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Transcript of Stylianos Bournazos, Ph.D.

Date: December 11, 2025
Case: CSPC Megalith Biopharmaceutical Co., Ltd -v- Shanghai Miracogen Inc.

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE PATENT TRIAL AND APPEAL BOARD

CSPC MEGALITH BIOPHARMACEUTICAL CO., LTD., Petitioner, vs. SHANGHAI MIRACOGEN INC., Patent Owner.
Case No. IPR2025-00685
U.S. Patent No. 10,792,370

REMOTE DEPOSITION OF

STYLIANOS BOURNAZOS, Ph.D.

THURSDAY, DECEMBER 11, 2025

Reported Stenographically By:
Cody Knacke, RDR, CSR No. 13691
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REMOTE DEPOSITION OF STYLIANOS BOURNAZOS, Ph.D., taken before Cody Knacke, RDR, CSR No. 13691, a Certified Shorthand Reporter for the State of California, commencing on Thursday, December 11, 2025, at 8:00 a.m., Pacific time.

(All Appearances Via Videoconference.)

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E - X - H - I - B - I - T - S

PREVIOUSLY MARKED EXHIBITS

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I N D E X
(Continued)

PREVIOUSLY MARKED EXHIBITS

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THURSDAY, DECEMBER 11, 2025
8:00 A.M.

REMOTE TECHNICIAN: Thank you to everyone for attending this proceeding remotely, which we anticipate will run smoothly. Please remember to speak slowly and do your best not to talk over one another. Please be aware that we are recording this for backup purposes. Any off-the-record discussions should be had away from the computer. Please remember to mute your mic for those conversations.

Please have your video enabled to help the reporter identify who is speaking. We will provide a complimentary, unedited recording of this deposition with the purchase of a transcript.

I apologize in advance for any technical-related interruptions.

Thank you.

THE STENOGRAPHER: This is Cody Knacke, CSR 13691. This deposition is being recorded stenographically.

STYLIANOS BOURNAZOS, Ph.D.,
called as a witness, having been first duly sworn, testified as follows:

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EXAMINATION

BY MR. QIU:

Q. Good morning, Dr. Bournazos.

A. Good morning.

Q. So let's start the deposition.

Have you been deposed before?

A. No. It's my first time.

Q. So let's go over a few ground rules just to get things started.

So you understand you are under oath to tell the truth today?

A. I do.

Q. We need verbal responses for today's deposition because this is being transcribed today. We need to make sure the court reporter can get your responses.

A. Yes. And if at some point the court reporter cannot understand me, I can speak more slowly or you can let me know.

Q. Great.

A. Can you hear me well?

Q. I'm sorry?

A. Can you hear me well?

Q. It's a little, slightly unclear. Don't know if you have a microphone near, other than the speaker --

A. It's in front of me, so I'll do my best.

Q. It's right -- okay. Okay. Thank you.

A. I can move it closer.

Okay. Hope it's better now because I have moved it closer.

Q. Okay. Thank you.

And we can take breaks today when you need to. I just ask that when we take a break, there's no question pending. Is that fair?

A. Yes.

Q. Do you understand you're not allowed to discuss your testimony with your counsel during breaks today?

A. Yes, I do.

Q. If you don't understand a question, let me know, and I will rephrase. Unless you say otherwise, I will assume you understand the question.

Is that fair?

A. Yes, I do.

Q. You have to answer my questions today unless your attorney instructs you otherwise.

Understood?

A. Yes.

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Q. Are you on any medication today?

A. No.

Q. Any reason that you wouldn't be able to provide accurate and truthful testimony today?

A. No.

Q. Are you here to give testimony in the Inter Partes Review proceedings involving U.S. Patent Number 10,792,370?

A. Yes.

Q. Today, we will refer to that patent as the '370 patent.

Is that all right?

A. Yes, that's correct.

Q. What documents do you have with you?

A. Nothing. I can see only the exhibits on my left side.

Q. And are you referring to the exhibits that was in the box that we mailed to you?

A. Yes, those exhibits.

Q. Okay. Do you have a computer in front of you?

A. No. Just my cell phone.

Q. Okay. So one of the things that we are probably going to talk about today is the concept of person of ordinary skill in the art.

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Are you familiar with that phrase?
A. Yes.
Q. If we use the term POSA, that's spelled, P-O-S-A, will you understand that that refers to the person of ordinary skill in the art?
A. Yes. You mean the acronym?
Q. Yes, yes.
A. Yes.
Q. Are there any errors in your declaration or anything you want to change?
A. I don't think so.
Q. How much time did you spend preparing your declaration?
A. Quite many hours. I don't recall the exact number of hours.
Q. Can you give me a ballpark estimate?
A. I would say maybe 20, 30 hours. But I don't really keep time.
Q. What did you review when preparing your declaration?
A. Can you repeat your question?
Q. I'm sorry? Can I repeat --
A. Can you repeat your question?
Q. So my question is, when you were preparing your declaration, what did you review -- what

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documents did you review?
A. Lots of documents, including patents, abstracts, conference abstracts, prior publications, sequences. Quite a few materials.
Q. Is there any document that you reviewed that was not listed in the list of exhibits shown in your declaration?
A. I believe we reviewed lots of different documents, papers, patents, and would include the most relevant ones. Yes. So during the process we reviewed many things.
Q. And some of the things were not listed in the exhibit list; is that right?
MR. SUH: Objection -- sorry. Objection to form.
You can answer, Doc.
THE WITNESS: Okay. I don't recall exactly, the type of materials and what exact materials we were going through.
BY MR. QIU:
Q. Right.
A. But at the end, we decided these are the most relevant for the case and for the -- for the arguments.
Q. Okay. Can you remember any document that

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you reviewed for preparing the declaration but was not listed in the declaration?
MR. SUH: Objection. Asked and answered.
THE WITNESS: I don't recall any. It's been almost a year, so I cannot remember every single paper that I reviewed back then.
BY MR. QIU:
Q. Did you draft your expert declaration in this proceeding?
A. Can you repeat the question, please?
Q. Did you draft the declaration that you signed for this proceeding?
A. I reviewed the draft.
Q. You reviewed the draft.
A. Yeah, I worked on the draft.
Q. So you didn't draft the initial declaration yourself.
MR. SUH: Objection. Form.
Sorry. Same objection.
THE WITNESS: I don't remember having prepared the first draft of the declaration. But there were several versions that I went through and edited.
BY MR. QIU:
Q. What did you do to prepare for this

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deposition?
A. I reviewed the materials, I refreshed my memory, because it's been a year, and had a good night's sleep.
Q. How long did you spend preparing for this deposition with counsel?
A. A few hours.
Q. Did you review any documents for preparing for this deposition?
A. Yes. I mentioned already I reviewed my declaration and then what it was included with the declaration previously.
Q. So in total, how much time have you spent reading and reviewing the '370 patent?
MR. SUH: Objection. Lacks foundation.
You can answer if you understand.
THE WITNESS: No, it's fine.
Total from the -- total number of hours or in preparation for the deposition?
BY MR. QIU:
Q. Yes, yes. Total number of hours.
A. I don't recall.
Q. Can you give an estimate for that?
A. No. I would say many hours.
Q. Have you ever reviewed the entire

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specification of the '370 patent?
A. What do you mean if I reviewed?
Q. Do you know the meaning of the specification in the context of a patent?
A. The claims.
Q. So you -- so your understanding is that the specification of a patent are the claims?
MR. SUH: Objection to form.
THE WITNESS: Can you rephrase your question or make it clearer?
BY MR. QIU:
Q. Sure.
Have you reviewed the entirety of the '370 patent?
A. Yes.
Q. Do you know what the specification of the '370 patent refers to?
MR. SUH: Objection to form. Vague.
You can answer if you understand the question.
THE WITNESS: What do you mean by specification? You mean the claims?
BY MR. QIU:
Q. Okay. Yeah, so by the specification, I mean the, yes, the content in the patent that goes

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before the claims, you know, the paragraphs.
A. Oh, the text.
Q. Uh-huh. Yeah.
A. Yes.
Q. Do you believe you have an adequate understanding of the '370 patent?
A. I think so.
Q. Is there anything you think is unclear about the '370 patent?
A. No.
Q. In your opinion, what qualifications does a person need to have to be a POSA?
A. According to my opinion, a POSA would be a person, as the name suggests, of ordinary skill in the art that will have a Ph.D. in immunology, molecular biology, biochemistry, or a related discipline, and at least five years of experience in research in the field of antibodies, antibody therapeutics, or any related field. It can also be an MD that has research experience as well. And I believe these were included in the petition as a definition of POSA.
Q. Did you qualify as a POSA in February 2015?
A. I believe so.
Q. What experiences did you have prior to

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February 2015 that qualified you to be a POSA?
A. My experiences are outlined in the deposition -- in the declaration, sorry. And I believe I fulfill these requirements as a POSA.
Q. What experiences listed in your declaration qualifies you to be a POSA?
A. Can I have a copy of the declaration -- of the declaration?
Q. Sure. You can open the declaration.
MR. SUH: Fred, do you want to mark it as an exhibit?
MR. QIU: Yeah. So the declaration is already marked as Exhibit 1002, I believe.
MR. SUH: All right. We're looking for it. Okay.
So, Fred, did you say this was marked already as an exhibit?
MR. QIU: Yeah. So this declaration is Dr. Bournazos's declaration that has been filed and stamped as Exhibit 1002 in this case.
(Exhibit 1002 was previously marked by the Certified Shorthand Reporter, and a copy is attached hereto.)
MR. SUH: Okay. Thank you.
And we're using the same exhibit numbers

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that were actually used in the actual filing of the papers?
MR. QIU: Yeah. I think that's -- that's a convenient way to do it, unless you have some other proposal. So for the --
MR. SUH: That's fine.
MR. QIU: Okay.
THE WITNESS: Okay. That's good. Thanks.
So do you have a copy of the declaration?
BY MR. QIU:
Q. I do, yeah.
A. Okay. Good. So then in Section 1, paragraphs 2 through 9, I have listed all my qualifications that are relevant to this case.
Q. Are all those qualifications relevant for determining whether you qualify as a POSA?
A. Yeah.
Q. Have you worked with any anti-EGFR antibody in your research?
A. Briefly, yes.
Q. Can you describe that experience?
A. It's an ongoing project, and I cannot really describe ongoing projects for this purpose.
MR. SUH: Yeah, and I just want to note for the record that, Doctor, to the extent that you have

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confidentiality agreements with respect to work that you currently have, that you do not disclose those.
BY MR. QIU:
Q. Do you have --
A. And don't -- yeah. No, sorry.
Q. Do you have any publications about anti-EGFR antibodies?
A. No.
Q. Have you worked with cetuximab in your research?
A. Yes.
Q. Is that something you can describe?
A. In very broad terms, yes.
Q. So can you please describe your experience researching about cetuximab.
A. So we have used cetuximab in the project that is still ongoing to assess the activity of the Fc domain in vivo and in vitro.
Q. Have you worked with antibody drug conjugates in your research?
A. Yes.
Q. Can you please describe your research about antibody drug conjugates.
A. Yes, of course. So one publication that was some years ago was in collaboration with a group

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at University of Maryland. So if you -- you have a copy of my CV; right?
Q. Yes.
A. Yeah. So -- or even in declaration. So page -- so publication in 2021 listed as One-pot conversion of free sialoglycans to functionalized glycan oxazolines. So this one was used in this publication, so actually --
(Speaking simultaneously.)
BY MR. QIU:
Q. On what page is that publication?
A. Is -- if you go to my CV, you see that?
Bibliography, Research Articles.
Q. Yes, yes. Research articles, yes.
A. So then you scroll to 2021. It's the last publication on the page before the end. Above the Review Articles.
Q. Okay.
A. So Ou, Li, Zhang, Yang, Zong, Dai, Francis, Bournazos, Ravetch, Wang, 2021.
Q. Is that at the top of that page or middle?
A. Because this is not marked.
Q. ELISA?
A. It's the eleventh publication from the end of the recent articles, the last on the previous

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page.
Q. Okay. Is it the eleventh -- oh, it's -- is it the eleventh from the end of that section? Like before --
A. Yeah.
Q. -- before Review Articles; right?
A. Before the Review Articles. So in the research.
Q. So it's the last article on the previous page.
A. Yeah, exactly.
Q. One-pot conversion of free sialoglycans to functionalized --
A. That's the one, yes.
MR. SUH: I just want to make sure that we're not talking over each other for the court reporter's purposes.
THE STENOGRAPHER: Thank you.
BY MR. QIU:
Q. So what is the title of this article?
A. What is that?
Q. What is the title of this article?
A. One-pot conversion of free sialoglycans to functionalized glycan oxazolines and efficient synthesis of homogenous antibody-drug conjugates

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through site-specific chemoenzymatic glycan remodeling.
Did you see?
Q. Can you briefly describe the subject of that research.
A. Yes. So this is basically testing different approaches of generating conjugation strategies of ADC to -- or conjugation strategies of the drug to the antibody and assessing the impact in vitro in the capacity of these antibodies to induce cell death.
Q. Do you have any other publications about ADCs?
A. The last one in 2024, this is -- again, it's not directly ADCs, but it's antibody drug and radioisotopes. Same chemistry, different approach.
Q. And can you -- sorry.
A. And there are also ongoing projects that I'm involved in direct assessing the activity of ADCs in vivo.
Q. Can you state the name of the -- this publication for the record in 2024?
A. Oh, the one I mention? Rodriguez. It's the last one on the list.
Q. Yeah, can you please state the title of

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this article?
A. Exploring the Interplay Between Radioimmunoconjugates and Fc Gamma Receptors in Genetically Engineered Mouse Models of Cancer.
Q. Thank you.
A. Thank you.
THE STENOGRAPHER: Excuse me, Counsel. May we go off the record, please.
(Recess.)
BY MR. QIU:
Q. Dr. Bournazos, can you please explain the differences between mouse antibody, chimeric antibody, and humanized antibody?
A. Mouse antibody is an antibody that has been produced in mouse and 100 percent of the sequence is mouse.
Your next question was chimeric?
Q. Yes.
A. Chimeric, as the name suggests, is an antibody that has sequence from a mouse or another species -- from two different species. Usually, when we -- specifically for this case, when we refer chimeric means that some part is mouse and the vast majority of the rest is human. So typically, the variations can be mouse because the antibody has

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been originated from a mouse, and then the rest is human.
And then your last -- your last question was humanized.
Q. Correct.
A. Humanized is usually an antibody that has as much human sequence as possible. It's not entirely human, but it has as high sequence similarity to humans as possible.
There is -- in the declaration, there is a nice cartoon -- cartoon that actually illustrates this. And it's very helpful. So if you go, for example, on page 22, you will see this.
Q. What are the benefits of humanization?
MR. SUH: Objection. Vague.
You can answer if you understand.
THE WITNESS: Benefits? So if you have a forwarding sequence from another species that is given to human, there is always going to be a reaction to that because the body is going to see this as a foreign object.
Think about in the context of transplantation. It's a foreign thing that is also immunogenic. So this process is called immunogenicity. So it's a reaction of the immune

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system against something else.
So one of the benefits of humanization is actually to reduce the potential of immunogenicity.
Is it clear?
BY MR. QIU:
Q. Do all humanized antibodies exhibit the same benefits over all chimeric antibodies?
A. What do you mean by "benefit"?
Q. You have just explained the benefits of humanization; correct?
A. I mentioned immunogenicity specifically.
Q. Okay. So do all humanized antibodies exhibit this same benefit over all chimeric antibodies?
MR. SUH: Objection. Vague.
THE WITNESS: In principle, yes. So any antibody that is closer to humans is expected to have lower immunogenicity.
BY MR. QIU:
Q. Are there any other benefits of humanization?
MR. SUH: Objection. Vague.
THE WITNESS: What other benefits do you have in mind?
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BY MR. QIU:
Q. Dr. Bournazos, I'm asking you a question. So my question is, are there any other benefits of humanization?
MR. SUH: Same objection. Vague.
THE WITNESS: Humanization, depending on how it's done, it can change the properties of the antibodies. It can lead to some benefits -- you can call them benefits. In my opinion, it's a change of property, but it really depends on the context of the antibody. But in principle, the main reason of humanization is to reduce immunogenicity.
BY MR. QIU:
Q. Is there any other property of an antibody that will be resulted from a humanization process?
A. It depends on what change is introduced during humanization.
(Stenographer clarification.)
THE WITNESS: On what changes, what modifications you introduced during the humanization process, and each process is different for each antibody.
BY MR. QIU:
Q. Can you give me an example of a property other than immunogenicity that's changed by the

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process of humanization?
A. So using the humanization invokes changes in the site where the antibody recognizes the antigen. So when you introduce these changes, you can also introduce variables that will influence the way that the antibody binds the antigen.
(Stenographer clarification.)
THE WITNESS: That the antibody recognizes the antigen.
BY MR. QIU:
Q. If you compare the humanized version of a first antibody and the chimeric version of a second antibody, will you always find the first antibody to have lower immunogenicity than the second antibody?
A. What is the first antibody and what is the second?
Q. They are two different antibodies.
A. Ah. Two different, we cannot make a comparison in two different antibodies.
Q. And why is that?
A. Because its antibody, if they are different, will organize different antigens.
Q. What if the two antibodies target the same antigen, but they are different antibodies?
A. Again, even if they target the same

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antigen, they can be from different clones. So binding different areas of the antigen, different epitopes. So we cannot make the assumptions that they are identical because they are different. You said they are different antibodies.
Q. Can you describe the history of anti-EGFR antibodies in clinical use?
MR. SUH: Objection. Vague. Lacks foundation.
You can answer if you understand, Doctor.
THE WITNESS: I understand the question, but I cannot really comment on the history or give you an overview, a very detailed overview that will be 100 percent scientifically accurate at this point. I'm not writing a review. I can give you a very -- like, what is EGFR, why antibodies used against EGFR, and so on, but to give you the history of EGFR, this is a subject of -- first of all, I will need to review literature on that, and I don't have anything in front of me. And it's also a subject of discussion that can take hours and hours.
BY MR. QIU:
Q. When did anti-EGFR antibodies first become available for clinical use?
A. I don't recall the exact year.

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Q. Does 2004 sound right to you, in the right time frame?
A. I believe so. I believe so.
Q. Was it right that cetuximab was initially approved for medical use in the U.S. in 2004?
A. I think so.
Q. To your knowledge, approximately how many anti-EGFR antibodies have been developed or described in the scientific literature?
A. Quite many.
Q. Do you have a ballpark estimate?
A. I would say hundreds. If we go over papers, literature, abstracts, patents, there are hundreds of antibodies out there.
Q. Are you familiar with efforts to create variants of cetuximab?
A. Yes.
Q. Why do researchers create variants of cetuximab?
A. Several reasons.
Q. Can you elaborate on the reasons?
A. One of the many reasons, for example, is a topic that we briefly discussed today about immunogenicity. So cetuximab is a chimeric antibody. So one of the efforts was to create

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humanized versions of cetuximab to reduce the potential for immunogenicity.
Q. Any other reason you can think of?
A. You always want to make an antibody better.
Q. What do you mean by "better" in this case?
A. And this -- and this is true for every other therapeutic antibody out there. So you want to increase the potency and reduce -- and improve the safety profile.
Q. Are there any other reason why researchers create variants of cetuximab?
A. There might be other reasons.
Q. Can you think of any at this point?
A. I can only speculate. If I'm allowed to do that, I can say cetuximab is owned by another company, so you want to make variants of that.
Q. What I would you -- strike that.
Was it common for researchers to create many cetuximab variants and then screen them for antibodies with desired properties?
MR. SUH: Objection. Vague.
THE WITNESS: Exactly what do you mean?
MR. QIU: Counsel, I have seen a pattern of you making an "Objection, vague," and then the witness will ask what I mean.

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According to the Board's rules, "Objection, vague" is not allowed as an objection for depositions. So I advise you to abstain from using that objection in this session.
MR. SUH: Well -- well, I'll ask you to articulate your questions more clearly.
MR. QIU: The Board has clear rules that speaking objections are not allowed in depositions for IPRs and --
MR. SUH: I don't believe -- I don't believe --
MR. QIU: And the Trial Practice Guide --
MR. SUH: I don't believe I've been making speaking objections.
MR. QIU: And the Trial Practice Guide explicitly states that "Objection, vague" is not allowed.
MR. SUH: Okay. We can discuss this off the record if you want to.
MR. QIU: Okay, yeah, let's go off the record and discuss this.
THE STENOGRAPHER: Off the record.
(Recess.)
THE STENOGRAPHER: Back on the record.
THE WITNESS: Can you please repeat your

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question?
BY MR. QIU:
Q. Yes. Let me do that.
Was it a common approach for researchers to create a number of cetuximab variants and then screen the variants to identify ones that have desirable properties?
MR. SUH: Objection. Unclear.
THE WITNESS: So your question is if it's common to create variants of cetuximab? Is that correct?
BY MR. QIU:
Q. So my question is -- so there's a research approach of creating a number of variants and screening the variants to identify ones that have desirable properties.
And my question is whether that was a common approach.
MR. SUH: Objection. That question lacks foundation.
THE WITNESS: At what time frame you are referring to?
BY MR. QIU:
Q. Sorry?
A. At what time frame you are referring to is

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it a generally common practice? I don't understand -- generally, I don't understand your question.
Q. Oh, the time frame.
Before 2015.
A. There is evidence that people were doing this. Now, how common, extensive, or how many groups were working on this, I cannot comment.
Q. When were ADCs initially invented?
A. When?
Q. Yes. At what time?
A. I don't recall -- I don't recall the exact year.
Q. Is it correct that the FDA approved an ADC for the first time in 2000?
A. I'm not sure.
Q. Does that time frame sound right to you?
A. Sounds a bit early, but it might be right. I cannot be 100 percent sure.
Q. Can you briefly explain the role of each component of an ADC molecule?
A. Yes. That's easy. So as the name suggests, it's antibody drug conjugates, so it's an antibody that has been conjugated to a drug, and usually the drug is a chemotherapy agent. But

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that's commonly used.
There are also later-on efforts to have other drugs instead of chemotherapy agents for other diseases, not neoplastic.
Q. What is the process of an ADC killing a tumor cell once it is administered to a patient?
A. Process? The mechanism, you mean?
Q. Sure. Mechanism.
A. So the first way that ADC act is to deliver the drug to tumor cells. So the exact mechanism, we still don't know. And there are several components that contribute to this antitumor process.
But basically, a very, very -- a very simplistic interpretation of how ADCs mediate antitumor activity is that they recognize a receptor on a tumor cell, commonly an extracellular membrane-expressed antigen, they recognize that, the receptor becomes internalized, and then the drug is released intracellularly in the tumor cell.
So this is a very simplistic way of how an ADC works, but we know that this process is much more complicated that we think, than this simplistic interpretation.
Q. What is the -- what is the main purpose of the antibody portion of an ADC?

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A. Most of the set -- in the context of tumor, most of the drugs that are used in the drug component of the ADC is very toxic to use it in humans. So you cannot administer these drugs in humans without killing the patient.

So what the ADC does, it brings this drug primarily to the tumor site. Think about chemotherapy but in a more targeted approach.

Q. So is it correct to say that the primary role of the antibody is to recognize and bind to target cells via specific antigens?

MR. SUH: Objection to form.

THE WITNESS: Can you repeat your question?

BY MR. QIU:

Q. Is it correct to say that the primary role of the antibody is to recognize and bind to target cells?

A. In the context of an ADC?

Q. Yes.

A. For most examples, yes, but there are always exceptions to the rule.

Q. What exceptions do you have in mind?

A. Of the antibody, in addition to do this function, to perform other functions.

Q. What other functions do you have in mind?

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A. It depends --

MR. SUH: Objection.

Sorry. Objection. Asked and answered.

You can go ahead.

THE WITNESS: It depends on the context on what receptor is targeted, what is not targeted, the nature of the receptor, the signaling downstream of the receptor, and so on. And this is mainly on the Fab portion of the antibody. Fc can also have effects.

BY MR. QIU:

Q. Can you give me an example of such other functions?

A. Yeah. We can -- I can give you an example specifically from the case, like cetuximab. It binds and blocks the activity of EGFR. So you see, in addition to blocking the receptor and internalizing the receptor, it can also block the signaling activity of the receptor.

Q. What are the important considerations when selecting an antibody for an ADC?

A. Too many. Selecting an antibody, you mean, or constructing an ADC?

Q. Yes.

A. The former or the latter? Selecting of the antibody or --

Q. Let me repeat my question.

A. Yeah, yeah, sorry, sorry.

Q. What are the important considerations when selecting an antibody for use in an ADC?

A. So selecting the antibody, there are several considerations that include among them the target that you are -- the target molecule that you are aiming to so that the antibody would be recognizing. And then it has to do primarily with the quality and the nature of the target.

Q. What is the main purpose of the linker within ADC?

A. So the linker, as the name suggests, links, in most cases, covalently the antibody to the cytotoxin, to the cytotoxic compound.

Q. How does the process of an ADC killing a tumor cell differ between ADCs with cleavable and noncleavable linkers?

A. The process of killing is -- depends on the cytotoxin, not on the linker. But the linker can influence when and where the cytotoxin will be released.

Q. How does a linker influence when and where the cytotoxin will be released?

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A. It does influence because of the nature of the linker. So you can have linkers that are cleavable and noncleavable. And among the cleavable linkers, it will also influence how these linkers are cleaved and under what conditions are cleavable. And this process will influence whether or not and to where the cytotoxin will be released.

Q. How does a cleavable linker and a noncleavable linker function differently in this mechanism?

A. In this? Can you repeat the last part of your question?

Q. How does a cleavable linker and a noncleavable linker function differently in the mechanism of the ADC?

A. It depends on the chemical nature of the linker. So I avoid using a global term of "cleavable linker" because even with this category, you can have linkers that can be cleaved under different conditions. And each different condition will influence how and when and where the tumor cell -- the cytotoxin will be released.

Q. If we use the same antibody and payload but either are cleavable or noncleavable linker, which ADC will generally be more potent?

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MR. SUH: Objection. Unclear.
THE WITNESS: Do you mean by having this exact same antibody and the exact same cytotoxin?
BY MR. QIU:
Q. That's correct.
A. It will really depend on the nature of the linker. So as I mentioned previously, I would avoid making the label of "cleavable linker" just to having a blank statement or designation of cleavable versus noncleavable because it depends on how the linker will be cleaved.
Q. What is the main therapeutic function of the payload in an ADC?
A. The main therapeutic function is to kill malignant cells. But it depends, again, on what this drug is. So I cannot comment on the mechanism of these drugs if I don't know the drug that you are referring to.
Q. What are the important considerations when selecting a payload for use in an ADC?
A. You always want to go with as potent as possible, but there are multiple considerations that you need to take into account when selecting a payload. But it's always a combination of the payload with a linker and with a target that you

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want to target. So it's not a one payload fits everything.
Q. What are the common payloads used in FDA-approved ADCs and those candidate ADCs in clinical trials?
A. I can refer to two. So one is DM-1 and the other is MMAE, also known as vedotin. These are the most commonly used, but there are several others.
Q. How do ADCs differ from unconjugated antibodies in terms of their components and mechanisms of action?
A. So antibody drug conjugates have a drug that's conjugated to the antibody. The other antibodies don't. So in terms of mechanism, ADCs will also bring any cytotoxic activities that come from the payload. Or cytotoxic or immunostimulator. So that's the main difference between antibodies and ADCs.
Q. Has ADC --
A. But not the only one.
Q. Sorry.
A. Yeah, go ahead.
Q. Does ADC provide increased efficacy in tumor eradication compared with unconjugated antibodies?

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A. It depends on the context.
Q. In what situations does ADC not provide increased efficacy in tumor eradication compared with unconjugated antibodies?
A. It depends on the target. So there -- there are examples of ADCs not conferring any benefit over naked antibodies. But it all depends on the context. Generally, having an ADC is expected to have better antitumor activity. But as I mentioned, a very -- some important consideration is the target. It all depends on what these antibodies or ADCs are targeting. I cannot -- we cannot really draw a conclusion and say ADCs are always better than antibodies.
Q. Is it correct to say that an antibody -- sorry. Strike that.
Is it correct to say that an ADC and antibody mainly provides the specificity and that the cytotoxic payload mainly performs the killing of tumor cells?
A. We already --
MR. SUH: Objection. I'm sorry.
Objection. Lacks foundation.
You can answer.
THE WITNESS: We already discussed this.

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BY MR. QIU:
Q. So you agree with my statement; correct?
A. We already discussed this. So your question is that if it merely provides binding to the enzyme. I mentioned before that this is not one single function of the antibody.
Q. What properties of the antibody determines the binding specificity to target cells?
A. So the antibodies don't bind directly to target cells. They bind to molecules that are expressed by target cells, if you mentioned this. Properties would be through a protein-protein interactions between the Fab atom of the antibody and the antigen that they recognize, the epitope that they recognize.
(Stenographer clarification.)
THE WITNESS: So the primary determiner would be how the Fab, F-A-B, the main atom antibody would recognize the epitope on the antigen that's expressed by the target cell. Is that clear?
THE STENOGRAPHER: Thank you.
THE WITNESS: Perfect. Thanks.
BY MR. QIU:
Q. Is binding specificity dictated by the structure of the antibody's variable region?

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A. Correct, along with sometimes post-translation modifications of this. So sometimes it's not protein-protein structure, but it can also have glycoproteins or glycans that are involved in this process.

Q. What properties of the antibody determines the binding affinity for a particular antigen?

A. I would -- properties? Did you mean determinants?

Q. Sure.

A. So the interaction is primarily through protein-protein context, but as I mentioned before, sometimes you can have glycans that participate in this interface.

Q. Does the binding of an antibody to cell surfaces depend on the expression level of antigen on cell surface?

MR. SUH: Objection. Lack of foundation.

You can answer if you understand.

THE WITNESS: Depends on the context. You can have high expression, but the antibody might not be able to bind. Or you can have very low expression, and the antibody can be binding really well.

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BY MR. QIU:

Q. In what situation can an antibody not bind well when you have high expression?

A. I can give you an example from SARS-CoV-2. So the spike protein has different components: The RBD, the NTD, and the S2 domains. So we know that -- how the spike protein, the S protein of SARS-CoV-2 is expressed by infected cells can influence how the antibody binds. This is because primarily of accessibility of the epitope, secondary structure or of how the spike is organized in the membrane, contact with other surface receptors, glycosylation, steric hindrance. There are many, many determinants that can determine how an antibody can bind to the antigen when the antigen is expressed on the cell surface.

Q. For a certain antibody, does its binding to cell surfaces depend on the expression level of antigen on the cell surface?

A. Not necessarily. I just mentioned the example of SARS-CoV-2. So you can have antibodies against a spike protein that might not bind very well to the spike. It depends on the antigen, it depends on the antibody and where the antibody binds.

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So overexpression or expression of something doesn't necessarily mean that the antibody is still able to bind to that.

Q. If an antigen is expressed at a very low -- at a very low level, is it accurate that even high-affinity antibodies may not bind efficiently?

A. No, that's not true. Because keep in mind --

Q. Because --

(Speaking simultaneously.)

A. No, go ahead.

Q. No, sorry. Please continue your answer.

A. Antibodies have two arms. So even if you don't have enough expression or you have very low affinity, avidity effects can compensate for that. That's why the context, the antibody, and the epitope matters when we discuss issues like that.

Q. So your opinion is if an antigen is expressed at a very low level, antibodies will still bind efficiently always?

A. No.

MR. SUH: Objection to form.

THE WITNESS: I already explained that it depends on the antibody, the target, and the molecule. It's all dependent on the context. I

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mentioned an example of SARS-CoV-2. This doesn't mean that the same principle applies to influenza.

BY MR. QIU:

Q. Is there typically a threshold or a minimum expression level of an antigen on cell surface for a significant antibody binding to a cell?

A. It depends on how you define "significant" and what you define as the threshold. It's -- it's very vague term to comment on that.

Q. Are you aware of any threshold or minimum expression level of an antigen needed for an antibody to bind to cells with the antigen?

MR. SUH: Objection. Unclear.

THE WITNESS: I'm not aware of a defined threshold. What I know is that you do need expression. With zero expression, you don't have recognition.

BY MR. QIU:

Q. But as long as the expression level is not zero, is it your opinion that an antibody targeting the antigen will always bind?

MR. SUH: Objection. Form.

THE WITNESS: No. I mentioned this already. So you can have expression but no binding. It's not -- let's say that you have a very, very low

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expression. One antibody can bind, another antibody cannot bind despite recognizing the same antigen.
BY MR. QIU:
Q. Does the expression level have an impact on how efficiently an antibody will bind to cells with an antigen?
A. Can you repeat the question?
Q. Does the expression level of an antigen have an impact on how efficiently an antibody can bind to cells with an antigen?
A. I explained this already. So the expression cannot guarantee binding because every antibody, every epitope is unique.
Q. Does the expression level of an antigen have an impact on how efficiently an antibody can bind to cells with an antigen other than guaranteeing binding?
A. Can you clarify your question because I think it's the same as your previous one.
Q. Sure.
I want to understand whether the expression level of an antigen have any impact on how efficiently an antibody can bind to cells with the antigen.
Your earlier answer talks about

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guaranteeing binding. So that's one way the expression level can impact.
But I'm asking about whether there are other impacts that the expression level of an antigen can have on how efficiently an antibody can bind to cells with an antigen?
A. What do you mean --
MR. SUH: Objection. Form. Misrepresents the testimony.
Go ahead, Doctor.
THE WITNESS: What do you mean other impacts? Other factors?
BY MR. QIU:
Q. Is the binding of an antibody to cells with an antigen in any way influenced by the expression level of the antigen on the cell.
MR. SUH: Objection. Asked and answered.
THE WITNESS: But I have already explained this. So you are asking me -- and I'm sorry if I don't get it. But you are asking me if the expression level can influence how efficiently the antibody can bind.
I have already explained that the level, the expression level of the antigen, it depends -- so how well -- how efficient the antibody binds to a

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cell surface antigen, it can -- it's not necessarily a function of expression level because it can be influenced because where the antibody binds, which epitope and so on, it all depends on the context.
Is it clear?
BY MR. QIU:
Q. Is there any case where the binding is a function of the expression level of antigen?
A. I'm sure there is a case. But every situation is unique. It's biology. Every system is so complex. It has evolved in this way.
MR. SUH: Fred, we've gone for more than an hour. Is this a good time for a break?
MR. QIU: Sure. Yeah, we can take a break.
MR. SUH: And if we could go off the record, we can talk about...
(Recess.)
BY MR. QIU:
Q. Is there a minimum of density of surface antibody binding required to trigger internalization of the target cell?
A. No, not an absolute minimum.
Q. For a specific antibody and the specific antigen being targeted, can a POSA determine an amount of density required to trigger

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internalization by the target cell?
A. Can you please repeat the question?
Q. Sure.
For a specific antibody and a specific antigen, can a POSA determine an amount of density required to trigger internalization by the target cell?
A. What do you mean "specific"? Is it a specific example or for an antibody -- an antigen?
Q. Yes.
So my question is if the POSA knows what the antibody is and what the antigen is, would the POSA have been able to determine the amount of density of a surface antibody binding that is required for internalization to happen?
A. Oh, okay. Got it. Thanks for clarifying.
It depends if the POSA knows the targeting antibody. Without this information, it's -- I don't think -- without knowing which antibody, which target is it, we cannot make the assumption about density.
Q. What antibody properties influence the threshold of binding required for internalization?
A. Let's take a step back. Antibody binding doesn't equate to internalization. You understand

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that?
Q. That's correct.
So my question is -- sorry. Strike that.
Let me rephrase my question.
A. Thank you.
Q. What properties of the antibody influence a threshold of binding density required for internalization to occur?
A. So I explained this. So antibody binding doesn't equate to internalization. So we cannot have properties of an antibody that will dictate whether or not an antibody will be internalized.
Q. Is antibody binding in any way related to internalization?
A. No. I just explained that. It depends on the enzyme that the antibody is targeting.
Q. When an antibody binds to an antigen, is binding with a single arm sufficient?
MR. SUH: Objection. Lacks foundation.
THE WITNESS: It depends on the context. For same-cell magnets [phonetic], it is sufficient. For others, it's not. For others -- for some antibodies, it is sufficient. For other antibodies, it is not sufficient.
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BY MR. QIU:
Q. When an antibody binds to a cell surface antigen, is binding via a single Fab typically sufficient to induce internalization, or is cross-linking generally required?
MR. SUH: Objection. Lacks foundation.
THE WITNESS: It depends on the target.
BY MR. QIU:
Q. Can adjusting an antibody's affinity alter the selectivity for cancer cells over normal cells based on differences --
(Speaking simultaneously.)
A. The antibody --
Q. Sorry.
A. No, no, sorry. Go ahead.
Q. Can adjusting the antibody's affinity alter the selectivity for cancer cells over normal cells based on their differences in antigen expression levels?
A. It can and cannot. Again, it depends on what antigen you're targeting and what antibodies.
Q. Would lowering the binding affinity of the antibody result in the antibody preferentially binding to and being internalized by cells with higher antigen expression, such as tumor cells,

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while sparing normal cells with low expression?
A. Can you repeat the question? I didn't get the first part.
Q. Sure.
Would lowering the binding affinity of the antibody result in the antibody preferentially binding to and being internalized by cells with higher antigen expression, such as tumor cells, while sparing normal cells with lower expression?
MR. SUH: Objection. Lacks foundation.
THE WITNESS: I don't like the generalization that you make. So as I mentioned, binding doesn't equate to internalization. Everything depends on the target and the antibody and epitope that this antibody is recognizing. So I cannot comment on this.
BY MR. QIU:
Q. Would you agree that one key scenario where affinity is intentionally lowered for an antibody is when the target antigen is expressed on both tumor and normal cells but at much higher levels on tumors?
MR. SUH: Objection to form.
THE WITNESS: Would I agree with -- can you please repeat or rephrase, if necessary?

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BY MR. QIU:
Q. One scenario in ADC development that often occurs is that binding affinity of the antibody is intentionally lowered when the target antigen is expressed on both tumor and normal cells but at much higher levels on tumors; is that correct?
MR. SUH: Objection to form.
THE WITNESS: So you are talking about a scenario -- I don't think I get the question correctly. So you are talking about a scenario where the affinity is lower and you -- what's the question? If I --
BY MR. QIU:
Q. Let me try to ask another question to make more sense.
In cases of ADCs with higher toxic -- sorry. Strike that.
In cases of ADCs with highly toxic payloads, would higher binding affinity increase the risk of the drug being delivered to normal tissues expressing low levels of the antigen?
A. Not necessarily. Also, keep in mind that ADCs have very toxic drugs.
Q. Would you agree that in the context of ADCs with highly toxic payloads, lowering antibody

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affinity is an established strategy to limit off-tumor toxicity?

A. Can you repeat the question, please?

Q. Would you agree that in the context of ADCs with highly toxic payloads, lowering antibody affinity is an established strategy to limit off-tumor toxicity?

A. I'm not aware that this being -- that this is an established strategy.

Q. If an ADC is found to be too toxic due to -- due to its payload being delivered to both tumor and normal cells, does increasing the antibody's binding affinity increase or decrease the risk of tumor toxicity?

A. It's very hard to speculate because everything depends on the expression level, on the dose. There are so many determinants.

Q. Are you aware of any case in the field where an ADC -- that it was too toxic with the initial antibody, was improved by switching to an antibody that has a higher binding affinity?

A. Compared to the parental [phonetic] antibody?

Q. Correct.

A. I'm not aware of any studies that have

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done -- assessed clinical efficacy and safety comparing antibodies with higher or lower affinity as ADCs.

Q. Is there a scientific rationale for expecting that switching to a higher affinity antibody will make an already too-potent and a too-toxic ADC less toxic to normal tissues?

A. It depends on the target. I won't exclude. It as a scenario, but everything needs to be considered, having in mind the nature of the antibody, the nature of the target, and the properties of the target.

Q. If an ADC is observed to be too toxic at therapeutic doses due to off-tumor targeting, would widening the therapeutic window be a primary goal in altering the ADC design?

MR. SUH: Objection. Foundation.

THE WITNESS: What do you mean, "widening of the therapeutic window"? Can you please define?

BY MR. QIU:

Q. Do you understand the term -- the meaning of the term "therapeutic window"?

A. Yes, I do, but not in the context of your question.

Q. What is the meaning of the "therapeutic

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window"?

A. It is the time where you have the opportunity to treat the patient.

Q. Do you understand what widening the therapeutic window means?

A. Yeah, I do.

Q. What does that mean?

A. To extend the time that you can treat the patient, if we are referring to the timing.

Q. Do you know the meaning of the term "therapeutic index"?

A. I'm not entirely sure what you mean. Can you please explain?

Q. So the term "therapeutic index" does not sound familiar to you; is that right?

A. I've heard it, but not in isolation as a single term.

Q. So do you understand the meaning of "therapeutic index"?

A. In general terms, yes.

Q. What is the meaning?

A. How a drug can be applied in the clinic, provide therapy against a disease.

Q. What are the factors that affect the likelihood of success of an ADC?

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A. Can you please define "success"?

Q. Do you understand what the phrase -- what the term "success" means in the field of ADC creation?

A. I do, but not in the context of your question.

Q. Can you please explain what you understand "success" to mean?

A. If a drug provides therapeutic benefit to the patient, I would personally consider it as a success. But this is my personal opinion. A company would consider it if it has a commercial success. So it's a very vague term. How do you define "success" in your context of your question?

Q. Can you please go to -- can you please open your declaration, which is Exhibit 1002.

A. Yeah.

Q. And go to paragraph 35 of that exhibit.

A. Yes.

Q. Can you please read the first sentence of that paragraph.

A. "ADC research has revealed several factors that affect the likelihood of success."

Q. What does the term "success" mean in that

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sentence?
A. In this -- in this context, it's not referring to a clinical benefit. It mostly refers to the antitumor activity of an ADC, because we can define success at different stages: Preclinical, clinical, post-market.
Q. So what does "success" mean in the context of creating an ADC?
A. In the context of paragraph 35 is for the ADC to exert antitumor activity.
Q. In determining whether there's a reasonable expectation of success in making an ADC, what factors would a POSA typically consider?
MR. SUH: Lack of foundation. Objection.
THE WITNESS: Can you please repeat the question?
MR. QIU: Can the court reporter read back my question.
THE STENOGRAPHER: Yes.
(The previous question was read back by the court reporter as follows:
"QUESTION: In determining whether there's a reasonable expectation of success in making an ADC, what factors would a POSA typically consider?")
MR. SUH: Same objection.
THE WITNESS: So the factors that are outlined primarily in section 35, paragraph 35. So: "First, the selected antigen should provide substantial tumor selectivity. Second, the cytotoxic drug should be highly potent as only a small amount of the ADC will reach the target cells." And: "Third, linker technologies are needed that result in stability of the ADC in circulation while also permitting efficient release of the cytotoxic drug following its internalization into target cells or localization in the tumor."
These are some of the factors that we -- a POSA would need to increase the likelihood of success.
BY MR. QIU:
Q. Are there any other factors that a POSA would have considered?
A. Yes, of course, but these are the main factors that I believe are important.
Q. Can you please provide a list of the other factors that the POSA would have considered.
A. It can be an extensive list.
Q. Can you please provide an example factor on that list.
A. Yeah. So for example, it can be the antigen that's targeted, if it can be internalized or not. It can be the selection of the drug itself. It can be the antigen, if it's expressed, where it is expressed, and when it is expressed. It can be the antibody.
So each component of the ADC we can -- we can specify a number of factors that can influence the likelihood of success. These are the three main, but there are several others.
Immunogenicity. That's another.
Q. What are some issues or obstacles that can make the effort of creating an ADC unsuccessful?
A. Can you repeat the question, please.
MR. QIU: Can the court reporter repeat the question.
THE STENOGRAPHER: Yes.
(The previous question was read back by the court reporter as follows:
"QUESTION: What are some issues or obstacles that can make the effort of creating an ADC unsuccessful?")
THE WITNESS: It can be toxicity, it can be an antigen that is not internalized, poor selection of antigen, unstable antibody, not efficient drug. These are some of the factors that I can think of, but there are several others.
BY MR. QIU:
Q. If a POSA knows the components that are used in an ADC, would the POSA would have been able to predict whether the ADC is likely to be successful?
A. Yes. Based on prior art, you can -- you -- a POSA will have the ability to determine whether a target is suitable, whether an antibody is suitable, whether a linker is suitable, whether a drug is suitable to increase the likelihood of success.
Q. What analysis would the POSA have performed to determine whether the ADC is likely to be successful?
A. By reading articles, by seeing publications, by attending conferences, by going over patent literature, see what other people have done before, check the nature of the target, be informed about advances in the technologies of payloads, of linkers. These are a few examples that a POSA can -- steps that the POSA can take to increase the likelihood -- likelihood of success.

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Q. Are there ways that a POSA can use to tell whether an anti-EGFR antibody is useful for use in an ADC?
A. Can you please repeat the question? We have some noise here.
Q. Sure.
Are there ways that a POSA can use to tell whether an anti-EGFR antibody is suitable for use in an ADC?
A. Are there ways that a POSA -- I believe so.
Q. What are they?
A. For example, selecting the right linker, the right payload, the right antibody, the right target, EGFR in that case. So all these factors would -- a POSA would consider for selecting and designing an ADC against an EGFR.
Q. What analysis would a POSA have performed to select the right antibody?
MR. SUH: Objection. Asked and answered.
THE WITNESS: Yeah, I believe I already answered that.
Again, understanding more about the antibodies, the target, seeking different sources of information, publications, patents, conference proceedings, be as informed as possible.

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BY MR. QIU:
Q. Would a POSA have analyzed the properties or characteristics of an antibody to determine whether it is the right antibody to use in an ADC?
A. How do you define "right"?
Q. You mentioned that, "the right antibody," in your earlier answer to my question.
A. Oh, okay.
Q. So I am asking you in that sense.
A. So the question was?
Q. Would a POSA have analyzed the properties or the characteristics of an antibody to determine whether it is the right antibody to use in an ADC?
A. Yes. Antibody is a critical component of an ADC. By analysis of the properties of the antibodies -- I believe that by analyzing the properties of the antibodies and selecting the right antibody is critical for the success of an ADC.
Q. How would a POSA have selected an antibody by analyzing its properties?
A. The most important is to know where it binds, the target.
Q. How does where an antibody binds to the target determine whether it is the right antibody?
A. No, no. I mentioned if it -- if it binds the target. So the expressed -- the molecule, the antigen itself, not where in the antigen.
Q. It is your opinion that all antibodies that binds to a target are suitable to be used in an ADC; correct?
A. Not at all because, as I mentioned, you need -- a requirement for an ADC to work would be that the target becomes internalized upon antibody binding.
Q. What properties of an antibody, other than whether it binds to the target, will decide -- will help a POSA to determine whether the antibody is suitable to use in an ADC?
A. Other than binding the antigen?
Q. Correct.
A. If the antibody triggers internalization. That's one important component.
Q. It is your opinion that all antibodies that binds to the target and triggers internalization are suitable to be used in an ADC; correct?
A. I believe so, unless this internalization is low or not efficient. But again, it depends on the context and the target. So expression density of a target and so on.
Q. Do you believe ADCs are useful tools for

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therapy?
A. Absolutely.
Q. Do you know whether companies have been trying to develop anti-EGFR ADCs?
A. I'm not 100 percent familiar with the field and what have -- what the efforts have been. But I believe that there are a few candidates of EGFR ADCs.
Q. When did researchers start to develop anti-EGFR ADCs?
A. I'm not entirely sure.
Q. Has any anti-EGFR ADC received regulatory approval?
A. I don't think so.
Q. Can you explain why no anti-EGFR ADCs have been approved in the 20 years since cetuximab was known?
A. Millions of -- it can be millions of factors. I cannot speculate.
Q. What do you think are the challenges preventing successful development of anti-EGFR ADCs?
A. Scientific challenges.
Q. Can you please provide a list of the scientific challenges that you have in mind.
A. I cannot speak list of challenges because

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there have been studies showing the in vivo efficacy of anti-EGFR ADCs. Now, why -- are these real challenges that have -- have prevented the clinical development of EGFR ADCs or not.

Scientifically, it's a very -- if I have to comment in a scientific basis, it's a very neat approach.

(Stenographer clarification.)

THE WITNESS: Neat, elegant.

BY MR. QIU:

Q. Sorry.

A. Yes?

Q. What are you referring to as a "neat approach"?

A. To develop ADCs as -- EGFR ADCs, the clinical development of EGFR ADCs. To me, based on existing literature and previous clinical studies, it seems a sophisticated approach.

Q. So what are the scientific challenges that prevent successful development of the anti-EGFR ADCs?

A. So I already answered this question. So to me, in reviewing the literature, going over the progress of anti-EGFR ADCs, and seeing the clinical -- them, the antitumor efficacy in

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preclinical models, I don't really see major scientific challenges that have prevented the clinical development on the anti-EGFR ADCs. It is an attractive target and I believe would have very good therapeutic benefits to patients.

Q. Why do you think ADCs for other targets have been developed sooner than anti-EGFR ADCs?

A. Again, a million of factors. It can be -- because we are talking about companies. Each company will have its own pipeline, its own strategy, what therapeutic areas to prioritize or not.

Yes, there are -- we still have cancer, so there is still cancer cases. And as a scientific community, we are trying to get the best out of that.

Now, why new drugs don't enter the market or targets that we believe are good do not enter the market, that's beyond me to comment.

Q. Why is it meaningful to develop an ADC based on anti-EGFR antibodies?

A. As my personal opinion, I would say it's a nice approach because we know the target, EGFR. Cetuximab has been in clinical use for so many years. And by combining cetuximab, the clinical

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benefit you see from cetuximab, along with the drug conjugate, to my opinion and based on preclinical data I have seen, it seems a nice therapeutic approach.

Q. Are there any characteristics of the EGFR antigen that would have motivated researchers to develop an ADC-targeted --

A. Sorry. Give me a second.

MR. SUH: Sorry. We have to go off the record. There's, like, some commotion going on outside. If we can just take a minute.

(Recess.)

BY MR. QIU:

Q. Are there any characteristics of the EGFR antigen that would have motivated researchers to develop an ADC targeting this antigen?

A. Yes. So it's if -- and that's the reason of why initially, EGFR was selected as a target for cetuximab. So it is abundantly expressed, abundantly expressed by multiple tumor types. And it's a receptor that, when targeted by cetuximab, can be internalized.

So naturally, it makes a lot of sense to generate now a cetuximab-based ADC.

Q. Do you think there has long been a need for

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anti-EGFR ADCs that's approved for clinical use?

A. What do you mean by "improved"? Like, improved compared to cetuximab?

Q. Let me repeat the question.

A. Yeah, yes.

Q. Do you think there has long been a need for anti-EGFR ADCs that are approved for clinical use?

A. I'm not aware of any EGFR ADCs that have been approved.

Now, your question is if there is a need for that?

Q. Correct.

A. Any drug is useful. People are still dying from cancer. So any drug, even if it extends the life of a patient by a few months, it's useful.

Q. Can you scroll to paragraph 35 of your declaration.

A. Yes.

Q. Which is Exhibit 1002.

Please let me know when you are there.

A. Yeah, I'm here. 35, you said?

Q. Yes.

In that paragraph, you stated there are -- you listed three factors that control -- affect the likelihood of success; correct?

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A. Yes.
Q. And those factors are from Exhibit 1021; correct?
A. Yes. Can we get Exhibit 1021?
MR. QIU: Yeah. Can you please get Exhibit 1021.
MR. SUH: Here we go.
THE WITNESS: Yeah. Got it. Yes.
(Exhibit 1021 was previously marked by the Certified Shorthand Reporter, and a copy is attached hereto.)
BY MR. QIU:
Q. Are you familiar with Exhibit 1021?
A. Yeah.
Q. Exhibit 1021 is concerned with the CD30 antigen; correct?
A. Exactly.
Q. Are you familiar with the CD30 antigen?
A. Yep.
Q. How does the EGFR antigen compare to the CD30 antigen in terms of their differentials of expression level between cancer cells and normal cells?
A. I believe there are differences, but these differences don't really extend to that. IF CD30

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and ADCs for CD30 target liquid cancers, EGFR primarily would target solid tumors.
Q. CD30 has higher expression difference between tumor and normal cells than EGFR; correct?
A. Correct.
Q. Given that EGFR has a smaller expression difference between the tumor and normal cells than CD30, that makes it harder to create an EGFR ADC than a CD30 ADC; correct?
MR. SUH: Objection to form. Foundation.
THE WITNESS: What do you mean "harder"? Like, the manufacturing would be challenging?
BY MR. QIU:
Q. By "harder," I'm referring to the difficulty of creating a useful ADC.
A. Ah, I see your point because CD30 is expressed only in tumors, whereas EGFR is expressed on tumors and also by normal cells, you mean. Is that correct?
Q. Correct.
A. No, not necessarily because EGFR -- we have to think a little bit out of the context between these two, CD30 and EGFR. HER2, HER2 is expressed on tumor cells, breast or gastric tumor, but it's also expressed on normal cells. But we have at

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least two or three, I believe, ADCs that are against HER2.
Another example is NECTIN4. NECTIN4 is expressed, I believe, by skin, primarily, and in some endothelial cells but overexpressed in bladder cancer and has been developed as a very successful ADC for the management of urothelial cancer.
Q. Is there any additional issue a POSA would have considered for creating an EGFR ADC but not for creating a CD30 ADC?
A. No. Given the success of other ADCs that target antigens that are expressed also by normal cells in physiological tissues, a POSA wouldn't really see a concern about this expression because by the time, like in 2015 Herceptin as an ADC has been developed, actually approved by FDA, and several others like NECTIN4 ADCs have been in clinical development.
Q. How does EGFR compare to CD -- strike that.
Are you familiar with the CD33 antigen?
A. Yes.
Q. How does EGFR compare to CD33 in terms of their differentials of expression level between cancer cells and normal cells?
A. I believe CD33 is expressed primarily by

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hematopoietic cells, whereas EGFR is expressed primarily by cells of endothelial origin -- epithelial origin, sorry.
Q. CD33 has higher expression difference between tumor and normal cells than EGFR; correct?
A. I haven't -- I'm not 100 percent sure. I -- I can do an analysis to see. I can do a database to check expression, but I cannot comment -- I don't remember the answer on the top of my head.
Q. Can you please access Exhibit 1002, your declaration, and go to paragraph 108. Please let me know when you are there.
A. On the declaration?
Yes.
Q. There, you mentioned that: "The background of the '370 patent recognizes 'it is highly complex and unpredictable whether an antibody drug conjugate becomes a safe and effective drug depending on a variety of factors.'"
Correct?
A. Yes.
Q. Do you agree with this statement in the '370 patent?
A. I have not made it there. Give me a

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second.
Yes, I do agree with this statement.
Q. In the same paragraph, you listed five factors from the '370 patent; correct?
A. Yeah.
Q. Do you agree that these factors affect the likelihood of successfully creating an ADC?
A. Yeah. All of them sound reasonable.
MR. SUH: Fred, sorry. Yeah, it's -- it's 1:20 here.
MR. QIU: Yeah, I was about to ask for -- whether you wanted a break as well.
MR. SUH: Yeah, sure. It's getting kind of late for a lunch, so if we could maybe just take a quick lunch, like 30 minutes.
MR. QIU: 30 minutes, okay. Sounds good. So it is 1:20 your time, and we come back at 1:50 Eastern time.
MR. SUH: We'll try, yeah.
(Luncheon recess taken at 10:19 a.m.)

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THURSDAY, DECEMBER 11, 2025
10:51 A.M.
STYLIANOS BOURNAZOS, Ph.D.,
having been previously duly sworn,
was examined and testified as follows:
BY MR. QIU:
Q. Dr. Bournazos, are you familiar with Exhibit 1005 in this case, which is the Wei reference?
A. Yes. I have it in front of me.
MR. QIU: Let me upload this reference for the court reporter.
(Exhibit 1005 was previously marked by the Certified Shorthand Reporter, and a copy is attached hereto.)
BY MR. QIU:
Q. So what is Wei's Y104D antibody?
A. It is a clone that is related to cetuximab.
Q. Can you point me to the sequence of this antibody?
A. Yeah. I believe the sequence is provided on Figure 1A.
Q. Figure 1A.
A. For the heavy chain, and then Figure 1B -- give me a second, because I'm looking --

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So if you go to paragraph 246, it has a description of the antibody. So Figure 1A and B, this is the "alignments of the exemplary heavy and light chains of cetuximab." So the sequences are there depicted in Figure 1A and B, and also, you can see them as SEQ ID NO: 5, for example, which is the heavy chain variable domain.
Q. So it's SEQ No. 5; correct?
A. I'm not 100 percent sure. Let me check. Searching sequences on a piece of paper is not easy.
I believe -- give me a second, because I'm a little lost with all the sequences.
I cannot comment on that because on the exhibit, I don't have a copy of the sequence listing. So I'm not 100 percent sure which specific sequence is there.
Q. Did you analyze the sequence of Wei's Y104D antibody as part of your analysis for creating the declaration?
A. I believe so.
Q. How is Wei's Y104D antibody different from cetuximab?
A. So this particular variant, 104D, is a replacement of a tyrosine on position 104 using aspartic acid.

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Q. Why did Wei try to modify cetuximab?
A. Modify the sequence, you mean, or to express it and formulate it as an ADC?
Q. Modify the sequence.
A. Modify the sequence.
So Wei made a few modifications. One among them is the Y104D. He also made some modifications actually to humanize it. And as we mentioned previously, humanization leads to reduced immunogenicity. So I believe among one of the motives was also to make a more appropriate and suitable cetuximab antibody by reducing immunogenicity.
Q. So it is your opinion that the Y104D antibody is a humanized; correct?
A. No. He made several versions. So if you read the patent, he made 104D -- actually, they. They made 104D, several other mutations and also a class of humanized antibodies based on cetuximab.
Q. So why did Wei try to modify cetuximab to arrive at the Y104D antibody?
A. His main rationale, you mean?
Q. Correct.
A. Yeah. So as Wei states, and we can see this in the background, for example: "The objects

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herein provide improved anti-EGFR antibodies that exhibit increased EGFR binding activity in a tumor microenvironment compared to in a nontumor environment." This is the objective of this application.

Q. Does that mean that the Y104D antibody has more selectivity than cetuximab in terms of targeting tumor cells rather than normal cells?

MR. SUH: Objection to form.

THE WITNESS: From the data that I have reviewed in the patent, I don't see that there is enough evidence to support this. So in my opinion, no.

BY MR. QIU:

Q. Is it true that the Y104D antibody exhibit greater activity under conditions of acidic pH than under conditions of neutral pH?

A. To my opinion, no, and I don't think -- if you can point me out -- point out evidence that supports this, please do so.

Q. So in your opinion, is there any difference between the properties of the Y104D antibody and cetuximab?

A. There are obvious differences. To start with, there is an amino acid substitution. So there

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are differences in the amino acid sequence between cetuximab and the 104D variant.

Q. Other than the difference between their sequences, is there any difference between their properties?

A. So Wei reports differences in some of the properties, but this is expected because it's -- any time that you make a difference, you expect -- and changes in the amino acid sequence, you expect differences.

Now, are these differences biologically meaningful? I doubt.

Q. So it is your opinion there is no biologically meaningful difference between Wei's Y104D antibody and cetuximab?

A. Yes. Upon a review of the data, I believe that Y104D does not have any significant biological differences compared to cetuximab.

Q. Does Y104D represent the only way to modify cetuximab?

A. No. There are millions of ways that you can modify cetuximab.

Q. So do all of the variants of cetuximab have the same properties?

A. The variants that Wei describes?

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Q. Is that your answer to the question?

A. No, no. I'm asking for a clarification.

Do you refer to the variants that Wei describes or generally, are any variants of cetuximab are expected to have different properties?

Q. Let's talk about the variants that Wei describes.

Do they all have the same properties?

A. No.

Q. What are their differences in properties?

A. I expect that some of them might have different stabilities used, express differently, and they have differences. Wei also made humanized versions of this antibody, so I expect that the humanized versions of these antibodies will have reduced immunogenicity in humans compared to cetuximab, since cetuximab is a chimeric antibody.

Q. Wei makes a large number of chimeric variants of cetuximab; correct?

A. Yes, correct.

Q. Is it true that they all differ from cetuximab by one amino acid?

A. I believe so. He lists many, many variants.

Q. Is it fair to say that the change of one

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amino acid in the sequence of an antibody can substantially change its properties?

MR. SUH: Objection to form.

THE WITNESS: Hard to predict.

BY MR. QIU:

Q. Why did Wei screen a large number of antibodies and decide to use the Y104D antibody?

A. For specifically Y104D, I don't know because I don't think -- I need to read it more carefully, but I don't think that we have data for all the variants presented in the Wei patent. But I might be wrong. I can check, if you'd like.

Q. Can you please go to -- take out Exhibit 1002, which is your declaration.

A. Yes.

Q. And go to paragraph 62.

A. Yep.

Q. Please let me know when you are there.

A. Yeah, I'm here.

Q. Can you please read that paragraph for the record.

A. Paragraph 62: "Wei states that these cetuximab variants 'exhibit greater activity (binding affinity) under conditions of acidic pH, such as present in a tumor microenvironment, than

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under conditions of neutral pH, such as exists in non-tumor tissue.'"
Then there is a reference.
"Wei further states that, 'By virtue of the pH-selective activity, the anti-EGFR antibodies provided produce fewer or lesser undesirable side-effects and/or exhibit improved efficacy in a treated subject by virtue of the ability to administer higher doses.'"
So that's paragraph 62.
Q. Based on reading this paragraph, do you want to change any of the testimony you have given just now?
A. No. These are statements that Wei makes, not me.
Q. Is it your opinion that these statements by Wei are incorrect?
A. According to the presented evidence in the Wei patent, I don't think that there is enough evidence to support these claims.
Q. Is it your opinion that a POSA reading Wei would have understood that these statements by Wei were incorrect?
A. Yeah, a POSA with understanding of the scientific process and being able to interpret the

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data, the presented data as presented in the Wei patent, would have agreed with me.
Q. So it is your opinion that a POSA reading Wei would have understood that the Y104D antibody does not have higher pH selectivity than --
A. Yes, correct.
Q. -- cetuximab?
A. Correct.
Q. Would a POSA -- sorry. Strike that.
Wei also disclosed a humanized version of the Y104D antibody; correct?
MR. SUH: Objection to form.
THE WITNESS: Correct, yes.
BY MR. QIU:
Q. And that antibody is named huY104D; correct?
A. Correct, yes.
Q. Is there any difference between the properties of the Y104D and the huY104D antibody?
A. I believe there are differences.
Q. What are the differences?
A. I need to check to be double sure -- double-check to be sure. Sorry.
Q. Yes, please check.
A. So from a quick look, maybe there are other

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things -- other differences as well. What I see is if you go to Table 42, for example.
Q. Table 42?
A. Mm-hmm. Table 42, yeah. Maybe there are other changes -- it's a big patent, so maybe there are other differences. But from what I see here on Table 42, in Table 42, is that Y104D-MMAE versus human, huY104D-MMAE and this is continuing on page 128, so there is some difference in the clinical -- in the tumor growth efficacy in this model. And this model is described in Figure -- I believe it's in paragraph 1118.
Then another difference that we see is also on Table 44. So this is comparing Y104D-MMAD versus human 104D-MMAD, same dose. Now it appears that the humanized version of the 104D has better activity than the chimeric. In the previous one it appeared that it has comparably maybe worse activity.
These are the two tables or external data that I see there is some difference between 104D and human 104D.
Q. Does the humanization of Y104D have any impact on the pH selectivity of the antibody?
A. I haven't seen some evidence, but give me a second. I can go back and then check again.

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Sorry, it's a big patent and it might take a while.
You meant pH selectivity between 104D and humanized 104D; right?
Q. Yes, mm-hmm.
A. Yes. It does appear that humanization resulted in difference in the pH binding of 104D to EGFR as assessed by ELISA.
Q. What is your basis in saying that?
A. So this is -- so if you go to Table 24.
Q. 1024? Okay.
A. Table 24.
Q. Table 24.
A. So this data described in Table 24 through 27. Without understanding the exact experimental procedures, you cannot really definitively say there is a difference in the pH selectivity between 104D and the humanized version of 104D.
If we take the conclusion of the -- of Wei that is in paragraph 1008 or 1007.
So Wei says that: "The results show that all tested variants exhibit a higher EC50 and hence weaker binding, at pH 7.4 than at pH 6.5 or pH 6.0."
So I'm not sure what are the units that they are measuring. If I take the statement as is,

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then it appears that there is a difference in pH selectivity that was better with humanization.
Q. Why do you agree with this statement of Wei but do not agree with the other statement of Wei that states that Y104D antibody has higher pH selectivity than cetuximab?
MR. SUH: Objection. Mischaracterizes testimony.
THE WITNESS: No. This one -- so we see Table 24. Y104D. And we assume that EC50 is a surrogate for pH selectivity, how well the antibody binds to EGFR.
So we see that it has an EC50 value. Again, I don't know the unit of that, so I'm not entirely sure how reproducible these results are, what's the intra-experimental variability. But we see that 104D has an EC50 of 8.33.
You see that? In Table 24.
BY MR. QIU:
Q. Please continue with your answer.
A. Yeah. Then the humanization, which is D-h has an EC50 of 30.2.
Without being able to comment how biologically significant this difference is, the 8.33 versus 30.2, I believe that is some difference.

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Now, why I don't think that the introduction, the replacement of the 104D does not generate a variant with a better pH selectivity comes from the fact that seeing, for example, on Table 18, wild-type versus 104D variants, the difference is from 3.3 to 5.07 or 6.18.
To me it appears that these differences are well within the experimental level.
Q. Can you please go to page 102 of Wei.
A. 102?
Q. Yes.
Can you please read Table 21 and the paragraph 0994.
A. How can I read Table 21?
MR. SUH: Do you want him to read it for the record?
BY MR. QIU:
Q. You can review them or you can read them to yourself.
A. So 994, you said.
Q. Yes.
A. "The results show that at pH 7.4, the wild-type cetuximab antibody exhibited a slightly higher EC50 than at pH 6.5 or pH 6.0. In contrast, for the Yl04 mutants and the FDP-h3 control, binding

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was substantially weaker at pH 7.4 than at pH 6.5 or pH 6.0 as evidenced by a higher EC50 under the neutral pH tested conditions than the acidic pH tested conditions. Thus, each of the mutants exhibit a greater ratio of binding at acidic pH 6.0 or 6.5 than at pH 7.4."
Q. Do you want to change any of your testimony provided in this deposition after reading Table 21 and paragraph 0994?
A. If we see at the values of pH 7.4, the binding of the wild-type and the 104 mutants, I consider this difference to be negligent, whereas in the humanization, the difference are a little bit more substantial.
So I still maintain the opinion that the introduction of the 104D mutation doesn't really influence its selectivity of cetuximab.
Q. Do you think pH selectivity is a positive property for an antibody for use in ADC?
A. It's neutral. I cannot comment on that. It can be positive, it can be negative. What it really matters is, is the new antibody better than cetuximab? And the results from the Wei patent are conflicting.
So in one tumor model the humanization made

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it better. In another tumor model, it made it worse.
Q. Do you think -- what do you think is the reason why humanization can enhance the pH dependency of the antibody in Wei?
A. I can only speculate. So humanization introduces changes to the amino acid sequence. Some of the changes might result in the recognition of the antigen with different affinity at different pHs. It's a chemical property of amino acids.
Q. Do you think this effect applies generally to humanization of chimeric antibodies?
A. I don't know if it applies generally. What I know is that any change that you introduce to the variable region of an antibody -- because remember humanization involves changes to the amino acid backbone of the antibody and to areas that recognize the antigen or participate directly or indirectly to this recognition.
So any of the changes might have impact on any function, including pH sensitivity recognition of an antigen.
Q. So it is your opinion that humanization always increases the pH selectivity of an antibody?
MR. SUH: Objection.

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THE WITNESS: No, I didn't say that.
BY MR. QIU:
Q. Is that correct?
A. No, I didn't say that. Humanization might change the prop- -- the how the antibody will recognize the antigen at different pH conditions. Not always. And we've seen this with Wei. So he humanized another antibody. It's not an absolute, like, every time that you humanize it will change the pH sensitivity.
Q. Would you say that Wei was successful in creating an ADC with the Y104D antibody?
A. Yeah. It showed potent antitumor activity.
Q. I want to turn to the Leanna reference, which is Exhibit 1006. Let me first upload that.
Actually, before moving on to -- to Leanna, let me -- let me ask some more questions on Wei.
So just to confirm, is it your opinion that Wei was successful in creating an ADC with the chimeric Y104D antibody?
A. Yes. I believe that Wei generated an ADC based on Y104D or in EGFR variants that have antitumor activity.
Q. Is it -- why do you believe it is -- why do you believe it is successful?

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A. Because of the demonstrated antitumor activity.
Q. You earlier testified that Wei's Y104D antibody has no biologically meaningful difference from cetuximab; correct?
A. Correct, correct.
Q. Is it your opinion that if Wei replaced the Y104D antibody with cetuximab, it will result in a successful ADC?
A. Yes.
Q. If we replace Wei's Y104D antibody with other cetuximab variants that Wei created, is it your opinion that the resulting ADC would have been successful?
A. If you can specifically mention one variant, I can look on the properties of his variant according to the data that Wei provides and then provide an opinion on that. But I don't believe that any of the variants that Wei created will be equally good as cetuximab.
Q. But Wei also created an ADC with humanized Y104D antibodies; correct?
A. Correct.
Q. Would you say that Wei was successful in creating that ADC?

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A. Yes.
Q. What is the basis of your opinion?
A. But -- and that's what I was -- I wanted to follow up.
So by saying "successful," my personal opinion is that if this molecule has antitumor activity in vivo. And what we see from Wei is that this molecule, one -- as an ADC, as an MMAE, it does have antitumor activity in vivo in different models that were -- that was tested.
Q. Do you believe -- strike that.
Let's move on to Leanna's -- Leanna, which is Exhibit 1006. I think I have uploaded a copy of that.
(Exhibit 1006 was previously marked by the Certified Shorthand Reporter, and a copy is attached hereto.)
BY MR. QIU:
Q. Actually, before moving on to Leanna, I want to ask a question?
So Dr. Bournazos, during the breaks, including the earlier ten-minute break and the lunch break, did you communicate with any person?
A. I called my sister.
Q. Is that all?

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A. Yeah, that's all.
Q. Okay. And you did communicate with counsel?
A. With who?
Q. With counsel present in your -- in the room that you were in.
A. We did communicate, like, what options for lunch we have.
This is acceptable; right?
Q. Okay.
A. Okay. Just to make sure.
Q. Yeah. I just want to make sure you didn't communicate about anything about this case.
A. No.
Q. What is Leanna's Antibody 1?
A. It's an antibody against EGFR.
Q. Does it have a name or sequence you can point me to?
A. No, I don't believe the sequence is provided in Leanna's reference.
Q. So to render your opinion you did not analyze Leanna's -- the sequence of Leanna's Antibody 1; correct?
MR. SUH: Objection to form.
THE WITNESS: I believe I did, but I'm not

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100 percent sure.
BY MR. QIU:
Q. If the sequence is not provided in the Leanna reference, where did you obtain the sequence?
A. So as I mentioned on paragraph 79 of the declaration, so Antibody 1 was previously described in WO 2011/041319. So I believe the sequence is there.
Now, I don't recall whether or not I have done any analysis of the sequence of Antibody 1 in preparation of the declaration.
Q. Do you believe analyzing the sequence of the Antibody 1 is relevant to rendering your opinion?
A. Not really.
Q. Does Leanna's Antibody 1 display tumor selectivity?
A. It's an antibody against EGFR, so it is specific for tumors.
Q. Does Leanna's Antibody 1 display higher activity against tumor cells than normal cells?
A. I'm not familiar with Antibody 1 to be able to make a conclusion of that. I haven't reviewed what is Antibody 1.
Q. Please go to paragraph 79 of your

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declaration, which is -- which is Exhibit 1002.
A. Yes. Do you need me to read it out loud?
Q. No.
A. Okay.
Q. There you mentioned that Antibody 1 is described in WO 2011/041319 and US20110076232; correct?
A. Yes, correct.
Q. Can you please open Exhibit 2015.
A. 2015, you said?
Q. Yes. I believe it's in the package that we sent.
MR. SUH: 13, 14... it's not in this pile, Fred, but I'm going to look at the other pile.
MR. QIU: Okay. Thank you. If it's not in there I'll...
MR. SUH: So we have 2002, 2003, 2004, 2005, 2006, 2007, 2008, 2009, 2011, 2012, 2013, 2014, and it skips to 2016.
MR. QIU: Oh, okay. In that case, let's -- let's have this exhibit electronically.
I have uploaded to the upload link. It would be great if you can download it.
MR. SUH: Fred?
MR. QIU: Yeah.

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MR. SUH: We actually have -- we have a set of 2015. Would you allow me to hand that over to the witness --
MR. QIU: Yeah, that'd be great. Is it --
MR. SUH: For the record, it's a clean copy, there's no notes or anything.
MR. QIU: Oh, that's perfect. Thank you.
MR. SUH: Okay.
THE WITNESS: Yeah, thanks.
Oh, that's big.
MR. QIU: Yeah.
(Exhibit 2015 was previously marked by the Certified Shorthand Reporter, and a copy is attached hereto.)
BY MR. QIU:
Q. Can you please go to this exhibit, Exhibit 2015.
Do you recognize this reference?
A. Looks familiar. I'm not sure if I have reviewed or not.
Q. Is it one of the --
A. Yeah.
Q. Is it one of the references that you have mentioned in your paragraph 79?
A. Yes. The number matches, yes.

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Q. Please go to paragraph 177 of Exhibit 2015.
A. 177. Give me a second because it's missing pages. What page is it? It might be easier to find like that.
Q. So it's on page 11.
A. Oh, okay. Paragraph?
Q. Yeah, paragraph 177 on page 11.
A. Got it.
Q. Can you please review that paragraph.
A. "Figures 55A and 55B show the hu806" --
MR. SUH: Dr. Bournazos, I think he wants you to review it.
THE WITNESS: Oh, review. Okay.
Yes. Let me go to the figures as well.
BY MR. QIU:
Q. So that paragraph indicates that the antibodies shown in Figure 55 is hu806 antibody; correct?
A. Correct.
Q. Can you please go to paragraph 15 of Exhibit 2015.
A. Paragraph 15.
Q. And that paragraph is on page 3.
A. Got it. Got it. Yes, I'm here.
Q. Can you please read paragraph 15 to

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yourself. You don't need to read it out loud.
A. Yeah, okay.
Yes.
Q. Does reading this paragraph change your opinion about whether Leanna's Antibody 1 is tumor selective?
A. I don't think it's -- don't -- give me a second.
These antibodies are different. I won't classify them as tumor selective, as you mentioned. And the reason for this opinion is that -- read paragraph 15. So it says: "Additionally, while these antibodies do not recognize the EGFR when expressed on the cell surface of a glioma cell line expressing normal amounts of EGFR..."
Gliomas are tumors. So based on this evidence, yeah, from what I read, Antibody 1 and the other antibodies recognize the surface of tumors while maintaining very low binding to normal -- they don't bind significantly to normal tissues.
But I wouldn't classify them as tumor selective because glioma cells are tumors.
Q. After reading this paragraph, do you now believe that Leanna's Antibody 1 has a higher activity on tumor cells than on normal cells?

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MR. SUH: Objection. Mischaracterizes the testimony.
THE WITNESS: On the contrary. By reading this paragraph, as I mentioned before, is that it appears, as they mentioned, I need to review the experiments. It appears that while this -- and I'm just citing what is in there in paragraph 15. These antibodies do not recognize the EGFR when expressed on the cell surface of a glioma cell line. Glioma cells are tumors.
So it appears to me that these antibodies bind but only to a subset of tumors.
So I would say tumor -- restricted to certain tumor types. Not selective.
BY MR. QIU:
Q. Do you agree that Antibody 1 is better at distinguishing tumor cells from normal cells than cetuximab?
A. I cannot comment on this because I haven't seen a head-to-head comparison between cetuximab and Antibody 1.
Q. Would you say that Leanna was successful in creating an ADC with Antibody 1?
A. So Leanna's objective was to describe the method of generating an ADC using a humanized anti-EGFR antibody as an example.
In this respect, yes. They were successful in creating an antibody against EGFR that is -- has -- is ADC, so it has a vcMMAE or vcMMAF drug.
Q. Would cetuximab bind to the mutant EGFR that Antibody 1 targets?
A. Do you mean the deletion 2-7?
Q. I'm sorry?
A. Do you mean the variant DDE2-7 mutant?
Q. Yes.
A. I believe this is the same, I might be wrong, but I believe that this is the variant 3 of EGFR, and cetuximab has activity against that variant.
MR. QIU: Okay. So, Doctor and Howard, the deposition has continued for, I think, more than an hour.
MR. SUH: Okay.
MR. QIU: I want to offer a break if you want to take one.
MR. SUH: Yes. Yes, thank you.
MR. QIU: Shall we take a break and come back ten minutes after 3:00 p.m. Eastern time?
MR. SUH: Yes. Thank you.
MR. QIU: Okay.

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(Recess.)
BY MR. QIU:
Q. Doctor, did you communicate with anyone during this past break?
A. No.
Q. Are you familiar with the reference Liu, which is 1007 and 1008 in this case?
A. Yes.
(Exhibit 1007 and Exhibit 1008 were previously marked by the reporter, and copies are attached hereto.)
BY MR. QIU:
Q. Can you point me to the sequence of Liu's BA03 antibody?
A. So Exhibit 1008, sequence of BA03 is, for the heavy chain, is sequence ID number 5, and for the light chain, sequence ID number 13.
So these sequences appear on Exhibit 1007 on page 19. So 5 and 6. 5 is there on page 19, 20 and sequence ID 15 is page 22. I believe it's also on the translated on page 12 and 13.
Q. How is Liu's antibody BA03 antibody different from cetuximab?
A. I believe it's a humanized version of cetuximab.

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Q. Is there any -- are there any variations other than humanization?
A. No. The humanization introduced changes. So the goal was to generate a humanized version. So the changes are amino acid changes from cetuximab to BA03.
Q. So it is your opinion that the BA03 antibody was created by humanizing cetuximab without any other variations?
MR. SUH: Objection to form.
THE WITNESS: So BA03 was constructed based on cetuximab. So they have introduced changes with the aim to humanize it.
Now, if these changes have resulted in humanization, some of them mice, some them not, have they changed the properties, if this is what you are asking, perhaps. But the goal was humanization.
BY MR. QIU:
Q. Is Liu's BA03 antibody substantially the same as Wei's humanized Y104D antibody?
A. Substantially the same. They both originate from the same clone from cetuximab. So they are related. So cetuximab is the parent. These are the siblings.
Now, the similarity between BA03 and Wei's,

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I'm not sure what degree of similarity would have.
Q. How is Liu's BA03 antibody different from Wei's humanized Y104D antibody?
A. Sequence, I presume.
Q. Are you aware of -- so how -- how do their sequences different -- sorry. Strike that.
How do the sequence of Liu's BA03 antibody differ from Wei's humanized Y104D antibody?
A. Hard to tell. I -- give me a second.
I cannot comment on how different they are, but they are not 100 percent identical. That's what I can say.
Q. Have you analyzed how the properties of Liu's BA03 antibody differ from those of Wei's humanized Y104D antibody?
A. Can you please define what do you mean by "property"? Is any specific aspect that you are interested in?
Q. Have you analyzed how any property of Liu's BA03 antibody differ from Wei's humanized Y104D antibody?
A. What I know by reviewing the Wei and the Liu patents is that both of them target the same epitope, they are clonal variants or variants of cetuximab. If there are any other changes or

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differences in the properties of these two antibodies, I don't know, mostly because there is no head-to-head comparison between these two antibodies that will enable me to say with confidence that BA03 differs from Liu's antibodies -- Liu's antibodies differs from Wei's.
Q. So you are not aware of any difference between the properties of Liu's BA03 antibody and Wei's humanized Y104D antibody; correct?
A. Because I don't have the data that can provide me with a head-to-head comparison between those two antibodies.
Q. Have you ever tried to determine the differences between the properties of Liu's BA03 antibody and Wei's humanized Y104D antibody?
A. No. That will require experimentation.
Q. Can you please go to paragraph 187 of Exhibit 1002, which is your declaration.
A. Yes. 187, you said?
Q. Mm-hmm. Yes.
A. Do I need to read this out loud?
Q. You don't.
Is it true that you stated that the humanized Y104D antibody and the BA03 antibody are substantially identical?

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A. Yes. And that's what I said previously. They come from the same clone, cetuximab. So they are related. So the parent cetuximab, siblings are Y104D and BA03.
Q. Is it your opinion that all cetuximab variants are substantially identical to each other?
A. All the variants disclosed by Wei.
Q. Is it your opinion that the BA03 antibody was created by Wei?
A. Can you rephrase -- can you repeat your question, please?
Q. Sure, sure.
It is your opinion that the BA03 antibody was created by Wei; correct?
A. By Liu. BA03 is Liu. Wei has the Y104D.
Q. So it is your opinion that all variants of cetuximab, regardless of who created them, are substantially identical to each other; correct?
MR. SUH: Objection. Mischaracterizes the testimony. Also object to the form.
THE WITNESS: Depends on which variant. So I can go ahead and generate a variant of cetuximab that has replaced all the amino acids. I wouldn't consider this to be substantially identical. A single amino acid substitution, it is substantially

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identical. It's -- again, it refers to the degree of changes.
BY MR. QIU:
Q. What is your basis in you saying that the BA03 antibody is substantially identical to the humanized Y104D antibody other than the fact that both are variants of cetuximab?
MR. SUH: Objection. Asked and answered.
THE WITNESS: Because they originate from the same parent. The parent is cetuximab. Humanized 103, 104D, BA03 are related from the same family, from the same parent. So that makes them substantially identical.
BY MR. QIU:
Q. So all embodiments -- strike that.
All antibodies that are generated from the same parent, like cetuximab, are substantially identical to each other, according to your opinion; correct?
MR. SUH: Objection. Mischaracterizes the testimony.
THE WITNESS: Not all of them. As I mentioned, if I go ahead and take cetuximab and I change everything, 99 out of 100 amino acids, it's not going to be substantially identical.

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Based on what I've seen from the 104D and BA03, the changes that have been introduced are not -- they haven't changed the characteristics of the antibody. The antibody still binds to EGFR. They are still related to cetuximab.
BY MR. QIU:
Q. Is it your opinion that all humanized antibodies generated from the same parent are substantially identical to each other?
A. Depends on the humanization strategy.
(Stenographer clarification.)
BY MR. QIU:
Q. Is it your opinion that all humanized versions of cetuximab are substantially identical to cetuximab?
A. It depends on the humanization strategy. But in principle, any humanization strategy will aim to maintain the least number of differences. So then it doesn't mess up with -- on cell binding.
Q. How many amino acids are -- strike that. Sorry.
Have you compared the humanization process of BA03 and Y104D?
A. No, I haven't.
Q. What aspect of the humanization process for

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the BA03 antibody and the Y104D antibody made you believe that they are substantially identical?
A. Because they come from the same parent with the cetuximab. They have very maintained binding to the target, which is EGFR.
Q. So it is your opinion that as long as two antibodies -- as long as two humanized antibodies come from the same parent, regardless of their humanization process, they are substantially identical; correct?
MR. SUH: Objection. Mischaracter- -- I'm sorry.
Objection. Mischaracterizes the testimony.
THE WITNESS: If they maintain binding properties, the same affinity or comparable affinity with a parent, if they maintain antigen specificity, I would consider them substantially identical compared to any other clone because the process of generating antibody diversity can lead to an infinite number antibodies in the combinations that you can have.
So in this very diverse spectrum of antibodies, even if there are changes from the parent, me, personally, I would consider them substantially identical.

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BY MR. QIU:
Q. Does the BA03 antibody have a higher or lower binding affinity than the humanized Y104D antibody?
A. I believe Liu never tested head-to-head BA03 with Y104D. So I cannot comment on that.
Q. Does Liu's BA03 antibody have a higher or lower antigen specificity as compared to the humanized Y104D antibody in Wei?
A. I believe I already answered this question. So there is no direct comparison between BA03 and humanized 104D or Y104D or any of the variants that Wei generated that would allow me to say that one has had affinity, has binding specificity over the other for EGFR.
Q. If two antibodies have different pH selectivity, will that make them substantially different from each other?
A. It depends on the definition of "substantially different." In the context of the paragraph 187, substantially -- my definition of substantially identical refers to the clone because we have endless possibility of generating antibody clones, these two are substantially identical.
Changing the pH or changing any other

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function it won't make them substantially different.
(Stenographer clarification.)
THE WITNESS: Any other properties will not make them.
BY MR. QIU:
Q. Is Liu's BA03 antibody substantially the same as Wei's chimeric Y104D antibody?
A. Can you please repeat the question?
MR. QIU: Can the court reporter help read the question.
THE STENOGRAPHER: Yes.
(The previous question was read back by the court reporter as follows:
"QUESTION: Is Liu's BA03 antibody substantially the same as Wei's chimeric Y104D antibody?")
THE WITNESS: I believe so. Both of them originate from the same clone, so this makes them substantially similar.
BY MR. QIU:
Q. Is there any difference between Liu's BA03 antibody and Wei's Y104D antibody?
A. Yes. They have differences in sequence, to begin with.
Q. Did you compare the sequence of Liu's BA03

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antibody and the sequence of Wei's chimeric Y104D antibody?
A. I don't think I did.
Q. Have you analyzed how the properties of Liu's BA03 antibody differ from those of Wei's chimeric Y104D antibody?
A. Again, we don't have a direct comparison between these two antibodies. So by comparing data from one patent to the other, it's not possible for us to lead to any conclusions in differences in any of the properties of these antibodies.
Q. Did you compare the properties of Liu's BA03 antibody and Wei's chimeric Y104D antibody in any way, including comparing data or other knowledge?
A. I cannot compare the activity or datasets that are generated by Wei and Liu because these differences, these experiments were done separately. So it won't allow me to draw any conclusions that one is different than the other.
Q. Have you analyzed whether Liu's BA03 antibody has a higher or lower binding affinity than Wei's Y104D antibody, either chimeric or humanized?
A. I cannot comment on that. There is no direct comparison in experiments between BA03 and

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Wei's Y104D.
Q. Have you ever analyzed whether Liu's BA03 antibody has a higher or lower immunogenicity than Wei's Y104D antibody, either chimeric or humanized?
A. If I have done the experiment by myself, you're asking?
Q. No. I'm asking for any type of analysis that you have performed.
A. Wei doesn't report immunogenicity, as far as I remember.
Q. So you do not know whether Liu's BA03 antibody has a higher or lower immunogenicity than Wei's Y104D antibody, either humanized or chimeric; correct?
A. Correct, because Wei doesn't provide any analysis on immunogenicity. So I cannot comment on something like that.
Q. Have you analyzed whether Liu's BA03 antibody has a higher or lower level of inhibitory activity in blocking interactions between EGFR and the EGF than Wei's Y104D antibody, either chimeric or humanized?
A. There is no head-to-head comparison between BA03 and Wei's Y104D that would allow me to draw any conclusions.

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Q. Do you know whether Liu's BA03 antibody has a stronger or weaker antibody in inhibiting phosphorylation of EGFR than Wei's Y104D antibody?
A. It's the same answer as before.
Q. Can you please provide the answer?
A. There is no direct comparison between BA03 in Liu's and Wei's Y104D in respect to this aspect.
So what Liu has done, and this is across different experiments that are described in Liu patent, is that BA03 has increased -- so they compared it only to cetuximab. So what I can do, if this is helpful, is to refer everything back to cetuximab. So BA03 has stronger activity in inhibiting phosphorylation of EGFR. It has higher ADCC activity. It has significantly lower immunogenicity compared to cetuximab.
I cannot comment on any of these aspects compared to Wei's antibodies because I don't know how they behave. They are different than cetuximab. They are substantially identical, but this change might influence one or some aspects.
Q. Have you analyzed whether Liu's BA03 antibody has a higher or lower ADCC activity than Wei's Y104D antibody, either chimeric or humanized?
A. Wei mentions that BA -- Liu mentions that

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BA03 has higher ADCC activity compared to cetuximab. No comparisons were made to Wei's Y104D antibody.

Q. So you do not know whether Liu's BA03 antibody has a higher or lower ADCC activity than Wei's Y104D antibody; correct?

A. Because such comparison was never done.

Q. Have you analyzed whether Liu's BA03 antibody has a higher or lower antitumor activity than Wei's Y104D antibody?

A. Can you repeat the question?

Q. Sure.

Have you analyzed whether Liu's BA03 antibody has a higher or lower antitumor activity than Wei's Y104D antibody, either chimeric or humanized?

A. As an ADCC or as a naked antibody?

Q. Either as ADCC or antibody.

A. I don't believe Liu has any experiments done with BA03 as ADCC. And Wei has never included in their analysis BA03. So I cannot comment on nonexisting data.

Q. Is it your opinion that as long as BA03 and Y104D have similar binding specificity and affinity, you don't need to review other data in order to arrive at the conclusion that they are substantially

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identical?

MR. SUH: Objection to form.

THE WITNESS: Can you please repeat the question?

MR. QIU: Can the court reporter read back the question.

THE STENOGRAPHER: Yes.

(The question was read back by the court reporter.)

MR. QIU: Sorry. Let me repeat the question.

BY MR. QIU:

Q. Is it your opinion that as long as BA03 and Y104D have similar binding specificity and the affinity, you don't need to review other data in order to arrive at the conclusion that they are substantially identical?

MR. SUH: Objection to form.

THE WITNESS: Substantially identical in which property?

BY MR. QIU:

Q. I mean, substantially identical in the sense in paragraph 187 of your declaration.

A. Yes. So these are -- they are substantially identical in terms of sequence. In

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terms of properties like antigen binding and specificity for the antigen, they both recognize the same epitope.

I cannot comment if one or the other has better activity in inhibiting phosphorylation in inducing ADCC unless an experiment is done to compare head-to-head these two antibodies.

Q. Is Liu's BA03 antibody substantially the same as Leanna's Antibody 1?

A. No.

Q. How is Liu's BA03 antibody different from Leanna's Antibody 1?

A. Liu's antibody is -- and Wei's -- come from the same parent, cetuximab, and they have the same properties. Leanna's Antibody 1 recognizes, I believe, a different epitope of EGFR, and that's the reason why it cannot bind on certain tumor types.

So these are substantially different. But in a bigger context, they both recognize EGFR.

Q. Have you analyzed how the properties of Liu's BA03 antibody differ from those of Leanna's Antibody 1?

A. I haven't done any comparison between Leanna's Antibody 1 and BA03. All I know is that both are anti-EGFR antibodies.

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Q. Does Liu teach how its BA03 antibody can be used?

A. I believe so.

Q. What are the use cases of BA03 that Liu teaches?

A. I believe these are described in paragraph 50 in Liu.

Q. Liu does not teach using BA03 in ADC; correct?

MR. SUH: Objection to form.

THE WITNESS: Not as ADC.

BY MR. QIU:

Q. Does Liu teach using cetuximab in ADC?

A. I don't believe so, but Wei does.

Q. Does your -- does Ground 1 and Ground 2 in your declaration rely on Wei's teaching of using cetuximab in ADC?

MR. SUH: Objection. Lacks foundation.

THE WITNESS: I believe it's a combination of both Wei and Liu.

BY MR. QIU:

Q. Does your declaration rely on Wei's embodiment that uses the Y104D antibody or does it rely on using ADC -- using cetuximab in ADC?

MR. SUH: Objection to form.

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THE WITNESS: Can you please repeat the question?
BY MR. QIU:
Q. Does your declaration rely on Wei's teaching of using the Y104D antibody in ADC or does it rely of Wei's teaching of using cetuximab in ADC?
MR. SUH: Same objection.
THE WITNESS: So Wei discloses that an anti-EGFR antibody drug conjugate include the variant that I describe. Knowing that this variant is a clonal variant of cetuximab, yes, my declaration depends -- uses Wei as this example.
BY MR. QIU:
Q. Are you familiar with the Tikhomirov reference that is Exhibit 1009?
A. 1009. Yes, I am.
Q. If we call it "Tikhomirov," would you understand that it refers to that exhibit?
A. Yes, but we can call it 009, if you prefer, 1009.
Q. Okay. Thanks.
Does Tikhomirov teach an anti-EGFR ADC with a cleavable linker?
A. Can you please repeat the question?
Q. Sure.

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Does Tikhomirov teach an anti-EGFR ADC with a cleavable linker?
A. Yes and no, because he teaches to use a cleavable linker unless the conjugation -- unless the drug is not an antimicrotubule agent.
Q. So it is your opinion that Tikhomirov does not teach an anti-EGFR ADC with a cleavable linker?
A. The conclusion from Tikhomirov -- their conclusion is that an anti-EGFR antibody or an antibody that targets -- that has agonistic activity -- antagonistic activity, it's better to have them as noncleavable linker.
My opinion upon reviewing the data is that the experiments do not support this notion.
Q. Is the Tikhomirov conclusion based on a certain anti-EGFR ADC that it performed experiments on?
A. They generated ADCs based on cetuximab.
Q. What is the linker and payload used?
A. So they used DM-1 as a noncleavable linker and then MMAE with a cleavable linker.
Q. What is the cleavable linker that was used?
A. The VC.
Q. If we keep the VC linker and the MMAE payload of Tikhomirov but increase the binding affinity of its antibody, would that increase or decrease the toxicity against normal cells?

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A. How we will increase the affinity?
Q. By replacing the antibody with another antibody that has a higher affinity.
A. If it's going to increase the toxicity? Most likely not.
Q. What is your basis in saying that?
A. Because a change in affinity, to my opinion, is not associated with toxicity. And I haven't seen any literature that would support this notion.
Q. Is the MMAE payload in Tikhomirov the same as that taught in Wei?
A. The same as Wei?
Q. Yeah, so is the MMAE payload in Tikhomirov the same as that taught in Wei?
A. It is the same as Wei, yes.
Q. Is the VC linker here also the same as that used by Wei?
A. I believe so.
Q. Is it your opinion that Wei's ADC has similar toxicity against normal cells as Tikhomirov's ADC with a cleavable linker?
MR. SUH: Objection to form. Foundation.

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THE WITNESS: I cannot comment on Wei's toxicity because he hasn't demonstrated toxicity data. And the experiments done in Tikhomirov do not allow me to draw any conclusions showing that -- saying that their antibody with the same -- with a vcMMAE linker has toxicity or not.
BY MR. QIU:
Q. Can you please go to page 31 of Exhibit 1009. Please let me know when you're there.
A. Yes.
(Exhibit 1009 was previously marked by the Certified Shorthand Reporter, and a copy is attached hereto.)
BY MR. QIU:
Q. Actually, it's page 30 of the reference of Tikhomirov and it's on page 31 of the stamp. Actually, let's go to page 29 of Tikhomirov. It's in the paragraph below Example 4.
Please let me know when you are there.
A. Yes, I'm there.
Q. At the end of this paragraph there's a sentence saying that Figure 13 shows that conjugation of cetuximab to MMAE by a cleavable linker, parenthetical, the VC linker, potentiates its toxicity against normal cells.

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Is that correct?
A. I don't believe the data. And the reason for this is if you go to Figure 13, this is on page -- page 42 of the exhibit, you will see there that it contains a comparison between cetuximab -- this is labeled as Cetux2C9-MMAE -- and then Cetux2C9-DM-1, along with cetuximab 2C9, which is the naked antibody, and then human Ig-DM-1, which I presume is an isotype control that has DM-1, and then human IgG, which is an irrelevant control.
So to make the statement that a cleavable linker potentiates toxicity, first of all you need to have a head-to-head comparison having cetuximab MMAE with a cleavable linker versus cetuximab MMAE with a noncleavable linker because the sensitivity of the cells to different drugs is going to be different. It's comparing apples and oranges.
So DM-1 would have different healing activity than MMAE.
Then if you even want to be precise, we also need an isotype control and a relevant control with MMAE with or without cleavable linkers.
So with the presented evidence, the lack of important controls, the lack of a payload-alone control, we cannot conclude that a cleavable linker

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will have more toxicity than a noncleavable linker.
Then in experiments in labs, what we do is we repeat the same experiment if we want to establish generality with different cleavable linkers.
So here in this patent they only used one linker, VC, and one noncleavable linker, different chemistries. By making this conclusion that all cleavable linkers are bad, all noncleavable linkers are good, you need to show data. So you need different cytotoxic drugs in addition to MMAE, different linkers, cleavable, noncleavable, and, ideally, different antibodies.
Q. Is the -- let me see.
Is it correct to say that the only difference between the ADC of Tikhomirov and the ADC of Wei is the antibody used?
A. If you are referring to cetuximab 2C9 MMAE, yes, the difference is the antibody; however, I'm not sure the purity of the antibody preparation, the drug-to-antibody ratio, and so on.
So there are several different aspects that can be different between these two patents in addition to the antibody.
Q. Is it your opinion that the payload and the

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linker used in Leanna are the same as the payload and linker in Tikhomirov?
A. Yes. It's in a vcMMAE linker, and the same linker has used in Wei as well.
Q. Is it fair to say that any property -- any differences between the properties of Wei and Tikhomirov's ADCs will be the result of their different antibodies?
MR. SUH: Objection to form.
THE WITNESS: I cannot comment on differences because, again, there is no head-to-head comparison on the activity of these two ADCs in vitro or in vivo.
BY MR. QIU:
Q. Do you use Tikhomirov as the basis of either ground of invalidity presented in your declaration?
A. I believe the reason we reviewed Tikhomirov -- probably I'm mispronouncing the name -- was that it was brought up during the patent prosecution of the '370 patent. And I had to review the evidence that support whether or not cleavable or noncleavable linkers are better or worse for anti-EGFR antibodies.
So upon reviewing the data, I concluded

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that the experiments -- there is almost zero experimental evidence to suggest that. And on the contrary, everyone at the time of Tikhomirov or even before that -- Leanna, Wei, or even brentuximab vedotin, so that's Exhibit 1021, a critical product at the time -- was using a vcMMAE linker, a cleavable linker.
Q. So to clarify, you do not use Tikhomirov for either ground in your declaration; correct?
A. To determine obviousness of the claims, no. Only -- only because it was part of the patent prosecution.
MR. QIU: Howard, we got to another good stopping point in my questions. Why don't you ask whether Dr. Bournazos would want a break or whether we should keep going.
MR. SUH: Let's take a break.
(Recess.)
BY MR. QIU:
Q. For Ground 1, you argue that the claims of the '370 patent are obvious in view of the combination of Wei and Liu; is that correct?
MR. SUH: Objection to form.
THE WITNESS: Can you refer me to the specific section in the declaration?

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BY MR. QIU:
Q. The section starting from page 86.
A. Got it. Yeah.
Q. Is it your opinion that the linker and payload in Wei's ADC respectively satisfied the '370 patent's limitations regarding linker and payload?
A. The linker in Wei is identical to the '370 patent. It's a vcMMAE linker.
Q. How about the payload?
A. Payload is the same, MMAE.
Q. Is it your opinion that the antibody in Wei's ADC is not what the '370 patent claims?
A. It is a substantial identical antibody compared to what patent '370 says.
Q. Is it your opinion that Liu teaches the antibody that the '370 patent claims?
A. Correct.
Q. Is it your opinion that a POSA would have found it obvious to replace the antibody of Wei's ADC with Liu's antibody to arrive at the challenged claims?
A. Yes, it's obvious.
Q. According to the Liu reference, the BA03 antibody has stronger activity than cetuximab in inhibiting phosphorylation of EGFR; correct?

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MR. SUH: Objection. Foundation. Form.
THE WITNESS: Correct. This is stated in the Liu patent.
BY MR. QIU:
Q. Is that comparison made on the basis of both antibodies being used as naked antibodies?
A. Correct.
Q. Would the benefit of stronger activity in inhibiting phosphorylation by BA03 be of the same magnitude when BA03 is used as part of ADC compared to when BA03 is used as a naked antibody?
A. In principle it's going to be the same. So the inhibition of EGFR phosphorylation will not be substantially impacted by the presence or not of the payload in the linker.
However, we need to consider two things: One is that the addition of the payload might change some of the properties of the antibody. And the second is that the dose that an ADC will be used in humans is going to be different than an antibody -- a naked antibody. But in principle, they will -- it's going to have comparable inhibitory activity against phosphorylation of EGFR.
Q. How will the dose be different?
A. Normally naked antibodies are administered

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at higher dose than ADCs. But it really depends on the tumor type. There's no one rule if it's everything.
(Stenographer clarification.)
BY MR. QIU:
Q. Is it accurate to say that in the context of an ADC the antibody's activity in inhibiting phosphorylation is not the primary therapeutic mechanism?
MR. SUH: Objection. Foundation.
THE WITNESS: Depends on the context. For me, in the context of EGFR, I would consider it a bonus. It's another antitumor function.
BY MR. QIU:
Q. When BA03 is incorporated into an ADC, does its effect on EGFR phosphorylation decrease or become clinically less significant compared to its payload-mediated cytotoxicity?
A. It depends on the context. So if we see -- for example, let's take Wei example. So in tumors that are resistant to classical EGFR therapy, cetuximab therapy, tumors that have KRAS or BRAF mutations, an ADC, despite the fact that the inhibition of EGFR signaling would be an added bonus, it's still -- the mechanism of killing is

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going to be primarily by internalization of the payload.
Now, in tumors that haven't mutated yet in terms of KRAS or BRAF, having an inhibitory activity against EGFR phosphorylation would still be one of the mechanisms by which an anti-EGFR ADC would mediate antitumor effects.
I don't really want to say what would be the primary or the secondary mechanism because everything depends on the tumor context, on the tumor type and the mutations of the tumor.
Q. How would you describe the relative clinical importance of EGFR phosphorylation inhibition in the ADC versus naked or unconjugated settings?
A. Can you please rephrase or repeat your question, just to make sure that I understand correctly?
Q. Sure.
I'm asking about the clinical importance of EGFR phosphorylation inhibition and whether that is more or less important between when the antibody is used naked or when the antibody is used in ADC?
A. Oh, okay. I got it. I got it. Thanks for clarifying.

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So again, it depends on the tumor type. So it is an important function, and for certain tumors that are still maintaining wild-type status KRAS or BRAF, it is another antitumor activity. I cannot, and I don't think anyone has done this comparison, quantified the precise contribution of this activity versus the cytotoxic activity of -- by the drug itself in contributing to antitumor activity.

And I don't think it's a feasible experiment, if you want to call it, to do.

(Stenographer clarification.)

BY MR. QIU:

Q. Would the activity inhibiting phosphorylation by BA03 have any correlation to its binding affinity?

A. Hard to tell. So Liu reports that BA03 has better inhibitory activity against phosphorylated -- phosphorylated EGFR and I believe higher affinity, but one is not a requirement for the other. So a higher affinity won't necessarily equate to better inhibitor activity.

Q. Does the activity of inhibiting phosphorylation affect both tumor and normal cells expressing EGFR?

A. Partly true because the tumor is always in

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a more constant, in much higher level of proliferation compared to normal tissues. And also we need to consider that the level of expression of EGFR is going to be substantially higher in the tumor compared to normal tissues.

So yes, the effects can be seen also in other cell types but are going to be -- expect to be way more prominent on tumor cells.

Q. So now you are saying the expression level of EGFR on the tissue would have a -- would be an important factor in controlling whether the ADC will impact the tissue; correct?

MR. SUH: Objection to form.

THE WITNESS: So if expressed --

BY MR. QIU:

Q. Oh, I'm sorry. Please strike that question.

Let me ask you: Is it your opinion that the expression level of EGFR on the tissue is an important factor in determining whether the antibody will have activities on the tissue?

A. Tissue, you mean, normal tissue?

Q. I mean any tissue, normal or tumor.

A. It really depends on how sensitive the tissue is to the drug, how much it's expressing. So

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saying that expression matters, you isolate just one component. What I see is that not all tumor cells -- or not all cell types -- tumor cells, malignant, or nonmalignant -- proliferate at the same rate and are sensitive -- have the same sensitivity to the drug payload.

And this is the basis of success for many ADCs out there that are currently in the clinic.

(Stenographer clarification.)

BY MR. QIU:

Q. Earlier I believe you indicated that you were not certain whether the expression level has an impact on antibody binding. Are you changing that opinion now?

MR. SUH: Objection. Mischaracterizes the testimony.

THE WITNESS: I still stand with my opinion because the question was very broad. So you asked me in the context of any antibody, any expression of any receptor, if this is true or not. I still maintain this posi- -- this opinion.

BY MR. QIU:

Q. Let's -- let's keep it in the context of the EGFR antigen and anti-EGFR antibody.

A. Okay.

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Q. Is it your opinion that the expression level does have an impact on antibody binding?

A. It is one of the determinants, certainly. But again, it depends on which epitope the antibody is recognizing. If we see Antibody 1, for example, it doesn't bind EGFR that's expressing on some glioma cells. But it's still -- an expression is there on these tumor cells.

So everything needs to be taken in a context and have specific examples for specific antibodies.

Q. In the context of EGFR, what properties of antibody determines the binding specificity to target cells?

A. The binding specificity. So the binding specificity is determined by the variable region of the Fab. So this determines how specific the antibody -- how specifically the antibody against EGFR binds EGFR. So this is the primary determinant.

Another determinant is how accessible the epitope that is recognized by EGFR is. Is it occluded? Is it mutated? Who knows.

Q. In the context of EGFR, the binding of an antibody to cell services depend on the expression

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level of antigen on the cell surfaces; correct?
A. No. In the context of cetuximab or in the context of any anti-EGFR antibody?
Q. In the context of EGFR. That's my question.
A. No. Remember, Antibody 1 is an anti-EGFR antibody that binds -- that also some glioma cells, as we have seen in the other example, express EGFR, it cannot bond, it cannot bind and recognize this EGFR positive tumor cells.
Q. So, Doctor, I'm a little confused.
A. Sorry.
Q. In the question of BA03, you said, you know, its effect on tissue would depend on the expression level of the EGFR antigen.
A. Yes, correct, correct.
Q. And here you are again saying it doesn't.
A. Because your question, your previous question was generally for all anti-EGFR antibodies. When I asked you specifically if you were referring to cetuximab, your response was no, for all anti-EGFR.
So for all anti-EGFR, what I can say is that it's not true. Expression does not equate with binding. And I gave you as a specific example

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Antibody 1. We have expression, for example, of EGFR on glioma cells, some cell types. Antibody 1, according to the patent, doesn't bind.
Is it clear now?
Q. So in the context of cetuximab, does the binding of the antibody-to-cell surface depend on the expression level of antigen?
A. Yes, unless as soon as the antigen is there and in a form that can be recognized by cetuximab. So if the epitope is preserved, yes.
Q. And this does not apply to -- sorry. Strike that.
And this also applies to variants of cetuximab; correct?
A. Correct. And again, depends on the variants. If I generate a variant of cetuximab that can no longer bind or have mutated extensively, it doesn't apply. So that's why it's helpful if we talk on specific examples. So which variants are you referring to?
Q. Does it apply to the Y104D variant and --
A. Yeah.
Q. -- it's either chimeric or humanized?
A. Yeah. So 104D binds EGFR. This has been demonstrated in Wei. BA03 does bind EGFR. This has

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been demonstrated by Liu.
Q. For cetuximab, Wei's Y104D antibody, and Liu's BA03, would you expect there to be a threshold or minimum expression level of the EGFR antigen on cell surface for significant antibody binding?
MR. SUH: Objection. Foundation. Form.
THE WITNESS: A threshold is an arbitrary term because I'm not sure how we would define the threshold. So you mean how many molecules were going to be expressed? What I know is that you need expression for binding.
BY MR. QIU:
Q. How do you evaluate the level of expression of an antigen?
A. There are several ways of doing this. You can do it by -- depends on the context. So you can assess by flow cytometry how much it is expressed. You can see it, for example, in tumor sections by immunohistochemistry. So this will tell you whether or not, for example, a tumor expresses EGFR or not.
Q. What is the unit that you used to quantify this level of expression?
A. I mean, in the clinic in biopsies, they do it based on a scoring system of plus, plus -- plus or minus. So it is the intensity of the staining.

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It's very arbitrary.
In the lab, for example, in flow cytometry, you can measure the median fluorescence intensity. We don't really quantify, unless absolutely necessary, how many more -- the absolute numbers of molecules that are expressed on the cell surface.
Q. So let's use whatever way to quantify the expression level that you are familiar with.
Is there typically a threshold or minimum expression level of the antigen, like, would you expect there to be a threshold or minimum expression level of the antigen on cell surface for a significant binding by cetuximab BA03 or Y104D?
MR. SUH: Objection to form.
THE WITNESS: This is a very vague question. What do you mean by "significant binding"? How many molecules do you mean? Because the number of molecules that you would consider significant binding, I would say it needs to match, approximately, the numbers of receptors that need to be expressed.
BY MR. QIU:
Q. By "significant binding" I mean enough binding to reduce EGFR activity.
A. To reduce EGFR activity?

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Q. Mm-hmm.
A. To reduce phosphorylation?
Q. Sure. We can talk about phosphorylation, yeah.
A. Yeah. So there is no arbitrary unit. So a cell line or a cell path needs to be paused before expression. I don't think that there is a right or wrong answer to this question. So whether I say 1,000 units, let's say. It's not typically done.
Q. In the context of the -- in the context of cetuximab BA03 and the Y104D, would you expect there to be a minimum density of surface antibody binding required to trigger internalization of the target cell?
A. Internalization, you will need at least two receptors. This is for sure because antibodies are by valent molecules. So the internalization would happen once two receptors are cross-linked.
Now, two molecules would be enough to internalize. My guess is yes. But in the context of an ADC, because I presume this is your -- your point, two receptors or one antibody, one drug, it might not be sufficient to kill a cell because everything depends on the dose of the drug and the express -- how much of the drug gets into the cell

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along with the sensitivity of the cell.
Q. So according to Liu, BA03 has a higher ADCC activity than cetuximab; correct?
A. Yes.
Q. Is that comparison made on the basis of both being used as naked antibodies?
A. Yeah, I believe so. They are all both compared as naked antibodies, so Erbitux, cetuximab, versus BA03.
Q. Would the benefit of stronger ADCC activity by BA03 be of the same magnitude when BA03 is used as part of ADC compared to when BA03 is used as naked antibody?
A. Maybe, maybe not. It's hard to speculate on this because it depends on the chemistry. So it depends where the MMAE would be conjugated.
If the conjugation happens to be near the Fc gamma receptor binding site, it might impact. But based on what we have seen before from what is typically used as a drug-antibody ratio, which is typically used for antibodies that are in the clinic, it does not impact any ADCC activity of cetuximab of any antibody when they are formulated as ADCs.
Q. Is it right that you have done extensive

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research in the area of Fc receptor-mediated effector functions and published some papers on it?
A. Yes, that's my main area of research.
MR. QIU: I'm introducing patent owner's Exhibit 2020. Let me upload it. This is a new exhibit. It's not in the paper files that we sent.
MR. SUH: Oh.
MR. QIU: Howard, do you have a way to either print it out or have Doctor look at it?
THE WITNESS: Can we print it out?
MR. SUH: We could try. Well, if you -- if you put it up on the screen, I don't know. Is there a way to print it out? We don't have it.
REMOTE TECHNICIAN: I can share it electronically if we want to go that route.
MR. QIU: That would be great.
MR. SUH: Okay.
REMOTE TECHNICIAN: Yeah, just let me know when it is uploaded.
MR. QIU: Yeah, I have uploaded it.
MR. DU: Is it in the Zoom?
MR. SUH: They said they are going to upload it on the Zoom.
REMOTE TECHNICIAN: Is it called Exhibit 2020? Is that what you said it was?

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MR. QIU: That's right. Exhibit 2020.
REMOTE TECHNICIAN: Okay. And this one needs to be marked, right, or is it already marked?
MR. QIU: We have already stamped it as Exhibit 2020.
REMOTE TECHNICIAN: Okay.
Okay, I just downloaded it.
MR. SUH: I think they're going to e-mail it to us.
REMOTE TECHNICIAN: I can -- I was just going to share it on my screen, but I can -- I can also share it in the chat and share it on the screen if that's also helpful.
MR. SUH: If we wanted to print it, how do we print it?
MR. QIU: Do you have the download link?
REMOTE TECHNICIAN: I believe the download link is just for me to access the exhibits.
MR. QIU: Oh, okay, sorry.
REMOTE TECHNICIAN: No, you're good.
Is it okay if I send it via chat now?
MR. QIU: Or I can e-mail it to you.
REMOTE TECHNICIAN: Is it all right if I send it in the chat here?
MR. SUH: Yeah, why don't we do both.

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REMOTE TECHNICIAN: Okay. And then I will share it on my screen.
MR. SUH: And then, Fred, if you want to e-mail it to us.
MR. QIU: Yes, I'm doing that.
THE WITNESS: I might have to stand.
MR. SUH: E-mail it to me and Erxin, please.
MR. QIU: I'll just e-mail it to the entire group.
THE WITNESS: No need to print it.
MR. SUH: We can proceed. Dr. Bournazos says that he doesn't need a paper copy.
MR. QIU: Okay.
(Exhibit 2020 was marked for identification by the Certified Shorthand Reporter, and a copy is attached hereto.)
BY MR. QIU:
Q. Doctor, do you recognize this exhibit?
A. Of course.
Q. What is it?
(Interruption in proceedings.)
THE STENOGRAPHER: We'll go off the record here, Counsel.
(Recess.)

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BY MR. QIU:
Q. So let me repeat my last question.
MR. QIU: Drew, can you share the exhibit on the screen again?
BY MR. QIU:
Q. Dr. Bournazos, what is Exhibit 2020?
A. It's a review that I wrote from 2017.
Q. Are you an author for this paper?
A. Yeah, I'm the first author.
Q. Can you please go to page 5 of this paper. Can you read the first paragraph to yourself.
A. Give me a second. Let me print this because it's too small.
Q. Sure.
THE WITNESS: Let's print it.
We're just trying to find a way to print it. I can move closer to the screen and read it out loud if you want.
MR. SUH: Why don't we do this. You can read it off my computer.
THE WITNESS: Yeah, okay, good.
So paragraph 1, you said, on page 5?
BY MR. QIU:
Q. Yes. The first paragraph of page 5.
A. So: "All cytotoxic effector functions

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induced upon Fc gamma receptor-IG interactions are mediated through activating Type I" --
Q. Doctor, you can feel free to review.
A. Oh, okay. Okay.
Q. You don't have to read it out loud.
A. Okay.
Yes.
Q. There you state that all cytotoxic effector functions induced upon the Fc gamma receptor IGG interactions are mediated through activating Type I Fc gamma receptors; correct?
A. Correct.
Q. Can you explain what that means?
A. Is there a figure in here that I can explain? No. Let me go back.
So antibodies when binding to cells that express the antigen can mediate effector functions through the Fc domain of the antibody. So there are several leukocytes, monocytes, dendritic cells, macrophages, NK cells, express activating and inhibitory receptors.
So particularly for cytotoxicity against antibody-coated targets, you need binding of the Fc domain of the antibody to this activating, we'll call them Type I, distinguish them from Type II,

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Fc gamma receptors.
So these effector functions that are mediated by the antibody are induced following the engagement of these activating Type I Fc gamma receptors.
Q. Does this mean that the antigen-binding portion of the antibody is not directly involved in the cytotoxic effector functions?
A. The cytotoxic function through the Fc domain is mediated by the Fc-Fc gamma interaction. However, our bodies have evolved. So we express Fc gamma receptors, and we also have in our circulations -- circulation about 10 mgs per mL of IgG, of antibodies.
So these receptors have evolved in a way that they will only bind with very low affinity to antibodies. So at steady states, steady state, none of the Fc gamma receptors are going to be occupied -- are going to be sufficiently activated by monomeric IgG. It is clear now.
Why do we have a virus or when we have an infected cell or a malignant cell? The antibody will bind to the antigens that are expressed by an infected cell. Think about an infected bronchial epithelial cell after flu infection. So this will

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express antigens against influenza.
So the antibody will come, will bind. So binding of the antibody is critical. So then the Fc gamma receptors are going to -- on the effector cells are going to recognize multiple antibodies that are bound on the surface of the infected cell, resulting in the clustering of the Fc gamma receptors on the effector cell, on a leukocyte, that will trigger cytotoxicity and killing of this infected cell.
So in conclusion, the activities are mediated through Fc-Fc gamma receptor interactions, but they require multiple, low -- multiple low-affinity hybrid interactions, and this results only when the antibody is presented to the Fc gamma receptor as an immune complex. In other words, complex to an antigen.
Q. Your declaration noted that the BA03 antibody is a humanized version of the cetuximab.
A. Correct.
Q. Is it correct that the humanization did not change the Fc portion of the antibody?
A. On the contrary. So cetuximab is chimeric. So cetuximab has the NFc that is human. So what humanization has done to BA03 is to keep it as

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human Z1 but also replace some of the residues that are on the variable region.
If we go to the declaration -- it's helpful if we go to the declaration on page 22 and you will see what I mean. So all the blue is human. All the red is mouse or other species. So chimeric, you notice that the Fc is human. The Fabs are mouse. In the humanized version, now, the vast majority of the antibody is now human, including Fc, but the Fc of cetuximab is human as well. The Fc domain of BA03 is human as well.
Q. So just to confirm, it is your opinion that the BA03 antibody and cetuximab, they have different Fc portions?
A. No, no, on the contrary. They have identical Fc portions.
Q. Oh, okay.
A. And they're both of human IgG 1.
Q. Since the BA03 antibody and cetuximab have the same Fc portion, what is your view on why BA03 has increased ADCC activity?
A. Very good point. And that question keeps bothering me almost every other night. Why by changing the Fab you change the Fc activity? It's -- it's not an easy question to answer. But

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scientifically it is one of the most important.
I wish we had the tools to solve this.
MR. QIU: Yeah, by the way, we can take off the exhibit from the screen.
BY MR. QIU:
Q. Would it be reasonable to believe that the increased ADCC arises from a higher amount of the antibody bound to EGFR on the cell surface for BA03?
MR. SUH: Objection to form.
THE WITNESS: Higher amount, no, because I don't think that they provide any data to explain this. To my opinion, I don't -- I can only speculate. The higher ADC activity might be because of some minor changes that the BA03 was -- were introduced in the way that it recognizes the antigen. I wouldn't say higher binding, but something is going on.
By the end of the day, BA03 seems to be a better version of cetuximab.
BY MR. QIU:
Q. But I thought you said earlier that the binding to a cell surface does impact ADCC activity, earlier.
A. It really depends on --
Q. Can you clarify this?

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A. It really depends on the context. So for the -- in the case of EGFR, I cannot comment if -- how ADCC is regulated. It's a line of investigation, of active investigation. We know from other antigen-antibody model systems that the expression is not a -- not just from my group, just several other groups have indicated this, that the expression of an antigen is not really -- the level of expression of an antigen is not -- cannot really predict whether an antibody will induce ADC activity or not.
Even if the antibody is expressed with the identical Fc domain, identical subclass, identical Fc glycan, this...
Q. Doctor, is that the end of your question [verbatim]? I thought we paused in the middle of a sentence.
A. No, no, no. I'm done.
Q. Does the ADCC activity affect both tumor and normal cells in expressing EGFR?
A. Potentially, yes.
Q. Does the BA03 antibody have pH selectivity?
A. I don't believe that Liu has tested this.
Q. So you do not know whether BA03 antibody has pH selectivity; correct?

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A. No.
MR. SUH: Objection to form.
THE WITNESS: I don't have data available to comment on that.
BY MR. QIU:
Q. Does the BA03 antibody have higher binding affinity for tumor cells than for normal cells?
A. It has equal activity to EGFR. Higher binding affinity, again, it depends on the density. But the absolute affinity, I don't expect to be higher or lower as soon as EGFR is expressed. One of the properties of BA02 [verbatim] and cetuximab is that it can bind a mutated variant that is predom- -- exclusively expressed by tumor cells.
So, yes, it has higher affinity for this variant and no affinity because there is no expression in normal cells.
Q. Is EGFR density a primary factor for cetuximab to distinguish tumor cells from normal cells?
A. Yes, I believe that's correct.
Q. How about the BA03 antibody? Is EGFR density a primary factor for BA03 to distinguish tumor cells from normal cells?
A. Given the fact that BA03 is substantially

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identical to cetuximab, I would assume so, yes. The level of receptor expression is going to determine whether cetuximab -- whether cetuximab or BA03 would bind to malignant or nonmalignant cells.
Q. Is EGFR density a primary factor for Wei's Y104D antibody or the humanized version to distinguish tumor cells from normal cells?
A. Given the fact that Wei's antibodies are variants of cetuximab, I would assume so. But neither Wei nor Liu have demonstrated that their antibody does or does not bind to normal cells.
My assumption is yes.
Q. So I understand that you don't believe Wei's Y104D antibody has pH selectivity.
Would Y104D still have some advantage over cetuximab in distinguishing tumor cells from normal cells?
A. Y104D, no, because there are no data to support this, that this particular mutation had changed from Y to D, but that position will make this antibody more selective for tumors compared to cetuximab.
Q. How about the humanized version of Y104D?
A. Again, no data presented for selectivity of tumor cells versus nontumor cells. Ideally you will

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need to do this experiment in vivo to see whether or not it can bind normal tissues or not. But these studies are not presented in Wei.
Q. Are you aware of petitioners' SYS6010 or CPO301 ADC candidate?
A. Which exhibit is this?
Q. No, that's a general question. I'm not showing an exhibit.
A. Can you please repeat the question, then?
MR. QIU: Can the court reporter repeat the question.
THE STENOGRAPHER: Yes.
(The previous question was read back by the court reporter as follows:
"QUESTION: Are you aware of petitioners' SYS6010 or CPO301 ADC candidate?")
MR. SUH: Objection. Lacks foundation.
THE WITNESS: I don't recall reviewing any of this. But again, it's a number, so I may have reviewed it but...
BY MR. QIU:
Q. Can you please open Paper 7 in this case, which is Petitioners' Response to Patent Owner's Request For Discretionary Denial of Institution.

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That is -- I believe that is included in the box.
MR. SUH: It's actually not in the box. Your POPR is not in the box, but we may have an extra copy.
MR. QIU: Oh, it's not the POPR. It's the Petitioners' Response to Patent Owner's Request For Discretionary Denial of Institution.
MR. SUH: Oh, okay.
MR. QIU: Is that in there?
MR. SUH: Hold on. Petitioners' response. Okay. Yes.
Here you go.
(Exhibit 7 was previously marked by the Certified Shorthand Reporter, and a copy is attached hereto.)
BY MR. QIU:
Q. Doctor, can you please go to page 45 of the Paper 7.
A. 45, yes.
Q. At the bottom of that page there's a paragraph starting with "Moreover"; correct?
A. Is there a specific section that you want me to review?
Q. Yeah. So I'm asking whether you see a paragraph starting with the term "Moreover," at the

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bottom of page 45?
A. I see it. I see it, yes.
Q. Can you please review that paragraph and the next paragraph that starts with "Notably" to yourself.
A. Yes.
Can we also review Exhibit 1103 and 2? Because there is a reference.
Q. Sure. I think it should be in the --
A. 1102 and 3.
Q. Yes. Yes, you can read those.
MR. SUH: 1102.
THE WITNESS: Oh, it's the same. 1101 here.
MR. SUH: Here's 1101.
THE WITNESS: Okay. Thank you.
(Exhibit 1101, Exhibit 1102, and Exhibit 1103 were previously marked by the Certified Shorthand Reporter, and copies are attached hereto.)
THE WITNESS: Yes, I have reviewed the paragraph.
And the next paragraph, you said, "Notably"?
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BY MR. QIU:
Q. Yes, the next paragraph starting with "Notably."
A. Can I have Exhibit 1100, please.
Q. It should be in the box as well.
A. Yes.
Q. Have you finished reviewing the two paragraphs?
A. I did, yes.
Q. Okay. In your opinion -- let me reframe my question.
Are you aware of any other anti-EGFR ADC that is further along in the regulatory approval process than petitioners' SYS6010 or CPO301 ADC?
A. I have -- I haven't reviewed this, so I'm not fully aware if there are any.
Q. In your opinion, does petitioners' SYS6010 or CPO301 ADC address a previously unmet need to develop a clinical -- clinically applicable anti-EGFR ADC?
MR. SUH: Objective. Lacks foundation. Objection. Lacks foundation.
THE WITNESS: Depending on how you define "clinically" and "medically," every drug helps. And you can see that, for example, from the trials,

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these will be applied or tested in patients who have already progressed. So these patients are in need.
BY MR. QIU:
Q. So I take that a "yes."
MR. SUH: Objection.
BY MR. QIU:
Q. Correct?
MR. SUH: Objection to the question.
THE WITNESS: Yes, sure, you can take it as a yes, but, again, it depends on the definition of "unmet need."
BY MR. QIU:
Q. Would you consider petitioners' development of the SYS6010 ADC to be a success?
MR. SUH: Objection. Form.
THE WITNESS: For me, my personal opinion, a success is any drug that saves even a single life. But I don't think my opinion matters to companies that develop drugs. So other companies have other standards. So -- or clinicians have other standards.
So a success for me is even one life saved is a success.
BY MR. QIU:
Q. Do you know what antibody is used in the

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SYS6010 ADC?
A. I'm not entirely sure. I believe it's the BA03.
Q. Do you think the BA0 --
A. I haven't reviewed any of this data. These are new to me.
Q. Do you think the BA03 antibody is a good antibody to use in ADCs because the SYS6010 ADC is advanced in the regulatory approval process?
MR. SUH: Objection to form.
THE WITNESS: If I believe that BA03 as an ADC is a good antibody, given the FDA, they have given the Phase III.
So what -- can you please rephrase or clarify your question?
BY MR. QIU:
Q. Given that petitioners' development of a -- the SYS6010 ADC has been advanced in the regulatory approval process, does that inform you that the BA03 antibody is a good antibody or suitable antibody to use in ADC?
A. It depends on the clinical data. I would assume that since it has received clearance for FDA Phase III, this is a very good indicator that it has shown -- I haven't reviewed the clinical data, so I

cannot comment on that, but given the fact that they have been initiated Phase III trials, I would assume that the signals from Phase I and II trials were positive.

Q. Are you aware of the -- sorry. Strike that question.

Are you aware of the patent owner's ADC candidate MRG003?

A. No, I am not.

Q. Do you have any comment on the fact that after so many years where cetuximab has been available, petitioners' SYS6010 ADC has been so advanced ahead of many other candidates?

MR. SUH: Objection to form. Foundation.

THE WITNESS: If I am --

Sorry. What was the question?

BY MR. QIU:

Q. Do you have any comment on the fact that after so many years of the industry trying to develop anti-EGFR ADCs, the SYS6010 ADC that uses the BA03 antibody is one of the earlier ones to be so advanced in the clinical regulatory approval process?

MR. SUH: Objection. Lacks foundation.

THE WITNESS: No substantive comment. I

don't know what to say here. Fine.

MR. QIU: Can we take a break here? We just want to make sure that we are finished with all the questions.

MR. SUH: Okay. That would be great. Yeah. We will note that it is 5:26 here, well past close of business.

MR. QIU: Let's take a ten-minute break.

(Recess.)

MR. QIU: Patent owner has no further questions. We will pass the witness.

MR. SUH: Petitioner has no questions, but the witness reserves the right to review and sign.

All right. All done.

THE WITNESS: All done.

MR. SUH: Off the record.

THE STENOGRAPHER: Mr. Suh, I don't have your firm's standing order. Would you require a rough draft also?

MR. SUH: Yeah. If you could send us a rough, that would be great, through an e-mail. That would be terrific.

(Deposition concluded at 2:35 p.m.)

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DECLARATION UNDER PENALTY OF PERJURY

I hereby declare under penalty of perjury that the foregoing is my deposition under oath; that I have read same; and that I have made the corrections, additions, or changes to my answers that I deem necessary.

In witness thereof, I hereby subscribe my name this day of , 2025.

____
STYLIANOS BOURNAZOS, Ph.D.

DEPONENT'S CHANGES OR CORRECTIONS

Note: If adding to your testimony, print the words you want to add. If deleting from your testimony, print the words you want to delete. Specify with "Add" or "Delete" and sign this form.

DEPOSITION OF: STYLIANOS BOURNAZOS, Ph.D.
DATE OF DEPOSITION: DECEMBER 11, 2025

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COUNTY OF LOS ANGELES,)
)
STATE OF CALIFORNIA,)

I, Cody Knacke, Registered Diplomate Reporter, Certified Shorthand Reporter in and for the State of California, License No. 13691, hereby certify that the deponent was by me first duly sworn and the foregoing testimony was stenographically reported by me and was thereafter transcribed with computer-aided transcription; that the foregoing is a full, complete, and true record of said proceedings.

I further certify that I am not of counsel or attorney for either or any of the parties in the foregoing proceedings and caption named or in any way interested in the outcome of the cause in said caption.

The dismantling, unsealing, or unbinding of the original transcript will render the reporter's certificate null and void.

In witness whereof, I have hereunto set my hand this day: December 18, 2025.

Cody Knacke

CODY KNACKE, RDR, CSR No. 13691

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