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

BICARA THERAPEUTICS, INC.
Petitioner

v.

THE JOHNS HOPKINS UNIVERSITY
Patent Owner

PGR2026-00025
U.S. Patent No. 12,295,968

DEPOSITION OF GEOFFREY HALE, PH.D.
TUESDAY, SEPTEMBER 29, 2026
9:41 A.M. - 2:43 P.M.
GEOFFREY HALE, PH.D
FENWICK & WEST LLP
ONE INTERNATIONAL PLACE
BOSTON, MASSACHUSETTS

REPORTED BY: Sandra A. Deschaine, CSR, RPR,
Job No. SF8456410

APPEARANCES:

ON BEHALF OF THE PATENT OWNER:
DLA PIPER LLP
James Heintz, Esquire
One Fountain Square
11911 Freedom Drive, Suite 300
Reston, Virginia 20190
703.773.4148
jim.heintz@dlapiper.com

ON BEHALF OF Y-TRAP:
FENWICK & WEST, LLP
David Tellekson, Esquire
Kelly Ndubuka, Esquire
401 Union Street
Seattle, Washington 98101
206.389.4560
dtellekson@fenwick.com
k.ndubuka@fenwick.com

(Appearances continued.)

APPEARANCES (continued.)

ON BEHALF OF THE PETITIONER:
GOODWIN PROCTER LLP:

Thomas McTigue, Esquire
100 Northern Avenue
Boston, Massachusetts 02210
617.570.1273
tmctigue@goodwinlaw.com

Also Present: David DesRosier, Esquire
Bicara Therapeutics

INDEX

EXAMINATION		PAGE
Geoffrey Hale, Ph.D.		
By Mr. Heintz		6

EXHIBITS

Exhibit	Description	Page
Exhibit 2036	United States Patent No. 11,939,387	128
Exhibit 2037	UK Patent Application 2535753A	160
Exhibit 2038	A modular IgG-scFv bispecific antibody topology	168
Exhibit 2039	Bates numbers PGR2026-00025, The first constant domain (CH1 and CL) of an antibody used as heterodimerization domain for bispecific miniantibodies	172

September 29, 2026

9:31 a.m.

Deposition of Geoffrey Hale, Ph.D., held at Fenwick & West, LLP, One International Place, Boston, Massachusetts, pursuant to Notice, before Sandra A. Deschaine, a Shorthand Reporter, Registered Professional Reporter, Certified LiveNote Reporter, and Notary Public in and for the Commonwealth of Massachusetts.

P R O C E E D I N G S

GEOFFREY HALE, PH.D., Deponent,
having first been satisfactorily identified
by the production of his United Kingdom of
Great Britain and Northern Ireland Passport, 09:31 AM
having duly been sworn by the Notary Public,
was examined and testified as follows:

EXAMINATION

BY MR. HEINTZ:

Q. Good morning, Dr. Hale. 09:33 AM

A. Good morning.

Q. Sir, we never met before today,
correct?

A. I think that's correct.

Q. All right. I know you've been 09:33 AM
deposed several times before, but I'm going
to go over a couple of ground rules with
today's deposition with you.

Is that all right?

A. Okay. 09:33 AM

Q. All right. So the first, most
important rule is that we not talk over each
other. So I'm going to ask that you wait for
me to complete my question before you start
answering, and I'll try to do the same with 09:33 AM

respect to your answer. Is that okay?

A. That's fine.

Q. All right. It's also important because the court reporter is recording your testimony that we answer in complete words. 09:33 AM

Verbal sounds like "uh-huh" and "ung-ung" will not work. Same with gestures, such as head nods or head shakes.

So will you please try to answer verbally to all my questions? 09:33 AM

A. I'll do my best.

Q. Thank you, sir.

Sir, if I ask you a question and you don't understand it, I'll ask you to ask me to clarify it. 09:33 AM

Is that all right?

A. That's fine.

Q. And if you answer my question, I'll assume you understood it.

Is that all right with you? 09:34 AM

A. Okay.

Q. All right. Sir, are you taking any medication or under any disability that would prevent you from giving full and complete answers to my questions today? 09:34 AM

A. No.
Q. Okay. Sir, did you review any documents in preparation for today's proceeding?
A. Yes. 09:34 AM
Q. Which documents did you review?
A. Quite a lot of documents, so in particular my report.
THE COURT REPORTER: I'm sorry.
What was that? 09:34 AM
THE WITNESS: I said quite a lot of documents.
THE COURT REPORTER: Right.
THE WITNESS: In particular my report, and many of the documents that I 09:34 AM considered in preparing that report.
BY MR. HEINTZ:
Q. Okay. And in terms of your preparation for today's deposition, did you review any documents in the last week? 09:34 AM
A. Yes.
Q. Which documents were those?
A. Those that I just mentioned.
Q. All right. Any others?
A. I may have looked at some -- some 09:35 AM

other documents. I can't remember all of them.

Q. Okay. Did you meet with anybody from Bicara?

A. No. 09:35 AM

Q. Did you meet with anybody from Biocon?

A. No.

Q. Okay. I'm going to hand you what's been previously marked as Exhibit 1004 and ask you if you recognize this document. 09:35 AM

A. Yes.

Q. And that's your CV, curriculum vitae; is that correct?

A. That's correct. 09:35 AM

Q. Are there any inaccuracies in the document of which you're aware?

A. Not that I'm aware of.

Q. Okay. Thank you.

In preparation for today's deposition, did you communicate with anyone other than the attorneys for Bicara? 09:36 AM

MR. MCTIGUE: I'm just going to tell the witness not to disclose any privileged information with 09:36 AM

communications with counsel, but the question is framed, so okay.

A. Okay. No, I didn't, so the only people I've spoken with are counsel.

BY MR. HEINTZ: 09:36 AM

Q. Okay. Would it be correct, Dr. Hale, to say that your primary expertise is in therapeutic monoclonal antibodies and antibody engineering?

A. That's -- that's certainly part of my expertise, yes. 09:36 AM

Q. Would that be the -- I'm sorry.

Would that be the primary area of your expertise?

MR. MCTIGUE: Objection to form. 09:36 AM

A. So I've worked in that area, I think, for quite a long time. You could call it primary area. I've got, you know, other areas as well.

BY MR. HEINTZ: 09:37 AM

Q. Okay. What are the other areas?

A. So I've worked in testing of biopharmaceuticals, things like measuring pharmacokinetics, anti-drug antibodies.

I trained as a biochemist 09:37 AM

originally, so I have experience in protein chemistry. I think it's all in the CV.

Q. All right. Have you designed a bifunctional fusion protein?

A. What exactly do you mean by that? 09:37 AM

Q. Do you know what a bifunctional fusion protein is?

A. You mean a fusion protein that's got two different parts to it?

Q. Correct. 09:37 AM

A. Yes, I think I have. I've certainly worked on something like that.

Q. Have you designed one of those?

A. Yes.

Q. Okay. Do you remember what it was? 09:37 AM

A. Well, one of the most recent ones I worked on was the fusion protein of an antibody with its antigen. That was something I designed for myself about a couple of years ago. 09:38 AM

Q. Why did you design it?

A. Sorry.

Q. Why did you design it?

A. I was interested in studying the 09:38 AM

structure and properties of that molecule, hoping that it might be useful for therapy in the future.

Q. I see.

Have you cloned a bifunctional fusion protein? 09:38 AM

A. What do you mean by "cloned"?

Q. I mean it in the common use of the term in your field.

A. Well, I've -- like I said, I've designed such proteins. I've -- a lot of my work involves working with subcontractors, so in that particular case that I described to you, I designed this and I ordered it to be made by a subcontractor, and they expressed the protein that I wanted, you know, based on the design I've given them. 09:38 AM

Q. All right. And have you yourself overseen the purification of a bifunctional fusion protein? 09:39 AM

A. Yes.

Q. Okay. Did you do it yourself or did you oversee it?

A. I mostly oversaw it. I was the leader of a team that did that. 09:39 AM

Q. Okay. So if you would, describe a project, one of the most recent projects you've done where you've purified or overseen the purification of a bifunctional fusion protein.

A. Well, I gave you that example just now. That was where I designed and had made for me, and then I tested a molecule which was an antibody fused to a peptide, which was its antigen.

That work has not been published, so it's not in the public domain.

Q. Okay. What was the outcome of that work?

A. It was quite difficult to design and predict the properties of the molecule. In fact, I made a number of different constructs, and I didn't know what was going to be the outcome.

It wasn't quite as good as I hoped it might be, and I haven't followed that work recently.

Q. You said you made a number of different constructs. Can you give me a sense for how large a number you're talking

09:39 AM 09:39 AM 09:40 AM 09:40 AM 09:40 AM

about?

A. I would think about 10 to 20.

Q. Would you say that was a small number for a research project?

MR. MCTIGUE: Objection to form. 09:40 AM

A. I think it would depend entirely on the research project.

BY MR. HEINTZ:

Q. I see. If the results had been promising, how many more would you have -- 09:40 AM how many different -- many more different constructs would you have tested?

MR. MCTIGUE: Objection to form.

A. It's hard to say. You know, it might have been another ten, it might have 09:41 AM been no more. I don't know, but it was a very -- you know, like a lot of these projects, in my experience most projects in this field are difficult, unpredictable.

I'd been working on that 09:41 AM particular project for about 15 years in total on and off, and none of the things I did were ultimately successful.

BY MR. HEINTZ:

Q. Have you worked with TGFbeta or 09:41 AM

TGFbetaRII in the laboratory?

A. No.

Q. Have you worked with cetuximab in the laboratory?

A. Not that I can remember. 09:41 AM

Q. Have you worked with any anti-EGFR antibodies in the laboratory?

A. I'm not sure of that, but I can't remember, as I sit here now, any.

Q. Have you ever designed, 09:42 AM constructed or expressed a fusion protein comprising a cetuximab-derived anti-EGFR antibody fragment fused to the TGFbetaRII extracellular domain?

MR. MCTIGUE: Objection to form. 09:42 AM

A. No.

BY MR. HEINTZ:

Q. Have you ever made any anti-EFG -- sorry. Let me start again.

Have you ever made any 09:42 AM anti-EFGR antibody TGFbetaRII fusion protein in any format?

A. No.

Q. Have you ever made any anti-TGF -- sorry, let me start again. 09:42 AM

PGR2026-00025 - JHU
Ex. 2042- Page 15

Have you ever made any anti-EGFR antibody TGFbetaRII fusion protein in any format?

MR. MCTIGUE: Objection to form.

A. No. 09:42 AM

BY MR. HEINTZ:

Q. Have you ever designed or expressed a Fab format construct in which the TGFbetaRII extracellular domain was fused to the C-terminus of the light chain? 09:43 AM

A. No.

Q. So your opinions here in this proceeding rest on general expertise and material supplied by counsel rather than firsthand experience with the claimed 09:43 AM molecules; is that correct?

MR. MCTIGUE: Objection to form.

A. No.

BY MR. HEINTZ:

Q. Why is that incorrect? 09:43 AM

A. Well, because my opinions are based on materials which I identified by my research, on my experience with different fusion proteins and antibodies, and conversations I've had over the years with 09:43 AM

many different scientists who worked in those areas, and conferences that I've attended, lectures that I've been to, you know, too numerous to really list.

But a lot of that is in my CV. 09:44 AM

Q. Okay. Were any of those conversations you had dealing in particular with, for instance, anti-EGFR antibodies, TGFbetaRII fusion proteins?

MR. MCTIGUE: Object to form. 09:44 AM

A. As I said, I've had so many conversations over the course of the past 45 years I can't really recall or describe all of them now.

BY MR. HEINTZ: 09:44 AM

Q. As you sit here today, you don't remember anything in particular; is that correct?

A. Well, I can remember being aware of anti-EGFR antibodies like cetuximab, for 09:44 AM example. I was aware of that.

I was aware of TGFbeta and its use in immunology. One of my colleagues, Dr. Stephen Cobbold, working with Herman Waldmann with studying that, so at the same 09:45 AM

time that I was working on antibodies. So I was part of a team that was aware of things like that.

Q. But you've never worked with that kind of thing in the lab, correct? 09:45 AM

A. Personally I've never picked up those -- you know, those molecules in my hands in the lab.

THE WITNESS: Can I have a drink of water? 09:45 AM

MR. HEINTZ: We'll go off the record while we get you a drink.

(Pause in proceedings.)

MR. HEINTZ: Back on.

BY MR. HEINTZ: 09:46 AM

Q. All right. Dr. Hale, when did your relationship with Bicara or its counsel begin?

A. I can't remember the exact day, so I think it was about in November or December 2025. 09:46 AM

Q. And was that in the context of this project or another project?

A. It was in the context of this project. 09:46 AM

Q. Other than this project, have you consulted or worked for Biocon or Bicara in the past?

A. No.

Q. Okay. Have you ever consulted or worked with Biocon at any time? 09:46 AM

A. Not that I can recall.

Q. Who first contacted you about this matter?

A. Counsel. 09:47 AM

Q. And who was that counsel?

A. I think it was -- it was Thomas here, but I'm not absolutely sure. It was one of the members of the Goodwin team.

Q. And what did that counsel ask you when they first contacted you? 09:47 AM

MR. MCTIGUE: I'm going to object to have the witness not disclose any privileged information with communications with counsel. 09:47 AM

MR. HEINTZ: Are you claiming privilege in this matter over something?

MR. MCTIGUE: With the communications with the witness regarding this proceeding. 09:47 AM

MR. HEINTZ: What privilege are you referring to, Counsel?

MR. MCTIGUE: Attorney-client privilege and work product.

MR. HEINTZ: You're claiming work product privilege in connection with an expert? You realize the Federal Rules of Civil Procedure do not apply here. 09:47 AM

MR. MCTIGUE: I do.

MR. HEINTZ: Okay. And yet you're claiming work product privilege and attorney-client communication privileges? 09:47 AM

MR. MCTIGUE: Yes.

MR. HEINTZ: And you're instructing your witness not to answer? 09:48 AM

MR. MCTIGUE: Yes.

MR. HEINTZ: Okay.

BY MR. HEINTZ:

Q. Dr. Hale, you're being compensated at your rate of 500 pounds per hour in this matter; is that correct? 09:48 AM

A. That's correct.

Q. How much time have you spent on this matter so far? 09:48 AM

A. I can't remember the exact amount, but in terms of preparing my reports, about 60 hours, and subsequent to that about 30 hours.

Q. So a total of about 90? 09:48 AM

A. About that.

Q. Okay. So roughly you've billed about 45,000 pounds so far?

A. I don't think I've billed all of it yet. 09:48 AM

Q. But eventually you will; is that correct?

A. I hope so.

Q. Have you worked as an expert for the law firm of Goodwin Procter in any other matter? 09:49 AM

A. Yes.

Q. How many times?

A. I think about five or six times.

Q. And what were your duties and obligations in those matters with Goodwin Procter? 09:49 AM

A. Well, they varied. Sometimes I was simply providing confidential advice, so those are matters which are not on any form 09:49 AM

of public record, and other times I was engaged in connection with some passing litigation, and I might have given -- written a report or --

THE COURT REPORTER: What reports? Written reports you said? 09:49 AM

THE WITNESS: Yeah. I said I was engaged in connection with patent litigation, and I may have provided reports or attended a deposition. 09:49 AM

BY MR. HEINTZ:

Q. Okay. Out of the five or six matters you mentioned earlier, do you recall how many of those involved patent litigation in which you provided a report and/or gave a deposition? 09:50 AM

A. I can't remember exactly. It might have been about three.

Q. Okay. Do you consult for or receive compensation from any other pharmaceutical or biotechnology companies? 09:50 AM

A. I've worked in the past for other law firms representing such companies. That's it.

Q. Okay. And how many prior 09:50 AM

proceedings involving patents have you provided expert opinions on enablement or written description?

A. I can't remember the exact number, but about maybe four or five or six. 09:51 AM

Q. And of those four or five or six, how many of those involve enablement or written description of fusion proteins?

A. I can't remember.

Q. Of those four or six prior cases that you mentioned earlier, how many of those did you testify that the specification lacked enablement for a fusion protein claim? 09:51 AM

MR. MCTIGUE: Objection to form.

A. Again, I can't remember which cases -- honestly, these cases very often people put me under confidentiality obligations, and I make it a point to forget as much as I can about the case afterwards, so I can't give you a lot of details. 09:51 AM 09:52 AM

BY MR. HEINTZ:

Q. Okay. Do you know if you've ever, prior to this proceeding, given an expert opinion as to enablement for a fusion protein claim? 09:52 AM

MR. MCTIGUE: Objection to form.

A. I can't remember.

BY MR. HEINTZ:

Q. Okay. And same question for written description? 09:52 AM

MR. MCTIGUE: Same objection.

A. I can't remember.

BY MR. HEINTZ:

Q. I'm going to hand you what's been previously marked as Exhibit 1003, and ask you if you recognize that document. 09:52 AM

A. Yes.

Q. On page 93 of Exhibit 1003, is that your signature?

A. Yes. 09:53 AM

Q. Did you write this document, Dr. Hale?

A. I prepared the draft of most of it. Counsel advised me on some parts, particularly the legal opinion -- the legal matters, you know, which are listed there in the contents, legal standards. 09:53 AM

Q. Okay. So you're referring to -- with respect to the table of contents, the section of the report labeled "II. Legal 09:54 AM

Standards"?

A. That's correct.

Q. The rest of this document is something for which you prepared the first draft; is that correct? 09:54 AM

A. Yes.

Q. Did you work with anyone else in preparing that first draft?

A. No.

Q. Have you identified any changes in Exhibit 1003 that you would like to make? 09:54 AM

A. No.

Q. Are there any statements in Exhibit 1003 that you think are incorrect?

A. Not to my knowledge. 09:54 AM

Q. Sir, on page 5 of your declaration you address a person of ordinary skill in the art, correct?

MR. MCTIGUE: Objection to form.

A. So I think that section on page 5 summarizes what I've been informed about the legal standards concerning a person of ordinary skill in the art. 09:55 AM

BY MR. HEINTZ:

Q. Could you please explain in your 09:55 AM

own words what a person of ordinary skill in the art means to you?

MR. MCTIGUE: Objection to form.

A. Well, I think you'd find that on page 53, because I've set out, in this case, what I think a person of ordinary skill in the art would be with regard to this particular patent, and it's all set out there in paragraph 111. 09:55 AM

BY MR. HEINTZ: 09:56 AM

Q. Do you think a person of ordinary skill in the art is someone of average skill in the art?

MR. MCTIGUE: Objection to form.

A. I think a person of ordinary skill in the art, as I've been informed, is a legal term, and, you know, the legal nature of it is set out there in the -- on page 5. So it's a particular sort of construct, a legal construct, really; that's how I understand it. 09:56 AM 09:56 AM

BY MR. HEINTZ:

Q. And I want to get a sense for what your understanding of this legal construct is. 09:56 AM

So if you could give me that understanding on your own words, that's fine; otherwise, I'll just ask you some questions like the one I just posed to you.

A. Okay. 09:57 AM

MR. MCTIGUE: Objection to form.

BY MR. HEINTZ:

Q. So how would you like to proceed?

A. Well, I'll do my best to explain that. 09:57 AM

I think a person of ordinary skill in the art would have an ordinary level of creativity, not really -- that doesn't mean to say they would be like someone who's capable of inventing new things, necessarily; 09:57 AM but they would just be able to follow instructions and carry out experiments diligently.

They'd be like the sort of people that I supervised, for example, and worked 09:57 AM with, you know, in my career. They'd have experience in the field. In this case, it might be biochemistry or molecular biology or immunology. They would be able to carry out experiments, and they would have knowledge of 09:58 AM

the prior art.

Q. Would they be able to design the experiments themselves?

MR. MCTIGUE: Objection to form.

A. I think they might have difficulty designing experiments, because in order to design experiments, you need to make creative choices sometimes between many different options. And so a person of ordinary skill in the art, you know, would have difficulty designing experiments that would lead to novel inventions. 09:58 AM

BY MR. HEINTZ:

Q. On page 5, in paragraph 17, second line from the bottom, it says that you understand that a person of skill in the art has ordinary creativity. 09:58 AM

A. Uh-huh.

Q. What's your understanding of "ordinary creativity"? 09:58 AM

MR. MCTIGUE: Objection to form.

MR. HEINTZ: What's the objection?

MR. MCTIGUE: To the extent it calls for a legal conclusion.

MR. HEINTZ: I'm asking for his 09:59 AM

understanding. Is that objectionable?

MR. MCTIGUE: I maintain my objection.

MR. HEINTZ: Okay.

BY MR. HEINTZ: 09:59 AM

Q. Go ahead, Dr. Hale, you can answer if you're able.

A. Okay. So my understanding is that, you know, when it says "ordinary creativity" here, that's probably a legal 09:59 AM term which is derived from some legal precedence that I'm not familiar with, but to me it means really what I've just told you in that previous answer.

Q. And that's that a person would 09:59 AM have difficulty designing experiments; is that correct?

A. I don't think I exactly said that, but I said they would have difficulty in designing experiments which would lead to 09:59 AM inventions.

Q. From whom did you obtain your understanding of a person of ordinary skill in the art as discussed in paragraphs 5 and -- I'm sorry -- in paragraph 17 and 18 of 10:00 AM

your declaration?

A. So I think -- 17 and 18, I think I said, before this information in this whole section, legal standards was communicated to me by counsel here. 10:00 AM

Q. Okay. And do you stand by your definition of a person of ordinary skill in the art as set out in Section 6, starting on page 53 of your declaration?

A. So I stand by what I've said there. 10:00 AM

Q. Would you have had experience with antibody domain and sequence manipulation and construction expression and purification of recombinant antibodies and/or fusion proteins and assays for expression levels and activity? 10:01 AM

A. Yes.

Q. Would that have been as of the priority date of the '968 patent at issue in this case? 10:01 AM

MR. MCTIGUE: Objection to form.

A. Whatever that priority date might be. What date are you thinking of?

MR. HEINTZ: So I'll hand the 10:01 AM

PGR2026-00025 - JHU
Ex. 2042- Page 30

witness what's been previously marked as Exhibit 1001, which is the '968 patent at issue.

BY MR. HEINTZ:

Q. So, Dr. Hale, I'll ask you if you recognize what's been marked as Exhibit 1001? 10:02 AM

A. Yes.

Q. And what is it?

A. This is Patent No. U.S. 12,295,968, which I believe is the patent at issue in this case. 10:02 AM

Q. Okay. Do you have an understanding as to what the term "priority date" means?

A. I have some sort of understanding, and I don't know if that was communicated to me in the legal section of this document. There's -- that's mentioned on page 7. 10:02 AM

Q. Okay. Do you know what the priority -- the earliest claimed priority date of the '968 patent is? 10:02 AM

MR. MCTIGUE: Objection to form.

A. So I understand that it's claiming priority to a whole sequence of earlier applications which go right back to a PCT 10:03 AM

filed on March the 4th, 2011, and then it claims priority to earlier provisional applications, including one filed on March the 5th, 2010.

BY MR. HEINTZ: 10:03 AM

Q. Correct, sir.

So I asked you if you had certain experience. Would you have had that experience that we discussed earlier as of that March 2011 claim priority date? 10:03 AM

MR. MCTIGUE: Objection.

A. Yes.

BY MR. HEINTZ:

Q. Thank you.

Would you also have had 10:03 AM collaborations with others experienced in the medicinal, pharmaceutical or biotech industry?

A. Yes.

Q. Okay. A person of ordinary skill 10:03 AM in the art, as you have defined that person, would have been familiar with standard recombinant DNA techniques, including PCR amplification, gene construction and cloning and subcloning into expression vectors, 10:04 AM

correct?

MR. MCTIGUE: Objection to form.

A. Yes. I don't think I've listed all those things in my opinion of a POSA. They may or may not have had experience of all those things, but that's the sort of thing they might have been experience of, yes. 10:04 AM

BY MR. HEINTZ:

Q. Would a POSI- -- sorry. I'm going to use the word "POSITA," and that's a shorthand for person of ordinary skill in the art. 10:04 AM

Is that okay?

A. That's okay with me. 10:04 AM

Q. All right. Thank you.

As you have defined a POSITA, would that person have been familiar with strategies used for designing antibody variants, including well-known antibody fragments, such as an Fab, a single-chain Fv and Fc? 10:04 AM

A. So, as I said, I don't think those particular experiences are in the list of things that I mentioned, but I think those 10:05 AM

are the sort of things that a POSITA, in your terms, might have had experience of.

Q. And that would be true in 2011, correct?

A. And I believe that would be true in 2011. 10:05 AM

Q. Okay. And a POSITA, as you have defined that person, would have been familiar with strategies and components used for designing fusion proteins, including the use of linkers, choice of domain orientation and ensuring the proper termini are incorporated into the design, correct? 10:05 AM

MR. MCTIGUE: Objection to form.

A. Well, now I think you're straying further away from the POSITA that I've described. 10:06 AM

So you're saying that this person would be able to design -- I didn't quite get all that. I don't know if you can -- 10:06 AM

BY MR. HEINTZ:

Q. I'll --

A. -- you know, go through it, just break it down a bit.

Q. So would a POSITA, as you have 10:06 AM

defined that person in your declaration, have been familiar with strategies and components used for designing fusion proteins, including the use of linkers, the choice of domain orientation and ensuring the proper termini are incorporated into the design? 10:06 AM

MR. MCTIGUE: Objection to form.

A. I don't think that that's necessarily a person of order skill would be able to do and know all of those things, because you're talking about very general ability to design, perhaps, novel fusion proteins, perhaps choose which linkers to use. Those would be things of an inventor level of skill, you know, something more than ordinary skill. 10:06 AM 10:07 AM

BY MR. HEINTZ:

Q. So choosing a linker, for instance, would be beyond the level -- hold on, let me finish my question. 10:07 AM

So choosing a linker, for example, when designing a protein, would have been something beyond the level of one of ordinary skill in the art, as you've defined that person, and as you've used in forming your 10:07 AM

opinions in this matter; is that correct?

MR. MCTIGUE: Objection to form.

A. No, I think it depends on the context.

BY MR. HEINTZ: 10:07 AM

Q. And how so?

A. Sorry?

Q. How so? How does it depend on the context?

A. I see. 10:07 AM

So if the context were putting together something which was already known in the art, making a fusion protein of a very familiar kind, then they might be able to go to the prior arts and find information about 10:07 AM the kind of linker that would be suitable.

If it was a project that involved making a totally novel kind of fusion protein with unpredictable properties, then they would have a lot more difficulty in choosing 10:08 AM the right linker or the right way to attach that linker. That would be much more difficult.

Q. So what about a fusion protein for a known molecule such as cetuximab? Would a 10:08 AM

person of ordinary skill in the art have been able to select an appropriate linker for a fusion molecule including cetuximab?

A. Again, it depends upon the context. You know, in the context of this particular case, this particular patent, what I noticed there is that there are some conventional kinds of fusion proteins are mentioned, and there are some very unusual, I would call them extraordinary kinds of molecules mentioned, which have not been described in the literature before. 10:08 AM 10:09 AM

So I think if one was tasking a person of ordinary skill with making one of those unusual exceptional molecules which had never been made before, then they would have difficulty in doing it. 10:09 AM

Q. So it's your opinion that a person of skill in the art, as you've defined it, would have had trouble choosing a linker for a fusion protein involving cetuximab if the thing being linked to the cetuximab had not been known in the art previously as being linked to cetuximab; is that correct? 10:09 AM

MR. MCTIGUE: Objection to form. 10:09 AM

A. I don't think that's quite what I said.

BY MR. HEINTZ:

Q. All right.

A. I don't know if we can have it, you know, played back, what I did say, but I think I put it a bit more clearly there. 10:09 AM

Q. Well, your answer was talking about an unusual exceptional molecule, correct; you mentioned that in your answer? 10:10 AM

A. I think I did.

Q. What did you mean by "an unusual exceptional molecule"?

A. Well, I was thinking particularly of the sort of molecule that's mentioned in the claims of the patent in this case. 10:10 AM

Q. Okay. So it's your opinion that a person of ordinary skill in the art, for example, if wishing to link TGFbetaRII to a cetuximab molecule and do so at the C-terminus, would not know which linker to choose? 10:10 AM

A. Again, I don't think that's what I said.

What I said was this hybrid 10:10 AM

molecule that's envisaged in the claims in this case, those are, in my opinion, unusual and exceptional molecules which would pose a great deal of difficulty for the person of ordinary skill to design and to make. 10:11 AM

Q. So let's take a look at Exhibit 1001, which is the '968 patent, if you wouldn't mind, and in particular I'll ask you to take a look at Claim 1.

I'm sorry. Let's look at Claim 9. 10:11 AM

A. Claim 9.

BY MR. HEINTZ:

Q. And if you let me know when you're done reviewing it, Doctor, I'll ask my questions. 10:11 AM

A. You mind if I --

Okay.

Q. All right. So Claim 9 says that "The amino acid sequence of Sequence ID No. 71 is fused to an N-terminus of the 10:12 AM polypeptide linker comprising the amino acid of the Sequence ID No. 104," correct?

A. That's what it says.

Q. Okay. Sequence ID No. 104 is the cetuximab light chain; is that correct? 10:13 AM

MR. MCTIGUE: Objection to form.

A. No.

BY MR. HEINTZ:

Q. Okay. What is Sequence ID No. 104? 10:13 AM

A. Well, that's a sequence which you can find in the listing a little bit earlier.

104, it's on page -- I apologize. There's no page numbers here. It's in Column 100 -- 89, Column 89. 10:13 AM

Q. I'm sorry. I misspoke.

So Sequence ID No. 104 is the linker, correct?

A. It is.

Q. Okay. So the linker, according to this claim in Sequence ID No. 104, links to the N-terminus of SEQ ID No. 71, correct? 10:13 AM

A. No.

MR. MCTIGUE: Objection.

BY MR. HEINTZ: 10:14 AM

Q. All right. I apologize, Doctor, I'm messing this up.

A. Don't worry. Take your time.

Q. All right. So in this claim, the linker is linked to the light chain, correct? 10:14 AM

A. In this claim, it says, "Light chain domain is fused to the linker."

Q. Okay. And the claim requires that TGFbetaRII is attached to the other end of the chain, correct? 10:14 AM

A. No.

Q. No. Okay.

A. I don't think the claim mentions TGFbetaRII.

Q. Claim 9 at line -- Column 98, line 53? 10:14 AM

A. Oh, my apologies. You're correct.

Q. Okay. So how is TGFbetaRII connected to the linker in Claim 9, if at all? 10:15 AM

A. So according to the last phrase of the claim, the amino acid sequence of the Sequence ID No. 87, which is the TGFbetaRII, is fused to the C-terminus of the linker.

Q. Okay. That's one end of the linker, correct? 10:15 AM

A. That's correct.

Q. And what is the other end of the linker attached to in this claim?

A. The other end of the linker is the 10:15 AM

N-terminus and that's attached to the light chain domain, which compromises the amino acid sequence of Sequence ID No. 71.

Q. Okay. So in simple terms, the linker connects the TGFbetaRII to the light chain in this claim, correct? 10:16 AM

A. That's correct.

Q. Okay. Is it your testimony that a person of ordinary skill in the art, as of 2011, wouldn't have known -- wouldn't have been able to select a linker to fuse the TGFbetaRII molecule to the EGFR molecule? 10:16 AM

MR. MCTIGUE: Objection to form.

A. Well, it depends, you know, what their project is. If the -- if the person had been told by a supervisor or an inventor I want you to link a light chain to a TGFbetaRII, it's possible that they could do that using such a linker. 10:16 AM

I think my objection to the idea that they would come up with the whole of this integrated claim, you know, revolves around the complexity and the originality of the molecule that's described. 10:17 AM

BY MR. HEINTZ: 10:17 AM

PGR2026-00025 - JHU
Ex. 2042- Page 42

Q. Okay. So I want to make sure I ask my question so that you understand it.

A. Thank you.

Q. So I'm going to pose a hypothetical to you. 10:17 AM

So a person of ordinary skill in the art is told that he needs to link a TGFbetaRII to a light chain of cetuximab and needs to select a linker in order to accomplish that goal. 10:17 AM

Would a person of ordinary skill in the art have been able to select such a linker, not being told to use the linker of Sequence ID No. 104?

MR. MCTIGUE: Objection to form. 10:18 AM

A. I think they'd need to understand the purpose of the experiments and the context in which it's being done, and so it's -- it's a hypothetical that really isn't based on, you know, anything that's likely to happen. You know, why should somebody be making a construct which is merely a light chain going to TGFbetaRII? They would need to understand the context of the whole project. 10:18 AM 10:18 AM

PGR2026-00025 - JHU
Ex. 2042- Page 43

BY MR. HEINTZ:

Q. And they'd need to understand that in order to select a suitable linker?

A. Yes.

Q. And if one of ordinary skill in the art had been given this context to which you referred, would that person then be able to select the linker? 10:18 AM

A. Well, if they'd been told everything that they needed to know, but that's a lot of things. You know, this is the problem with a person of ordinary skill, and the difference between such a person and an inventor. They've got to take into account so many different things. 10:18 AM 10:19 AM

You know, for instance, would it matter if this hypothetical fusion protein was susceptible to being -- to proteolysis? Is that important in its use or application?

If so, that might influence the design of the linker. Is it important whether the molecule can be purified, and it retains its biological activity? You know, that would dictate, perhaps, the choice of the linker, among other things. 10:19 AM 10:19 AM

So there's a lot of different factors that would have been to be taken into account, and that's the problem for the person of ordinary skill in the art, that they don't necessarily have the overarching knowledge to put all of that together. 10:20 AM

Q. Okay. So if a person of ordinary skill in the art were told in the hypothetical I've just asked that it is important that the molecule be soluble, would that person then have been able to select the linker? 10:20 AM

MR. MCTIGUE: Objection to form.

A. Well, I'm still saying there's so many other factors. It may be soluble. It may be free from aggregates. It may be sensitive to proteolysis. Perhaps they want it to be susceptible to proteolysis. Some linkers are, and that's desirable in some situations, so you need to know the whole context. 10:20 AM

BY MR. HEINTZ:

Q. And if a person of ordinary skill in the art had been given that context and told to select the linker, would that person 10:20 AM

have been able to do so?

A. So if they'd been told everything that they need to know, then they would be able to follow the instructions that they'd been given. 10:21 AM

Q. Would there be any -- any number -- let me rephrase that.

If they'd been given these instructions, would there still be choices to be made as to which linker to select? 10:21 AM

A. Yes.

Q. Okay. And the person of skill in the art would be able to make those choices?

A. I don't know.

Q. So you don't have an opinion on that? 10:21 AM

MR. MCTIGUE: Objection to form.

A. That's correct.

BY MR. HEINTZ:

Q. Thank you. 10:21 AM

Sir, I apologize. Earlier I mentioned a priority date of 2011. It's actually 2010.

Does the change of 2011 to 2010 as the priority date, or at least claimed 10:21 AM

priority date, change any of your answers?

A. Whatever you -- the priority date is alleged to be, it doesn't affect my answers.

Q. All right. Thank you, Doctor. 10:21 AM

Would a POSITA, as you have defined that person, in 2010 have been familiar with binding assays used to confirm antigen binding specificity?

A. Yes, I expect they would. 10:22 AM

Q. Would a POSITA, as you have defined that person, know how to design a recombinant expression construct including a fusion protein?

MR. MCTIGUE: Objection to form. 10:22 AM

A. I give the same answer as before. It would depend upon the context and the complexity of the project, and whether or not it was straightforward and routine or whether it was unusual and extraordinary. 10:22 AM

BY MR. HEINTZ:

Q. Assuming it's not unusual and extraordinary, would a POSITA have known how to design a recombinant expression construct that encodes a fusion protein? 10:23 AM

PGR2026-00025 - JHU
Ex. 2042- Page 47

A. They would certainly have some knowledge of the methods used in those constructions, yes.

Q. Would a POSITA know how to select an appropriate expression vector and host cell? 10:23 AM

MR. MCTIGUE: Objection to form.

A. It's another area where it's tremendously dependent on context, and in some cases I think they would not know how to select such a host cell. 10:23 AM

BY MR. HEINTZ:

Q. But in some cases they would?

A. In some cases they would.

Q. Would a POSITA know how to transfect or infect a host cell with the construct? 10:23 AM

MR. MCTIGUE: Objection to form.

A. Again, I think that's dependent on context, and in some cases they might know that, in other cases it would be difficult to know. 10:23 AM

BY MR. HEINTZ:

Q. Can you give me an example of a case in which it would be difficult to know 10:23 AM

how to transfect or infect a host cell with a construct?

A. Well, if the host cell had never been transfected before, if there was no record in the literature of how it was done or if the record was inadequate, there was only a partial description, that would make it difficult. 10:24 AM

Q. Okay. Would a POSITA know how to assess whether the recombinant protein was expressed? 10:24 AM

A. Same sort of answer; it would depend upon the context.

Q. Would a POSITA know how to conduct binding assays to confirm antigen specificity? 10:24 AM

A. Again, it would depend upon the context.

Q. Mammalian expression systems such as CHO and HEK293 were standard choices for antibody and fusion protein expression by 2010, correct? 10:25 AM

MR. MCTIGUE: Objection to form.

A. What do you mean by "standard choices"? 10:25 AM

BY MR. HEINTZ:

Q. Let's turn to paragraph 62 of your declaration, which is Exhibit 1003. There you say that "By 2010, the manufacture of conventional recombinant IgG antibodies was a comparatively predictable and routine process," correct? 10:25 AM

A. That's what I say.

Q. And you say, "This included (1) transfection of a suitable host cell with a plasmid or viral vector which encoded the antibody, (2) selection of a stable transfectant, (3) culture of the cells, and (4) purification of the antibody from the culture supernatant," if I pronounced that correctly. 10:26 AM

Is that correct?

A. That's correct. I go on to say, "Such predictability could not be said for fusion proteins." 10:26 AM

Q. Okay. So with this understanding, was CHO a standard choice for antibody and fusion protein expression by 2010?

MR. MCTIGUE: Objection to form.

A. It was at least a common choice. 10:26 AM

PGR2026-00025 - JHU
Ex. 2042- Page 50

BY MR. HEINTZ:

Q. And the same question for HEK293. Was that also a common choice?

MR. MCTIGUE: Same objection.

A. In this context it was not a common choice. I was talking about selecting stable transfectants. That's because you need a stable transfectant for long-term production of antibody, and HEK cells are usually used for transient transfection. 10:27 AM

BY MR. HEINTZ:

Q. Was that a common choice for transient transfection?

A. It was commonly used.

Q. All right. So, sir, we've been going for about an hour. Would you like to take a short break now? 10:27 AM

A. That would be fine if you like. I don't mind.

MR. HEINTZ: Go off the record. 10:28 AM

(Recess taken at 10:28 a.m. to 10:42 a.m.)

MR. HEINTZ: Back on the record whenever you're ready.

BY MR. HEINTZ:

Q. Dr. Hale, would you agree that a 10:42 AM

PGR2026-00025 - JHU
Ex. 2042- Page 51

POSITA, as you have defined that person, would have been familiar with the significant protein and antibody literature?

A. Yes.

Q. Dr. Hale, are you familiar with the journal named "Protein Engineering Design and Selection," PEDS? 10:42 AM

A. I'm not very familiar with it.

Q. Do you know whether it's a peer-reviewed journal by Oxford University Press? 10:43 AM

A. I don't know that.

Q. Do you know if the -- that journal, PEDS, would qualify as one of the significant journals for antibody engineering in 2009 and 2010? 10:43 AM

A. I don't know that. There's a lot of journals in those days, and even more now. Some are reliable.

Q. Are you familiar with Sir Alan Fersht? 10:43 AM

A. I knew him long time ago.

Q. How about Sir Gregory Winter?

A. I knew him as well.

Q. Those two folks were on the 10:43 AM

editorial team for PEDS. Does that help inform your opinion as to whether PEDS would have been an important or significant journal for antibody engineering in 2009, 2010?

A. Well, that would enhance it in my opinion. There's certainly people with a high reputation in the field. 10:44 AM

Q. Okay. You state in your declaration that "By 2010 the manufacture of conventional recombinant IgG antibodies was a comparatively predictable and routine process," correct? 10:44 AM

And I'll refer you to paragraph 62, if you care to see.

A. That's what I said. 10:44 AM

Q. Okay. And that's correct?

A. And that's correct.

Q. All right. And that would be within the level of ordinary skill in the art, as you've defined a POSITA, correct? 10:45 AM

A. Yes. Notice what I said exactly, "conventional recombinant IgG antibodies." Each of those words is important.

Q. And would you agree that by 2010 numerous fusion proteins have been described 10:45 AM

and a number of different peptide -- sorry -- peptide linkers were known?

A. Yes.

Q. And you would agree that by 2010 there were a number of fusion proteins in clinical development, and some had been approved and marketed, most including one or more immunoglobulin domains; is that correct? 10:45 AM

A. I believe that is correct. I described some of those fusion proteins in my report. 10:45 AM

Q. One of them would be abatacept; is that correct?

You can look in paragraph 59 if you'd like to refer. 10:46 AM

A. Thank you. One of them would be abatacept.

Q. And, in fact, all of the --

A. Sorry, can you just go back to the question, one of -- were we saying they've been approved? 10:46 AM

Q. Had been approved. Some of these had been approved and marketed by 2010.

A. Yeah, okay. I didn't say that in my reports, and I'm not quite sure whether 10:46 AM

all those molecules mentioned in the reports had been approved and marketed by 2010.

I think that abatacept might have been, but I'm not -- as I sit here today, I'm not certain of that. It had been given an INN name. It had entered clinical trials by 2010. That's what I said in the report. 10:47 AM

Q. How about for the other ones listed there of the nine?

A. I think from memory, but I might not be reliable, possibly two or three of them had been approved for marketing by 2010. I'm not quite sure which ones. 10:47 AM

Q. And whether or not they had been approved for marketing, they were known in the art by 2010; is that correct? 10:47 AM

A. They were known in the art by then.

Q. And you would also agree that antibody fusion proteins were also known by March 2010, correct? 10:47 AM

MR. MCTIGUE: Objection to form.

A. There were some antibody fusion proteins which were known by March 2010, and I've listed some of them in paragraph 60. 10:48 AM

BY MR. HEINTZ:

Q. Okay. Were all of those listed in paragraph 60 known by 2010?

MR. MCTIGUE: Objection to form.

BY MR. HEINTZ: 10:48 AM

Q. In particular, March of 2010?

A. I believe that all of those listed in paragraph 60 were known by March 2010. I've cited references there for all of them, and I believe that all those references date 10:48 AM before March 2010.

Q. Thank you, Doctor.

Earlier we talked about linkers before the break. Do you recall that?

A. Yes. 10:48 AM

Q. I'm going to direct your attention to paragraph 61 of your report now, and ask you if you would agree that a short flexible linker consisting of one or more copies of four glycine residues and one serine residue, 10:49 AM i.e., GGGGS, was commonly used as of March 2010 to link protein domains to a fusion protein?

MR. MCTIGUE: Objection to form.

A. I believe it was quite often used. 10:49 AM

PGR2026-00025 - JHU
Ex. 2042- Page 56

I'm not certain how commonly it was used, but it was quite often.

BY MR. HEINTZ:

Q. And so that kind of linker, in other words, four glycine residues and one serine residue, was well-known before March of 2010, correct? 10:49 AM

MR. MCTIGUE: Objection to form.

A. Depends what you mean by well-known, but it was known by people who were working in the field. 10:49 AM

BY MR. HEINTZ:

Q. And well-known -- I'm sorry, known by a POSITA, as you've defined that term, in March 2010, correct? 10:49 AM

MR. MCTIGUE: Same objection.

A. So just remind me the question.

BY MR. HEINTZ:

Q. Yes. That kind of linker was well-known to a person of ordinary skill in the art by March of 2010, correct? 10:50 AM

MR. MCTIGUE: Same objection.

A. Yes, I think it was well-known. It depends, of course, on the context as to what it might be used for. 10:50 AM

BY MR. HEINTZ:

Q. TGFbetaRII, which is the immunomodulatory moiety we cite in Claims 1 and 9, is a receptor extracellular domain, correct? 10:50 AM

A. I believe so.

Q. Would you agree that the general concept of fusing a receptor ectodomain to an immunoglobulin domain have been demonstrated and commercialized by 2010? 10:51 AM

A. I'm not sure.

Q. So in paragraph 59, none of those involve a fusion of a receptor ectodomain to a immunoglobulin domain that had been commercialized and demonstrated by 2010? 10:51 AM

A. In paragraph 59, no.

Q. Is that because they hadn't been marketed -- I'm sorry, hadn't been commercialized?

A. No. It's because those are not antibody fusion proteins. Those are Fc fusion proteins. 10:51 AM

So you're looking at paragraph 59?

Q. Yes.

A. Yeah, you might want to look at 10:52 AM

paragraph 60.

Q. All right. What about paragraph 60? So does your answer change in respect to paragraph 60?

A. So can you just give me the question again? 10:52 AM

Q. Okay. Let me see if I can get the exact words.

Would you agree that the general concept of fusing a receptor ectodomain to an immunoglobulin domain have been demonstrated and commercialized by March of 2010? 10:52 AM

MR. MCTIGUE: Objection to form.

A. If by "commercialized" you mean that there was a product on the market, then I think the answer is no, I am not aware, as I sit here today, of any of those products being on the market by March 2010. 10:52 AM

BY MR. HEINTZ:

Q. Would it be fair to say that it had been demonstrated and known in the art by March of 2010, correct? 10:53 AM

MR. MCTIGUE: Objection to form.

A. Sorry, I sort of lost the trail of the question. 10:53 AM

BY MR. HEINTZ:

Q. I'll --

A. Can you rephrase that without the commercialization, perhaps?

Q. All right. So by March of 2010, the general concept of fusing a receptor ectodomain to an immunoglobulin domain was known in the art? 10:53 AM

A. Well, by March 2010, people had made some of these antibody fusion proteins where they contained an antibody fused with a non-immunoglobulin protein, which might be a toxin or an enzyme or a cytokine. 10:53 AM

So most of those molecules I mentioned there are not immunomodulatory molecules necessarily, at least not in the way we understand it in the context of this patent. 10:54 AM

So whether any of them -- maybe one or two were fused with immunomodulatory molecules like Il2. That will be considered to be an immunomodulatory molecule. So there are a few examples, but I wouldn't say that they were necessarily generally widely known, because there weren't lots of examples. So 10:54 AM

whether or not one could make others would be a matter of uncertainty.

Q. So in each of the examples you identify in paragraph 59, for example -- I'm sorry, let me rephrase it. 10:55 AM

In each of the examples you identify in paragraph 60, such as Zemab, the antibody or antibody fragment retained the ability to specifically bind its target antigen after fusion, correct? 10:55 AM

MR. MCTIGUE: Objection to form.

A. I can't say that I specifically checked that. It seems plausible.

BY MR. HEINTZ:

Q. You would expect that to be the case, wouldn't you? 10:55 AM

A. I would hope that it is the case, but I know that there are some examples where activity of antibodies or proteins attached to them has changed when they've been joined together. So the activity isn't -- it's not a given that the activity will remain the same. 10:55 AM

Q. But nonetheless, it has been demonstrated several times, including for 10:56 AM

Zemab MFECP1 and EMD 273066, that there was retention of the ability to bind the target antigen after the fusion, correct?

A. Yeah, I expect that was the case. Those are three examples. 10:56 AM

Q. Sequence ID No. 104, which is the linker recited in Claim 9, is a GGGGS repetition three times of the same GGGS motif we discussed earlier. If I missed a G it's four Gs in this. Is that correct, Doctor? 10:56 AM

MR. MCTIGUE: Objection to form.

A. I believe it's correct. The sequence of that linker you're talking about is in Sequence ID No. 104.

BY MR. HEINTZ: 10:57 AM

Q. Right. And that sequence ID is a repeat of the general GGGGS motif, correct?

MR. MCTIGUE: Same objection.

A. Yes.

BY MR. HEINTZ: 10:57 AM

Q. Okay. A POSITA would have known how to incorporate that linker by encoding its nucleotide sequence between the two protein domains, correct?

MR. MCTIGUE: Objection to 10:57 AM

PGR2026-00025 - JHU
Ex. 2042- Page 62

form.

A. Well, it would depend upon the context.

BY MR. HEINTZ:

Q. In Claim 9 of the '968 patent. 10:57 AM

A. Sorry. Can I just have another look at that?

Q. Yeah, sure.

A. Yeah, I think my answer remains the same. It would depend upon the context, 10:58 AM so -- yep.

Q. So the context in particular is Claim 9, where we have a TGFbetaRII?

A. Uh-huh.

Q. Linked to the light chain of 10:58 AM cetuximab, right?

And are you saying that a POSITA would not have known how to incorporate that linker by encoding its nucleotide sequence between those two protein domains? 10:58 AM

A. What I meant by the context is they would have to take into account the whole context of the -- you know, of the experiment. They're really trying to make, according to Claim 9, an isolated molecule, 10:58 AM

which comprises a lot of things, including this.

Have I got that right?

Q. Yeah, I think so.

A. Yeah. And in order to make that isolated molecule, they need to carry out a lot of different steps, and I've set those out in a sort of hypothetical research plan in my report that's not described in the patent. It doesn't describe any of those steps. 10:59 AM

So in that context, they would need to make many inventive decisions. They need to -- for example, they need to choose the cell line that they were going to transfect out of all the many possible cell lines known in the art, of which there are, I don't know how many, lots. 10:59 AM

They need to choose an expression system, a vector, that is, the nucleic acid that carries it in, and all of those things would have a bearing on the decision about encoding the linker in the -- in the DNA that encodes for it. 10:59 AM

So there's a complicated set of 11:00 AM

decisions that needs to be made, and that's the part that requires a great deal of skill.

Q. And so you're saying that those decisions would have been beyond one of ordinary skill in the art as of March 2010? 11:00 AM

A. They could be. It's hard to say. I knew people of ordinary skill who attempted to do that sort of project and had great difficulty in achieving it, even though they had access to all this information at that 11:00 AM sort of time.

Q. And to be clear, we are talking about the particular linker in Sequence ID No. 104?

A. Yes. 11:00 AM

Q. Okay. So even then --

A. Even then.

Q. -- given that information --

A. Even then. Even now. I mean, I've been involved in such a project where 11:00 AM such a linker was used even today, and the decision as to how to encode it in DNA is not a straightforward one.

So you're probably aware that there are many difference codons which encode 11:01 AM

glycine and amino acid, so there's different ways --

THE COURT REPORTER: Encode glycine and what?

THE WITNESS: So there are many different codons which encode the amino acid glycine, and the POSA would need to choose the particular codons which should be used, and the choice of those codons will depend upon the factors that I mentioned earlier, such as cell type, such as expression vector and so on. 11:01 AM

BY MR. HEINTZ:

Q. All right.

A. So it complicates -- it's not a simple matter. There's a lot of choices to be made and making these choices requires a high level of skill and experience. 11:01 AM

Q. Beyond the level of ordinary skill? 11:02 AM

A. Maybe, maybe.

THE COURT REPORTER: Hold on.

THE WITNESS: Sorry. Excuse me.

BY MR. HEINTZ:

Q. Well, you're saying "maybe," and 11:02 AM

I'm asking you in particular about Claim 9 and the particular Sequence ID No. 104, and we've been talking about TGFbetaRII and the light chain of cetuximab.

And even then, I just want to make my record clear, it may be beyond the level of ordinary skill in the art to be able to get that linker in Sequence ID No. 104 to connect those two molecules in the way that's required in Claim 9? 11:02 AM

A. Yes.

Q. Okay. Thank you.

All right. Let's go to your declaration at paragraphs 24 to 29, and in particular, I want to ask you about what "written description" means to you, your understanding of it, Doctor. 11:03 AM

A. So your question is what does written description mean to me?

Q. Yes. How do you understand what's been written, starting at paragraph 24 and continuing through 29, which I understand you obtained from counsel. You didn't write this yourself, correct? 11:03 AM

A. Correct. 11:03 AM

Q. So what's your understanding of the written description requirement?

A. I think it's described quite clearly there. It's -- I understand that the written description, you know, it helps to ensure that the inventor has actually invented the claimed subject matter, and in a sense possesses that invention. 11:03 AM

That means they understand exactly how the invention could be reduced to practice, and they've got to demonstrate to the POSA that they've got that possession, and they've got to do that within the -- what's described here as the four corners of the specification. 11:04 AM

And I understand that to mean the actual specification as we have it, the text, the figures.

Q. Okay. So you understand the specification includes all of the text, correct? 11:04 AM

A. Apart from the claims, and maybe the preamble -- the legal matter at the beginning. I mean, the -- you know, the first page, which has got numbers and dates 11:04 AM

and that sort of thing on it.

Q. I understand.

The abstract is on the first page. Do you understand whether that's all the specification or not? 11:05 AM

A. I don't know.

Q. Okay. And you said that the specification in your opinion did not include the claims; is that correct?

A. That's how I understand it. 11:05 AM

Q. Okay. So when you did your analysis for the purposes of your report, did you consider whether the originally filed claims were -- sorry.

Did you consider whether the written description requirement could be satisfied in part by the originally filed claims that were filed with the application? 11:05 AM

MR. MCTIGUE: Objection to form. 11:05 AM

A. So when you say "the originally filed claims," which application are you talking about?

BY MR. HEINTZ:

Q. So let's start with application 11:06 AM

serial number 18883719, which was the application number that led to the '968 patent.

A. Okay. And so the question related to the original claims in that application? 11:06 AM

Q. Correct.

A. And the question was did I consider them?

Q. Correct, in your analysis of the written description requirement. 11:06 AM

A. Well, I did consider those claims, and I would expect that in order to satisfy the written description requirements, those claims would have to find supports, you know, elsewhere in the specification. 11:06 AM

Q. So earlier when I asked you about the claims, you said they weren't part of the specification. Now you've told me that you did consider those claims in analyzing the written description requirement. 11:07 AM

It seems like there's an inconsistency there. Can you help explain how you consider the claims in your analysis of the written description requirement?

MR. MCTIGUE: Objection to form, 11:07 AM

asked and answered.

A. I think so. I think the question about written description is does the specification provide the written description support for the claims. 11:07 AM

Claims are one thing. They have to be supported by what's written in the specification, the specification, not the claims. I think that's what I said, and I'm sorry if I didn't make it clear. 11:07 AM

BY MR. HEINTZ:

Q. Got it. Okay.

Do you -- let me rephrase that.

Do you agree that the written description requirement is satisfied if the 11:08 AM patent disclosure reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the effective filing date?

MR. MCTIGUE: Objection to form. 11:08 AM

BY MR. HEINTZ:

Q. Do you want me to read it to you again?

A. Yes, please. Sorry.

Q. Do you agree that the written 11:08 AM

description requirement is satisfied if the patent disclosure reasonably conveys to those skilled in the art that the inventor had possession of the claim subject matter as of the effective filing date? 11:08 AM

MR. MCTIGUE: Same objection.

A. Yes.

BY MR. HEINTZ:

Q. Okay. And just to be clear, you consider the entire specification when making the determination as to whether the claims of the '968 patent satisfied the written description requirement? 11:08 AM

A. Yes.

Q. And you would agree that this written description requirement can be satisfied by any combination of the words, the structures, the figures, the diagrams, the formula or anything else contained in the patent specification, correct? 11:09 AM

A. Well, I'm not sure about that, because I think it needs to be clear in terms of conveying to the POSA that the inventor was in possession of what is claimed.

And just to put together words and 11:09 AM

phrases from different parts of the specification may concoct something entirely different that wasn't in the specification at all.

Q. Well, you do agree that the entire specification, including everything in the figures, everything in the text, whether it be tables or formulas or equations, all of that needs to be considered? 11:09 AM

A. Yes. 11:10 AM

Q. Okay.

A. But you couldn't just take words and phrases and jumble them up in some different order and then produce a claim out of that. 11:10 AM

Q. And so you would agree, for example, that Figure 3 is part of the written description of the patent, correct?

A. Yes.

Q. And just to be clear, we're talking about Figure 3 of the '968 patent, correct? 11:10 AM

A. Yes.

Q. Okay. Is there anything about Figure 3 of the '968 patent that would not be 11:10 AM

understood by a person of ordinary skill in the art?

A. I think it would need to be understood in the context of the rest of the specification. I think I can understand it. 11:11 AM

Q. Do you think a person of ordinary skill in the art would have been able to understand Figure 3 in light of the entire specification?

A. I think they would have a reasonable understanding of what it is, and they would understand it to be describing what it says in the title, "Fusion proteins comprising anti-EGFR antibody and TGFbetaRII extracellular domain." 11:11 AM

Q. For example, in Figure 3 a POSITA would understand what the underlying portion Sequence ID No. 2 represents, correct?

A. Well, they would notice the key which says "Underlined: Anti-EGFR antibody variable region," and so they may well come to the conclusion that that was intended to indicate the variable region of the heavy chain and the light chain. 11:12 AM

Q. Okay. And the light chain is 11:12 AM

what's further down under Sequence ID No. 71 in Figure 73, correct?

A. Correct.

Q. Okay. So a person of ordinary skill in the art understands that those underlying portions of Sequence ID No. 2 and Sequence ID No. 71 in Figure 3 are the variable regions of the heavy and light chains respectively, correct? 11:12 AM

A. I think so. 11:12 AM

Q. Okay. What about the bold text, would a POSITA understand what that represents?

A. Well, according to the legend, it indicates that the text in bold is the amino acid sequence of the TGFbetaRII ectodomain, and so that's what they would understand it to mean. 11:13 AM

Q. How about the italics? Would a POSITA understand what the italics in Figure 3 represent? 11:13 AM

A. In the same way. It says, "Italic: Linker," and the letters in italics are -- that's repeated motif GGGGS, three times. They would understand that to be a 11:13 AM

linker, specifically a linker between the heavy chain and the TGFbetaRII ectodomain.

Q. All right. Let's turn to paragraph 95 of your declaration, which again is Exhibit 1003. 11:14 AM

MR. MCTIGUE: Do you mind if I refer to the page?

MR. HEINTZ: Oh, certainly, sorry. Page 39.

MR. MCTIGUE: Thank you. 11:14 AM

THE WITNESS: Thank you.

BY MR. HEINTZ:

Q. So, Dr. Hale, on page 39 we see the start of paragraph 95, in which you state you reproduced Figure 3 below, and that's 11:15 AM actually on the next page in page 40, correct?

A. Correct.

Q. And so this is Figure 3 from the -- from the patent, correct? 11:15 AM

A. Yes, it is.

Q. Okay. So with respect to the underlying portion of Sequence ID No. 2 in Figure 3, that is the variable domain of the heavy chain, correct? 11:15 AM

MR. MCTIGUE: Objection to form.

A. Yes, I believe it is.

BY MR. HEINTZ:

Q. Okay. And a person of ordinary skill in the art would have understood that from Figure 3, as we discussed earlier, correct? 11:16 AM

A. I believe so.

Q. Okay. And that underlying portion of Sequence ID No. 2 is amino acids 1 to 119, correct? 11:16 AM

A. Do you want me to count them or take your word for it?

Q. You can take my word for it.

A. I'll take your word for it. 11:16 AM

Q. Okay. And again, we talked about this earlier, but the italicized portion of Sequence ID No. 2 is the linker sequence, correct?

A. Correct. 11:16 AM

Q. Okay. And that is the same -- I'm sorry.

Did you compare the bolded sequence in Sequence ID No. 2 to the Sequence ID No. 87 to confirm that it's the same? 11:17 AM

A. Yes.

Q. Okay. Let's turn to Sequence ID No. 71 in Figure 3.

The underlying portion of Sequence ID No. 71 is the variable domain sequence, correct? 11:17 AM

A. Yes, it's the variable domain of the light chain.

Q. And what is the plain portion of Sequence ID No. 71, the one in plain text? 11:17 AM

A. That's not identified in the figure. I believe it is the light chain constant domain.

Q. And a person of ordinary skill in the art would have had that understanding upon reading the '968 patent, correct? 11:17 AM

A. I think they would have done. They would have had to, you know, check that, but that's what it appears to be.

Q. Okay. And just for the record, same question with respect to Sequence ID No. 2. The plain text portion of Sequence ID No. 2 would have been understood by a person of ordinary skill in the art to be the constant reagent of the heavy chain, correct? 11:18 AM 11:18 AM

A. In the same way, I think that's probably correct.

Q. So Figure 3 marks out by underlining exactly the variable domain sequences that make up amino acids 1 through 119 of Sequence ID No. 2, and the variable portion of Sequence ID No. 71, correct? 11:18 AM

A. So that's correct.

Q. Do you explain anywhere in your declaration why the underlining of the verbal domain sequences in Figure 3 fails to function as guidance, direction for other suggested directing of POSITA in interpreting Claim 1 or Claim 9? 11:19 AM

A. I don't -- I never thought that they were. That was -- that was helpful. I don't see anything in the patent's description or specification to indicate that. 11:19 AM

Q. So in Figure 3 we have plain text, and then we have other text that's highlighted in some way, such as underlining or bolding or italicization, correct? 11:19 AM

A. Uh-huh.

Q. You don't think that had any 11:19 AM

significance to one of ordinary skill in the art, upon reading the '968 patent?

A. Well, other than what we've just described. I mean, they indicate that they -- the underlining texts, I think it would indicate to them that that represents the variable region and the plain text, the constant region. 11:20 AM

And so, you know, that's -- that sort of description is not uncommon in the field, but I don't think there's anything there to direct a person of ordinary skill in the art to imagine that you would create a completely new construct not described in Figure 3, but that's had only the variable region from the heavy chain and then the whole of the light chain. 11:20 AM

I mean, that would be something way beyond I think what a person of ordinary skill would ever imagine. 11:20 AM

Q. In Figure 3 -- let me rephrase that.

In the standard IgG, the heavy chain variable region is a distinct structural unit, correct? 11:21 AM

A. It's a unit of protein which folds up, to some extent, independently of the constance domains. I don't know that you could say it's an independent unit.

Q. Well, I said distinct. 11:21 AM

A. Oh, sorry. Repeat your question then.

Q. Yes.

In a standard IgG the heavy chain variable region is a distinct structural unit, correct? 11:21 AM

A. I think that's a way of looking at it. I mean, in representations of IgG antibodies, they're often represented as being made up of different domains, and the heavy variable domain is one of those domains. 11:21 AM

Q. The variable chain -- sorry, the variable region of a heavy chain of a humanized or human antibody typically comprises about 115 to 125 amino acids, correct? 11:22 AM

MR. MCTIGUE: Objection to form.

A. You know, I can't remember the exact number, as I sit here today, but it 11:22 AM

sounds about right.
BY MR. HEINTZ:
Q. Right. And in Figure 3, the underlying portion of Sequence ID No. 2 spans 119, correct? 11:22 AM
And, again, you can take a --
A. I'll take your word for it.
Q. Okay. So, in other words, that length of 119 is about what somebody would expect for a variable region of a heavy 11:22 AM chain?
MR. MCTIGUE: Objection to form.
BY MR. HEINTZ:
Q. A person of ordinary skill in the art would expect, correct? 11:23 AM
A. I think that's reasonable.
Q. Okay. So with respect to the amino acid positions we cited in Claim 1, each of those are identified in Figure 3 by underlying, correct? 11:23 AM
MR. MCTIGUE: Objection to form.
A. I don't think that's correct.
BY MR. HEINTZ:
Q. I'm sorry. In Claim 1 the underlying portion of the anti-EGFR antibody 11:23 AM

variable region is identified by underlining and labeling, correct?

A. No, I don't think it is. Sorry. I don't think Claim 1 -- firstly, it doesn't say anything about underlining, and secondly, you know, even if you refer to Figure 3, Claim 1 has got some amino acids which are underlined and some which are not underlined. 11:24 AM

So there's no -- there's nothing in the underlining that conveys any understanding of Claim 1. 11:24 AM

Q. Let me ask you to turn to your declaration at paragraphs 131 and 132, and those are on page -- starting on page 60, and then goes on to page 62. 11:25 AM

A. Okay.

Q. All right. So you say in your declaration that you identified a single molecule disclosed in the '968 patent that is covered by Claim 1, and that in particular is the fusion protein disclosed in Figure 3; is that correct? 11:25 AM

A. Yes.

Q. Okay. So in the '968 patent specification, there is at least one 11:25 AM

disclosed molecule that a POSITA would recognize as falling within the literal scope of Claim 1, correct?

A. I believe so.

Q. Okay. Did you express an opinion anywhere in your declaration that it would take undue experimentation to make the choices between including the entirety of Sequence ID No. 2 or only the underlined portion of Sequence ID No. 2 in determining what was going to be part of a fusion protein? 11:25 AM 11:26 AM

A. I'm not sure I understand the question.

Q. So in Figure 3, for Sequence ID No. 2 there is an underlying portion, and then there is the entirety of Sequence ID No. 2, right? 11:26 AM

A. Okay.

Q. Let's refer to the portion of Sequence ID No. 2 that precedes the linker. 11:26 AM

Do you understand what I'm referring to?

A. Okay.

Q. All right. So in that portion of 11:26 AM

Sequence ID No. 2 that precedes the linker, some portion is underlined and some portion is in plain text, correct?

A. Correct.

Q. Okay. So a POSITA would have a choice in creating a fusion protein that includes some part of Sequence ID No. 2 to include the entirety of Sequence ID No. 2 before the linker or only the underlined portion of Sequence ID No. 2 before the linker. 11:27 AM

And you agree that there would be a choice that a person of ordinary skill in the art had to make?

A. Well, there would, but, of course, if they wanted to practice the full scope of the invention they'd have to make, presumably, both, at least both, if not others. 11:27 AM

Q. And you don't express anywhere in your declaration an opinion that making that choice would require undue experimentation, do you, Doctor? 11:27 AM

A. I think making those molecules would certainly require undue 11:27 AM

experimentation. So if the POSA was to attempt to -- you know, or was asked to, you know, produce the molecules which are covered by Claim 1, even, you know, a proportion of them to enable that full scope of that claim, then I think it would involve undue experimentation, and I've set out the reasons for that, you know, in detail in the report. 11:28 AM

Q. How many choices does Figure 3 present to one of skill in the art in making a fusion protein? 11:28 AM

A. Well, it only presents one choice, and that is to make the fusion protein which I've illustrated in figure -- in my paragraph 131. 11:28 AM

I mean, the important question is how many choices there are in Claim 1, which are, of course, many, many more.

Q. How many choices do you think there are in Claim 1? 11:29 AM

A. Uncountable.

Q. How about Claim 9?

A. Similarly uncountable.

Q. Why do you say it's uncountable?

A. Because both those claims involve 11:29 AM

the language "comprise," and comprise, as I understand it, means that they could have other parts to them. And those other parts, if you look at the specification, could be many, many different things, antibodies of different isotype, different species by specific antibodies, all sorts of things. 11:29 AM

I couldn't count them.

Q. Are you familiar with patents or different kinds of fusion proteins generally? 11:29 AM

MR. MCTIGUE: Objection to form.

A. Are you thinking of the particular patent?

BY MR. HEINTZ:

Q. No, just -- 11:30 AM

A. Just in general?

Q. Yeah.

A. I've read, you know, probably hundreds of patents. I can't remember all of them. 11:30 AM

Q. Okay. Have you -- let me withdraw that question.

Let me ask you to turn your attention to the '968 patent, which again, is Exhibit 1001, at Column 29, lines 24 to 35. 11:30 AM

MR. MCTIGUE: Can you remind me of the lines?

MR. HEINTZ: Sure. Column 29, lines 24 through 35.

MR. MCTIGUE: Thank you. 11:30 AM

MR. HEINTZ: Sort of the middle paragraph in Column 29.

THE WITNESS: Okay.

BY MR. HEINTZ:

Q. Okay. The beginning of that passage states that the targeted -- sorry -- "the targeting moiety includes an antibody, antibody fragment, ScFV or Fc-containing polypeptide," correct? 11:31 AM

A. Correct. 11:31 AM

Q. Okay. That same passage identifies EGFR as one of the targeting moieties that may -- sorry -- has one target the targeting moiety may specifically bind, correct? 11:31 AM

A. It's one of a long list of possible targets and moieties. It just says "in one aspect," yes.

Q. And you reviewed this passage before you signed your declaration, correct? 11:32 AM

A. Yes.

Q. Okay. The specification separately states that "An antibody includes single-chain antibodies, Fab fragments, Fab prime fragments, fragments produced by" -- 11:32 AM

A. Sorry. Could you point me to the place?

Q. Let's go to Column 34, lines 23 to 60.

A. Okay. Okay. So this is the paragraph which starts, "Antibodies in one embodiment"? 11:32 AM

Q. Correct.

A. Thank you.

Q. Okay. And if you let me know when you're ready for the question, I'll ask it. 11:33 AM

A. Okay.

Q. All right. The specification also states that "An antibody includes single-chain antibodies, Fab fragments, Fab prime fragments, fragments produced by a Fab expression library," that's F-a-b; is that correct? 11:33 AM

A. That's part of what it includes, so known antibodies among many other things, 11:33 AM

yes.

Q. Okay. And the specification states that "An antibody fragment includes Fab, Fab prime, Fab prime II, Fd, single-chain Fvs" -- that's F-v plural -- "such as ScFV, single-chain antibodies, disulfide linked Fvs such as svFv, and fragments including either a variable light or variable heavy chain domain," correct? 11:34 AM

A. Yes, that's what it says, and yeah, there's a lot of different things that could be meant by the term antibodies. 11:34 AM

Q. All right. And with respect to Column 34, lines 46 to 49, the specification states that "An antigen-binding antibody fragment may include the variable regions alone," correct? 11:34 AM

MR. MCTIGUE: Objection to form.

A. So an antibody -- antigen-binding antibody fragments may include the variable regions alone. That's line 46 onwards, yes. 11:35 AM

BY MR. HEINTZ:

Q. Okay. And now referring to Column 35, lines 56 to 62, just let me know when you're there and I'll continue. 11:35 AM

A. Okay.

Q. All right. "The specification separately identifies antibody fragments including Fab, Fab prime, Fab II prime, and Fv fragments, Fc fragments or Fc fusion products, diabodies, linear antibodies, single-chain antibody molecules and multispecific antibodies formed from antibody fragments," correct? 11:35 AM

MR. MCTIGUE: Objection to form. 11:36 AM

A. Yes, that's what it says. You said "separately," so I'm not sure why that would be separately. It's just a long list of things that's -- yeah.

BY MR. HEINTZ: 11:36 AM

Q. Okay. An Fv fragment consists of a VH variable heavy chain domain and a VL variable light chain domain without the antibody's constant regions, correct?

A. Correct. 11:36 AM

Q. You're not offering an opinion that a targeting moiety compromising only a variable heavy chain region and a light chain sequence was, as a general structural matter, unknown to a person of ordinary skill in the 11:37 AM

art as of March 2010, are you?

MR. MCTIGUE: Objection to form.

A. Can you just repeat exactly the question? It's very particular.

BY MR. HEINTZ: 11:37 AM

Q. Yeah. So you are not offering an opinion that a targeting moiety compromising only a variable chain heavy region -- sorry.

A. Yeah.

Q. A variable heavy chain region -- 11:37 AM

A. Yes.

Q. -- and a light chain sequence was, as a general structural matter, unknown to a person of ordinary skill in the art as of March 2010, are you? 11:37 AM

MR. MCTIGUE: Same objection.

A. Yes, I am offering that opinion, because I think that's the molecule that I've represented. If it is as I understand it in my figure -- well, let's find it so 11:37 AM there's -- I'll make sure I understand the same thing that you're talking about.

Sorry.

So that would be in my report, paragraph 117, and my Figure G. And I think 11:38 AM

this is the molecule you've just described.

BY MR. HEINTZ:

Q. And so you're saying that was unknown to a POSITA as of March 2010?

A. Yes. It's still unknown. 11:38 AM

Q. Would you agree that a POSITA reading Figure 3 together with the fragment disclosure passages that we just read in the '968 patent would support a targeting moiety comprising less than the full-length 11:39 AM cetuximab heavy chain?

A. No.

Q. You would not agree?

A. If I understood your question correctly -- just say it again so that I'm 11:39 AM quite clear.

Q. Sure. A POSITA reading Figure 3, together with the fragment disclosure passages we just read of the '968 patent, would understand the specification to support 11:39 AM the targeting moiety comprising less than the full-length heavy chain of cetuximab?

A. I don't think the POSITA would understand that from Figure 3, no.

Q. Let's go to paragraph 154 of your 11:40 AM

PGR2026-00025 - JHU
Ex. 2042- Page 93

declaration, and that is on page -- starting on page 69.

A. Uh-huh.

Q. In discussing Claim 9, you quote the specification statement that "In another aspect, the immunomodulatory moiety is a polypeptide that is fused to the C-terminus of the light chain of a targeting antibody," correct? 11:40 AM

A. Correct. 11:40 AM

Q. Okay. That is the exact architecture that Claim 9 requires, an immunomodulatory moiety fused via a linker to the light chain, correct?

MR. MCTIGUE: Objection to form. 11:40 AM

A. Well, it isn't, of course, the exact architecture. You've just said it yourself.

BY MR. HEINTZ:

Q. I'm sorry, what did I say myself? 11:41 AM

A. You said -- well, quoting from my paragraph 154, which quotes from the specification, "The immunomodulatory moiety is a polypeptide that is fused to the C-terminus of the light chain of a targeting 11:41 AM

antibody," and Claim 9, as you just said, doesn't have that.

It has the immunomodulatory moiety linked via a linker.

Q. Okay. 11:41 AM

MR. NDUBUKA: To the C chain of the linker?

MR. MCTIGUE: Objection.

THE WITNESS: Sorry. So am I expected to answer that question? 11:41 AM

MR. MCTIGUE: No, you're not answering any questions for counsel from Y-Trap.

BY MR. HEINTZ:

Q. Okay. Claim 9 does require that the immunomodulatory -- to the C-terminus of the linker, correct? 11:42 AM

MR. HEINTZ: Let's go off the record.

(Recess taken at 11:42 a.m. to 11:44 a.m.) 11:42 AM

BY MR. HEINTZ:

Q. So, Dr. Hale, in paragraph 154 of your declaration you cite a passage of the '968 patent that says, "In another aspect, the immunomodulatory moiety is a polypeptide 11:45 AM

that is fused to the C-terminus of the light chain of a targeting antibody."

Do you see that?

A. Yes, and that comes from Column 35 of the patent specification. 11:45 AM

Q. Okay. Is it your testimony that a POSITA reading that disclosure of the '968 patent would understand that the polypeptide is fused directly to the light chain without any linker? 11:45 AM

A. Yes.

Q. Wouldn't the POSITA, as of March 2010, reading the patent, understand that a linker could be used to accomplish that fusion? 11:46 AM

A. I don't think that's the relevant question.

In -- if you look at Column 35 of the patent, line -- well, starting at line 31, but it talks about in one embodiment, a hybridoma can produce a targeted fusion protein compromising a targeting moiety -- 11:46 AM

THE COURT REPORTER: Doctor, you can't read that fast.

THE WITNESS: I'm sorry. 11:47 AM

THE COURT REPORTER: In one embodiment what? It talks about one embodiment.

THE WITNESS: A hybridoma can produce a targeted fusion protein comprising a targeting moiety and an immunomodulatory moiety. And it goes on to say that they may be fused together with a linker or without a linker. It describes the linker. 11:47 AM

And then further down, we come to the section that I described -- sorry, I've lost it. 48, 50. Here we are.

"In another aspect the immunomodulatory moiety is a polypeptide that is fused to the C-terminus fused to the C-terminus of the light chain." And so in the context, I think the POSA would understand that other aspect to be an aspect where the immunomodulatory moiety is fused to the C-terminus of the light chain. 11:47 AM 11:48 AM

And particularly in the context of Claim 9, where it talks about fusion, you can see that fusion means, as it 11:48 AM

normally would mean, that those two things are directly connected together. That's -- you go from the C-terminus of one to the N-terminus of the other, and that's the way that fusion is used or fused is used in Claim 9.

It talks about the linker being fused to the light chain or the immunomodulatory molecule being fused to the linker. So in Claim 9 there has to be a linker. In this section there's no linker. 11:48 AM

BY MR. HEINTZ:

Q. So in Column 35, starting at line 33, it says, "In one embodiment a targeting moiety compromising an antibody, an antibody fragment or polypeptide, is linked or fused to an immunomodulatory moiety consisting of a polypeptide with a linker or without a linker." 11:49 AM

A. Exactly.

Q. Doesn't that tell one of ordinary skill in the art that when we talk -- when the patent talks about linking or fusing, that can be accomplished either with a linker 11:49 AM

or without a linker?

A. Well, you might think that, but I would think that when it says linked or fused with a linker or without a linker, it means linked with a linker or fused without a linker. 11:49 AM

Q. So you're telling me, in your opinion, that fusion can only be accomplished without a linker?

MR. MCTIGUE: Objection to form. 11:50 AM

A. No, I'm telling you what I think a POSA would reasonably understand by reading the specification.

BY MR. HEINTZ:

Q. In March of 2010, if a POSITA was told that he needed to connect the targeting moiety to the polypeptide, and he can do it by fusion or -- that he could do it by fusion, would that person understand that a linker could be used to accomplish the fusion? 11:50 AM

A. It's very difficult. I'm not giving an opinion about what in general terms a POSA would or would not be able to do in March 2010. It's what -- how they would 11:50 AM

understand the instructions that are given in this specification, and that's what I've tried to test out.

Q. And you understand, do you not, that when a POSITA reads this specification he does so with the background knowledge that's available to him. And you think, then, that in paragraph -- sorry, in Column 35, lines 33 to 35 or so, that the specification is defining the word "fusion" to be something exclusively accomplished without a linker. Is that your opinion? 11:50 AM 11:51 AM

MR. MCTIGUE: Objection to form.

A. Well, I don't think the specification -- it's unhelpful that the specification doesn't define those terms, but the plain and ordinary meaning of the specification is, I believe, as I've described to you. 11:51 AM

BY MR. HEINTZ: 11:51 AM

Q. All right. Thank you.

And so you believe that that passage of the specification we just read excludes accomplishing a fusion with a linker, as we cited in Claim 9? 11:51 AM

PGR2026-00025 - JHU
Ex. 2042- Page 100

A. Well, I believe it doesn't describe -- it doesn't -- it doesn't say anything about the linker, does it? So it doesn't include it or exclude it. It just doesn't describe it. It's lacking any description of a linker. 11:51 AM

Q. It says you can link or fuse with a linker or without a linker, doesn't it?

MR. MCTIGUE: Objection to form.

A. But -- sorry, I was talking about the bit about the light chain. So it's -- it's quite clear that linkers are present throughout the specification with regard to the heavy chain, but with regard to the light chain this is the only place that light chain fusions are mentioned in the specifications, so far as I'm aware, and it doesn't talk about linkers there. 11:52 AM

BY MR. HEINTZ:

Q. So if I -- in your opinion, when the specification talks about the heavy chain it mentions fusion that can be accomplished with or without a linker, but for the light chain, when we talk about -- 11:52 AM

A. I -- 11:52 AM

Q. Let me finish my question.

But when we talk -- when the specification talks about the light chain and fusion, there the fusion can only be accomplished without a linker. 11:52 AM

Do I understand your opinion correctly?

A. Well, perhaps you can point me to a place in the specification where it says that fusion is accomplished with a linker in the heavy chain. I don't know about that. 11:52 AM

Q. Well, whether or not I can point you to that place, I think I already have, but you disagree, I understand.

I just want your opinion. So when the patent talks fusion in the context of a heavy chain, can that be accomplished both with and without a linker? 11:53 AM

A. Well, not according to this paragraph. The problem is that the patent has all sorts of language. 11:53 AM

You may be able to point me to some other bit that says something different. I don't know, but this bit that we're looking at here, as I said, it seems to be that it 11:53 AM

uses the language linked when there's a linker, fusion when they're directly joined.

Q. Okay. So I'm going to ask my question again, and let's see if we can get an answer this time. 11:53 AM

Would a POSITA reading this specification understand that when the specification talks about fusing in the context of a heavy chain, that fusion must happen without a linker? Yes or no? 11:53 AM

A. I don't know.

Q. You don't know. Okay.

Same question for the light chain. Would a POSITA reading this specification understand in the context of fusion in a 11:54 AM light chain that any fusion must happen without a linker?

A. Yes.

Q. And that's on the basis of the portions of Column 35 we've been discussing? 11:54 AM

A. Yes.

Q. Okay.

MR. HEINTZ: I've lost track of time. Are we scheduled for a break now?

MR. MCTIGUE: I don't know when 11:54 AM

lunch was going to happen, but yeah, I think it's --

MR. HEINTZ: Why don't we go off the record, and we'll break for lunch.

(Recess taken at 11:54 a.m. to 12:42 p.m.) 12:42 PM

BY MR. HEINTZ:

Q. So welcome back, Dr. Hale.

A. Thank you.

Q. During the break, did you discuss the substance of this deposition with anybody? 12:42 PM

A. No.

Q. All right. So I'm going to go back just briefly to something you said earlier today. 12:42 PM

You had mentioned that there was a difference on your mind with respect to a POSITA for claims that are about molecules that are unusual and/or exceptional.

Do you remember that testimony? 12:42 PM

A. I think so.

Q. Okay. What is it about the molecules of Claim 1 and 9 that make them unusual and/or exceptional?

A. I think one of the features that 12:42 PM

makes things unusual and exceptional is the thing that you got a complete light chain and just the variable portion of the heavy chain. So it's a kind of fragment which I'm not aware has been in the -- described in the literature before or since. 12:43 PM

And so I think a POSITA would not quite know what to expect with a fragment like that, how to make it, whether it could be made. Because the problem with it is that it's got a light chain constant region that doesn't have a partner. Normally the light chain constant region would be -- have a partner in the heavy chain. 12:43 PM

Q. Okay. The claim says compromising, right? 12:43 PM

A. It does.

Q. So the claims don't exclude there be a partner to the light chain constant region and the heavy chain, right? 12:43 PM

A. That's right. But, of course, you know, they do include this species I just described.

Q. Yep. Fair enough. Okay.

So I'd like to direct your 12:44 PM

attention back to the Column 35 of the '968 patent that we were discussing before.

So on line 30 -- I guess it's 33. It says, "In one embodiment, a targeting moiety compromising an antibody, antibody fragment or polypeptide is linked or fused to an immunomodulatory moiety consisting of a polypeptide, with a linker or without a linker," correct? 12:44 PM

A. Correct. 12:44 PM

Q. So the phrase "with or without a linker," what word or words in this sentence does that phrase modify?

A. You're asking me a question about English language? 12:45 PM

Q. I am. And, in particular, how one of skill in the art would understand this passage.

A. Yeah. Well, I think I said earlier you might interpret it one way. You might interpret it another way. The way I would interpret it is that it's linked with a linker. It seems the linker is a thing for linking or it's fused without a linker. That's what I -- that's the way I would read 12:45 PM

that.

Q. Are you familiar with a Rule of Ramon known as the doctrine of last antecedent?

MR. MCTIGUE: Objection to form. 12:45 PM

A. No.

BY MR. HEINTZ:

Q. Okay. So that grammatical concept says that when you have a phrase like with a linker or without a linker, it modifies the 12:46 PM word that immediately precedes it.

Now, here it's fused to an immunomodulatory moiety consisting of a polypeptide, right, but the with or without a linker -- sorry -- with a linker or without a 12:46 PM linker is modifying at least the word "fused," correct?

A. So are you referring to -- is this like -- is this concept I hadn't heard of, is that a legal concept or a concept in patent 12:46 PM law?

Q. It's a legal concept not limited to patent law. It's also implied in discussing general --

A. Okay. 12:46 PM

PGR2026-00025 - JHU
Ex. 2042- Page 107

Q. -- grammatical --

A. Yeah. Well, if it's a legal matter, I can't really give you any more than opinion on that than I've already given you. It's probably something to ask the lawyers. 12:46 PM

Q. Okay. See if I can find one and ask them.

Let me ask you this: Is it possible to link something without a linker? 12:47 PM

A. I wouldn't have thought so. I mean the word "links" implies a linker.

Q. So saying linked with a linker or without a linker makes no sense then; is that right? 12:47 PM

A. Well, exactly. That's why I think it's linked with a linker or fused without a linker.

Q. Well, saying linked with a linker would just be redundant, wouldn't it? 12:47 PM

A. Well, there's a lot of redundancies in this specification, I think.

Q. In this instance, saying linked with a linker would just be redundant, wouldn't it? 12:47 PM

A. It's quite possible.

Q. Yeah. So wouldn't the understanding of a person of ordinary skill in the art be that you can accomplish fusion without or without a linker? 12:47 PM

MR. MCTIGUE: Objection to form.

A. Well, I think I've answered that already. You know, I said -- looking at this sentence, I think that fusion is something that you do without a linker. You might have a different view. And as I say, that's probably a legal matter. 12:48 PM

BY MR. HEINTZ:

Q. What's your understanding of the definition of fusion in this context? 12:48 PM

MR. MCTIGUE: Objection to form.

A. I'm not sure that there's a definition of fusion here in this context. It's not a word that's been described. But the plain and ordinary meaning of the word seems to me that the two things are directly joined together. 12:48 PM

BY MR. HEINTZ:

Q. And you believe that's the plain and ordinary meaning of fusion in the art; is 12:48 PM

that correct?

MR. MCTIGUE: Objection to form.

A. I think we're talking about the context of this particular passage.

BY MR. HEINTZ: 12:49 PM

Q. Well, let's talk about outside this patent.

So putting aside this patent, if you said fusion to one of skill in the art, and, in particular, if you talked about a 12:49 PM targeting moiety being fused to a polypeptide, what would one of skill in the art understand that to mean?

MR. MCTIGUE: Objection to form.

A. You're asking me about something 12:49 PM which I've not been asked to give an opinion on, and I haven't done the research on that.

And, you know, if I were to attempt to answer that question, it would need going into literature and seeing 12:49 PM what's -- have the words they used in different context and so on and so forth, and I can't, sitting here today, give an answer to that.

BY MR. HEINTZ: 12:49 PM

PGR2026-00025 - JHU
Ex. 2042- Page 110

Q. And you don't have such an opinion in your declaration, correct?

MR. MCTIGUE: Objection to form.

A. I don't believe so.

BY MR. HEINTZ: 12:49 PM

Q. All right. I want to direct your attention to Figure 3 of the '968 patent.

In particular, I'll refer you to the Sequence ID No. 2 of Figure 3. Okay?

A. Okay. 12:50 PM

Q. All right. In Sequence ID No. 2, we discussed this earlier, but there is an underlying portion, a plain text portion, then an italicized portion and a bolded portion, correct? 12:50 PM

A. Correct.

Q. Okay. So I just want to refer you some numbers to refer to these various portions.

Now, we've established earlier, 12:50 PM you've taken my word for it, that the underlined portion is SEQ ID 1 to 119, correct?

A. Correct.

Q. I want to come up with some 12:51 PM

nomenclature to refer to the portion of Sequence ID No. 2 that includes the underlined portion and the plain text portion right up to the linker. I haven't counted the numbers, so I can't tell you it's one -- I have a vague sense that it might be 440. I don't know the number off the top of my head. But I want to pick some term we can use to designate the entire underlined portion and the entire plain text portion of Sequence ID No. 2? 12:51 PM

A. Okay. Is there not such a term anywhere in the specification.

Q. I don't know off the top of my head. But I'm just going to propose that we say it's 400, just for the sake of reference. 12:51 PM

A. Okay.

Q. I'm not representing to you that's the accurate number. I haven't done the counting. But we'll just say 1 to 400 -- that's that we mean when we say 1 to 400 is the entire underlined portion and the entire plain text portion right up before the linker in Sequence ID No. 2. Okay? 12:51 PM

A. Okay. Okay. Yeah. 12:52 PM

Q. And if you know the answer, I'm happy to use the exact number. It doesn't matter for the series of questions I'm going to ask you.

A. Okay. 12:52 PM

Q. Now, I'd like you to turn to Claim 9.

A. Okay.

Q. Okay. So you've given an opinion that Claim 9 is invalid for lack of written description, correct? 12:52 PM

A. Correct.

Q. Okay. Now, I understand that you believe that there is no disclosure in the specification of having the TGFbetaRII connected to the light chain using a linker. 12:53 PM

Do I understand that correctly?

A. Correct.

Q. Okay. So that's one reason that Claim 9 is invalid for lack of written description according to you. 12:53 PM

Is there any other reason that Claim 9 is invalid for lack of written description?

MR. MCTIGUE: Objection to form. 12:53 PM

A. Yeah, I think I've set that out in my report.

BY MR. HEINTZ:

Q. And is that the issue about just the variable region of the heavy chain and the entire light chain as specified in Claim 9? 12:53 PM

A. That's one of the reason, yes.

Q. Okay.

A. I think -- well, it's all there. Can I just check? 12:53 PM

Q. Yeah, sure.

A. Yeah. So my reports, page 60, paragraph 127 onwards, I think right through until paragraph 134. 12:54 PM

That sets out my opinions regarding the lack of written disclosure in Claim 9.

Q. Okay. So I want to get to the bottom of some of this stuff and in particular something you mentioned earlier today about the word "compromising." 12:54 PM

A. Uh-huh.

Q. So I want you to think about Claim 9, and if Claim 9 were to recite 1 to 12:54 PM

400 of Sequence ID 2, where 400 means the part of Sequence ID 2 right up until the linker -- right before the linker, right?

A. Uh-huh.

Q. Would Claim 9 be invalid for any other reason than the first reason we mentioned, which is the lack of disclosure of the TGFbetaRII being fused to the light chain via the linker? 12:55 PM

MR. MCTIGUE: Objection to form. 12:55 PM

BY MR. HEINTZ:

Q. So putting aside that issue, okay, and assuming that Claim 9 said 1 to 400, would there be any other reason that Claim 9 in that form is invalid? 12:55 PM

A. Well, I don't think sitting here I can give you a definitive answer to that question because that's not a question I've been asked to consider. I wasn't asked to consider, you know, hypothetical claims, which are not the same as the claims in the patent. 12:56 PM

You know, when I consider whether a claim is supported by written description, then a lot of work goes into that analysis. 12:56 PM

And so to answer your question would require a lot more work which I haven't been asked to do.

So maybe I'll be asked to do it in the future. So I reserve the right to give a fuller answer in that case. 12:56 PM

But, as I sit here, I can't give you a complete answer.

Q. Okay. Earlier today in discussing written description, you mentioned the fact that Claim 9 includes the word "compromising" in the preamble? 12:56 PM

A. I believe I did. I might have said that about Claim 1, but perhaps I said it about Claim 9. 12:56 PM

Q. Okay. Nonetheless, Claim 9 does --

THE COURT REPORTER: Hold on.

Nonetheless, doesn't?

BY MR. HEINTZ: 12:56 PM

Q. It does include the word "compromising" in the preamble?

A. Yes, it does.

Q. So that would mean, for example, that Claim 9, in the form we're discussing in 12:57 PM

the hypothetical that recites 1 to 40 -- I'm sorry -- 1 to 400 of Sequence ID No. 2, could include other things that are attached. For example, at the end of the heavy chain and that attachment could be via a linker or it could be fused directly without a linker, right, all those things would be within the scope of Claim 9 in the hypothetical that we're talking about where it recites 1 to 400, right? 12:57 PM

MR. MCTIGUE: Objection to form.

A. So in your hypotheticals, if you still got the word "compromised," then it could include all sorts of other things, just as it does at the moment. 12:57 PM

BY MR. HEINTZ:

Q. Right. Does that make the Claim invalid?

MR. MCTIGUE: Objection to form.

BY MR. HEINTZ: 12:57 PM

Q. For lack of written description.

A. Sorry. The fact that it includes all sorts of other things?

Q. That it could, yes, due to the word "compromising." 12:58 PM

A. I see.

You know, the word "compromised" per se doesn't necessarily make it invalid. But the question is, regarding written description, has the inventor got possession of the full scope of the invention. So that's the question the POSA has to try to determine by looking at the four corners of the specification. 12:58 PM

And, you know, when the inventor using the word "compromising," and that could compromise almost an unlimited number of things, it certainly makes it more difficult for the POSA to appreciate that they're in possession of that full scope. 12:58 PM

Q. Yeah. And it's not almost a unlimited number, it is, in fact, unlimited, correct?

MR. MCTIGUE: Objection.

A. Well, it's uncountable anyway. 12:58 PM

BY MR. HEINTZ:

Q. I'm sorry?

A. It's uncountable anyway.

Q. Uncountable. All right.

So regardless of whether Claim 1 12:58 PM

says 1 to 119 or 1 to 400, in either case there are an uncountable number of additional things that could be added to what's in Claim 9 and that would make the claim invalid in either case, wouldn't it? 12:59 PM

MR. MCTIGUE: Objection to form.

A. Well, I'll take your word for it, yes.

BY MR. HEINTZ:

Q. Well, I'm asking your opinion. 12:59 PM

A. My opinion, whether -- well, whether uncountable things makes it invalid?

Q. Yes. Whether the fact that Claim 9 includes the word "compromising," and therefore includes an uncountable number of 12:59 PM things that could be attached to whatever part of a heavy chain is in the claim, doesn't that, in your opinion, mean that Claim 9 is invalid for lack of written description? 12:59 PM

MR. MCTIGUE: Objection to form.

A. It not quite what I said, I don't think.

I said -- the question is whether the POSA can appreciate that the inventor is 12:59 PM

in possession of the full scope of the invention, and so it makes it more difficult for the POSA to appreciate that if there is a vast range, if there's a -- if the invention is very broad in its scope, like it is here, it doesn't necessarily mean that it's because the number is uncountable per se, that that makes it invalid. It's the fact that it's the lack of description of the scope of the invention that makes it invalid. 01:00 PM

BY MR. HEINTZ:

Q. So there is no description anywhere in this patent, the '968 patent, of any of the myriad of things that could be attached at the end of a heavy chain if the TGFbetaRII is attached to the light chain. 01:00 PM

Would you agree with that?

MR. MCTIGUE: Objection to form.

A. That's very hard to tell, because the specification, you know, includes so many possible things, including, for example, bispecific antibodies. So it's really hard to tell from the specification, which has got this vast number of different possibilities as to what is there and what is not there. 01:00 PM 01:01 PM

PGR2026-00025 - JHU
Ex. 2042- Page 120

The problem is for the POSA that it seems like the inventor has just picked a few little bits here and there from this huge menu that's provided in this specification.

So I think the question is practically impossible to answer. 01:01 PM

BY MR. HEINTZ:

Q. Okay. One of the passages that you identified in your opinion as to why the '968 is invalid for lack of written description. 01:01 PM

Did you say it starts at paragraph 127; is that right?

A. Yes. It starts at 127 with regard to Claim 9. I think if you want to go back to the beginning -- it's earlier than that. Excuse me. 01:01 PM

So the lack of written description section starts -- Section 8 is paragraph 113.

Q. Okay. Let's talk specifically not claim -- 01:02 PM

MR. MCTIGUE: To clarify, it's Section 7.

THE WITNESS: Oh, I'm sorry. I'm not counting Roman numbers. 01:02 PM

BY MR. HEINTZ:

Q. I want to talk particularly about why Claim 9 is invalid for lack of written description.

So can you point me to where you identify the particular reasons why Claim 9 is invalid for lack of written description? 01:02 PM

MR. MCTIGUE: Objection to form.

A. Well, there's different reasons. In page 55, paragraph 117, that describes the problem with the targeting moiety limitation, and that problem with lack of description applies to both Claim 1 and Claim 9, and, of course, to all the subsequent claims as a consequence, the dependent claims. 01:02 PM 01:03 PM

BY MR. HEINTZ:

Q. Now that problem wouldn't exist if Claim 1 were modified to say 1 through 400, correct?

MR. MCTIGUE: Objection to form. 01:03 PM

A. I've not analyzed that hypothetical.

BY MR. HEINTZ:

Q. But that particular problem, you're saying, is the reason it's invalid is 01:03 PM

because you've claimed just the heavy chain variable region plus the entire light chain.

If we have the 1 through 400, now we've claimed the entire heavy chain as well as the entire light chain; so clearly, what you're describing in 117 would not be an invalidity problem for Claim 9 modified in that way, correct? 01:04 PM

MR. MCTIGUE: Objection to form.

A. Well, as you say, that might appear to be correct, but I haven't analyzed that in detail. 01:04 PM

BY MR. HEINTZ:

Q. Okay. So we've got one reason why Claim 9 is invalid. That's the -- we'll call it the mismatch in the targeting moiety for shorthand. All right? 01:04 PM

A. Okay.

Q. Is there any other reason why Claim 9 is invalid, for lack of written description, in your opinion? 01:04 PM

A. Well, we talk in paragraph 147 onwards about the lack of disclosure, the lack of the blaze marks to the whole -- the integrated whole of Claim 9. 01:05 PM

Q. Help me understand that.

A. Okay. So that's --

Q. So what do you mean by "lack of blaze marks" in connection with Claim 9?

A. So that's the lack of any direction -- as I understand it, the specification has a vast number of difference aspects to it. Some of those aspects involve targeting moieties. Some involve immunomodulatory moieties, some involve linkers. They might be connected together in many different ways. 01:05 PM 01:06 PM

What's happened, in my view in the claims of this patent, is that little bits have been picked from here and there throughout the specification and put together to make these new claims, which didn't appear anywhere before. 01:06 PM

And, as I understand, if that is done, it needs something to point the POSA towards an understanding that a particular combination is preferred or desirable or is going to be claimed. And I've heard the language "blaze marks" used to describe how they could be identified. 01:06 PM 01:07 PM

In my experience, I've usually seen in patent that I reviewed before the term "preferred" being used. So somebody would say in a preferred aspect, such and such. And that seems to me to point the POSA towards the particular combination which the inventor is going to claim.

I don't see anything like that here. This is just a sort of -- I've called it a concoction, if you like, little bits and pieces put together. There's no blaze marks. There's nothing to point the POSA towards this particular combination.

Does that make sense? 01:07 PM

Q. Not entirely.

You say there's nothing to point the POSITA to the particular combination. And by that combination you're referring to what you've depicted in the figure at the top of page 68 of Exhibit 1003? 01:08 PM

A. Yes.

Q. Okay. And so the issue here is that each of the things depicted in the Figure 1 that you've drawn on page 68 is present in Figure 3, and is formatted in 01:08 PM

Figure 3 with something other than plain text. That's true for the variable region heavy chain, the light region -- I'm sorry. Let me rephrase. Let me start again.

Everything that you've shown in your Figure 1 on page 68 is in Figure 3 of the '968 patent, right? 01:08 PM

MR. MCTIGUE: Objection to form.

A. So not quite everything. Just for clarity, I think I've identified the TGFbetaRII as being Sequence ID No. 87, I don't think that comes in Figure 3 anywhere. I've identified the linker as being Sequence ID No. 104. I don't think that identification comes in Figure 3. I've labeled the domains VH, VL, CL, that doesn't explicitly come in Figure 3. The way I constructed that figure was based on claim, Claim 9, the things that are claimed there. 01:09 PM

BY MR. HEINTZ: 01:10 PM

Q. Okay. I apologize.

I think you told me earlier today you've seen a number of patents in the fusion protein art; is that correct?

A. I don't remember saying that. 01:11 PM

Q. Have you seen a number of patents in the fusion protein art?

A. I think I said I've seen quite a lot of patents, and it's quite possible or likely that some of them will be in the fusion protein arts, but I can't remember the details apart from the ones I've looked at in this case. 01:12 PM

Q. Do you have an understanding as to whether it's common in the fusion protein art to claim fusion protein molecules by specifying only the variable regions of the heavy and light chains? 01:12 PM

MR. MCTIGUE: Objection to form.

A. I don't know. 01:12 PM

MR. HEINTZ: I'm going to mark as Exhibit 2032 -- excuse me -- 2036, U.S. Patent No. 11,939,387.

THE WITNESS: Can I just tidy up these for a minute? 01:12 PM

MR. HEINTZ: Yep.

THE WITNESS: I could deal with a bigger table if you're going to give me a lot more stuff.

/ 01:13 PM

PGR2026-00025 - JHU
Ex. 2042- Page 127

(Exhibit 2036, United States Patent No. 11,939,387, marked for identification.)

BY MR. HEINTZ:

Q. Okay. I assume the answer is no. But have you seen the patent before, Dr. Hale? 01:13 PM

A. No, I don't think so.

Q. Okay. I'll ask you to turn to the last page of Exhibit 2036, which is Column 79. 01:13 PM

All right. And I'd like you to look at Claim 1, and go ahead and read it to yourself and let me know when you're done.

A. Okay.

Q. All right. So you see in the Claim HCDR1 sequence and similarly HCDR2 and HCDR3 sequence. 01:15 PM

Do you see that?

A. Yes.

Q. Do you know generally what those acronyms refer to? I'm not asking for the particular proteins, just generally, what's a CDR? 01:15 PM

A. I mean, generally, I've seen those CDR is -- refers to 01:15 PM

PGR2026-00025 - JHU
Ex. 2042- Page 128

complementarity-determining regions. I don't know what -- perhaps H refers to heavy chain maybe in this context.

Q. Yes.

A. That's my guess. I've obviously not had any time to review or analyze the whole of this passage, you understand. 01:16 PM

Q. Sure. And I'll represent to you that's my understanding too, the H stands for heavy, and the L stands for light. 01:16 PM

A. Okay.

Q. And the CDR has its normal meaning, and then 1, 2, 3 just depict particular ones. Okay?

A. Okay. 01:16 PM

Q. And you would agree, would you not, that the CDRs in one of these molecules are all in the variable regions of the heavy and light chains?

A. As I've said, I've not analyzed in this detail but usually that would be the case. 01:16 PM

Q. I'm sorry. Generally, when you talk --

A. Generally, when -- 01:16 PM

Q. -- about the CDRs, they're the variable regions of heavy or light chains, correct?

A. Yes.

Q. Okay. So this claim specifies that we've got, in particular, an antibody that includes three heavy chain CDRs and three light chain CDRs, and all of those are in the variable regions of the heavy or light chains. Fair enough? 01:16 PM 01:17 PM

A. I'm prepared to accept that.

Q. Okay. There is nothing in Claim 1 that specifies what the heavy chains or the light chain constant regions are.

Would you agree with that based on your reading of Claim 1? 01:17 PM

A. Based on my reading of it right now, yes.

Q. Okay. So, for example, this claim 1 would include, and I'm going to refer you to paragraph 68 of your declaration -- I'm sorry -- page 68 of your declaration, Figure 1. 01:17 PM

MR. MCTIGUE: I think it's Figure I for 68. 01:17 PM

MR. HEINTZ: I apologize. Figure I on page 68.

THE WITNESS: Uh-huh.

BY MR. HEINTZ:

Q. Okay. So Claim 1 is to an antibody, and the heavy chain and light chain constant regions are not specified in Claim 1, correct? 01:18 PM

MR. MCTIGUE: Objection to form, outside the scope.

A. I'm sorry, Claim 1 of what? Claim 1 of --

BY MR. HEINTZ:

Q. The '387 patent.

A. This patent -- this new '387 patent? 01:18 PM

Q. Correct, Exhibit 2036.

A. And you said that the claim is to an antibody?

Q. Yes. 01:18 PM

A. And what is not specified?

Q. The heavy or light chain constant regions.

MR. MCTIGUE: Same objection.

A. Indeed. So far as I can see from 01:18 PM

what I'm looking at, just Claim 1, that seems to be the case.

BY MR. HEINTZ:

Q. Is there an infinite number of possible heavy chain and light chain constant regions that could be included within the scope of Claim 1? 01:19 PM

MR. MCTIGUE: Objection to form, outside the scope.

A. I don't know. 01:19 PM

BY MR. HEINTZ:

Q. Okay. Is there an uncountable number of heavy chains and light chains, constant regions, that could be within the scope of Claim 1? 01:19 PM

MR. MCTIGUE: Same objections.

A. Again, I wouldn't be able to count them, so at least uncountable for me.

BY MR. HEINTZ:

Q. Okay. Given that there are an uncountable number of heavy and light chain constant regions that could be within the scope of Claim 1, does that render Claim 1 invalid for lack of written description and/or enablement, in your opinion? 01:19 PM 01:20 PM

MR. MCTIGUE: Objection, outside the scope. And just for clarity, you're referring to Claim 1 of the '387 patent?

MR. HEINTZ: I am.

A. I can't answer that because, you know, I haven't analyzed this '387 patent for validity. I don't know whether it is valid or not valid and, you know, I just don't know. 01:20 PM

BY MR. HEINTZ: 01:20 PM

Q. So I'll represent to you that there is a disclosure of what -- an example of a heavy chain for both -- sorry.

I'll represent to you that there is an example of a constant region of the heavy chain and a constant region of the light chain given in the specification in this patent. I'll also represent to you that there is nothing in this patent that limits the claimed invention to either -- to any example of either the heavy chain or light chain constant regions. 01:20 PM

A. Uh-huh.

Q. Now that you have this information, knowing that there's nothing in 01:21 PM

the patent that limits the scope of claims to any particular constant region for either the heavy or the light chain, that there's only one example of the constant region for both chains given, is the claim invalid for lack of written description or lack of enablement?

MR. MCTIGUE: Objection to form, outside the scope.

A. Yeah. I mean, ultimately this decision as whether it's valid or invalid is a legal, you know, conclusion, and I've not been asked to make any legal conclusions based on this patent '387. So I really can't answer the question.

It seems to me that it's not invalid based on your representations, but it's not something that I'm giving an opinion on today. 01:21 PM

BY MR. HEINTZ:

Q. So you say it's not invalid based on my representations. Why do you say that? 01:21 PM

MR. MCTIGUE: Objection to form, scope.

A. Well, because you represented so, yeah. 01:22 PM

BY MR. HEINTZ:

Q. I represented nothing about whether it's valid or invalid or written description.

What I've told you is that the claim doesn't limit the constant region of the heavy chain or constant region of the light chain in any way. You've agreed with that. 01:22 PM

A. Uh-huh. 01:22 PM

Q. I've told you there's an example of a constant region of a heavy chain and an example of a constant of a light chain given in the specification but just one example. There's nothing in the specification that limits, in any way, what the heavy or light chain constant regions can be. It doesn't limit it to that example. It doesn't include anything, right? 01:22 PM

A. Uh-huh. 01:22 PM

Q. And my question is, given that information, is the claim invalid for lack of written description or indefiniteness --

A. Yeah.

Q. Sorry. Written description or 01:22 PM

enablement in your opinion? You told me yes, and I want to understand why you think that's the case.

MR. MCTIGUE: Same objections. Mischaracterizes testimony. 01:23 PM

BY MR. HEINTZ:

Q. You told me no, and I want to understand why the answer is no.

A. I think you've got me really confused. Sorry. 01:23 PM

Q. It's a simple hypothetical. Right?

A. Yeah, it's really confusing.

Perhaps you can explain to me where you're going in connection with the 01:23 PM case that we're talking about, because it seems to me this is a very different case.

Q. Well, I'm trying to find out if one of your agreements here is that because the heavy chain is not specified -- the 01:23 PM constant region in the heavy chain is not specified and there are an uncountable number of possibilities that the heavy chain can be, whether there's lack of written description or enablement. 01:23 PM

MR. MCTIGUE: Objection to form.

A. I think -- part of my confusion is that you're mixing the two things together, the written description and enablement. So the problem with enablement is that the patent -- the specification needs to enable the POSA to make the full scope of the invention which could include numerous different things. 01:23 PM

And the problem with this particular passage, to my mind in regards to enablement, it doesn't enable the POSA to make any form of the molecules according to Claim 9. It doesn't describe any of them or how to make them. 01:24 PM

With regard to written description, then the problem is for the POSA to understand whether the inventor was in possession of the full scope of that invention. And, again, it seems to me that because of the concoction of different little bits, a little bit from here, a little bit from here, Figure 3 seems to be cut and spliced in lots of different ways, which were never described in the specification, so the 01:24 PM

PGR2026-00025 - JHU
Ex. 2042- Page 137

problem then is that there's no description of molecules corresponding to Claim 9 in the specification.

BY MR. HEINTZ:

Q. Yeah, we're not talking about Claim 9 or Figure 3 of the '968 patent now. We're talking about Exhibit 2036, the '387 patent. 01:25 PM

So my question to you again, okay, the '387 patent discloses one example of a constant portion of a heavy chain, one example of a constant portion of a light chain; it includes no discussion that would limit the scope of Claim 1 of the '387 patent to those examples of the heavy and light chain constant regions. 01:25 PM

In light of that, is Claim 1 of the '387 patent invalid for lack of written description?

MR. MCTIGUE: Objection to form, scope. 01:26 PM

A. Yeah, I think -- honestly, I've answered that question to the best of my ability. I've not analyzed this new patent. I've not been asked to look at it, and I 01:26 PM

PGR2026-00025 - JHU
Ex. 2042- Page 138

haven't really got any more to add to the answers I've already given.

BY MR. HEINTZ:

Q. Okay. So you can't tell me whether something -- a specification that includes one example of a heavy chain constant region and one example of a light chain constant region but nothing further that limits it in any way to those examples, you can't tell me whether that renders the claim invalid for lack of written description? 01:26 PM

MR. MCTIGUE: Same objections, asked and answered.

A. I've got nothing extra to add. 01:26 PM

BY MR. HEINTZ:

Q. Okay. And then your answer would be the same for enablement; is that correct?

MR. MCTIGUE: Same objections.

A. Yeah, I've got nothing extra to add. 01:26 PM

BY MR. HEINTZ:

Q. So even though there are an uncountable number of heavy chains, constant regions that could be used and an uncountable 01:27 PM

number of light chain constant regions that could be used, you can't say whether the claim would be invalid for lack of enablement?

MR. MCTIGUE: Same objections. 01:27 PM

A. I can't say, because in different situations the conclusion may be different.

BY MR. HEINTZ:

Q. I'm going to ask you to turn to paragraph 62 of your declaration and that 01:27 PM starts on page 25.

A. Okay.

Q. We talked about this earlier.

Do you recall?

A. We did. 01:28 PM

Q. Okay. All right.

Now, I want to turn to paragraph 172 of your declaration. That's on page 80 or starts on page 80.

MR. MCTIGUE: Do you want to have 01:28 PM him keep the paragraphs side by side.

MR. HEINTZ: No. We can --

BY MR. HEINTZ:

Q. And you can take your time and read it. But my first question will be, this 01:29 PM

is that 9-step research plan you talked about earlier, correct?

A. Correct.

Q. If you want to read it further, that's fine. But I'm not going to start asking you questions about particular parts of it. So when you're ready for me to continue, let me know. 01:29 PM

A. Okay.

Q. All right. So in Step (A), that's on page 80, you talk about deciding whether to express the three polypeptide chains separately or from the same cell, correct? 01:30 PM

A. Yes, that's correct.

And just before we go further, can I just say there is nothing in the specification, so far as I'm aware, that sets out any of these steps. 01:30 PM

Q. Okay. Wasn't that standard recombinant protein design work by 2010, making that decision? 01:30 PM

MR. MCTIGUE: Objection to form.

A. No.

BY MR. HEINTZ:

Q. What was standard in 2010 for 01:30 PM

recombinant protein design?

A. Lots of things were standard.

Q. With respect to expression separately or from the same cell, which was the standard? 01:30 PM

A. Well, in this particular case, I'm just talking here about Claim 1. So I'm not trying to discuss the standard ways of making recombinant polypeptides in general. I'm trying my best to scope out what might be a 01:31 PM plan for preparing and testing molecules which fall within the scope of that claim.

And the first thing is deciding whether these three polypeptide chains should be expressed separately or from the same 01:31 PM thing. Well, that depends upon the exact structure of the molecule that you want to make.

And the problem is that, as I've set out I think a few pages earlier, there's 01:31 PM a plethora of different formats, some of which have got linkers joining different parts together, some of which are noncovalently linked, some of which are linked by a chemical linker. 01:32 PM

And so depending upon the particular format which is going to be made and to make the full scope of the claim, you have to make many different formats. Sometimes you might be able to express them in the same cell. Sometimes you might need to express them in separate cells. It's difficult to tell.

Q. And would a POSITA know for any particular case whether to express them from the same cell or different cells? 01:32 PM

A. I think they would be uncertain.

Q. Are there any cases for which a POSITA would be certain as to what to do?

A. I suppose in the case where all three polypeptide chains were linked together with linkers so that you only had one polypeptide chain, that might be a case where they would say -- they would be expressed from the same cell because they would be one molecule. That might be a case. 01:32 PM 01:33 PM

Q. Would the same be true if they were fused together as you understand fusion?

A. It might be the case.

But, as I say, there is 01:33 PM

uncertainty about the immunomodulatory moiety, TGF beta being linked to this maybe light chain, maybe heavy chain. We don't know in the case of Claim 1.

Q. If it's linked to the heavy chain, do we know whether it's going to be from the same cell or separate cells? 01:33 PM

A. Well, the problem there is we don't know whether a given cell is going to be suitable for the production of both molecules. So if they're linked together, some cells might be able to make that fusion protein but other cells might not. It would depend upon the particular cell and the properties of those moieties that are being linked. 01:33 PM 01:34 PM

Q. Is that going to change depending on where the TGF beta is linked, whether to the light chain or the heave chain; it's still all one molecule, is it? 01:34 PM

A. It could change; it could change, yep. Yeah, might do. It's just uncertain, because there isn't any guidance. That's the problem. If one of these molecules had been made and described in an example, that's what 01:34 PM

I'd usually expect to see in a patent, then it would be all be straightforward.

Q. You would expect the patent to tell you whether for this molecule it's going to be expressed from the same cell or from a different cell, that's the kind of detail that's necessary in a patent disclosure in order to -- 01:34 PM

A. It's the kind of detail, yeah.

MR. MCTIGUE: Objection for form. 01:34 PM

A. Lots of detail.

BY MR. HEINTZ:

Q. Okay. Great.

Let's go to Step (B), which starts on the bottom of page 80 and goes on to page 81. 01:35 PM

There you say selecting an expression vector and host cell while considering secretion, glycoslation cites on usage and related factors. 01:35 PM

Wasn't that standard protein engineering work done by 2010, meaning wasn't that the kind of thing that a person who is practicing standard -- sorry -- protein 01:35 PM

engineering would do in 2010?

A. It's the kind of thing, but it's not spelled out.

And so there's two sort of problems for the POSA here. One is this molecule or this large family of molecules presumably have never been made before, they cannot be described, at least in this patent, and I've not evaluated whether there's a presence for these molecules in the literature, but I'm assuming there isn't, otherwise the patent would have been invalidated for lack of novelty. 01:35 PM 01:36 PM

So the POSA doesn't know which cells and which methods would be particularly suitable for this particular construct of all the many different methods that there might be and all the different cell lines that there might be available in the prior arts. They would have to choose one, and they wouldn't have certainty that it would work. 01:36 PM 01:36 PM

Q. Would they have a good idea of which ones would work, whether or not they were certain they would?

A. They might have some that they 01:36 PM

would prefer. But, you know, it's not necessarily clear. I mentioned glycosylation. Glycosylation is a post-translational modification of proteins, which is particularly important for their structure and function.

And in the case of the molecule depicted in Figure 3, there are numerous glycosylation sites. So, in particular, I think I described in my reports, there are at least two glycosylation sites in the TFG beta component, possibly there are more. And also there's a glycosylation site in the variable domain of the heavy chain and that's quite unusual. 01:37 PM 01:37 PM 01:38 PM

And so the POSA would not know what would be the consequence of trying to express a molecule with that combination of polypeptides being made in one protein, with different glycosylation cites possibly requiring different glycosylation machinery to ensure that they're expressed in a functional form. 01:38 PM

Q. Let's take a look at Step (C).

There you refer to designing the 01:38 PM

PGR2026-00025 - JHU
Ex. 2042- Page 147

vector with a promoter and enhancer, single peptide and related expression elements.

Wasn't that recombinant design work that was done on a daily basis by those of skill in the art in 2010? 01:39 PM

A. Well, as I say there, those elements are quite conventional. Those are elements that all of those individually would be known in the art, but there's many possible options. 01:39 PM

And my experience, you know, working in the laboratory where the molecular biology was being used for the expression of fusion proteins, antibodies, and so on, was that the particular choice of which vector or promoter or enhancer or other elements, which one was actually used would have an impact on the outcome. And that choice is, you know, a difficult high-level thing which a person of ordinary skill would find difficult. 01:39 PM 01:40 PM

Q. Would it be capable of making the decision?

A. He might make the wrong decision.

Q. He might have to try again?

A. And then he'd have to try again. 01:40 PM

And so this is where the amount of experimentation for a person of ordinary skill become undue, because there's always different steps. Each of them might involve choices among options which are perhaps conventional or well known in the art; but for each single step, there's a lot of choices to be made, and a single misstep, making the wrong choice could result in a failure and then having to go back. 01:40 PM

This is something we've experienced in my lab in the days very frequently. A little -- a mistake would be made, and then it would mean that you have to go back to square one and start over again. 01:40 PM

And so the effort is extraordinary, and sometimes would take many, many years.

I remember an example of an antibody that we were working on, it was very difficult to express, and we didn't know why. 01:41 PM

And it took us I think 10 or 15 years before we understood the reason. And you would have thought that it was just a straightforward antibody. It was just made from conventional, what we thought at the time was 01:41 PM

conventional technology, yet that particular antibody was very difficult.

Q. You yourself have not attempted to carry out your 9-step plan for any molecule within the scopes of claims 1 or 9 of the '968, correct? 01:41 PM

A. Correct.

Q. Are you aware of any person of ordinary skill in the art who attempted that research plan for Claim 1 or Claim 9 and failed? 01:41 PM

A. No. I'm not aware of anybody who succeeded either.

Q. You say you offer this plan in the absence of any guidance or working examples, correct? That's the paragraph 17 -- 01:41 PM

A. I said there's no guidance or working examples that I'm aware of in the specification.

Q. The specification does supply the amino acid sequences, though, correct? 01:42 PM

MR. MCTIGUE: Objection to form.

A. Which sequence are you referring to?

BY MR. HEINTZ: 01:42 PM

Q. Sequence ID 2, Sequence ID 104, Sequence ID 87, Sequence ID 71.

A. So those sequences are in the specification indeed. But, of course, to make this molecule you have to cut and splice different -- little bits of those sequence, and there's no guidance on that. 01:42 PM

Q. And the specification includes Figure 3, correct?

A. Correct. 01:42 PM

Q. And Figure 3 includes those domain-identifying annotations we talked about earlier, the underlining, the italicization, the bolding, correct?

A. It certainly does include those markings. But it doesn't give any guidance to the POSA as to whether those are bits that should be included in some molecule to be made or bits to be excluded. Maybe the underlining are the bits that you shouldn't include. 01:42 PM 01:43 PM

Q. And it supplies a particular GGGGS linker, correct?

A. There is a particular linker in the middle of, I think, Sequence ID No. 2, 01:43 PM

that's the -- so it's directing -- if it's directing the POSA anywhere, it's directing them to use that linker to link the TGF beta to the heavy chain.

Q. Right. Let's turn to Column 43, and lines 40 to 52 of the '968 patent. 01:43 PM

A. Can I give you this other patent back?

Q. Why don't you hold on to it. We might need it again. 01:43 PM

MR. MCTIGUE: Can you remind me of the lines? I have got the columns.

MR. HEINTZ: 40 to 52, so to be clear, Column 43, lines 40 to 52.

BY MR. HEINTZ: 01:44 PM

Q. So my question is going to be, those lines supply the recombinant DNA production instruction, correct?

MR. MCTIGUE: Objection to form.

BY MR. HEINTZ: 01:44 PM

Q. I'm sorry. Recombinant DNA production instruction.

MR. MCTIGUE: Same objection.

A. I'm sorry. What's the question?

BY MR. HEINTZ: 01:45 PM

Q. Yes. Those lines supply the recombinant DNA production instruction?

MR. MCTIGUE: Same objection.

A. I'm sorry. I don't see that.

BY MR. HEINTZ: 01:45 PM

Q. All right.

Let me go to paragraph 174 of your declaration. All right.

There you say, "for the reasons discussed above, practicing the full scope of 01:46 PM the claims will require undue experimentation."

A. Uh-huh.

Q. Okay. Just to be clear, what exactly are the reasons you're referring to 01:46 PM in that portion of the first sentence of paragraph 174?

A. Well, I think that section that I'm referring to above, it goes from paragraph 155 up to 173. 01:46 PM

Q. Do you have any literature you can point to that would establish that a POSITA would have difficulty making the fusion proteins of Claim 1 and 9?

A. As I sit here, no. As I said 01:47 PM

earlier, I don't recall seeing any example of somebody making that full range of proteins successfully or unsuccessfully.

Q. So the term "fusion protein" could apply to any two or more proteins that are genetically fused where in nature they are not fused, correct? 01:48 PM

A. It could do. I think that's correct.

Q. Okay. But here we're talking about a particular class of fusion proteins, and by here I mean the '968 patent, where one of the partners in the fusion protein is antibody or antibody fragment, correct? 01:48 PM

MR. MCTIGUE: Objection to form. 01:48 PM

A. So are you talking about the claims of the patent now or a particular claim, or are you talking about the specifications as a whole?

BY MR. HEINTZ: 01:48 PM

Q. I'm talking about Claim 1 and 9.

A. Okay.

Q. They're talking about a particular class of fusion proteins where one of the parts that are fused is an antibody or 01:48 PM

antibody fragment, correct?

A. Yes, strictly speaking, the claims don't mention fusion protein, I don't think. I think they just talked about isolated molecule and say an isolated molecule. 01:49 PM

Q. They are fusion proteins, though, are they not?

A. I believe they likely are.

Q. And they are fusion proteins where one of the parts of the molecule is an antibody or antibody fragment, correct? 01:49 PM

A. Right.

Q. Okay. And those were the most common types of fusion proteins in the therapeutic world, correct? 01:49 PM

MR. MCTIGUE: Objection to form.

A. I don't think that was correct, no.

BY MR. HEINTZ:

Q. What was incorrect about it? 01:49 PM

A. I think at the time and probably even now, in the therapeutic world, if by that you mean you know, drugs that are in the -- in the therapeutic world if by that you mean drugs that were approved for 01:49 PM

administration to humans, I think there were more molecules of the type of Fc fusion proteins. So that's not an antibody attached to another molecule but a molecule attached to an Fc.

Q. Well, my example was not just an antibody but an antibody or antibody fragment.

Does that change your answer?

A. No. 01:50 PM

Q. Okay. Nonetheless, if they weren't the most common type, they were still very common in a therapeutic world, correct?

MR. MCTIGUE: Objection for form. 01:50 PM

BY MR. HEINTZ:

Q. In March 2010?

MR. MCTIGUE: Same objection.

A. No, I wouldn't say they were very common in those days, no. it's a relative term. But if you compare it with regular antibodies or other fusion proteins, they weren't common. 01:50 PM

BY MR. HEINTZ:

Q. Would it be correct that the 01:51 PM

PGR2026-00025 - JHU
Ex. 2042- Page 156

antibody or antibody fragment component of the protein fusion would be soluble by itself?

MR. MCTIGUE: Objection to form.

A. Do you mean the antibody or antibody fragments of Claim 1? 01:51 PM

BY MR. HEINTZ:

Q. Or 9, yes.

A. Or 9.

I don't think it would be known. But particularly the minimum molecule that I've described, I'd be particularly unsure as to whether that would be soluble or not. 01:51 PM

Q. Now, with respect to Claim 1 and 9 of the '968 patent, the non-antibody part of the molecule can come from a number of sources, such as signaling molecules, toxins, extracellular domains of cell surface, receptors, enzymes, peptides or other proteins, correct? 01:51 PM

MR. MCTIGUE: Objection to form.

A. I think at the beginning of that question you said claims 1 and 9. I don't think that is correct. 01:52 PM

PGR2026-00025 - JHU
Ex. 2042- Page 157

Are you talking about the specifications as a whole now?

BY MR. HEINTZ:

Q. No, the claims.

A. In the claims. 01:52 PM

Q. Oh, forgive me. Yes, let's say the specification as a whole.

A. Do you want to rephrase the question?

Q. In fact, I'll withdraw it. 01:52 PM

A. Okay.

Q. Let me turn to your declaration of paragraph 65.

Are you there, Dr. Hale?

A. Okay. 01:52 PM

Q. So there in paragraph 65 you state that during work at the Native Antigen Company, you attempted to make a large number of fusion proteins, some of which proved to be extremely difficult for reasons that were 01:53 PM never obvious to you, correct?

A. Correct.

Q. Okay. And you state that in 2015 you filed a patent application number GB2535753, but then withdraw it due to lack 01:53 PM

of success in actually making the proposed fusion proteins, correct?

A. Correct.

Q. Nothing in your declaration discusses what the specific fusion proteins that you were trying to make were; is that correct? 01:53 PM

A. That's correct.

Q. And the patent that -- the patent that I just mentioned, the Great Britain patent -- 01:53 PM

A. Uh-huh.

Q. -- was about a novel fusion protein of your own design, correct?

A. I think that's correct. I haven't, you know, got all the details of that in my mind at the moment; but yes, it was -- we certainly thought it was novel at the time, that's why we filed a patent application. 01:53 PM 01:54 PM

MR. HEINTZ: Let's mark as Exhibit 2037, Great Britain Patent number 2535753A.

THE WITNESS: You don't need to mark it. 01:54 PM

PGR2026-00025 - JHU
Ex. 2042- Page 159

(Exhibit 2037, UK Patent Application 2535753A, marked for identification.)

MR. MCTIGUE: And you said this is the patent application, right, not the patent? 01:54 PM

MR. HEINTZ: This is the Great Britain application with the number in the upper right-hand corner.

BY MR. HEINTZ:

Q. Okay. I'll ask you a question, and I don't know if you need to review the application or not, but we'll see. 01:55 PM

So my question is, were the fusion proteins that are described in Exhibit 2037 structurally different from the claimed anti-EGFR antibody-TGFbetaRII fusion proteins that I described in the '968 patent? 01:55 PM

A. Well, I'll just say in advance that this isn't a document which I listed with the documents considered, you know, in forming my opinions on this patent. 01:55 PM

But, of course, it's a document that I've seen before. And, you know, I haven't had the opportunity to review it in detail. It's quite some time ago since I saw 01:56 PM

this patent and thought about these problems.

But to the best of my recollection, I think the answer to your question is that this is a different construct from the one that's described in Claim 1 or Claim 9. 01:56 PM

Q. Were they anti-EGFR antibody-TGFbetaRII fusion proteins of any kind?

A. No. 01:56 PM

Q. Were the fusion proteins in Exhibit 2037 that you were unsuccessful in making an Fc or antibody fusion?

A. No.

Q. Were they fusions of two soluble components? 01:57 PM

A. Well, that's difficult to say because they should have been soluble in the form that we were aiming to make them. But as I said, they were difficult to make, and we didn't, in the end, get consistent results from our experiments. 01:57 PM

Q. One of the components was a hydrophobic membrane-spanning sequence, correct? 01:57 PM

MR. MCTIGUE: Objection to form.

MR. HEINTZ: Sorry. Hydrophobic membrane-spanning sequence.

THE WITNESS: Are you reading that from some particular place? 01:57 PM

MR. MCTIGUE: Are we looking at the claims or the spec?

THE WITNESS: As I said, it's a long time. Ten years since I reviewed this, so I don't remember every detail 01:58 PM of it. I just remember it was difficult.

So I've got the claims on page 55, if that's helpful.

BY MR. HEINTZ: 01:58 PM

Q. Well, are you able to tell from the claims the answer to my question? In other words, was one of the components a hydrophobic membrane-spanning sequence?

A. Well, it was a membrane-spanning 01:58 PM sequence. So the whole -- the claim related to a core polypeptide, which was, to the best of my recollection, a soluble polypeptide and a membrane-spanning polypeptide, that was the second component, so the idea was to fuse the 01:59 PM

two together.

Q. But you don't know whether that membrane-spanning polypeptide was hydrophobic or not?

A. I don't think you can describe such a polypeptide as being hydrophobic as a whole. All polypeptides have some hydrophobic parts and some hydrophilic parts just as, for instance, TGFbetaII receptor itself, the one we've been talking about all along. So that's an example of a membrane-spanning polypeptide as well. 01:59 PM 01:59 PM

Q. So let's see, Sequence ID 38 in here. Can you find that?

There's discussion of that -- 02:00 PM

A. You may not have provided me with a sequence listing. I'm not sure.

Q. I'm not sure. Yeah, okay.

A. I think, you know, we probably supplied the sequence listing as an electronic file. 02:00 PM

Q. Well, let me ask you this. One of the challenges you faced in connection with this application is inventing a completely new fusion protein technology. Isn't that 02:01 PM

correct?

A. A new technology? I mean, all inventions are sort of new technologies, aren't they? So you just might -- you could well say the '968 is a new technology. I supposed everything has to be new to be an invention. 02:01 PM

Q. The fusion proteins you're talking about in Exhibit 2037 were for a totally different purpose than the fusion proteins of Claim 1 and 9, correct? 02:01 PM

MR. MCTIGUE: Objection to form.

A. I think the purpose was different, whether it was totally different, it was -- we were -- our intention was to make medicaments for therapy in the broad sense, and in that sense the patents, you know, ensued here is also about making a fusion protein with the intention of making a medicament for therapy. Ours was a different kind of fusion protein, and it was a different set of applications. 02:02 PM 02:02 PM

My point was that sometimes it's unpredictable and difficult and requires a vast amount of experimentation to make fusion 02:03 PM

proteins in contrast with antibodies which can usually be made quite predictably. This was one example. And as you saw in paragraph 65 and 66 of my reports, I was aware of the other examples. 02:03 PM

BY MR. HEINTZ:

Q. Let's go to page 12, Exhibit 2037. I'm talking about native page 12. That's with the 12 across the top.

A. Got it. Well, I haven't got it. 02:03 PM I'm nearly there.

Q. And about halfway, a little more than halfway down the page there's a heading that begins "Membrane-spanning domain."

Do you see that? 02:04 PM

A. I see it.

Q. Do you see there the second sentence that refers to "hydrophobic amino acids"?

A. It says, "mostly hydrophobic amino 02:04 PM acids," yes.

Q. So does that refresh your memory as to whether these membrane-spanning domains were hydrophobic?

MR. MCTIGUE: Object to form, 02:04 PM

asked and answered.

A. Yeah, I think -- I described that earlier. So what we were attempting to do was to fuse a membrane protein with what we call a core protein, I think. And the membrane protein, like all proteins, has some hydrophobic regions and some hydrophilic regions. The membrane-spanning domain is more hydrophobic in general, as in the examples that we used here as well. 02:04 PM 02:05 PM

And I said, that's just like the TGFbetaII receptor that we've been talking about earlier.

Q. So you think the problems you had in making the inventions that were claimed in Exhibit 2037 were comparable to the kinds of problems that would be faced by a POSITA in practicing Claims 1 and 9 of this '968 patent; is that correct? 02:05 PM

A. I don't think that's what I said. 02:05 PM

Q. I'm asking you.

A. You know, I don't know what the problems were. I'm saying that, you know, we -- in general, myself and all the people I've read in the literature, I cited a number 02:05 PM

of different literature references, we've all found that making fusion proteins is comparatively more difficult and unpredictable than, for example, making conventional IgG antibodies, and so I'm just citing a number of examples to support that assertion. 02:06 PM

And I've given this as one example, where we put a lot of efforts into making fusion proteins, ultimately unsuccessfully, and I've given some other examples from my own experience, and I've given other examples from other people's experience in the literature. 02:06 PM

So I think a POSA looking at the literature would come to the conclusion that there's unpredictability in the art in making fusion proteins and that's backed up by my experience. 02:06 PM

BY MR. HEINTZ: 02:06 PM

Q. Okay.

MR. HEINTZ: We've been going for an hour. Why don't we take a quick break, and I think I'm getting close to the end, so give you guys a heads up. 02:07 PM

(Recess taken at 2:07 p.m. to 2:26 p.m.)
(Exhibit 2038, A modular IgG-scFv bispecific antibody topology, marked for identification.)
BY MR. HEINTZ: 02:26 PM
Q. Dr. Hale, we had during the break marked as Exhibit 2038 a paper entitled "A modular IgG-scFv bispecific antibody topology."
You've got Exhibit 2038, do you not, Dr. Hale? 02:27 PM
A. Yes.
Q. Have you seen Exhibit 2038 prior to today?
A. No. 02:27 PM
Q. Earlier we had discussed how Claim 9 requires the TGFbetaRII to be fused to the light chain rather than the heavy chain, correct?
A. Uh-huh. 02:27 PM
THE COURT REPORTER: Is that a yes, Doctor?
THE WITNESS: The question was Claim 9?
BY MR. HEINTZ: 02:27 PM

PGR2026-00025 - JHU
Ex. 2042- Page 168

Q. Claim 9 requiring that the TGFbetaRII be fused to light chain rather than the heavy chain, correct?

A. Well, you'll remember that it was linked through a linker rather than fused. 02:27 PM

Q. I see. Okay. Connected to the light chain?

A. Connected, using the link, yep.

Q. And connected using the linker. Okay. 02:28 PM

Before the earliest priority date of the March 2010 for the '968 patent, Orcutt discusses fusing a non-antibody domain to a C-terminus of an antibody light chain, and that's -- again, Orcutt is Exhibit 2038 that 02:28 PM I've handed you; is that correct?

MR. MCTIGUE: Objection to form.

A. Whoo. As I've said, I haven't seen this paper before to the best of knowledge. I would need to review it. I've 02:28 PM not, you know, been asked to express any opinion about this paper, so you take that step by step.

BY MR. HEINTZ:

Q. All right. Well, let me ask you 02:29 PM

this. Putting aside Exhibit 2038, do you have an opinion as to whether it was known to connect a non-antibody portion to a light chain of an antibody or antibody fragment in a fusion protein prior to March 2010? 02:29 PM

A. I think there may have been a few examples in the prior art, not many. But it's likely in my opinion that there would have been a small number of examples. It was more commonly fused to the heavy chain, but 02:29 PM there were some examples, I expect.

Q. All right. So let's take a look at the first page of Exhibit 2038, which is native page 221, and I'll direct you to the summary in the upper left corner and 02:30 PM particularly the first sentence.

Do you see that? It begins "Here we present."

MR. MCTIGUE: Is this the bolded -- 02:30 PM

MR. HEINTZ: Bolded summary.

THE WITNESS: Oh, I see, yes. Yeah, okay. Just give me a moment.

Okay.

BY MR. HEINTZ: 02:31 PM

Q. So here's an example where we have -- let me get the terminology correct. Here's an example where we have a non-antibody domain being fused to the C-terminus of an antibody light chain, correct? 02:31 PM

MR. MCTIGUE: Objection to form.

A. Well, that's not what I see here.

BY MR. HEINTZ:

Q. What do you see there? 02:31 PM

A. Well, I see a single-chain Fv, which is -- I think we've established is composed of an antibody variable regions and that's been fused to a whole IgG. So I think it is an antibody, but it's likely two antibody domains. 02:31 PM

Q. Okay. It's not an entire antibody, though, it's something less than a antibody --

A. It's a fragment, yeah. It's an antibody fragment, just as we've been discussing earlier. It's certainly a very different kind of molecule from the one we've been looking at in Claim 1 and Claim 9 for '968. 02:31 PM 02:32 PM

Q. But that fragment is nonetheless fused to the C-terminus of the light chain of an IgG antibody, correct?

And you can look further on page 223 and the results -- under the "Results" heading if you'd like. 02:32 PM

A. Okay.

Q. Okay. So my question was, that fragment is nonetheless fused to the C-terminus of the light chain of an IgG antibody, correct? 02:33 PM

MR. MCTIGUE: Objection to form.

A. Yes, I believe that's what it says in the summary, as, again, I just read it just now. 02:33 PM

BY MR. HEINTZ:

Q. Okay.

MR. HEINTZ: We'll have marked as Exhibit 2039 a document entitled, "The first constant domain (CH1 and CL) of an antibody used as heterodimerization domain for bispecific miniantibodies." 02:33 PM

(Exhibit 2039, Bates numbers PGR2026-00025, The first constant domain (CH1 and CL) of an antibody used as heterodimerization domain 02:34 PM

for bispecific miniantibodies, marked for identification.)

BY MR. HEINTZ:

Q. Dr. Hale, have you seen Exhibit 2039 prior to today? 02:34 PM

A. I'm not sure. I don't remember seeing it. I might have seen it.

Q. Okay. I'll direct your attention to the abstract on page 1 of Exhibit 2039.

MR. MCTIGUE: Just to clarify the question -- 02:35 PM

MR. HEINTZ: I'm sorry. Let me rephrase this.

BY MR. HEINTZ:

Q. What's been marked today as Exhibit 2039 has also previously been marked as Exhibit 2031 in the PGR. 02:35 PM

So I'll refer to 2039 as Exhibit 2031 for the rest of the day.

MR. MCTIGUE: Understood. 02:35 PM

A. Okay.

BY MR. HEINTZ:

Q. All right. The abstract on page 1 states that, "Bispecific miniantibodies were constructed by genetically fusing the CH1 02:36 PM

domain of an IgG 1 to the C-terminus of a single-chain Fv fragment," in part, correct?

A. Correct.

Q. So this is another example of something being connected to a C-terminus of a light chain, correct? 02:37 PM

MR. MCTIGUE: Objection to form.

A. I don't think so, no.

BY MR. HEINTZ:

Q. Okay. What is discussed there then? 02:37 PM

A. So I think here we've got a single-chain Fv fragment which is fused to the N-terminus of the CH1 domain and a different single-chain Fv fragment fused to the N-terminus of the constant light chain domain. 02:37 PM

I think they've illustrated the construct in Figure 1, Figure 1A.

So I understand that in Figure 1A, at the top left-hand side, it's labeled "Anti-EFGR," that's the single-chain Fv, which is fused to the N-terminus of the CH1 domain, and on the other side is the anti-CD2 single-chain Fv, which is fused to the 02:38 PM 02:39 PM

PGR2026-00025 - JHU
Ex. 2042- Page 174

N-terminus of the light chain constant domain, and what they're making is a bispecific antibody or more particularly a bispecific miniantibody.

So, again, this is something -- the construct is very different from anything claimed in the '968 patent. 02:39 PM

Q. In Figure 1A, there is something that is fused to the N-terminus of a light chain, correct? 02:39 PM

A. I don't think so.

Q. Well, there's a light chain in the figure somewhere, isn't there?

A. You can't actually see that in the figure. What you've got in the figure is a single-chain Fv, anti-CD2, which is linked to the light chain constant domain, the CL. 02:40 PM

Q. Yes.

A. That's not the N-terminus of the light chain. It's unclear from the figures to whether you've got a -- you know, which orientation the single-chain Fv is. 02:40 PM

Q. Okay.

A. I'd have to study the paper in much more detail to understand that. 02:40 PM

Q. Nonetheless there is a light chain in Figure A and that's designated by CL, correct?

A. I don't think CL designates a light chain. It only designates a constance domain from the light chain. 02:40 PM

Q. I apologize. The constant domain of a light chain?

A. I think that's what's depicted in Figure 1A. 02:41 PM

Q. And something is fused to that, correct?

A. Well, it seems to be linked to it, anyway.

Q. Why do you say it's linked? 02:41 PM

A. Well, honestly, I haven't had them to review this in great detail because Figure 1A is not disclosing the amino acid sequence. It's a sort of topological picture and from that you can't quite see the detail of a fusion or a link or anything else. 02:41 PM

Q. But you believe, I think you said earlier, you chose linking?

A. I mean, that's my impression from just the quick reading of the abstracts and 02:41 PM

the figure.

Q. Okay.

MR. HEINTZ: All right. Dr. Hale, no further questions.

THE WITNESS: Okay. 02:42 PM

MR. HEINTZ: But your counsel may have some.

MR. MCTIGUE: Bicara has no questions. Thank you, Dr. Hale, for your time. 02:42 PM

MR. HEINTZ: Thank you for your time. We're off the record.

THE COURT REPORTER: So, Mr. Heintz, you're getting the original, correct? 02:42 PM

MR. HEINTZ: Yes.

THE COURT REPORTER: And, Mr. Tellekson, you're ordering a copy, right?

MR. HEINTZ: He's not in the case yet, so we're just going to order one copy. 02:43 PM

THE COURT REPORTER: Mr. McTigue, you're ordering a copy?

MS. LAROCHELLE: Regular delivery 02:43 PM

is fine. We don't need a rush.

THE COURT REPORTER: Do you want a rough?

MS. LAROCHELLE: We'll take a rough. 02:43 PM

(Deposition concluded at 2:43 p.m.)

PGR2026-00025 - JHU
Ex. 2042- Page 178

COMMONWEALTH OF MASSACHUSETTS
SUFFOLK, SS.

I, Sandra A. Deschaine, Registered Professional Reporter and Notary Public within and for the Commonwealth of Massachusetts at large, do hereby certify that the deposition of Geoffrey Hale, Ph.D., in the matter of BICARA THERAPEUTICS, INC., VS. THE JOHNS HOPKINS UNIVERSITY, held at the offices of Fenwick & White, LLP, One International Place, Boston, Massachusetts, on September 29, 2026, taken and transcribed by me; that the witness provided satisfactory evidence of identification as prescribed by Executive Order 455 (03-13) issued by the Governor of the Commonwealth of Massachusetts; that the transcript produced by me is a true record of the proceedings to the best of my ability; that the witness is reading and signing; that I am neither counsel for, related to, nor employed by any of the parties to the action in which this deposition was taken, and further that I am not a relative or employee of any attorney or counsel employed by the parties thereto, nor financially or otherwise interested in the outcome of the action, on this 30th of September 2026.



Sandra A. Deschaine
Registered Professional Reporter

My Commission Expires:
July 3, 2031

James Heintz, Esquire
jim.heintz@dlapiper.com

September 30, 2026

RE: Bicara Therapeutics, Inc. v. The Johns Hopkins University
9/29/2026, Geoffrey Hale, PH.D. (#8456410)

The above-referenced transcript is available for review.

Within the applicable timeframe, the witness should read the testimony to verify its accuracy. If there are any changes, the witness should note those with the reason, on the attached Errata Sheet.

The witness should sign the Acknowledgment of Deponent and Errata and return to the deposing attorney. Copies should be sent to all counsel, and to Veritext at (production-ca@veritext.com).

Return completed errata within 30 days from receipt of testimony.

If the witness fails to do so within the time allotted, the transcript may be used as if signed.

Yours,
Veritext Legal Solutions

Bicara Therapeutics, Inc. v. The Johns Hopkins University

Geoffrey Hale, PH.D. (#8456410)

E R R A T A S H E E T

PAGE_____ LINE_____ CHANGE_____

_____

REASON_____

PAGE_____ LINE_____ CHANGE_____

_____

REASON_____

PAGE_____ LINE_____ CHANGE_____

_____

REASON_____

PAGE_____ LINE_____ CHANGE_____

_____

REASON_____

PAGE_____ LINE_____ CHANGE_____

_____

REASON_____

PAGE_____ LINE_____ CHANGE_____

_____

REASON_____

_____ _____

Geoffrey Hale, PH.D. Date

Bicara Therapeutics, Inc. v. The Johns Hopkins University
Geoffrey Hale, PH.D. (#8456410)

ACKNOWLEDGEMENT OF DEPONENT

I, Geoffrey Hale, PH.D., do hereby declare that I have read the foregoing transcript, I have made any corrections, additions, or changes I deemed necessary as noted above to be appended hereto, and that the same is a true, correct and complete transcript of the testimony given by me.

_____ _____

Geoffrey Hale, PH.D. Date

*If notary is required

SUBSCRIBED AND SWORN TO BEFORE ME THIS

_____ DAY OF _____, 20___.

_____

NOTARY PUBLIC

&

& 1:20 2:13 5:6 179:7

0

01:00 120:5,10 120:15,20
01:01 120:25 121:5,10,15
01:02 121:20 121:25 122:5 122:10
01:03 122:15 122:20,25
01:04 123:5,10 123:15,20
01:05 123:25 124:5
01:06 124:10 124:15,20
01:07 124:25 125:5,10,15
01:08 125:20 125:25 126:5
01:09 126:10 126:15
01:10 126:20
01:11 126:25
01:12 127:5,10 127:15,20
01:13 127:25 128:5,10
01:15 128:15 128:20,25
01:16 129:5,10 129:15,20,25 130:5
01:17 130:10 130:15,20,25
01:18 131:5,10 131:15,20,25
01:19 132:5,10 132:15,20
01:20 132:25 133:5,10,15,20
01:21 133:25 134:5,10,15,20
01:22 134:25 135:5,10,15,20 135:25
01:23 136:5,10 136:15,20,25 137:5
01:24 137:10 137:15,20,25
01:25 138:5,10 138:15
01:26 138:20 138:25 139:5 139:10,15,20
01:27 139:25 140:5,10
01:28 140:15 140:20
01:29 140:25 141:5
01:30 141:10 141:15,20,25 142:5
01:31 142:10 142:15,20
01:32 142:25 143:5,10,15
01:33 143:20 143:25 144:5 144:10
01:34 144:15 144:20,25 145:5,10
01:35 145:15 145:20,25 146:5
01:36 146:10 146:15,20,25
01:37 147:5,10
01:38 147:15 147:20,25
01:39 148:5,10 148:15
01:40 148:20 148:25 149:5 149:10,15
01:41 149:20 149:25 150:5 150:10,15
01:42 150:20 150:25 151:5 151:10,15
01:43 151:20 151:25 152:5 152:10
01:44 152:15 152:20
01:45 152:25 153:5
01:46 153:10 153:15,20
01:47 153:25
01:48 154:5,10 154:15,20,25
01:49 155:5,10 155:15,20,25
01:50 156:5,10 156:15,20
01:51 156:25 157:5,10,15,20
01:52 157:25 158:5,10,15
01:53 158:20 158:25 159:5 159:10,15
01:54 159:20 159:25 160:5
01:55 160:10 160:15,20
01:56 160:25 161:5,10
01:57 161:15 161:20,25 162:5
01:58 162:10 162:15,20
01:59 162:25 163:5,10

02210 3:7
02:00 163:15 163:20
02:01 163:25 164:5,10
02:02 164:15 164:20
02:03 164:25 165:5,10
02:04 165:15 165:20,25 166:5
02:05 166:10 166:15,20,25
02:06 167:5,10 167:15,20
02:07 167:25
02:26 168:5
02:27 168:10 168:15,20,25 169:5
02:28 169:10 169:15,20
02:29 169:25 170:5,10
02:30 170:15 170:20
02:31 170:25 171:5,10,15,20
02:32 171:25 172:5
02:33 172:10 172:15,20
02:34 172:25 173:5
02:35 173:10 173:15,20
02:36 173:25
02:37 174:5,10 174:15
02:38 174:20
02:39 174:25 175:5,10
02:40 175:15 175:20,25 176:5
02:41 176:10 176:15,20,25
02:42 177:5,10 177:15
02:43 177:20 177:25 178:5
03-13 179:10
09:31 6:5
09:33 6:10,15 6:20,25 7:5,10 7:15
09:34 7:20,25 8:5,10,15,20
09:35 8:25 9:5 9:10,15
09:36 9:20,25 10:5,10,15
09:37 10:20,25 11:5,10,15
09:38 11:20,25 12:5,10,15
09:39 12:20,25 13:5,10
09:40 13:15,20 13:25 14:5,10
09:41 14:15,20 14:25 15:5
09:42 15:10,15 15:20,25 16:5
09:43 16:10,15 16:20,25
09:44 17:5,10 17:15,20
09:45 17:25 18:5,10
09:46 18:15,20 18:25 19:5
09:47 19:10,15 19:20,25 20:5 20:10
09:48 20:15,20 20:25 21:5,10
09:49 21:15,20 21:25 22:5,10
09:50 22:15,20 22:25
09:51 23:5,10 23:15
09:52 23:20,25 24:5,10
09:53 24:15,20
09:54 24:25 25:5,10,15
09:55 25:20,25 26:5
09:56 26:10,15 26:20,25
09:57 27:5,10 27:15,20
09:58 27:25 28:5,10,15,20
09:59 28:25 29:5,10,15,20

1

1 39:9 50:9 58:3 77:10 79:5,14 82:18 82:24 83:4,7 83:11,20 84:3 86:4,17,20 104:23 111:22 112:20,21 114:25 115:13 116:14 117:1,2 117:9 118:25 119:1,1 122:13 122:18,18 123:3 125:24 126:6 128:12 129:13 130:12 130:16,20,23 131:5,8,11,12 132:1,7,15,23 132:23 133:3 138:14,17 142:7 144:4 150:5,10 153:24 154:21

157:6,15,24 161:6 164:11 166:18 171:24 173:9,23 174:1 174:19
10 14:2 149:21
100 3:6 40:10
1001 31:2,6 39:7 87:25
1003 24:10,13 25:11,14 50:3 76:5 125:20
1004 9:10
104 39:22,24 40:5,8,12,16 43:14 62:6,14 65:14 67:2,8 126:14 151:1
10:00 29:25 30:5,10
10:01 30:15,20 30:25
10:02 31:5,10 31:15,20
10:03 31:25 32:5,10,15,20
10:04 32:25 33:5,10,15,20
10:05 33:25 34:5,10
10:06 34:15,20 34:25 35:5,10
10:07 35:15,20 35:25 36:5,10
36:15
10:08 36:20,25 37:5
10:09 37:10,15 37:20,25 38:5
10:10 38:10,15 38:20,25
10:11 39:5,10 39:15
10:12 39:20
10:13 39:25 40:5,10,15
10:14 40:20,25 41:5,10
10:15 41:15,20 41:25
10:16 42:5,10 42:15
10:17 42:20,25 43:5,10
10:18 43:15,20 43:25 44:5,10
10:19 44:15,20 44:25
10:20 45:5,10 45:15,20,25
10:21 46:5,10 46:15,20,25 47:5
10:22 47:10,15 47:20
10:23 47:25 48:5,10,15,20 48:25
10:24 49:5,10 49:15
10:25 49:20,25 50:5
10:26 50:10,15 50:20,25
10:27 51:5,10 51:15
10:28 51:20,21
10:42 51:21,25 52:5
10:43 52:10,15 52:20,25
10:44 53:5,10 53:15
10:45 53:20,25 54:5,10
10:46 54:15,20 54:25
10:47 55:5,10 55:15,20
10:48 55:25 56:5,10,15
10:49 56:20,25 57:5,10,15
10:50 57:20,25 58:5
10:51 58:10,15 58:20
10:52 58:25 59:5,10,15
10:53 59:20,25 60:5,10
10:54 60:15,20 60:25
10:55 61:5,10 61:15,20
10:56 61:25 62:5,10
10:57 62:15,20 62:25 63:5
10:58 63:10,15 63:20,25
10:59 64:5,10 64:15,20
11,939,387 4:8 127:18 128:2
111 26:9
113 121:19
115 81:21
117 92:25 122:10 123:6
119 77:10 79:6 82:5,9 111:22 119:1
11911 2:7
11:00 64:25 65:5,10,15,20
11:01 65:25 66:5,10,15
11:02 66:20,25 67:5,10
11:03 67:15,20 67:25 68:5
11:04 68:10,15 68:20,25

11:05 69:5,10 69:15,20
11:06 69:25 70:5,10,15
11:07 70:20,25 71:5,10
11:08 71:15,20 71:25 72:5,10
11:09 72:15,20 72:25 73:5
11:10 73:10,15 73:20,25
11:11 74:5,10 74:15
11:12 74:20,25 75:5,10
11:13 75:15,20 75:25
11:14 76:5,10
11:15 76:15,20 76:25
11:16 77:5,10 77:15,20
11:17 77:25 78:5,10,15
11:18 78:20,25 79:5
11:19 79:10,15 79:20,25
11:20 80:5,10 80:15,20
11:21 80:25 81:5,10,15
11:22 81:20,25 82:5,10
11:23 82:15,20 82:25
11:24 83:5,10
11:25 83:15,20 83:25 84:5
11:26 84:10,15 84:20,25
11:27 85:5,10 85:15,20,25
11:28 86:5,10 86:15
11:29 86:20,25 87:5,10
11:30 87:15,20 87:25 88:5
11:31 88:10,15 88:20
11:32 88:25 89:5,10
11:33 89:15,20 89:25
11:34 90:5,10 90:15
11:35 90:20,25 91:5
11:36 91:10,15 91:20
11:37 91:25 92:5,10,15,20
11:38 92:25 93:5
11:39 93:10,15 93:20
11:40 93:25 94:5,10,15
11:41 94:20,25 95:5,10
11:42 95:15,20 95:20
11:44 95:20
11:45 95:25 96:5,10
11:46 96:15,20
11:47 96:25 97:5,10,15
11:48 97:20,25 98:5,10
11:49 98:15,20 98:25 99:5
11:50 99:10,15 99:20,25 100:5
11:51 100:10 100:15,20,25 101:5
11:52 101:10 101:15,20,25 102:5,10
11:53 102:15 102:20,25 103:5,10
11:54 103:15 103:20,25 104:5
12 165:7,8,9
12,295,968 1:13 31:10
125 81:21
127 114:14 121:13,14
128 4:8
12:42 104:5,5 104:10,15,20 104:25
12:43 105:5,10 105:15,20
12:44 105:25 106:5,10
12:45 106:15 106:20,25 107:5
12:46 107:10 107:15,20,25 108:5
12:47 108:10 108:15,20,25 109:5
12:48 109:10 109:15,20,25
12:49 110:5,10 110:15,20,25 111:5
12:50 111:10 111:15,20
12:51 111:25 112:5,10,15,20
12:52 112:25 113:5,10

12:53 113:15 113:20,25 114:5,10
12:54 114:15 114:20,25
12:55 115:5,10 115:15
12:56 115:20 115:25 116:5 116:10,15,20
12:57 116:25 117:5,10,15,20
12:58 117:25 118:5,10,15,20 118:25
12:59 119:5,10 119:15,20,25
131 83:13 86:15
132 83:13
134 114:15
147 123:22
15 14:21 149:21
154 93:25 94:22 95:22
155 153:20
160 4:9
168 4:11
17 28:14 29:25 30:2 150:16
172 4:13 140:18
173 153:20
174 153:7,17
18 29:25 30:2
18755 179:19
18883719 70:1
1a 174:19,20 175:8 176:10 176:18

2

2 50:12 74:18 75:6 76:23 77:10,18,24 78:22,23 79:6 82:4 84:9,10 84:16,18,21 85:1,7,8,10 111:9,11 112:2 112:11,24 115:1,2 117:2 129:13 151:1 151:25
20 14:2 182:15
2009 52:16 53:4
2010 32:4 46:23,24 47:7 49:22 50:4,23 52:16 53:4,9 53:24 54:4,23 55:2,7,12,16,21 55:24 56:3,6,8 56:11,22 57:7 57:15,21 58:10 58:15 59:12,18 59:22 60:5,9 65:5 92:1,15 93:4 96:13 99:15,25 141:20,25 145:23 146:1 148:5 156:17 169:12 170:5
2011 32:1,10 34:3,6 42:10 46:22,24
2015 158:23
20190 2:8
2025 18:21
2026 1:17 5:1 179:8,16 180:3
2031 173:17,19 179:25
2032 127:17
2036 4:8 127:17 128:1,9 131:17 138:7
2037 4:9 159:22 160:1 160:14 161:12 164:9 165:7 166:16
2038 4:11 168:2,7,10,13 169:15 170:1 170:13
2039 4:13 172:19,23 173:5,9,16,18
206.389.4560 2:18
221 170:14
223 172:5
23 89:8
24 67:14,21 87:25 88:4
25 140:11
2535753a 4:10 159:23 160:2
273066 62:1
29 1:17 5:1 67:14,22 87:25 88:3,7 179:8
2:07 168:1
2:26 168:1
2:43 1:18 178:6

3

3 50:13 73:17 73:21,25 74:8 74:16 75:7,21 76:15,19,24 77:6 78:3 79:3 79:11,20 80:15 80:21 82:3,19 83:6,21 84:15 86:9 93:7,17 93:24 111:7,9 125:25 126:1,6 126:12,15,17 129:13 137:23 138:6 147:8

151:9,11 179:25
30 21:3 106:3 180:3,16
300 2:7
30th 179:16
31 96:20
33 98:15 100:9 106:3
34 89:8 90:14
35 87:25 88:4 90:24 96:4,18 98:14 100:9,9 103:20 106:1
38 163:13
387 131:14,15 133:3,6 134:13 138:7,10,14,18
39 76:9,13

4

4 50:14
40 76:16 117:1 152:6,13,14
400 112:16,20 112:21 115:1,1 115:13 117:2 117:10 119:1 122:18 123:3
401 2:16
43 152:5,14
440 112:6
45 17:12
45,000 21:8
455 179:10
46 90:14,21
48 97:13
49 90:14
4th 32:1

5

5 25:16,20 26:18 28:14 29:24
50 97:13
500 20:21
52 152:6,13,14
53 26:5 30:9 41:11
55 122:10 162:13
56 90:24
59 54:14 58:12 58:16,23 61:4
5th 32:4

6

6 4:4 30:8
60 21:3 55:25 56:3,8 59:1,3,4 61:7 83:14 89:9 114:13
61 56:17
617.570.1273 3:8
62 50:2 53:14 83:15 90:24 140:10
65 158:13,16 165:4
66 165:4
68 125:20,24 126:6 130:21 130:22,25 131:2
69 94:2

7

7 31:18 121:23
703.773.4148 2:9
71 39:20 40:17 42:3 75:1,7 78:3,5,10 79:7 151:2
73 75:2
79 128:10

8

8 121:19
80 140:18,19 141:11 145:16
81 145:17
8456410 180:5 181:2 182:2
87 41:18 77:25 126:11 151:2
89 40:10,10

9

9 39:10,11,18 41:10,14 58:4 62:7 63:5,13 63:25 67:1,10 79:14 86:22 94:4,12 95:1 95:15 97:24 98:6,10 100:25 104:23 113:7 113:10,20,23 114:7,18,25,25 115:5,13,14 116:11,15,16 116:25 117:8 119:4,14,19 121:15 122:3,6 122:13 123:7 123:15,20,25 124:4 126:19 137:14 138:2,6 141:1 150:4,5 150:10 153:24 154:21 157:8,9 157:15,24 161:6 164:11 166:18 168:17 168:24 169:1 171:24
9/29/2026 180:5
90 21:5
93 24:13
95 76:4,14
968 30:20 31:2 31:21 39:7 63:5 70:2 72:12 73:21,25

78:16 80:2 83:19,24 87:24 93:9,19 95:24 96:7 106:1 111:7 120:13 121:10 126:7 138:6 150:6 152:6 154:12 157:16 160:17 164:5 166:18 169:12 171:25 175:7
98 41:10
98101 2:17
9:31 5:3
9:41 1:18

a

a.m. 1:18 5:3 51:21,21 95:20 95:20 104:5
abatacept 54:12,17 55:3
ability 35:12 61:9 62:2 138:24 179:12
able 27:16,24 28:2 29:7 34:19 35:10 36:14 37:2 42:11 43:12 44:7 45:11 46:1,4,13 67:7 74:7 99:24 102:22 132:17 143:5 144:12 162:16
above 153:10 153:19 180:6 182:7
absence 150:15
absolutely 19:13
abstract 69:3 173:9,23
abstracts 176:25
accept 130:11
access 65:10
accomplish 43:10 96:14 99:20 109:4
accomplished 98:25 99:8 100:11 101:22 102:5,10,17
accomplishing 100:24
account 44:15 45:3 63:22
accuracy 180:9
accurate 112:19
achieving 65:9
acid 39:19,21 41:17 42:3 64:20 66:1,7 75:16 82:18 150:21 176:18
acids 77:10 79:5 81:21 83:7 165:19,21
acknowledge... 182:3
acknowledg... 180:12
acronyms 128:21
action 179:13 179:16
activity 30:17 44:23 61:19,21 61:22
actual 68:17
actually 46:23 68:6 76:16 148:17 159:1 175:14
add 139:1,15 139:21
added 119:3
additional 119:2
additions 182:6
address 25:17
administration 156:1
advance 160:18
advice 21:24
advised 24:19
affect 47:3
aggregates 45:16
ago 11:21 52:22 160:25
agree 51:25 53:24 54:4 55:19 56:18 58:7 59:9 71:14,25 72:15 73:5,16 85:12 93:6,13 120:17 129:16 130:15
agreed 135:8
agreements 136:19
ahead 29:6 128:12
aiming 161:19
alan 52:20
alleged 47:3
allotted 180:19
amino 39:19,21 41:17 42:2 66:1,6 75:15 77:10 79:5 81:21 82:18 83:7 150:21 165:18,20 176:18
amount 21:1 149:1 164:25
amplification 32:24

analysis 69:12 70:9,23 115:25
analyze 129:6
analyzed 122:21 123:11 129:20 133:6 138:24
analyzing 70:19
annotations 151:12
answer 7:1,5,9 7:18 20:16 29:6,14 38:8 38:10 47:16 49:12 59:3,16 63:9 95:10 103:5 110:19 110:23 113:1 115:17 116:1,6 116:8 121:6 128:4 133:5 134:14 136:8 139:17 156:9 161:3 162:17
answered 71:1 109:7 138:23 139:14 166:1
answering 6:25 95:12
answers 7:25 47:1,4 139:2
antecedent 107:4
anti 10:24 15:6 15:12,18,21,24 16:1 17:8,20 74:14,20 82:25 160:16 161:7 174:22,24 175:16
antibodies 10:8 10:24 15:7 16:24 17:8,20 18:1 30:15 50:5 53:10,22 61:19 81:14 87:5,7 89:4,11 89:20,25 90:6 90:12 91:7,8 120:22 148:14 156:22 165:1 167:5
antibody 4:11 4:14 10:9 11:19 13:9 15:13,21 16:2 30:13 33:19,20 49:21 50:12,14 50:22 51:9 52:3,15 53:4 55:20,23 58:21 60:10,11 61:8 61:8 74:14,20 81:20 82:25 88:12,13 89:3 89:19 90:3,15 90:19,20 91:3 91:7,9 94:8 95:1 96:2 98:16,16 106:5 106:5 130:6 131:6,19 149:19,24 150:2 154:14 154:14,25 155:1,11,11 156:3,7,7,7 157:1,1,5,6,16 160:16 161:8 161:13 168:3,8 169:13,14 170:3,4,4 171:4,5,13,15 171:16,18,19 171:21 172:3 172:11,21,25 175:3
antibody's 91:19
antigen 11:19 13:10 47:9 49:15 61:10 62:3 90:15,19 158:17
anybody 9:3,6 104:11 150:12
anyway 118:20 118:23 176:14
apart 68:22 127:7
apologies 41:12
apologize 40:8 40:21 46:21 126:21 131:1 176:7
appeal 1:2
appear 123:11 124:17
appearances 2:1,25 3:1
appears 78:19
appended 182:7
applicable 180:8
application 4:9 44:19 69:19,22 69:25 70:2,5 158:24 159:20 160:1,4,7,12 163:24
applications 31:25 32:3 164:22
applies 122:13
apply 20:8 154:5
appreciate 118:14 119:25 120:3
appropriate 37:2 48:5
approved 54:7 54:21,22,23

55:2,12,15 155:25
architecture 94:12,17
area 10:13,16 10:18 48:8
areas 10:19,21 17:2
art 25:18,23 26:2,7,12,13,16 27:12 28:1,10 28:16 29:24 30:8 32:21 33:13 35:24 36:13 37:1,19 37:23 38:18 42:9 43:7,12 44:6 45:4,8,24 46:13 53:20 55:16,17 57:21 59:21 60:8 64:17 65:5 67:7 71:17 72:3 74:2,7 75:5 77:5 78:15,24 80:2 80:13 82:15 85:14 86:10 92:1,14 98:23 106:17 109:4 109:25 110:9 110:13 126:24 127:2,10 148:5 148:9 149:6
150:9 167:17 170:7
arts 36:15 127:6 146:19
aside 110:8 115:12 170:1
asked 32:7 45:9 70:16 71:1 86:2 110:16 115:19,19 116:2,4 134:12 138:25 139:14 166:1 169:21
asking 28:25 67:1 106:14 110:15 119:10 128:21 141:6 166:21
aspect 88:23 94:6 95:24 97:14,19,20 125:4
aspects 124:8,8
assays 30:16 47:8 49:15
assertion 167:7
assess 49:10
assume 7:19 128:4
assuming 47:22 115:13 146:11
attach 36:21
attached 41:4 41:24 42:1
61:19 117:3 119:16 120:15 120:16 156:3,4 180:11
attachment 117:5
attempt 86:2 110:19
attempted 65:7 150:3,9 158:18
attempting 166:3
attended 17:2 22:10
attention 56:16 87:24 106:1 111:7 173:8
attorney 20:3 20:12 179:14 180:13
attorneys 9:22
available 100:7 146:19 180:6
avenue 3:6
average 26:12
aware 9:17,18 17:19,21,22 18:2 59:16 65:24 101:17 105:5 141:17 150:8,12,18 165:4

b

b 89:22 145:15
back 18:14 31:25 38:6 51:22 54:19 104:7,14 106:1 121:15 149:10 149:15 152:8
backed 167:18
background 100:6
based 12:16 16:22 43:20 126:18 130:15 130:17 134:13 134:16,20
basis 103:19 148:4
bates 4:13 172:23
bearing 64:22
beginning 68:24 88:10 121:16 157:23
begins 165:14 170:17
behalf 2:3,12 3:3
believe 31:10 34:5 54:9 56:7 56:10,25 58:6 62:12 77:2,8 78:12 84:4

100:18,22 101:1 109:24 111:4 113:14 116:13 155:8 172:13 176:22
best 7:11 27:9 138:23 142:10 161:2 162:22 169:19 179:12
beta 144:2,18 147:11 152:3
beyond 35:19 35:23 65:4 66:19 67:6 80:19
bicara 1:4 3:12 9:4,22 18:17 19:2 177:8 179:6 180:4 181:1 182:1
bifunctional 11:4,6 12:5,19 13:4
bigger 127:23
billed 21:7,9
bind 61:9 62:2 88:19
binding 47:8,9 49:15 90:15,19
biochemist 10:25
biochemistry 27:23
biocon 9:7 19:2 19:6
biological 44:23
biology 27:23 148:13
biopharmace... 10:23
biotech 32:17
biotechnology 22:21
bispecific 4:11 4:15 120:22 168:2,8 172:22 173:1,24 175:3 175:4
bit 34:24 38:7 40:7 101:11 102:23,24 137:22,22
bits 121:3 124:14 125:10 137:22 151:6 151:17,19,20
blaze 123:24 124:4,24 125:11
board 1:2
bold 75:11,15
bolded 77:23 111:14 170:20 170:21
bolding 79:23 151:14
boston 1:22 3:7 5:7 179:8
bottom 28:15 114:20 145:16
break 34:24 51:17 56:14 103:24 104:4,9 167:24 168:6
briefly 104:14
britain 6:5 159:10,22 160:7
broad 120:5 164:16

c

c 6:1 16:10 38:21 41:19 94:7,25 95:6 95:16 96:1 97:16,17,21 98:3 147:24 169:14 171:5 172:2,10 174:1 174:5
ca 180:15
call 10:17 37:10 123:15 166:5
called 125:9
calls 28:24
capable 27:15 148:21
care 53:14
career 27:21
carries 64:21
carry 27:17,24 64:6 150:4
case 12:13 23:19 26:5 27:22 30:21 31:11 37:6 38:16 39:2 48:25 61:16,17 62:4 116:6 119:1,5 127:8 129:22 132:2 136:3,16,17 142:6 143:10 143:15,18,21 143:24 144:4 147:7 177:20
cases 23:10,16 23:16 48:10,13 48:14,20,21 143:13
cd2 174:24 175:16
cdr 128:23,25 129:12
cdrs 129:17 130:1,7,8
cell 48:6,11,16 49:1,3 50:10 64:15,16 66:11 141:13 142:4 143:6,11,20

144:7,9,14 145:5,6,19 146:18 157:19
cells 50:13 51:9 143:7,11 144:7 144:12,13 146:15
certain 32:7 55:5 57:1 143:14 146:24
certainly 10:10 11:12 48:1 53:6 76:8 85:25 118:13 151:15 159:18 171:22
certainty 146:21
certified 5:10
certify 179:5
cetuximab 15:3 15:12 17:20 36:25 37:3,21 37:22,24 38:20 39:25 43:8 63:16 67:4 93:11,22
ch1 4:14 172:20,24 173:25 174:14 174:23
chain 16:10 33:21 39:25 40:25 41:2,5 42:2,6,17 43:8 43:23 63:15 67:4 74:24,24 74:25 76:2,25 78:8,12,25 80:16,17,24 81:9,18,19 82:11 89:4,20 90:5,6,9 91:7 91:17,18,23,23 92:8,10,12 93:11,22 94:8 94:14,25 95:6 96:2,9 97:17 97:22 98:8 101:11,14,15 101:15,21,24 102:3,11,17 103:9,13,16 105:2,3,11,13 105:14,19,20 113:16 114:5,6 115:8 117:4 119:17 120:15 120:16 123:1,2 123:4,5 126:3 129:2 130:7,8 130:14 131:6,6 131:22 132:5,5 132:21 133:13 133:16,17,21 133:22 134:3 135:7,8,12,13 135:17 136:20 136:21,23 138:11,13,16 139:6,8 140:1 143:18 144:3,3 144:5,19,19 147:14 152:4 168:18,19 169:2,3,7,14 170:4,10 171:5 171:11 172:2 172:10 174:2,6 174:13,15,16 174:22,25 175:1,10,12,16 175:17,20,22 176:1,5,6,8
chains 75:9 127:13 129:19 130:2,10,13 132:13,13 134:5 139:24 141:12 142:14 143:16
challenges 163:23
change 46:24 47:1 59:3 144:17,21,21 156:9 181:4,7 181:10,13,16 181:19
changed 61:20
changes 25:10 180:10 182:6
check 78:18 114:11
checked 61:13
chemical 142:25
chemistry 11:2
cho 49:20 50:22
choice 34:11 35:4 44:24 50:22,25 51:3 51:6,12 66:9 85:6,13,22 86:12 148:15 148:18 149:9
choices 28:8 46:9,13 49:20 49:25 66:16,17 84:8 86:9,17 86:19 149:5,8
choose 35:13 38:22 64:14,19 66:8 146:20
choosing 35:18 35:21 36:20 37:20
chose 176:23
cite 58:3 95:23
cited 56:9 82:18 100:25 166:25
cites 145:20 147:20

citing 167:6
civil 20:8
cl 4:14 126:16 172:20,24 175:17 176:2,4
claim 23:13,25 32:10 39:9,10 39:11,18 40:16 40:24 41:1,3,8 41:10,14,17,24 42:6,22 62:7 63:5,13,25 67:1,10 72:4 73:14 79:14,14 82:18,24 83:4 83:7,11,20 84:3 86:4,5,17 86:20,22 94:4 94:12 95:1,15 97:24 98:6,10 100:25 104:23 105:15 113:7 113:10,20,23 114:7,18,25,25 115:5,13,14,24 116:11,14,15 116:16,25 117:8,17 118:25 119:4,4 119:14,17,19 121:15,21 122:3,6,13,13 122:18 123:7 123:15,20,25 124:4 125:7 126:18,19 127:11 128:12 128:16 130:5 130:12,16,20 131:5,8,11,11 131:18 132:1,7 132:15,23,23 133:3 134:5 135:6,22 137:14 138:2,6 138:14,17 139:11 140:3 142:7,12 143:3 144:4 150:10 150:10 153:24 154:18,21 157:6,15 161:6 161:6 162:21 164:11 168:17 168:24 169:1 171:24,24
claimed 16:15 31:20 46:25 68:7 71:18 72:24 123:1,4 124:23 126:19 133:20 160:15 166:15 175:7
claiming 19:21 20:5,11 31:23
claims 32:2 38:16 39:1 58:3 68:22 69:9,14,18,22 70:5,11,14,17 70:19,23 71:5 71:6,9 72:11 86:25 104:18 105:18 115:20 115:21 122:14 122:15 124:14 124:17 134:1 150:5 153:11 154:17 155:2 157:24 158:4,5 162:7,13,17 166:18
clarify 7:15 121:22 173:10
clarity 126:10 133:2
class 154:11,24
clear 65:12 67:6 71:10 72:9,22 73:20 93:16 101:12 147:2 152:14 153:14
clearly 38:7 68:4 123:5
client 20:3,12
clinical 54:6 55:6
cloned 12:5,7
cloning 32:24
close 167:24
cobbold 17:24
codons 65:25 66:6,8,10
collaborations 32:16
colleagues 17:23
column 40:9,10 41:10 87:25 88:3,7 89:8 90:14,23 96:4 96:18 98:14 100:8 103:20 106:1 128:9 152:5,14
columns 152:12
combination 72:17 124:22 125:6,13,17,18 147:18
come 42:21 74:21 97:11 111:25 126:17 157:17 167:16
comes 96:4 126:12,15
commercializ... 60:4
commercializ... 58:10,15,19 59:12,14
commission 179:24

common 12:8 50:25 51:3,6 51:12 127:10 155:14 156:12 156:13,20,23
commonly 51:14 56:21 57:1 170:10
commonwealth 5:12 179:1,5 179:10
communicate 9:21
communicated 30:4 31:16
communication 20:12
communicati... 10:1 19:20,24
companies 22:21,23
company 158:18
comparable 166:16
comparatively 50:6 53:11 167:3
compare 77:23 156:21
compensated 20:20
compensation 22:20
complementa... 129:1
complete 6:24 7:5,25 105:2 116:8 182:8
completed 180:16
completely 80:14 163:24
complexity 42:23 47:18
complicated 64:25
complicates 66:15
component 147:12 157:1 162:25
components 34:9 35:2 161:16,23 162:18
composed 171:13
comprise 87:1 87:1
comprises 64:1 81:21
comprising 15:12 39:21 74:14 93:10,21 97:6
compromise 118:12
compromised 117:13 118:2
compromises 42:2
compromising 91:22 92:7 96:22 98:16 105:16 106:5 114:22 116:11 116:22 117:25 118:11 119:14
concept 58:8 59:10 60:6 107:8,19,20,20 107:22
concerning 25:22
concluded 178:6
conclusion 28:24 74:22 134:11 140:7 167:16
conclusions 134:12
concoct 73:2
concoction 125:10 137:21
conduct 49:14
conferences 17:2
confidential 21:24
confidentiality 23:17
confirm 47:8 49:15 77:25
confused 136:10
confusing 136:13
confusion 137:2
connect 67:9 99:16 170:3
connected 41:14 98:2 113:16 124:11 169:6,8,9 174:5
connection 20:6 22:2,8 124:4 136:15 163:23
connects 42:5
consequence 122:15 147:17
consider 69:13 69:15 70:8,11 70:19,23 72:10 115:19,20,23
considered 8:16 60:21 73:9 160:20
considering 145:20

consistent 161:21
consisting 56:19 98:18 106:7 107:13
consists 91:16
constance 81:3 176:5
constant 4:14 78:13,25 80:8 91:19 105:11 105:13,19 130:14 131:7 131:22 132:5 132:14,22 133:15,16,22 134:2,4 135:6 135:7,12,13,17 136:21 138:11 138:12,16 139:7,8,24 140:1 172:20 172:24 174:16 175:1,17 176:7
construct 16:8 26:19,20,24 43:22 47:13,24 48:17 49:2 80:14 146:16 161:5 174:19 175:6
constructed 15:11 126:18 173:25
construction 30:14 32:24
constructions 48:3
constructs 13:18,24 14:12
consult 22:19
consulted 19:2 19:5
contacted 19:8 19:16
contained 60:11 72:19
containing 88:13
contents 24:22 24:24
context 18:22 18:24 36:4,9 36:11 37:5,5 43:18,24 44:6 45:21,24 47:17 48:9,20 49:13 49:18 51:5 57:24 60:17 63:3,10,12,21 63:23 64:12 74:4 97:18,23 102:16 103:9 103:15 109:15 109:18 110:4 110:22 129:3
continue 90:25 141:8
continued 2:25 3:1
continuing 67:22
contrast 165:1
conventional 37:8 50:5 53:10,22 148:7 149:6,25 150:1 167:5
conversations 16:25 17:7,12
conveying 72:23
conveys 71:16 72:2 83:10
copies 56:19 180:14
copy 177:18,22 177:24
core 162:22 166:5
corner 160:8 170:15
corners 68:14 118:8
correct 6:13,14 9:14,15 10:6 11:10 16:16 17:18 18:5 20:22,23 21:12 25:2,5,18 29:17 32:6 33:1 34:4,13 36:1 37:24 38:10 39:22,25 40:13,17,25 41:5,12,21,22 42:6,7 46:18 49:22 50:7,17 50:18 53:12,16 53:17,20 54:8 54:9,13 55:16 55:21 57:7,15 57:21 58:5 59:22 61:10 62:3,10,12,17 62:24 67:24,25 68:21 69:9 70:6,9 72:20 73:18,22 74:18 75:2,3,9 76:17 76:18,20,25 77:7,11,19,20 78:6,16,25 79:2,7,8,23 80:25 81:11,22 82:5,15,20,22 83:2,22 84:3 85:3,4 88:14 88:15,20,25 89:13,23 90:9 90:17 91:9,19 91:20 94:9,10 94:14 95:17 106:9,10 107:17 110:1 111:2,15,16,23

111:24 113:11
113:12,18
118:18 122:19
123:8,11
126:24 130:3
131:8,17
139:18 141:2,3
141:13,14
150:6,7,16,21
151:9,10,14,23
152:18 154:7,9
154:14 155:1
155:11,15,17
156:13,25
157:21,25
158:21,22
159:2,3,7,8,14
159:15 161:25
164:1,11
166:19 168:19
169:3,16 171:2
171:6 172:3,11
174:2,3,6
175:10 176:3
176:12 177:15
182:8
corrections
182:6
correctly 50:16
93:15 102:7
113:17
corresponding
138:2
counsel 10:1,4
16:14 18:17
19:10,11,15,20
20:2 24:19
30:5 67:23
95:12 177:6
179:13,15
180:14
count 77:12
87:8 132:17
counted 112:4
counting
112:20 121:25
couple 6:17
11:21
course 17:12
57:24 85:15
86:18 94:16
105:21 122:14
151:4 160:22
court 7:4 8:9
8:13 22:5 66:3
66:22 96:23
97:1 116:18
168:21 177:13
177:17,23
178:2
covered 83:20
86:3
create 80:13
creating 85:6
creative 28:7
creativity
27:13 28:17,20
29:10
csr 1:24
culture 50:13
50:15
curriculum
9:13
cut 137:23
151:5
cv 9:13 11:2
17:5
cytokine 60:13

d

d 6:1
daily 148:4
date 30:20,23
30:24 31:14,21
32:10 46:22,25
47:1,2 56:10
71:19 72:5
169:11 181:24
182:12
dates 68:25
david 2:14 3:11
day 18:19
173:19 182:15
days 52:18
149:12 156:20
180:16
deal 39:4 65:2
127:22
dealing 17:7
december
18:20
deciding
141:11 142:13
decision 64:22
65:22 134:10
141:21 148:22
148:23
decisions 64:13
65:1,4
declaration
25:16 30:1,9
35:1 50:3 53:9
67:14 76:4
79:10 83:13,18
84:6 85:21
88:25 94:1
95:23 111:2
130:21,22
140:10,18
153:8 158:12
159:4
declare 182:4
deemed 182:6
define 100:16
defined 32:21
33:17 34:8
35:1,24 37:19
47:7,12 52:1
53:20 57:14
defining 100:10
definition 30:7
109:15,18
definitive
115:17

delivery 177:25
demonstrate 68:11
demonstrated 58:9,15 59:11 59:21 61:25
depend 14:6 36:8 47:17 49:13,17 63:2 63:10 66:10 144:14
dependent 48:9 48:19 122:15
depending 143:1 144:17
depends 36:3 37:4 42:14 57:9,24 142:16
depict 129:13
depicted 125:19,23 147:8 176:9
deponent 6:2 180:13 182:3
deposed 6:16
deposing 180:13
deposition 1:16 5:5 6:18 8:19 9:21 22:10,16 104:10 178:6 179:6,14
derived 15:12 29:11
deschaine 1:24 5:9 179:4,20
describe 13:1 17:13 64:10 101:2,5 124:24 137:14 163:5
described 12:13 34:17 37:12 42:24 53:25 54:10 64:9 68:3,14 80:4,14 93:1 97:12 100:19 105:5,23 109:19 137:25 144:25 146:8 147:10 157:12 160:14,17 161:5 166:2
describes 97:10 122:10
describing 74:12 123:6
description 4:7 23:3,8 24:5 49:7 67:16,19 68:2,5 69:16 70:10,13,20,24 71:3,4,15 72:1 72:13,16 73:18 79:18 80:10 101:6 113:11 113:21,24 115:24 116:10 117:21 118:5 119:20 120:9 120:12 121:11 121:18 122:4,7 122:12 123:21 132:24 134:6 135:4,23,25 136:24 137:4 137:17 138:1 138:19 139:12
design 11:22,24 12:17 13:15 28:2,7 34:13 34:19 35:6,12 39:5 44:21 47:12,24 52:6 141:20 142:1 148:3 159:14
designate 112:9
designated 176:2
designates 176:4,5
designed 11:3 11:13,20 12:11 12:14 13:7 15:10 16:7
designing 28:6 28:11 29:16,20 33:19 34:10 35:3,22 147:25
desirable 45:19 124:22
desrosier 3:11
detail 86:8 123:12 129:21 145:6,9,12 160:25 162:10 175:25 176:17 176:20
details 23:20 127:7 159:16
determination 72:11
determine 118:8
determining 84:10 129:1
development 54:6
diabodies 91:6
diagrams 72:18
dictate 44:24
difference 44:13 65:25 104:17 124:7
different 11:9 13:17,24 14:11 14:11 16:23 17:1 28:8 44:15 45:1 54:1 64:7 66:1 66:6 73:1,3,14 81:15 87:5,6,6 87:10 90:11 102:23 109:11 110:22 120:24

122:9 124:12 136:17 137:9 137:21,24 140:6,7 142:21 142:22 143:4 143:11 145:6 146:17,18 147:20,21 149:4 151:6 160:15 161:4 164:10,13,14 164:20,22 167:1 171:23 174:15 175:6
difficult 13:15 14:19 36:23 48:21,25 49:8 99:22 118:13 120:2 143:8 148:19,20 149:20 150:2 158:20 161:17 161:20 162:12 164:24 167:3
difficulty 28:5 28:10 29:16,19 36:20 37:17 39:4 65:9 153:23
diligently 27:18
direct 56:16 80:12 105:25 111:6 170:14 173:8
directing 79:13 152:1,2,2
direction 79:12 124:6
directly 96:9 98:2 103:2 109:21 117:6
disability 7:23
disagree 102:14
disclose 9:24 19:18
disclosed 83:19 83:21 84:1
discloses 138:10
disclosing 176:18
disclosure 71:16 72:2 93:8,18 96:7 113:14 114:17 115:7 123:23 133:12 145:7
discuss 104:9 142:8
discussed 29:24 32:9 62:9 77:6 111:12 153:10 168:16 174:10
discusses 159:5 169:13
discussing 94:4 103:20 106:2 107:24 116:9 116:25 171:22
discussion 138:13 163:15
distinct 80:24 81:5,10
disulfide 90:7
dla 2:4
dlapiper.com 2:10 180:2
dna 32:23 64:23 65:22 152:17,21 153:2
doctor 39:14 40:21 47:5 56:12 62:10 67:17 85:23 96:23 168:22
doctrine 107:3
document 9:11 9:17 24:11,16 25:3 31:17 160:19,22 172:19
documents 8:3 8:6,7,12,15,20 8:22 9:1 160:20
doing 37:17
domain 4:14,15 13:12 15:14 16:9 30:13 34:11 35:4 41:2 42:2 58:4 58:9,14 59:11 60:7 74:15 76:24 78:5,7 78:13 79:4,11 81:16 90:9 91:17,18 147:14 151:12 165:14 166:8 169:13 171:4 172:20,22,24 172:25 174:1 174:14,17,24 175:2,17 176:6 176:7
domains 54:8 56:22 62:24 63:20 81:3,15 81:17 126:16 157:19 165:23 171:16
dr 6:10 10:7 17:24 18:16 20:20 24:17 29:6 31:5 51:25 52:5 76:13 95:22 104:7 128:6 158:14 168:6 168:11 173:4 177:3,9
draft 24:18 25:5,8

drawn 125:24
drink 18:9,12
drive 2:7
drug 10:24
drugs 155:23 155:25
dtellekson 2:19
due 117:24 158:25
duly 6:6
duties 21:20

e

e 6:1,1 181:3,3 181:3
earlier 22:13 23:11 31:24 32:2,9 40:7 46:21 56:13 62:9 66:11 70:16 77:6,17 104:15 106:20 111:12,20 114:21 116:9 121:16 126:22 140:13 141:2 142:20 151:13 154:1 166:3,13 168:16 171:22 176:23
earliest 31:20 169:11
ectodomain 58:8,13 59:10 60:7 75:16 76:2
editorial 53:1
effective 71:19 72:5
effort 149:16
efforts 167:9
efg 15:18
efgr 15:21 174:22
egfr 15:6,12 16:1 17:8,20 42:12 74:14,20 82:25 88:17 160:16 161:7
either 90:8 98:25 119:1,5 133:20,21 134:2 150:13
electronic 163:21
elements 148:2 148:7,8,16
embodiment 89:12 96:20 97:2,3 98:15 106:4
emd 62:1
employed 179:13,15
employee 179:14
enable 86:5 137:6,12
enablement 23:2,7,13,24 132:25 134:6 136:1,25 137:4 137:5,12 139:18 140:4
encode 65:22 65:25 66:3,6
encoded 50:11
encodes 47:25 64:24
encoding 62:22 63:19 64:23
engaged 22:2,8
engineering 10:9 52:6,15 53:4 145:23 146:1
english 106:15
enhance 53:5
enhancer 148:1 148:16
ensued 164:18
ensure 68:6 147:22
ensuring 34:12 35:5
entered 55:6
entire 72:10 73:5 74:8 112:9,10,22,22 114:6 123:2,4 123:5 171:17
entirely 14:6 73:2 125:15
entirety 84:8 84:17 85:8
entitled 168:7 172:19
envisaged 39:1
enzyme 60:13
enzymes 157:20
equations 73:8
errata 180:11 180:13,16
esquire 2:5,14 2:15 3:5,11 180:1
establish 153:22
established 111:20 171:12
evaluated 146:9
eventually 21:11
evidence 179:9
exact 18:19 21:1 23:4 59:8 81:25 94:11,17 113:2 142:16
exactly 11:5 22:17 29:18 53:21 68:9 79:4 92:3 98:21 108:16

153:15
examination 4:2 6:8
examined 6:7
example 13:6 17:21 27:20 35:21 38:19 48:24 61:4 64:14 73:17 74:16 116:24 117:4 120:21 130:19 133:12 133:15,21 134:4 135:11 135:13,14,18 138:10,12 139:6,7 144:25 149:18 154:1 156:6 163:11 165:3 167:4,9 171:1,3 174:4
examples 60:23 60:25 61:3,6 61:18 62:5 138:15 139:9 150:15,18 165:5 166:10 167:6,12,13 170:7,9,11
exceptional 37:15 38:9,13 39:3 104:19,24 105:1
exclude 101:4 105:18
excluded 151:19
excludes 100:24
exclusively 100:11
excuse 66:23 121:17 127:17
executive 179:10
exhibit 4:7,8,9 4:11,13 9:10 24:10,13 25:11 25:14 31:2,6 39:7 50:3 76:5 87:25 125:20 127:17 128:1,9 131:17 138:7 159:21 160:1 160:14 161:12 164:9 165:7 166:16 168:2,7 168:10,13 169:15 170:1 170:13 172:19 172:23 173:5,9 173:16,17,18
exhibits 4:6
exist 122:17
expect 47:10 61:15 62:4 70:12 82:10,15 105:8 145:1,3 170:11
expected 95:10
experience 11:1 14:18 16:15,23 27:22 30:12 32:8,9 33:5,7 34:2 66:18 125:1 148:11 167:12,14,19
experienced 32:16 149:12
experiences 33:24
experiment 63:24
experimentat... 84:7 85:22 86:1,7 149:2 153:12 164:25
experiments 27:17,25 28:3 28:6,7,11 29:16,20 43:17 161:22
expert 20:7 21:14 23:2,23
expertise 10:7 10:11,14 16:13
expires 179:24
explain 25:25 27:9 70:22 79:9 136:14
explicitly 126:17
express 84:5 85:20 141:12 143:5,7,10 147:18 149:20 169:21
expressed 12:15 15:11 16:8 49:11 142:15 143:19 145:5 147:22
expression 30:14,16 32:25 47:13,24 48:5 49:19,21 50:23 64:19 66:12 89:22 142:3 145:19 148:2 148:13
extent 28:23 81:2
extra 139:15,20
extracellular 15:14 16:9 58:4 74:15 157:19
extraordinary 37:10 47:20,23 149:16
extremely 158:20

f
f 89:22 90:5
fab 16:8 33:21 89:4,4,20,20,21 90:4,4,4 91:4,4 91:4
faced 163:23 166:17
fact 13:17 54:18 116:10 117:22 118:17 119:13 120:8 158:10
factors 45:2,15 66:10 145:21
failed 150:11
fails 79:11 180:18
failure 149:10
fair 59:20 105:24 130:10
fall 142:12
falling 84:2
familiar 29:12 32:22 33:18 34:8 35:2 36:14 47:8 52:2,5,8,20 87:9 107:2
family 146:6
far 20:25 21:8 101:17 131:25 141:17
fast 96:24
fc 33:22 58:21 88:13 91:5,5 156:2,5 161:13
fd 90:4
features 104:25
federal 20:7
fenwick 1:20 2:13 5:6 179:7
fenwick.com 2:19,20
fersht 52:21
field 12:9 14:19 27:22 53:7 57:11 80:11
figure 73:17,21 73:25 74:8,16 75:2,7,21 76:15,19,24 77:6 78:3,12 79:3,11,20 80:15,21 82:3 82:19 83:6,21 84:15 86:9,14 92:20,25 93:7 93:17,24 111:7 111:9 125:19 125:24,25 126:1,6,6,12,15 126:17,18 130:23,24 131:1 137:23 138:6 147:8 151:9,11 174:19,19,20 175:8,13,15,15 176:2,10,17 177:1
figures 68:18 72:18 73:7 175:20
file 163:21
filed 32:1,3 69:13,17,18,22 158:24 159:19
filing 71:19 72:5
financially 179:15
find 26:4 36:15 40:7 70:14 92:20 108:6 136:18 148:20 163:14
fine 7:2,17 27:2 51:18 141:5 178:1
finish 35:20 102:1
firm 21:15
firms 22:23
first 4:13 6:3 6:21 19:8,16 25:4,8 68:25 69:3 115:6 140:25 142:13 153:16 170:13 170:16 172:20 172:24
firsthand 16:15
firstly 83:4
five 21:19 22:12 23:5,6
flexible 56:18
folds 81:1
folks 52:25
follow 27:16 46:4
followed 13:21
follows 6:7
foregoing 182:5
forget 23:18
forgive 158:6
form 10:15 14:5,13 15:15 16:4,17 17:10 21:25 23:14 24:1 25:19 26:3,14 27:6 28:4,21 30:22 31:22 33:2 34:14 35:7 36:2 37:25 40:1 42:13 43:15 45:13 46:17 47:15 48:7,18 49:23 50:24 55:22 56:4,24 57:8 59:13,23 61:11 62:11 63:1

69:20 70:25
71:20 77:1
81:23 82:12,21
87:11 90:18
91:10 92:2
94:15 99:10
100:13 101:9
107:5 109:6,16
110:2,14 111:3
113:25 115:10
115:15 116:25
117:11,19
119:6,21
120:18 122:8
122:20 123:9
126:8 127:14
131:9 132:8
134:7,22 137:1
137:13 138:20
141:22 145:11
147:23 150:22
152:19 154:15
155:16 156:15
157:4,22
161:19 162:1
164:12 165:25
169:17 171:7
172:12 174:7

format 15:22
16:3,8 143:2

formats 142:21
143:4

formatted
125:25

formed 91:8

forming 35:25
160:21

formula 72:19

formulas 73:8

forth 110:22

found 167:2

fountain 2:6

four 23:5,6,10
56:20 57:5
62:10 68:14
118:8

fragment 15:13
61:8 88:13
90:3,16 91:16
93:7,18 98:17
105:4,8 106:6
154:14 155:1
155:11 156:8
157:1 170:4
171:20,21
172:1,9 174:2
174:13,15

fragments
33:21 89:4,5,5
89:20,21,21
90:8,20 91:3,5
91:5,9 157:6

framed 10:2

free 45:16

freedom 2:7

frequently
149:13

full 7:24 85:16
86:5 93:10,22
118:6,15 120:1
137:7,19 143:3
153:10 154:2

fuller 116:6

function 79:12
147:6

functional
147:23

further 34:16
75:1 97:11
139:8 141:4,15
172:4 177:4
179:14

fuse 42:11
101:7 162:25
166:4

fused 13:9
15:13 16:9
39:20 41:2,19
60:11,20 94:7
94:13,24 96:1
96:9 97:8,16
97:16,21 98:6
98:8,9,17 99:3
99:5 106:6,24
107:12,17
108:17 110:11
115:8 117:6
143:23 154:6,7
154:25 168:17
169:2,5 170:10
171:4,14 172:2
172:9 174:13
174:15,23,25
175:9 176:11

fusing 58:8
59:10 60:6
98:24 103:8
169:13 173:25

fusion 11:4,7,8
11:18 12:6,20
13:4 15:11,21
16:2,24 17:9
23:8,13,24
30:15 34:10
35:3,13 36:13
36:18,24 37:3
37:8,21 44:17
47:14,25 49:21
50:20,23 53:25
54:5,10 55:20
55:23 56:22
58:13,21,22
60:10 61:10
62:3 74:13
83:21 84:11
85:6 86:11,13
87:10 91:6
96:15,21 97:5
97:24,25 98:5
99:8,18,19,21
100:10,24
101:22 102:4,4
102:10,16
103:2,9,15,16
109:4,9,15,18

109:25 110:9 126:23 127:2,6 127:10,11 143:23 144:12 148:14 153:23 154:4,11,13,24 155:3,6,9,14 156:2,22 157:2 158:19 159:2,5 159:13 160:13 160:16 161:8 161:11,13 163:25 164:8 164:10,18,21 164:25 167:2 167:10,18 170:5 176:21
fusions 101:16 161:15
future 12:3 116:5
fv 33:21 91:5 91:16 171:11 174:2,13,15,22 174:25 175:16 175:22
fvs 90:5,7

g

g 6:1 62:9 92:25
gb2535753 158:25
gene 32:24
general 16:13 35:12 58:7 59:9 60:6 62:17 87:16 91:24 92:13 99:23 107:24 142:9 166:9,24
generally 60:24 87:10 128:20 128:22,24 129:23,25
genetically 154:6 173:25
geoffrey 1:16 1:19 4:3 5:5 6:2 179:6 180:5 181:2,24 182:2,4,12
gestures 7:7
getting 167:24 177:14
ggggs 56:21 62:7,17 75:24 151:22
gggs 62:8
give 13:24 23:20 27:1 47:16 48:24 59:5 108:3 110:16,23 115:17 116:5,7 127:23 151:16 152:7 167:25 170:23
given 12:17 22:3 23:23 44:6 45:24 46:5,8 55:5 61:22 65:18 100:1 108:4 113:9 132:20 133:17 134:5 135:13,21 139:2 144:9 167:8,11,13 182:9
giving 7:24 99:23 134:17
glycine 56:20 57:5 66:1,4,7
glycoslation 145:20
glycosylation 147:3,3,9,11,13 147:20,21
go 6:17 18:11 29:6 31:25 34:23 36:14 50:18 51:20 54:19 67:13 89:8 93:25 95:18 98:3 104:3,13 121:15 128:12 141:15 145:15 149:10,15 153:7 165:7
goal 43:10
goes 83:15 97:7 115:25 145:16 153:19
going 6:16,23 9:9,23 13:18 19:17 24:9 33:10 43:4,23 51:16 56:16 64:15 84:11 103:3 104:1,13 110:20 112:15 113:3 124:23 125:7 127:16 127:23 130:20 136:15 140:9 141:5 143:2 144:6,9,17 145:4 152:16 167:22 177:21
good 6:10,11 13:20 146:22
goodwin 3:4 19:14 21:15,21
goodwinlaw.... 3:9
governor 179:10
grammatical 107:8 108:1
great 6:5 39:4 65:2,8 145:14 159:10,22 160:6 176:17

gregory 52:23
ground 6:17
gs 62:10
guess 106:3 129:5
guidance 79:12 144:23 150:15 150:17 151:7 151:16
guys 167:25

h

h 129:2,9 181:3
hale 1:16,19 4:3 5:5 6:2,10 10:7 18:16 20:20 24:17 29:6 31:5 51:25 52:5 76:13 95:22 104:7 128:6 158:14 168:6 168:11 173:4 177:3,9 179:6 180:5 181:2,24 182:2,4,12
halfway 165:12 165:13
hand 9:9 24:9 30:25 160:8 174:21
handed 169:16
hands 18:8
happen 43:21 103:10,16 104:1
happened 124:13
happy 113:2
hard 14:14 65:6 120:19,22
hcdr1 128:16
hcdr2 128:16
hcdr3 128:17
head 7:8,8 112:7,15
heading 165:13 172:6
heads 167:25
heard 107:19 124:23
heave 144:19
heavy 74:23 75:8 76:2,25 78:25 80:16,23 81:9,16,19 82:10 90:9 91:17,23 92:8 92:10 93:11,22 101:14,21 102:11,17 103:9 105:3,14 105:20 114:5 117:4 119:17 120:15 123:1,4 126:3 127:13 129:2,10,18 130:2,7,9,13 131:6,22 132:5 132:13,21 133:13,16,21 134:3 135:7,12 135:16 136:20 136:21,23 138:11,15 139:6,24 144:3 144:5 147:14 152:4 168:18 169:3 170:10
heintz 2:5 4:4 6:9 8:17 10:5 10:20 14:8,24 15:17 16:6,19 17:15 18:11,14 18:15 19:21 20:1,5,10,15,18 20:19 22:11 23:21 24:3,8 25:24 26:10,22 27:7 28:13,22 28:25 29:4,5 30:25 31:4 32:5,13 33:9 34:21 35:17 36:5 38:3 39:12 40:3,20 42:25 44:1 45:22 46:19 47:21 48:12,23 50:1 51:1,11 51:20,22,24 56:1,5 57:3,12 57:18 58:1 59:19 60:1 61:14 62:15,20 63:4 66:13,24 69:24 71:11,21 72:8 76:8,12 77:3 82:2,13 82:23 87:14 88:3,6,9 90:22 91:15 92:5 93:2 94:19 95:14,18,21 98:13 99:14 100:20 101:19 103:23 104:3,6 107:7 109:13 109:23 110:5 110:25 111:5 114:3 115:11 116:20 117:16 117:20 118:21 119:9 120:11 121:7 122:1,16 122:23 123:13 126:20 127:16 127:21 128:3 131:1,4,13 132:3,11,19 133:4,10 134:19 135:1 136:6 138:4 139:3,16,22 140:8,22,23

141:24 145:13 150:25 152:13 152:15,20,25 153:5 154:20 155:19 156:16 156:24 157:7 158:3 159:21 160:6,9 162:2 162:15 165:6 167:20,22 168:5,25 169:24 170:21 170:25 171:9 172:16,18 173:3,12,14,22 174:9 177:3,6 177:11,14,16 177:20 180:1
hek 51:9
hek293 49:20 51:2
held 5:6 179:7
help 53:1 70:22 124:1
helpful 79:16 162:14
helps 68:5
hereto 182:7
herman 17:24
heterodimeri... 4:15 172:21,25
high 53:7 66:18 148:19
highlighted 79:22
hold 35:19 66:22 116:18 152:9
honestly 23:16 138:22 176:16
hope 21:13 61:17
hoped 13:20
hoping 12:2
hopkins 1:8 179:7 180:4 181:1 182:1
host 48:5,11,16 49:1,3 50:10 145:19
hour 20:21 51:16 167:23
hours 21:3,4
huge 121:3
huh 7:6 28:18 63:14 79:24 94:3 114:23 115:4 131:3 133:23 135:10 135:20 153:13 159:12 168:20
human 81:20
humanized 81:20
humans 156:1
hundreds 87:19
hybrid 38:25
hybridoma 96:21 97:4
hydrophilic 163:8 166:7
hydrophobic 161:24 162:2 162:19 163:3,6 163:8 165:18 165:20,24 166:7,9
hypothetical 43:5,19 44:17 45:9 64:8 115:20 117:1,8 122:22 136:11
hypotheticals 117:12

i

i.e. 56:21
idea 42:20 146:22 162:25
identification 126:15 128:2 160:2 168:4 173:2 179:9
identified 6:3 16:22 25:10 78:11 82:19 83:1,18 121:9 124:25 126:10 126:13
identifies 88:17 91:3
identify 61:4,7 122:6
identifying 151:12
igg 4:11 50:5 53:10,22 80:23 81:9,13 167:5 168:2,8 171:14 172:3,10 174:1
ii 24:25 90:4 91:4
il2 60:21
illustrated 86:14 174:18
imagine 80:13 80:20
immediately 107:11
immunoglob... 54:8 58:9,14 59:11 60:7,12
immunology 17:23 27:24
immunomod... 58:3 60:15,20 60:22 94:6,13 94:23 95:3,16 95:25 97:7,15 97:20 98:9,18 106:7 107:13 124:10 144:1

impact 148:17
implied 107:23
implies 108:12
important 6:22 7:3 44:19,21 45:10 53:3,23 86:16 147:5
impossible 121:6
impression 176:24
inaccuracies 9:16
inadequate 49:6
include 69:8 85:8 90:16,20 101:4 105:22 116:21 117:3 117:14 130:20 135:18 137:8 151:15,21
included 50:9 132:6 151:18
includes 68:20 85:7 88:12 89:3,19,24 90:3 112:2 116:11 117:22 119:14,15 120:20 130:7 138:13 139:6 151:8,11
including 32:3 32:23 33:20 34:10 35:3 37:3 47:13 54:7 61:25 64:1 73:6 84:8 90:8 91:4 120:21
inconsistency 70:22
incorporate 62:22 63:18
incorporated 34:12 35:6
incorrect 16:20 25:14 155:20
indefiniteness 135:23
independent 81:4
independently 81:2
index 4:1
indicate 74:23 79:18 80:4,6
indicates 75:15
individually 148:8
industry 32:18
infect 48:16 49:1
infinite 132:4
influence 44:20
inform 53:2
information 9:25 19:19 30:3 36:15 65:10,18 133:25 135:22
informed 25:21 26:16
inn 55:6
instance 17:8 35:19 44:16 108:23 163:9
instructing 20:16
instruction 152:18,22 153:2
instructions 27:17 46:4,9 100:1
integrated 42:22 123:25
intended 74:22
intention 164:15,19
interested 11:25 179:15
international 1:21 5:7 179:8
interpret 106:20,21,22
interpreting 79:13
invalid 113:10 113:20,23 115:5,15 117:18 118:3 119:4,12,19 120:8,10 121:10 122:3,7 122:25 123:15 123:20 132:24 134:5,10,16,20 135:3,22 138:18 139:11 140:3
invalidated 146:13
invalidity 123:7
invented 68:7
inventing 27:15 163:24
invention 68:8 68:10 85:17 118:6 120:2,4 120:10 133:20 137:8,20 164:7
inventions 28:12 29:21 164:3 166:15
inventive 64:13
inventor 35:14 42:16 44:14 68:6 71:17 72:3,23 118:5 118:10 119:25

121:2 125:7 137:18
involve 23:7 58:13 86:6,25 124:8,9,10 149:4
involved 22:14 36:17 65:20
involves 12:12
involving 23:1 37:21
ireland 6:5
isolated 63:25 64:6 155:4,5
isotype 87:6
issue 30:20 31:3,11 114:4 115:12 125:22
issued 179:10
italic 75:23
italicization 79:23 151:14
italicized 77:17 111:14
italics 75:19,20 75:23

j

james 2:5 180:1
jim.heintz 2:10 180:2
job 1:25
johns 1:8 179:7 180:4 181:1
182:1
joined 61:20 103:2 109:22
joining 142:22
journal 52:6,10 52:14 53:3
journals 52:15 52:18
july 179:25
jumble 73:13

k

k.ndubuka 2:20
keep 140:21
kelly 2:15
key 74:19
kind 18:5 36:14 36:16,18 57:4 57:19 105:4 145:6,9,24 146:2 161:9 164:21 171:23
kinds 37:8,10 87:10 166:16
kingdom 6:4
knew 52:22,24 65:7
know 6:15 10:18 11:6 12:16 13:18 14:14,16,17 17:3 18:7 23:22 24:21 26:17 27:21 28:10 29:9 31:16,19 34:20 34:23 35:10,15 37:5 38:5,6,21 39:13 42:14,22 43:20,21 44:10 44:11,16,23 45:20 46:3,14 47:12 48:4,10 48:15,20,22,25 49:9,14 52:9 52:12,13,17 61:18 63:23 64:18 68:5,24 69:6 70:14 78:18 80:9 81:3,24 83:6 86:2,3,4,8 87:18 89:15 90:24 102:11 102:24 103:11 103:12,25 105:8,22 109:8 110:18 112:7 112:14 113:1 115:20,23 118:2,10 120:20 127:15 128:13,20 129:2 132:10 133:6,7,8,9 134:11 141:8 143:9 144:4,6 144:9 146:14 147:1,16 148:11,18 149:20 155:23 159:16 160:11 160:20,23 163:2,19 164:17 166:22 166:22,23 169:21 175:21
knowing 133:25
knowledge 25:15 27:25 45:6 48:2 100:6 169:20
known 33:20 36:12,25 37:23 42:10 47:23 54:2 55:15,17 55:20,24 56:3 56:8 57:6,10 57:10,13,13,20 57:23 59:21 60:8,24 62:21 63:18 64:17 89:25 107:3 148:9 149:6 157:10 170:2

l

l 129:10
lab 18:5,8 149:12

labeled 24:25 126:16 174:21
labeling 83:2
laboratory 15:1,4,7 148:12
lack 113:10,20 113:23 114:17 115:7 117:21 119:19 120:9 121:10,18 122:3,7,12 123:20,23,24 124:3,5 132:24 134:5,6 135:22 136:24 138:18 139:11 140:3 146:13 158:25
lacked 23:12
lacking 101:5
language 87:1 102:21 103:1 106:15 124:24
large 13:25 146:6 158:18 179:5
larochelle 177:25 178:4
law 21:15 22:23 107:21 107:23
lawyers 108:5
lead 28:11 29:20
leader 12:25
lectures 17:3
led 70:2
left 170:15 174:21
legal 24:20,20 24:22,25 25:22 26:16,17,19,24 28:24 29:10,11 30:4 31:17 68:23 107:20 107:22 108:2 109:12 134:11 134:12 180:23
legend 75:14
length 82:9 93:10,22
letters 75:23
level 27:12 35:15,19,23 53:19 66:18,19 67:6 148:19
levels 30:16
library 89:22
light 16:10 39:25 40:25 41:1 42:1,5,17 43:8,22 63:15 67:4 74:8,24 74:25 75:8 78:8,12 80:17 90:8 91:18,23 92:12 94:8,14 94:25 96:1,9 97:17,22 98:8 101:11,14,15 101:23 102:3 103:13,16 105:2,11,12,19 113:16 114:6 115:8 120:16 123:2,5 126:3 127:13 129:10 129:19 130:2,8 130:9,14 131:6 131:22 132:5 132:13,21 133:17,21 134:3 135:8,13 135:16 138:12 138:15,17 139:7 140:1 144:3,19 168:18 169:2,7 169:14 170:3 171:5 172:2,10 174:6,16 175:1 175:9,12,17,20 176:1,5,6,8
likely 43:20 127:5 155:8 170:8 171:15
limit 135:6,18 138:14
limitation 122:11
limited 107:22
limits 133:19 134:1 135:16 139:9
line 28:15 41:10,10 64:15 90:21 96:19,19 98:14 106:3 181:4,7,10,13 181:16,19
linear 91:7
lines 64:17 87:25 88:2,4 89:8 90:14,24 100:9 146:18 152:6,12,14,17 153:1
link 38:19 42:17 43:7 56:22 101:7 108:9 152:3 169:8 176:21
linked 37:22,24 40:25 63:15 90:7 95:4 98:17 99:3,5 103:1 106:6,22 108:13,17,19 108:23 142:24 142:25 143:16 144:2,5,11,16 144:18 169:5 175:16 176:13 176:15

linker 35:18,21 36:16,21,22 37:2,20 38:21 39:21 40:13,15 40:25 41:2,14 41:19,21,24,25 42:5,11,19 43:9,13,13 44:3,8,21,25 45:12,25 46:10 56:19 57:4,19 62:7,13,22 63:19 64:23 65:13,21 67:8 75:23 76:1,1 77:18 84:21 85:1,9,11 94:13 95:4,7 95:17 96:10,14 97:9,9,10 98:7 98:10,11,12,19 98:20,25 99:1 99:4,4,5,6,9,20 100:12,25 101:3,6,8,8,23 102:5,10,18 103:2,10,17 106:8,9,12,23 106:23,24 107:10,10,15 107:15,16 108:10,12,13 108:14,17,18 108:19,24 109:5,10 112:4 112:23 113:16 115:3,3,9 117:5,6 126:13 142:25 151:23 151:24 152:3 169:5,9
linkers 34:11 35:4,13 45:19 54:2 56:13 101:12,18 124:11 142:22 143:17
linking 98:24 106:24 176:23
links 40:16 108:12
list 17:4 33:24 88:21 91:13
listed 24:21 33:3 55:9,25 56:2,7 160:19
listing 40:7 163:17,20
literal 84:2
literature 37:12 49:5 52:3 105:6 110:20 146:11 153:21 166:25 167:1,14,16
litigation 22:3 22:9,14
little 40:7 121:3 124:14 125:10 137:21,22,22 149:13 151:6 165:12
livenote 5:10
llp 1:20 2:4,13 3:4 5:6 179:7
long 10:17 51:8 52:22 88:21 91:13 162:9
look 39:6,9,10 54:14 58:25 63:7 87:4 96:18 128:12 138:25 147:24 170:12 172:4
looked 8:25 127:7
looking 58:23 81:12 102:24 109:8 118:8 132:1 162:6 167:15 171:24
lost 59:24 97:13 103:23
lot 8:7,11 12:11 14:17 17:5 23:20 36:20 44:11 45:1 52:17 64:1,7 66:16 90:11 108:21 115:25 116:2 127:4,24 149:7 167:9
lots 60:25 64:18 137:24 142:2 145:12
lunch 104:1,4

m

machinery 147:21
made 12:15 13:7,17,23 15:18,20,24 16:1 37:16 46:10 60:10 65:1 66:17 81:15 105:10 143:2 144:25 146:7 147:19 149:8,14,24 151:19 165:2 182:5
maintain 29:2
make 23:18 25:11 28:7 39:5 43:1 46:13 49:7 61:1 63:24 64:5,13 67:5 71:10 79:5 84:7 85:14,17 86:13 92:21 104:23 105:9 117:17 118:3 119:4 124:17

125:14 134:12
137:7,13,15
142:18 143:3,4
144:12 148:23
151:5 158:18
159:6 161:19
161:20 164:15
164:25
makes 105:1
108:14 118:13
119:12 120:2,8
120:10
making 36:13
36:18 37:14
43:22 66:17
72:10 85:21,24
86:10 141:21
142:8 148:21
149:9 153:23
154:2 159:1
161:13 164:18
164:19 166:15
167:2,4,10,17
175:2
mammalian
49:19
manipulation
30:13
manufacture
50:4 53:9
march 32:1,3
32:10 55:21,24
56:6,8,11,21
57:6,15,21
59:12,18,22
60:5,9 65:5
92:1,15 93:4
96:12 99:15,25
156:17 169:12
170:5
mark 127:16
159:21,25
marked 9:10
24:10 31:1,6
128:2 160:2
168:3,7 172:18
173:1,15,16
market 59:15
59:18
marketed 54:7
54:23 55:2
58:18
marketing
55:12,15
markings
151:16
marks 79:3
123:24 124:4
124:24 125:11
massachusetts
1:22 3:7 5:7,12
179:1,5,8,11
material 16:14
materials 16:22
matter 19:9,22
20:22,25 21:16
36:1 44:17
61:2 66:16
68:7,23 71:18
72:4 91:24
92:13 108:3
109:12 113:3
179:6
matters 21:21
21:25 22:13
24:21
mctigue 3:5
9:23 10:15
14:5,13 15:15
16:4,17 17:10
19:17,23 20:3
20:9,14,17
23:14 24:1,6
25:19 26:3,14
27:6 28:4,21
28:23 29:2
30:22 31:22
32:11 33:2
34:14 35:7
36:2 37:25
40:1,19 42:13
43:15 45:13
46:17 47:15
48:7,18 49:23
50:24 51:4
55:22 56:4,24
57:8,16,22
59:13,23 61:11
62:11,18,25
69:20 70:25
71:20 72:6
76:6,10 77:1
81:23 82:12,21
87:11 88:1,5
90:18 91:10
92:2,16 94:15
95:8,11 99:10
100:13 101:9
103:25 107:5
109:6,16 110:2
110:14 111:3
113:25 115:10
117:11,19
118:19 119:6
119:21 120:18
121:22 122:8
122:20 123:9
126:8 127:14
130:24 131:9
131:24 132:8
132:16 133:1
134:7,22 136:4
137:1 138:20
139:13,19
140:5,20
141:22 145:10
150:22 152:11
152:19,23
153:3 154:15
155:16 156:14
156:18 157:4
157:22 160:3
162:1,6 164:12
165:25 169:17
170:19 171:7
172:12 173:10

173:20 174:7 177:8,23
mean 11:5,8 12:7,8 27:13 38:12 49:24 57:9 59:14 65:19 67:19 68:16,24 75:18 80:4,18 81:13 86:16 98:1 108:12 110:13 112:21 116:24 119:18 120:6 124:3 128:24 134:9 149:14 154:12 155:23 155:25 157:5 164:2 176:24
meaning 100:17 109:20 109:25 129:13 145:23
means 26:2 29:13 31:14 67:16 68:9 87:2 97:25 99:4 115:1
meant 63:21 90:12
measuring 10:23
medicament 164:20
medicaments 164:16
medication 7:23
medicinal 32:17
meet 9:3,6
members 19:14
membrane 161:24 162:3 162:19,20,24 163:3,12 165:14,23 166:4,6,8
memory 55:10 165:22
mention 155:3
mentioned 8:23 22:13 23:11 31:18 33:25 37:9,11 38:10 38:15 46:22 55:1 60:15 66:11 101:16 104:16 114:21 115:7 116:10 147:2 159:10
mentions 41:8 101:22
menu 121:4
merely 43:22
messing 40:22
met 6:12
methods 48:2 146:15,17
mfecp1 62:1
middle 88:6 151:25
mind 39:8,16 51:19 76:6 104:17 137:11 159:17
miniantibodies 4:16 172:22 173:1,24
miniantibody 175:4
minimum 157:11
minute 127:20
mischaracteri... 136:5
mismatch 123:16
missed 62:9
misspoke 40:11
misstep 149:8
mistake 149:13
mixing 137:3
modification 147:4
modified 122:18 123:7
modifies 107:10
modify 106:13
modifying 107:16
modular 4:11 168:2,8
moieties 88:18 88:22 124:9,10 144:15
moiety 58:3 88:12,19 91:22 92:7 93:9,21 94:6,13,23 95:3,25 96:22 97:6,7,15,21 98:16,18 99:17 106:5,7 107:13 110:11 122:11 123:16 144:2
molecular 27:23 148:12
molecule 12:1 13:8,16 36:25 37:3 38:9,13 38:15,20 39:1 42:12,12,24 44:22 45:10 60:22 63:25 64:6 83:19 84:1 92:18 93:1 98:9 142:17 143:21 144:20 145:4 146:6 147:7,18 150:4 151:5,18 155:5,5,10

156:4,4 157:12 157:17 171:23
molecules 16:16 18:7 37:11,15 39:3 55:1 60:14,16 60:21 67:9 85:24 86:3 91:8 104:18,23 127:11 129:17 137:13 138:2 142:11 144:11 144:24 146:6 146:10 156:2 157:18
moment 117:15 159:17 170:23
monoclonal 10:8
morning 6:10 6:11
motif 62:8,17 75:24
multispecific 91:8
myriad 120:14

n

n 6:1 39:20 40:17 42:1 98:4 174:14,16 174:23 175:1,9 175:19
name 55:6
named 52:6
native 158:17 165:8 170:14
nature 26:17 154:6
ndubuka 2:15 95:6
nearly 165:11
necessarily 27:15 35:9 45:5 60:16,24 118:3 120:6 147:2
necessary 145:7 182:6
need 28:7 43:16 43:23 44:2 45:20 46:3 51:8 64:6,13 64:14,14,19 66:7 74:3 110:20 143:6 152:10 159:24 160:11 169:20 178:1
needed 44:10 99:16
needs 43:7,9 65:1 72:22 73:9 124:20 137:6
neither 179:12
never 6:12 18:4 18:6 37:16 49:3 79:15 137:25 146:7 158:21
new 27:15 80:14 124:17 131:15 138:24 163:25 164:2,3 164:5,6
nine 55:9
nods 7:8
nomenclature 112:1
non 60:12 157:16 169:13 170:3 171:4
noncovalently 142:24
normal 129:12
normally 98:1 105:12
northern 3:6 6:5
notary 5:11 6:6 179:4 182:13 182:19
note 180:10
noted 182:7
notice 5:8 53:21 74:19
noticed 37:7
novel 28:12 35:12 36:18 159:13,18
novelty 146:13
november 18:20
nucleic 64:20
nucleotide 62:23 63:19
number 13:17 13:23,25 14:4 23:4 46:7 54:1 54:5 70:1,2 81:25 112:7,19 113:2 118:12 118:17 119:2 119:15 120:7 120:24 124:7 126:23 127:1 132:4,13,21 136:22 139:24 140:1 157:17 158:18,24 159:22 160:7 166:25 167:6 170:9
numbers 4:13 40:9 68:25 111:18 112:5 121:25 172:23
numerous 17:4 53:25 137:8 147:8

o

o 6:1
object 17:10 19:17 165:25
objection 10:15 14:5,13 15:15 16:4,17 23:14 24:1,6 25:19 26:3,14 27:6 28:4,21,22 29:3 30:22 31:22 32:11 33:2 34:14 35:7 36:2 37:25 40:1,19 42:13,20 43:15 45:13 46:17 47:15 48:7,18 49:23 50:24 51:4 55:22 56:4,24 57:8 57:16,22 59:13 59:23 61:11 62:11,18,25 69:20 70:25 71:20 72:6 77:1 81:23 82:12,21 87:11 90:18 91:10 92:2,16 94:15 95:8 99:10 100:13 101:9 107:5 109:6,16 110:2,14 111:3 113:25 115:10 117:11,19 118:19 119:6 119:21 120:18 122:8,20 123:9 126:8 127:14 131:9,24 132:8 133:1 134:7,22 137:1 138:20 141:22 145:10 150:22 152:19 152:23 153:3 154:15 155:16 156:14,18 157:4,22 162:1 164:12 169:17 171:7 172:12 174:7
objectionable 29:1
objections 132:16 136:4 139:13,19 140:5
obligations 21:21 23:18
obtain 29:22
obtained 67:23
obvious 158:21
obviously 129:5
offer 150:14
offering 91:21 92:6,17
office 1:1
offices 179:7
oh 41:12 76:8 81:6 121:24 158:6 170:22
okay 6:20 7:1 7:21 8:2,18 9:3 9:9,19 10:2,3,6 10:21 11:15 12:22 13:1,13 17:6 19:5 20:10,18 21:7 22:12,19,25 23:22 24:4,23 27:5 29:4,8 30:6 31:12,19 32:20 33:14,15 34:7 38:17 39:17,24 40:4 40:15 41:3,7 41:13,20 42:4 42:8 43:1 45:7 46:12 49:9 50:21 53:8,16 54:24 56:2 59:7 62:21 65:16 67:12 68:19 69:7,11 70:4 71:12 72:9 73:11,24 74:25 75:4,11 76:22 77:4,9 77:16,21 78:2 78:20 82:8,17 83:16,24 84:5 84:19,24 85:5 87:21 88:8,10 88:16 89:2,10 89:10,15,17 90:2,23 91:1 91:16 94:11 95:5,15 96:6 103:3,12,22 104:22 105:15 105:24 107:8 107:25 108:6 111:9,10,17 112:12,17,24 112:25,25 113:5,8,9,13,19 114:9,19 115:12 116:9 116:16 121:8 121:20 123:14 123:18 124:2 125:22 126:21 128:4,8,14 129:11,14,15 130:5,12,19 131:5 132:12 132:20 138:9 139:4,17 140:12,16 141:9,19 145:14 153:14 154:10,22

155:13 156:11 158:11,15,23 160:10 163:18 167:21 169:6 169:10 170:23 170:24 171:17 172:7,8,17 173:8,21 174:10 175:23 177:2,5
ones 11:17 55:8 55:13 127:7 129:14 146:23
onwards 90:21 114:14 123:23
opinion 23:24 24:20 33:4 37:18 38:17 39:2 46:15 53:2,6 69:8 84:5 85:21 91:21 92:7,17 99:8,23 100:12 101:20 102:6 102:15 108:4 110:16 111:1 113:9 119:10 119:11,18 121:9 123:21 132:25 134:17 136:1 169:22 170:2,8
opinions 16:12 16:21 23:2 36:1 114:16 160:21
opportunity 160:24
options 28:9 148:10 149:5
orcutt 169:12 169:15
order 28:6 35:9 43:9 44:3 64:5 70:12 73:14 145:8 177:21 179:10
ordered 12:14
ordering 177:18,24
ordinary 25:17 25:23 26:1,6 26:11,15 27:11 27:12 28:9,17 28:20 29:9,23 30:7 32:20 33:12 35:16,23 37:1,14 38:18 39:5 42:9 43:6 43:11 44:5,12 45:4,7,23 53:19 57:20 65:5,7 66:19 67:7 74:1,6 75:4 77:4 78:14,24 80:1 80:12,19 82:14 85:13 91:25 92:14 98:22 100:17 109:3 109:20,25 148:20 149:2 150:9
orientation 34:11 35:5 175:22
original 70:5 177:14
originality 42:23
originally 11:1 69:13,17,21
outcome 13:13 13:19 148:18 179:16
outside 110:6 131:10 132:9 133:1 134:8
overarching 45:5
oversaw 12:24
oversee 12:23
overseen 12:19 13:3
own 26:1 27:2 159:14 167:12
owner 1:9 2:3
oxford 52:10

p

p 6:1

p.m. 1:18 104:5 168:1,1 178:6
page 4:2,7 24:13 25:16,20 26:5,18 28:14 30:9 31:18 40:8,9 68:25 69:3 76:7,9,13 76:16,16 83:14 83:14,15 94:1 94:2 114:13 122:10 125:20 125:24 126:6 128:9 130:22 131:2 140:11 140:18,19 141:11 145:16 145:16 162:13 165:7,8,13 170:13,14 172:4 173:9,23 181:4,7,10,13 181:16,19
pages 142:20
paper 168:7 169:19,22 175:24
paragraph 26:9 28:14 29:25 50:2 53:13 54:14 55:25 56:3,8 56:17 58:12,16 58:23 59:1,2,4

61:4,7 67:21 76:4,14 86:14 88:7 89:11 92:25 93:25 94:22 95:22 100:8 102:20 114:14,15 121:12,19 122:10 123:22 130:21 140:10 140:17 150:16 153:7,17,20 158:13,16 165:3
paragraphs 29:24 67:14 83:13 140:21
part 10:10 18:2 65:2 69:17 70:17 73:17 84:11 85:7 89:24 115:2 119:17 137:2 157:16 174:2
partial 49:7
particular 8:8 8:14 12:13 14:21 17:7,17 26:8,19 33:24 37:6,6 39:8 56:6 63:12 65:13 66:8 67:1,2,15 83:20 87:12 92:4 106:16 110:4,10 111:8 114:21 122:6 122:24 124:21 125:6,13,17 128:22 129:14 130:6 134:2 137:11 141:6 142:6 143:2,10 144:14 146:16 147:9 148:15 150:1 151:22 151:24 154:11 154:17,23 162:5
particularly 24:20 38:14 97:23 122:2 146:15 147:5 157:11,13 170:16 175:3
parties 179:13 179:15
partner 105:12 105:14,19
partners 154:13
parts 11:9 24:19 73:1 87:3,3 141:6 142:23 154:25 155:10 163:8,8
passage 88:11 88:16,24 95:23 100:23 106:18 110:4 129:7 137:11
passages 93:8 93:19 121:8
passing 22:2
passport 6:5
past 17:12 19:3 22:22
patent 1:1,2,9 1:13 2:3 4:8,9 22:8,14 26:8 30:20 31:2,9 31:10,21 37:6 38:16 39:7 60:18 63:5 64:10 70:3 71:16 72:2,12 72:20 73:18,21 73:25 76:20 78:16 80:2 83:19,24 87:13 87:24 93:9,19 95:24 96:5,8 96:13,19 98:24 102:16,20 106:2 107:20 107:23 110:7,8 111:7 115:22 120:13,13 124:14 125:2 126:7 127:18 128:1,5 131:14 131:15,16 133:3,6,18,19 134:1,13 137:6 138:6,8,10,14 138:18,24 145:1,3,7 146:8,12 152:6 152:7 154:12 154:17 157:16 158:24 159:9,9 159:11,19,22 160:1,4,5,17,21 161:1 166:19 169:12 175:7
patent's 79:17
patents 23:1 87:9,19 126:23 127:1,4 164:17
pause 18:13
pcr 32:23
pct 31:25
peds 52:7,14 53:1,2
peer 52:10
people 10:4 23:17 27:19 53:6 57:10 60:9 65:7 166:24
people's 167:13
peptide 13:9 54:1,2 148:2
peptides 157:20

person 25:17 25:22 26:1,6 26:11,15 27:11 28:9,16 29:15 29:23 30:7 32:20,21 33:12 33:18 34:8,18 35:1,9,25 37:1 37:14,18 38:18 39:4 42:9,15 43:6,11 44:7 44:12,13 45:4 45:7,11,23,25 46:12 47:7,12 52:1 57:20 74:1,6 75:4 77:4 78:14,23 80:12,19 82:14 85:13 91:25 92:14 99:19 109:3 145:24 148:19 149:2 150:8
personally 18:6
petitioner 1:5 3:3
pgr 173:17
pgr2026-00025 1:12 4:13 172:23
ph.d 1:19
ph.d. 1:16 4:3 5:6 6:2 179:6 180:5 181:2,24 182:2,4,12
pharmaceutical 22:21 32:17
pharmacokin... 10:24
phrase 41:16 106:11,13 107:9
phrases 73:1,13
pick 112:8
picked 18:6 121:2 124:15
picture 176:19
pieces 125:11
piper 2:4
place 1:21 5:7 89:7 101:15 102:9,13 162:5 179:8
plain 78:9,10 78:22 79:20 80:7 85:3 100:17 109:20 109:24 111:13 112:3,10,23 126:1
plan 64:8 141:1 142:11 150:4 150:10,14
plasmid 50:11
plausible 61:13
played 38:6
please 7:9 25:25 71:24
plethora 142:21
plural 90:5
plus 123:2
pm 104:5,10,15 104:20,25 105:5,10,15,20 105:25 106:5 106:10,15,20 106:25 107:5 107:10,15,20 107:25 108:5 108:10,15,20 108:25 109:5 109:10,15,20 109:25 110:5 110:10,15,20 110:25 111:5 111:10,15,20 111:25 112:5 112:10,15,20 112:25 113:5 113:10,15,20 113:25 114:5 114:10,15,20 114:25 115:5 115:10,15,20 115:25 116:5 116:10,15,20 116:25 117:5 117:10,15,20 117:25 118:5 118:10,15,20 118:25 119:5 119:10,15,20 119:25 120:5 120:10,15,20 120:25 121:5 121:10,15,20 121:25 122:5 122:10,15,20 122:25 123:5 123:10,15,20 123:25 124:5 124:10,15,20 124:25 125:5 125:10,15,20 125:25 126:5 126:10,15,20 126:25 127:5 127:10,15,20 127:25 128:5 128:10,15,20 128:25 129:5 129:10,15,20 129:25 130:5 130:10,15,20 130:25 131:5 131:10,15,20 131:25 132:5 132:10,15,20 132:25 133:5 133:10,15,20 133:25 134:5 134:10,15,20 134:25 135:5 135:10,15,20 135:25 136:5

136:10,15,20
136:25 137:5
137:10,15,20
137:25 138:5
138:10,15,20
138:25 139:5
139:10,15,20
139:25 140:5
140:10,15,20
140:25 141:5
141:10,15,20
141:25 142:5
142:10,15,20
142:25 143:5
143:10,15,20
143:25 144:5
144:10,15,20
144:25 145:5
145:10,15,20
145:25 146:5
146:10,15,20
146:25 147:5
147:10,15,20
147:25 148:5
148:10,15,20
148:25 149:5
149:10,15,20
149:25 150:5
150:10,15,20
150:25 151:5
151:10,15,20
151:25 152:5
152:10,15,20
152:25 153:5
153:10,15,20
153:25 154:5
154:10,15,20
154:25 155:5
155:10,15,20
155:25 156:5
156:10,15,20
156:25 157:5
157:10,15,20
157:25 158:5
158:10,15,20
158:25 159:5
159:10,15,20
159:25 160:5
160:10,15,20
160:25 161:5
161:10,15,20
161:25 162:5
162:10,15,20
162:25 163:5
163:10,15,20
163:25 164:5
164:10,15,20
164:25 165:5
165:10,15,20
165:25 166:5
166:10,15,20
166:25 167:5
167:10,15,20
167:25 168:5
168:10,15,20
168:25 169:5
169:10,15,20
169:25 170:5
170:10,15,20
170:25 171:5
171:10,15,20
171:25 172:5
172:10,15,20
172:25 173:5
173:10,15,20
173:25 174:5
174:10,15,20
174:25 175:5
175:10,15,20
175:25 176:5
176:10,15,20
176:25 177:5
177:10,15,20
177:25 178:5
point 23:18
89:6 102:8,12
102:22 122:5
124:20 125:5
125:12,16
153:22 164:23
polypeptide
39:21 88:14
94:7,24 95:25
96:8 97:15
98:17,19 99:17
106:6,8 107:14
110:12 141:12
142:14 143:16
143:18 162:22
162:23,24
163:3,6,12
polypeptides
142:9 147:19
163:7
portion 74:17
76:23 77:9,17
78:4,9,22 79:7
82:4,25 84:10
84:16,20,25
85:2,2,10
105:3 111:13
111:13,14,15
111:22 112:1,3
112:3,9,10,22
112:23 138:11
138:12 153:16
170:3
portions 75:6
103:20 111:19
posa 33:4 66:7
68:12 72:23
86:1 97:18
99:12,24 118:7
118:14 119:25
120:3 121:1
124:20 125:5
125:12 137:7
137:12,17
146:5,14
147:16 151:17
152:2 167:15
pose 39:3 43:4
posed 27:4
posi 33:10

posita 33:11,17 34:1,7,16,25 47:6,11,23 48:4,15 49:9 49:14 52:1 53:20 57:14 62:21 63:17 74:16 75:12,20 79:13 84:1 85:5 93:4,6,17 93:23 96:7,12 99:15 100:5 103:6,14 104:18 105:7 125:17 143:9 143:14 153:22 166:17
positions 82:18
possesses 68:8
possession 68:12 71:18 72:4,24 118:5 118:15 120:1 137:19
possibilities 120:24 136:23
possible 42:18 64:16 88:22 108:9 109:1 120:21 127:4 132:5 148:10
possibly 55:11 147:12,20
post 147:4
pounds 20:21 21:8
practically 121:6
practice 68:11 85:16
practicing 145:25 153:10 166:18
preamble 68:23 116:12,22
precedence 29:12
precedes 84:21 85:1 107:11
predict 13:16
predictability 50:19
predictable 50:6 53:11
predictably 165:2
prefer 147:1
preferred 124:22 125:3,4
preparation 8:3,19 9:20
prepared 24:18 25:4 130:11
preparing 8:16 21:2 25:8 142:11
prescribed 179:9
presence 146:10
present 3:11 86:10 101:12 125:25 170:18
presents 86:12
press 52:11
presumably 85:18 146:7
prevent 7:24
previous 29:14
previously 9:10 24:10 31:1 37:23 173:16
primary 10:7 10:13,18
prime 89:5,21 90:4,4 91:4,4
prior 22:25 23:10,23 28:1 36:15 146:19 168:13 170:5,7 173:5
priority 30:20 30:23 31:13,20 31:20,24 32:2 32:10 46:22,25 47:1,2 169:11
privilege 19:22 20:1,4,6,11
privileged 9:25 19:19
privileges 20:13
probably 29:10 65:24 79:2 87:18 108:5 109:12 155:21 163:19
problem 44:12 45:3 102:20 105:10 121:1 122:11,12,17 122:24 123:7 137:5,10,17 138:1 142:19 144:8,24
problems 146:5 161:1 166:14 166:17,23
procedure 20:8
proceed 27:8
proceeding 8:4 16:13 19:25 23:23
proceedings 18:13 23:1 179:11
process 50:7 53:12
procter 3:4 21:15,22
produce 73:14 86:3 96:21 97:5

produced 89:5 89:21 179:11
product 20:4,6 20:11 59:15
production 6:4 51:9 144:10 152:18,22 153:2 180:15
products 59:17 91:6
professional 5:10 179:4,21
project 13:2 14:4,7,21 18:23,23,25 19:1 36:17 42:15 43:25 47:18 65:8,20
projects 13:2 14:18,18
promising 14:10
promoter 148:1 148:16
pronounced 50:15
proper 34:12 35:5
properties 12:1 13:16 36:19 144:15
proportion 86:4
propose 112:15
proposed 159:1
protein 11:1,4 11:7,8,18 12:6 12:16,20 13:5 15:11,21 16:2 23:13,24 35:22 36:13,18,24 37:21 44:17 47:14,25 49:10 49:21 50:23 52:3,6 56:22 56:23 60:12 62:24 63:20 81:1 83:21 84:12 85:6 86:11,13 96:22 97:5 126:24 127:2,6,10,11 141:20 142:1 144:13 145:22 145:25 147:19 154:4,13 155:3 157:2 159:14 163:25 164:19 164:21 166:4,5 166:6 170:5
proteins 12:11 16:24 17:9 23:8 30:15 34:10 35:3,13 37:8 50:20 53:25 54:5,10 55:20,24 58:21 58:22 60:10 61:19 74:13 87:10 128:22 147:4 148:14 153:24 154:2,5 154:11,24 155:6,9,14 156:3,22 157:21 158:19 159:2,5 160:14 160:16 161:8 161:11 164:8 164:10 165:1 166:6 167:2,10 167:18
proteolysis 44:18 45:17,18
proved 158:19
provide 71:4
provided 22:9 22:15 23:2 121:4 163:16 179:9
providing 21:24
provisional 32:2
public 5:11 6:6 13:12 22:1 179:4 182:19
published 13:11
purification 12:19 13:4 30:14 50:14
purified 13:3 44:22
purpose 43:17 164:10,13
purposes 69:12
pursuant 5:8
put 23:17 38:7 45:6 72:25 124:16 125:11 167:9
putting 36:11 110:8 115:12 170:1

q

qualify 52:14
question 6:24 7:13,18 10:2 24:4 35:20 43:2 51:2 54:20 57:17 59:6,25 67:18 70:4,7 71:2 78:21 81:6 84:14 86:16 87:22 89:16 92:4 93:14 95:10 96:17 102:1 103:4,13 106:14 110:19 115:18,18 116:1 118:4,7 119:24 121:5

134:14 135:21 138:9,23 140:25 152:16 152:24 157:24 158:9 160:10 160:13 161:4 162:17 168:23 172:8 173:11
questions 7:10 7:25 27:3 39:15 95:12 113:3 141:6 177:4,9
quick 167:23 176:25
quite 8:7,11 10:17 13:15,20 34:19 38:1 54:25 55:13 56:25 57:2 68:3 93:16 101:12 105:8 109:1 119:22 126:9 127:3,4 147:14 148:7 160:25 165:2 176:20
quote 94:4
quotes 94:22
quoting 94:21

r

r 6:1 181:3,3
ramon 107:3
range 120:4 154:2
rate 20:21
rather 16:14 168:18 169:2,5
read 71:22 87:18 93:8,19 96:24 100:23 106:25 128:12 140:25 141:4 166:25 172:14 180:9 182:5
reading 78:16 80:2 93:7,17 96:7,13 99:12 103:6,14 130:16,17 162:4 176:25 179:12
reads 100:5
ready 51:23 89:16 141:7
reagent 78:25
realize 20:7
really 17:4,13 26:20 27:13 29:13 43:19 63:24 108:3 120:22 134:13 136:9,13 139:1
reason 113:19 113:22 114:8 115:6,6,14 122:25 123:14 123:19 149:22 180:11 181:6,9 181:12,15,18 181:21
reasonable 74:11 82:16
reasonably 71:16 72:2 99:12
reasons 86:7 122:6,9 153:9 153:15 158:20
recall 17:13 19:7 22:13 56:14 140:14 154:1
receipt 180:17
receive 22:20
recent 11:17 13:2
recently 13:22
receptor 58:4,8 58:13 59:10 60:6 163:9 166:12
receptors 157:20
recess 51:21 95:20 104:5 168:1
recite 114:25
recited 62:7
recites 117:1,9
recognize 9:11 24:11 31:6 84:2
recollection 161:3 162:23
recombinant 30:15 32:23 47:13,24 49:10 50:5 53:10,22 141:20 142:1,9 148:3 152:17 152:21 153:2
record 18:12 22:1 49:5,6 51:20,22 67:6 78:20 95:19 104:4 177:12 179:11
recording 7:4
reduced 68:10
redundancies 108:22
redundant 108:20,24
refer 53:13 54:15 76:7 83:6 84:20 111:8,17,18 112:1 128:21 130:20 147:25 173:18
reference 112:16

referenced 180:6
references 56:9 56:10 167:1
referred 44:7
referring 20:2 24:23 84:23 90:23 107:18 125:18 133:3 150:23 153:15 153:19
refers 128:25 129:2 165:18
refresh 165:22
regard 26:7 101:13,14 121:14 137:16
regarding 19:25 114:17 118:4
regardless 118:25
regards 137:11
region 74:21,23 80:7,8,16,24 81:10,19 82:10 83:1 91:23 92:8,10 105:11 105:13,20 114:5 123:2 126:2,3 133:15 133:16 134:2,4 135:6,7,12 136:21 139:7,8
regions 75:8 90:16,21 91:19 127:12 129:1 129:18 130:2,9 130:14 131:7 131:23 132:6 132:14,22 133:22 135:17 138:16 139:25 140:1 166:7,8 171:13
registered 5:9 179:4,21
regular 156:21 177:25
related 70:4 145:21 148:2 162:21 179:13
relationship 18:17
relative 156:20 179:14
relevant 96:16
reliable 52:19 55:11
remain 61:22
remains 63:9
remember 9:1 11:15 15:5,9 17:17,19 18:19 21:1 22:17 23:4,9,15 24:2 24:7 81:24 87:19 104:20 126:25 127:6 149:18 162:10 162:11 169:4 173:6
remind 57:17 88:1 152:11
render 132:23
renders 139:10
repeat 62:17 81:6 92:3
repeated 75:24
repetition 62:8
rephrase 46:7 60:3 61:5 71:13 80:21 126:4 158:8 173:13
report 8:8,15 8:16 22:4,15 24:25 54:11 55:7 56:17 64:9 69:12 86:8 92:24 114:2
reported 1:24
reporter 5:9,10 5:11 7:4 8:9,13 22:5 66:3,22 96:23 97:1 116:18 168:21 177:13,17,23 178:2 179:4,21
reports 21:2 22:5,6,10 54:25 55:1 114:13 147:10 165:4
represent 75:21 129:8 133:11,14,18
representations 81:13 134:16 134:21
represented 81:14 92:19 134:24 135:2
representing 22:23 112:18
represents 74:18 75:13 80:6
reproduced 76:15
reputation 53:7
require 85:22 85:25 95:15 116:1 153:11
required 67:10 182:13
requirement 68:2 69:16 70:10,20,24 71:15 72:1,13 72:16
requirements 70:13
requires 41:3 65:2 66:17

94:12 164:24 168:17
requiring 147:21 169:1
research 14:4,7 16:23 64:8 110:17 141:1 150:10
reserve 116:5
residue 56:20 57:6
residues 56:20 57:5
respect 7:1 24:24 59:3 76:22 78:21 82:17 90:13 104:17 142:3 157:15
respectively 75:9
rest 16:13 25:3 74:4 173:19
reston 2:8
result 149:9
results 14:9 161:21 172:5,5
retained 61:8
retains 44:23
retention 62:2
return 180:13 180:16
review 8:2,6,20 129:6 160:11 160:24 169:20 176:17 180:7
reviewed 52:10 88:24 125:2 162:9
reviewing 39:14
revolves 42:22
right 6:15,19 6:21 7:3,16,20 7:22 8:13,24 11:3 12:18 18:16 31:25 33:16 36:21,21 38:4 39:18 40:21,24 47:5 51:15 53:18 59:2 60:5 62:16 63:16 64:3 66:14 67:13 76:3 82:1,3 83:17 84:18,25 89:18 90:13 91:2 100:21 104:13 105:16,20,21 107:14 108:15 111:6,11 112:4 112:23 114:14 115:2,3,3 116:5 117:7,10 117:17 118:24 121:13 123:17 126:7 128:11 128:15 130:17 135:19 136:12 140:16 141:10 152:5 153:6,8 155:12 160:4,8 169:25 170:12 173:23 177:3 177:19
roman 121:25
rough 178:3,5
roughly 21:7
routine 47:19 50:6 53:11
rpr 1:24
rule 6:22 107:2
rules 6:17 20:7
rush 178:1

s

s 6:1 181:3
sake 112:16
sandra 1:24 5:8 179:4,20
satisfactorily 6:3
satisfactory 179:9
satisfied 69:17 71:15 72:1,12 72:17
satisfy 70:12
saw 160:25 165:3
saying 34:18 45:14 54:20 63:17 65:3 66:25 93:3 108:13,19,23 122:25 126:25 166:23
says 28:15 29:9 39:18,23 41:1 74:13,20 75:22 88:22 90:10 91:11 95:24 98:15 99:3 101:7 102:9,23 105:15 106:4 107:9 119:1 165:20 172:13
scfv 4:11 88:13 90:6 168:2,8
scheduled 103:24
scientists 17:1
scope 84:2 85:16 86:5 117:8 118:6,15 120:1,5,9 131:10 132:7,9 132:15,23 133:2 134:1,8 134:23 137:7 137:19 138:14 138:21 142:10 142:12 143:3 153:10

scopes 150:5
se 118:3 120:7
seattle 2:17
second 28:14 162:25 165:17
secondly 83:5
secretion 145:20
section 24:25 25:20 30:4,8 31:17 97:12 98:11 121:19 121:19,23 153:18
see 12:4 14:9 36:10 53:14 59:7 76:13 79:17 96:3 97:25 103:4 108:6 118:1 125:8 128:15 128:18 131:25 145:1 153:4 160:12 163:13 165:15,16,17 169:6 170:17 170:22 171:8 171:10,11 175:14 176:20
seeing 110:20 154:1 173:7
seems 61:13 70:21 102:25 106:23 109:21 121:2 125:5 132:1 134:15 136:17 137:20 137:23 176:13
seen 125:2 126:23 127:1,3 128:5,24 160:23 168:13 169:19 173:4,7
select 37:2 42:11 43:9,12 44:3,8 45:11 45:25 46:10 48:4,11
selecting 51:6 145:18
selection 50:12 52:7
sense 13:25 26:23 68:8 108:14 112:6 125:14 164:16 164:17
sensitive 45:17
sent 180:14
sentence 106:12 109:9 153:16 165:18 170:16
separate 143:7 144:7
separately 89:3 91:3,12,13 141:13 142:4 142:15
september 1:17 5:1 179:8,16 180:3
seq 40:17 111:22
sequence 30:13 31:24 39:19,19 39:22,24 40:4 40:6,12,16 41:17,18 42:3 42:3 43:14 62:6,13,14,16 62:23 63:19 65:13 67:2,8 74:18 75:1,6,7 75:16 76:23 77:10,18,18,24 77:24,24 78:2 78:4,5,10,21,22 79:6,7 82:4 84:9,10,15,17 84:21 85:1,7,8 85:10 91:24 92:12 111:9,11 112:2,10,24 115:1,2 117:2 126:11,13 128:16,17 150:23 151:1,1 151:2,2,6,25 161:24 162:3 162:19,21 163:13,17,20 176:18
sequences 79:5 79:11 150:21 151:3
serial 70:1
series 113:3
serine 56:20 57:6
set 26:5,8,18 30:8 64:7,25 86:7 114:1 142:20 164:22
sets 114:16 141:17
several 6:16 61:25
sf8456410 1:25
shakes 7:8
sheet 180:11
short 51:17 56:18
shorthand 5:9 33:12 123:17
shown 126:5
side 140:21,21 174:21,24
sign 180:12
signaling 157:18
signature 24:14 179:19
signed 88:25 180:19

significance 80:1
significant 52:2 52:15 53:3
signing 179:12
similarly 86:23 128:16
simple 42:4 66:16 136:11
simply 21:24
single 33:21 83:18 89:4,20 90:5,6 91:7 148:1 149:7,8 171:11 174:2 174:13,15,22 174:25 175:16 175:22
sir 6:12 7:12,13 7:22 8:2 25:16 32:6 46:21 51:15 52:20,23
sit 15:9 17:16 55:4 59:17 81:25 116:7 153:25
site 147:13
sites 147:9,11
sitting 110:23 115:16
situations 45:20 140:7
six 21:19 22:12 23:5,6,10
skill 25:17,23 26:1,6,12,12,15 27:11 28:9,16 29:23 30:7 32:20 33:12 35:9,15,16,24 37:1,14,19 38:18 39:5 42:9 43:6,11 44:5,12 45:4,8 45:23 46:12 53:19 57:20 65:2,5,7 66:18 66:20 67:7 74:1,7 75:5 77:5 78:14,24 80:1,12,20 82:14 85:13 86:10 91:25 92:14 98:23 106:17 109:3 110:9,12 148:5 148:20 149:3 150:9
skilled 71:17 72:3
small 14:3 170:9
soluble 45:10 45:15 157:2,14 161:15,18 162:23
solutions 180:23
somebody 43:21 82:9 125:3 154:2
sorry 8:9 10:12 11:23 15:19,25 29:25 33:10 36:7 39:10 40:11 54:1,19 57:13 58:18 59:24 61:5 63:6 66:23 69:14 71:10,24 76:8 77:22 81:6,18 82:24 83:3 88:11,18 89:6 92:8,23 94:20 95:9 96:25 97:12 100:8 101:10 107:15 117:2 117:22 118:22 121:24 126:3 129:23 130:22 131:11 133:13 135:25 136:10 145:25 152:21 152:24 153:4 162:2 173:12
sort 26:19 27:19 31:15 33:6 34:1 38:15 49:12 59:24 64:8 65:8,11 69:1 80:10 88:6 125:9 146:4 164:3 176:19
sorts 87:7 102:21 117:14 117:23
sounds 7:6 82:1
sources 157:18
spanning 161:24 162:3 162:19,20,24 163:3,12 165:14,23 166:8
spans 82:4
speaking 155:2
spec 162:7
species 87:6 105:22
specific 87:7 159:5
specifically 61:9,12 76:1 88:19 121:20
specification 23:12 68:15,17 68:20 69:5,8 70:15,18 71:4 71:8,8 72:10 72:20 73:2,3,6 74:5,9 79:18 83:25 87:4 89:2,18 90:2 90:14 91:2

93:20 94:5,23 96:5 99:13 100:2,5,10,15 100:16,18,23 101:13,21 102:3,9 103:7 103:8,14 108:22 112:13 113:15 118:9 120:20,23 121:4 124:7,16 133:17 135:14 135:15 137:6 137:25 138:3 139:5 141:17 150:19,20 151:4,8 158:7
specifications 101:16 154:19 158:2
specificity 47:9 49:16
specified 114:6 131:7,21 136:20,22
specifies 130:5 130:13
specifying 127:12
spelled 146:3
spent 20:24
splice 151:5
spliced 137:24
spoken 10:4
square 2:6 149:15
ss 179:2
stable 50:12 51:7,8
stand 30:6,10
standard 32:22 49:20,24 50:22 80:23 81:9 141:19,25 142:2,5,8 145:22,25
standards 24:22 25:1,22 30:4
stands 129:9,10
start 6:24 15:19,25 69:25 76:14 126:4 141:5 149:15
starting 30:8 67:21 83:14 94:1 96:19 98:14
starts 89:11 121:12,14,19 140:11,19 145:15
state 53:8 76:14 158:16 158:23
statement 94:5
statements 25:13
states 1:1 4:8 88:11 89:3,19 90:3,15 128:1 173:24
step 141:1,10 145:15 147:24 149:7 150:4 169:23,23
stephen 17:24
steps 64:7,11 141:18 149:4
straightforward 47:19 65:23 145:2 149:23
strategies 33:19 34:9 35:2
straying 34:15
street 2:16
strictly 155:2
structural 80:25 81:10 91:24 92:13
structurally 160:15
structure 12:1 142:17 147:6
structures 72:18
study 175:24
studying 11:25 17:25
stuff 114:20 127:24
subcloning 32:25
subcontractor 12:15
subcontractors 12:12
subject 68:7 71:18 72:4
subscribed 182:14
subsequent 21:3 122:14
substance 104:10
succeeded 150:13
success 159:1
successful 14:23
successfully 154:3
suffolk 179:2
suggested 79:13
suitable 36:16 44:3 50:10 144:10 146:16
suite 2:7
summarizes 25:21
summary 170:15,21

172:14
supernatant 50:15
supervised 27:20
supervisor 42:16
supplied 16:14 163:20
supplies 151:22
supply 150:20 152:17 153:1
support 71:5 93:9,20 167:6
supported 71:7 115:24
supports 70:14
suppose 143:15
supposed 164:6
sure 15:8 19:13 43:1 54:25 55:13 58:11 63:8 72:21 84:13 88:3 91:12 92:21 93:17 109:17 114:12 129:8 163:17,18 173:6
surface 157:19
susceptible 44:18 45:18
svfv 90:7
sworn 6:6 182:14
system 64:20
systems 49:19

t

t 181:3,3
table 24:24 127:23
tables 73:8
take 39:6,9 40:23 44:14 51:17 63:22 73:12 77:13,14 77:15 82:6,7 84:7 119:7 140:24 147:24 149:17 167:23 169:22 170:12 178:4
taken 45:2 51:21 95:20 104:5 111:21 168:1 179:8,14
talk 6:22 98:23 101:17,24 102:2 110:6 121:20 122:2 123:22 129:24 141:11
talked 56:13 77:16 110:10 140:13 141:1 151:12 155:4
talking 13:25 35:11 38:8 51:6 62:13 65:12 67:3 69:23 73:21 92:22 101:10 110:3 117:9 136:16 138:5,7 142:7 154:10 154:16,18,21 154:23 158:1 163:10 164:8 165:8 166:12
talks 96:20 97:2,24 98:7 98:24 101:21 102:3,16 103:8
target 61:9 62:2 88:18
targeted 88:11 96:21 97:5
targeting 88:12 88:17,19 91:22 92:7 93:9,21 94:8,25 96:2 96:22 97:6 98:15 99:16 106:4 110:11 122:11 123:16 124:9
targets 88:22
tasking 37:13
team 12:25 18:2 19:14 53:1
techniques 32:23
technologies 164:3
technology 150:1 163:25 164:2,5
tell 9:24 98:22 112:5 120:19 120:23 139:4 139:10 143:8 145:4 162:16
tellekson 2:14 177:18
telling 99:7,11
ten 14:15 162:9
term 12:9 26:17 29:11 31:13 51:8 57:14 90:12 112:8,12 125:3 154:4 156:21
termini 34:12 35:5
terminology 171:2
terminus 16:10 38:21 39:20 40:17 41:19 42:1 94:7,25 95:16 96:1 97:16,17,21 98:3,4 169:14

171:5 172:2,10 174:1,5,14,16 174:23 175:1,9 175:19
terms 8:18 21:2 34:2 42:4 72:22 99:23 100:16
test 100:3
tested 13:8 14:12
testified 6:7
testify 23:12
testimony 7:5 42:8 96:6 104:20 136:5 180:9,17 182:8
testing 10:22 142:11
text 68:17,20 73:7 75:11,15 78:10,22 79:20 79:21 80:7 85:3 111:13 112:3,10,23 126:2
texts 80:5
tfg 147:11
tgf 15:24 144:2 144:18 152:3
tgfbeta 14:25 17:22
tgfbetaii 163:9 166:12
tgfbetarii 15:1 15:13,21 16:2 16:9 17:9 38:19 41:4,9 41:13,18 42:5 42:12,18 43:8 43:23 58:2 63:13 67:3 74:14 75:16 76:2 113:15 115:8 120:16 126:11 160:16 161:8 168:17 169:2
thank 7:12 9:19 32:14 33:16 43:3 46:20 47:5 54:16 56:12 67:12 76:10,11 88:5 89:14 100:21 104:8 177:9,11
therapeutic 10:8 155:15,22 155:24 156:13
therapeutics 1:4 3:12 179:6 180:4 181:1 182:1
therapy 12:2 164:16,20
thereto 179:15
thing 18:5 33:7 37:22 69:1 71:6 92:22 105:2 106:23 142:13,16 145:24 146:2 148:19
things 10:23 14:22 18:2 27:15 33:4,6 33:25 34:1 35:11,14 44:11 44:15,25 64:1 64:21 87:5,7 89:25 90:11 91:14 98:2 105:1 109:21 117:3,7,14,23 118:13 119:3 119:12,16 120:14,21 125:23 126:19 137:3,9 142:2
think 6:14 10:17 11:2,11 14:2,6 18:20 19:12 21:9,19 25:14,20 26:4 26:6,11,15 27:11 28:5 29:18 30:2,2 33:3,23,25 34:15 35:8 36:3 37:13 38:1,7,11,23 41:8 42:20 43:16 48:10,19 55:3,10 57:23 59:16 63:9 64:4 68:3 71:2 71:2,9 72:22 74:3,5,6,10 75:10 78:17 79:1,25 80:5 80:11,19 81:12 82:16,22 83:3 83:4 85:24 86:6,19 92:18 92:25 93:23 96:16 97:18 99:2,3,11 100:7,14 102:13 104:2 104:21,25 105:7 106:19 108:16,22 109:7,9 110:3 114:1,10,14,24 115:16 119:23 121:5,15 126:10,12,14 126:22 127:3 128:7 130:24 136:2,9 137:2 138:22 142:20 143:12 147:10 149:21 151:25 153:18 154:8 155:3,4,17,21 156:1 157:10

157:23,25 159:15 161:3 163:5,19 164:13 166:2,5 166:14,20 167:15,24 170:6 171:12 171:14 174:8 174:12,18 175:11 176:4,9 176:22
thinking 30:24 38:14 87:12
thomas 3:5 19:12
thought 79:15 108:11 149:23 149:25 159:18 161:1
three 22:18 55:11 62:5,8 75:24 130:7,8 141:12 142:14 143:16
tidy 127:19
time 10:17 18:1 19:6 20:24 40:23 52:22 65:11 103:5,24 129:6 140:24 149:25 155:21 159:19 160:25 162:9 177:10 177:12 180:18
timeframe 180:8
times 6:16 21:18,19 22:1 61:25 62:8 75:25
title 74:13
tmctigue 3:9
today 6:12 7:25 17:16 55:4 59:17 65:21 81:25 104:15 110:23 114:22 116:9 126:22 134:18 168:14 173:5,15
today's 6:18 8:3,19 9:20
together 36:12 45:6 61:21 72:25 93:7,18 97:8 98:2 109:22 124:11 124:16 125:11 137:3 142:23 143:16,23 144:11 163:1
told 29:13 42:16 43:7,13 44:9 45:8,25 46:2 70:18 99:16 126:22 135:5,11 136:1 136:7
took 149:21
top 112:7,14 125:19 165:9 174:21
topological 176:19
topology 4:12 168:3,9
total 14:22 21:5
totally 36:18 164:9,14
towards 124:21 125:6,12
toxin 60:13
toxins 157:18
track 103:23
trademark 1:1
trail 59:24
trained 10:25
transcribed 179:8
transcript 179:11 180:6 180:19 182:5,8
transfect 48:16 49:1 64:16
transfectant 50:13 51:8
transfectants 51:7
transfected 49:4
transfection 50:10 51:10,13
transient 51:10 51:13
translational 147:4
trap 2:12 95:13
tremendously 48:9
trial 1:2
trials 55:6
tried 100:3
trouble 37:20
true 34:3,5 126:2 143:22 179:11 182:8
try 6:25 7:9 118:7 148:24 148:25
trying 63:24 136:18 142:8 142:10 147:17 159:6
tuesday 1:17
turn 50:2 76:3 78:2 83:12 87:23 113:6 128:8 140:9,17 152:5 158:12
two 11:9 52:25 55:11 60:20 62:23 63:20 67:9 98:1 109:21 137:3 146:4 147:11 154:5 161:15

163:1 171:15
type 66:11 156:2,12
types 155:14
typically 81:20

u

u.s. 1:13 31:9 127:17
uh 7:6 28:18 63:14 79:24 94:3 114:23 115:4 131:3 133:23 135:10 135:20 153:13 159:12 168:20
uk 4:9 160:1
ultimately 14:23 134:9 167:10
uncertain 143:12 144:22
uncertainty 61:2 144:1
unclear 175:20
uncommon 80:10
uncountable 86:21,23,24 118:20,23,24 119:2,12,15 120:7 132:12 132:18,21 136:22 139:24
139:25
under 7:23 23:17 75:1 172:5
underlined 74:20 83:8,8 84:9 85:2,9 111:22 112:3,9 112:22
underlining 79:4,10,22 80:5 83:1,5,10 151:13,20
underlying 74:17 75:6 76:23 77:9 78:4 82:4,20 82:25 84:16 111:13
understand 7:14 26:20 28:16 31:23 43:2,16,24 44:2 60:17 67:20,22 68:4 68:9,16,19 69:2,4,10 74:5 74:8,12,17 75:12,17,20,25 84:13,22 87:2 92:19,21 93:20 93:24 96:8,13 97:19 99:12,19 100:1,4 102:6
102:14 103:7 103:15 106:17 110:13 113:13 113:17 124:1,6 124:19 129:7 136:2,8 137:18 143:23 174:20 175:25
understanding 26:24 27:2 28:19 29:1,8 29:23 31:13,15 50:21 67:17 68:1 74:11 78:15 83:11 109:3,14 124:21 127:9 129:9
understands 75:5
understood 7:19 74:1,4 77:5 78:23 93:14 149:22 173:20
undue 84:7 85:22,25 86:6 149:3 153:11
ung 7:6,6
unhelpful 100:15
union 2:16
unit 80:25 81:1 81:4,11
united 1:1 4:8 6:4 128:1
university 1:8 52:10 179:7 180:4 181:1 182:1
unknown 91:25 92:13 93:4,5
unlimited 118:12,17,17
unpredictabil... 167:17
unpredictable 14:19 36:19 164:24 167:4
unsuccessful 161:12
unsuccessfully 154:3 167:11
unsure 157:13
unusual 37:9 37:15 38:9,12 39:2 47:20,22 104:19,24 105:1 147:15
upper 160:8 170:15
usage 145:21
use 12:8 17:22 33:11 34:10 35:4,14 43:13 44:19 112:8 113:2 152:3

used 4:14 33:19 34:9 35:3,25 47:8 48:2 51:10,14 56:21 56:25 57:1,25 65:21 66:9 96:14 98:5,6 99:20 110:21 124:24 125:3 139:25 140:2 148:13,17 166:10 172:21 172:25 180:19
useful 12:2
uses 103:1
using 42:19 113:16 118:11 169:8,9
usually 51:10 125:1 129:21 145:1 165:2

v

v 1:6 90:5 180:4 181:1 182:1
vague 112:6
valid 133:7,8 134:10 135:3
validity 133:7
variable 74:21 74:23 75:8 76:24 78:5,7 79:4,6 80:7,15 80:24 81:10,16 81:18,19 82:10 83:1 90:8,9,16 90:20 91:17,18 91:23 92:8,10 105:3 114:5 123:2 126:2 127:12 129:18 130:2,9 147:13 171:13
variants 33:20
varied 21:23
various 111:18
vast 120:4,24 124:7 164:25
vector 48:5 50:11 64:20 66:12 145:19 148:1,15
vectors 32:25
verbal 7:6 79:10
verbally 7:10
verify 180:9
veritext 180:14 180:23
veritext.com 180:15
vh 91:17 126:16
view 109:11 124:13
viral 50:11
virginia 2:8
vitae 9:14
vl 91:17 126:16
vs 179:7

w

wait 6:23
waldmann 17:25
want 26:23 42:17 43:1 45:17 58:25 67:5,15 71:22 77:12 102:15 111:6,17,25 112:8 114:19 114:24 121:15 122:2 136:2,7 140:17,20 141:4 142:17 158:8 178:2
wanted 12:16 85:16
washington 2:17
water 18:10
way 36:21 60:17 67:9 75:22 79:1,22 80:19 81:12 98:5 106:20,21 106:21,25 123:8 126:17 135:8,16 139:9
ways 66:2 124:12 137:24 142:8
we've 51:15 67:3 80:3 103:20 111:20 123:4,14 130:6 149:11 163:10 166:12 167:1 167:22 171:12 171:21,23 174:12
week 8:20
welcome 104:7
west 1:20 2:13 5:6
white 179:7
whoo 169:18
widely 60:24
winter 52:23
wishing 38:19
withdraw 87:21 158:10 158:25
witness 8:11,14 9:24 18:9 19:18,24 20:16 22:7 31:1 66:5 66:23 76:11 88:8 95:9 96:25 97:4 121:24 127:19 127:22 131:3 159:24 162:4,8

168:23 170:22
177:5 179:9,12
180:8,10,12,18
word 33:11
77:13,14,15
82:7 100:10
106:12 107:11
107:16 108:12
109:19,20
111:21 114:22
116:11,21
117:13,25
118:2,11 119:7
119:14
words 7:5 26:1
27:2 53:23
57:5 59:8
72:17,25 73:12
82:8 106:12
110:21 162:18
work 7:7 12:12
13:11,14,21
20:4,5,11 25:7
115:25 116:2
141:20 145:23
146:21,23
148:4 158:17
worked 10:16
10:22 11:12,18
14:25 15:3,6
17:1 18:4 19:2
19:6 21:14
22:22 27:20
working 12:12
14:20 17:24
18:1 57:11
148:12 149:19
150:15,18
world 155:15
155:22,24
156:13
worry 40:23
write 24:16
67:23
written 22:3,6
23:3,8 24:5
67:16,19,21
68:2,5 69:16
70:10,13,20,24
71:3,4,7,14,25
72:12,16 73:17
113:10,20,23
114:17 115:24
116:10 117:21
118:4 119:19
121:10,18
122:3,7 123:20
132:24 134:6
135:3,23,25
136:24 137:4
137:16 138:18
139:11
wrong 148:23
149:9

y

y 2:12 95:13
yeah 22:7
54:24 58:25
62:4 63:8,9
64:4,5 87:17
90:11 91:14
92:6,9 104:1
106:19 108:2
109:2 112:25
114:1,12,13
118:16 134:9
134:25 135:24
136:13 138:5
138:22 139:20
144:22 145:9
163:18 166:2
170:23 171:20
years 11:21
14:21 16:25
17:13 149:17
149:21 162:9
yep 63:11
105:24 127:21
144:22 169:8

z

zemab 61:7
62:1