UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MERCK SHARP & DOHME LLC,

Petitioner,

v.

HALOZYME, INC.,

Patent Owner.

ORAL AND VIDEOTAPED 30(B)(6) and 30(B)(1)

DEPOSITION OF

JAMES J. MOON, PH.D

November 18, 2025

Reported By: SUSAN ASHE, CER

Job No.: 7005314

1 Tuesday, November 18, 2025
2 8:40 a.m. Eastern Standard Time
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7 Oral and videotaped deposition of JAMES J.
8 MOON, PH.D. taken on behalf of the Petitioner,
9 beginning at 8:40 a.m., on Tuesday, November 18,
10 2025, at the law offices of Sterne Kessler Goldstein
11 & Fox, 1101 K~Street, Northwest, Washington, D.C.,
12 before Susan Ashe, Certified Electronic Reporter and
13 a Notary Public of the District of Columbia.
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APPEARANCE OF COUNSEL:

On behalf of the Petitioner:

SIDLEY AUSTIN LLP
BY: JEFFREY P. KUSHAN, ESQ.
BY: CHELSEA M. HIMES, ESQ.
BY: AMIT BHATLA, ESQ.
1501 K Street, Northwest, Suite 600
Washington, D.C. 20005
(202) 736-8000
jkushan@sidley.com
chimes@sidley.com
abhatla@sidley.com

- and -

DECHERT LLP
BY: BRIAN M. GOLDBERG, ESQ.
Cira Centre
2929 Arch Street
Philadelphia, Pennsylvania 19104-2808
(215)994-4000
brian.goldberg@dechert.com

1 APPEARANCE OF COUNSEL (Continued):
2 On behalf of the Patent Owner and the Witness:
3 STERNE KESSLER GOLDSTEIN & FOX
4 BY: PRATIBHA KHANDURI, PH.D., ESQ.
5 BY: R. WILSON "TREY" POWERS, III, PH.D, ESQ.
6 BY: ELDORA L. ELLISON, PH.D., ESQ.
7 1101 K Street, Northwest, Tenth Floor
8 Washington, D.C. 20005
9 (202) 371-2600
10 pkhanduri@sternekessler.com
11 tpowers@sternekessler.com
12 eellison@sternekessler.com
13 - and -
14 QUINN EMANUEL URQUHART & SULLIVAN, LLP
15 BY: ELLIOT CHOI, ESQ.
16 295 5th Avenue, Ninth Floor
17 New York, New York 10016
18 (212) 849-7000
19 elliotchoi@quinnemanuel.com
20 - and -
21 BY: NANCY L. ZHANG, ESQ.
22 50 California Street, Suite 22
23 San Francisco, California 94111
24 (415) 875-6600
25 nancyzhang@quinnemanuel.com

1 ALSO PRESENT:
2 Aubrey Haddach, Esq., Halozyme (Via Zoom)
3 Joshua Mack, Esq., Halozyme (Via Zoom)
4 Sue Wang (Via Zoom)
5 Jason Levin, Videographer
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1 MOTION TO STRIKE

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22 (REPORTER'S NOTE: All quotations from exhibits are

23 reflected in the manner in which they were read into

24 the record and do not necessarily denote an exact

25 quote from the document.)

1 TUESDAY, NOVEMBER 18, 2025;
2 8:40 A.M. EASTERN STANDARD TIME
3 --o0o--
4 VIDEOGRAPHER: We are now on the
5 record. The time is 8:40 a.m. Eastern on
6 November 18, 2025.
7 This is the video-recorded
8 deposition of James Moon, Ph.D., in the
9 matter of Merck Sharp & Dohme LLC versus
10 Halozyme, Incorporated.
11 This proceeding is being held at
12 the offices of Sterne Kessler in
13 Washington, D.C.
14 My name is Jason Levin. I'm a
15 videographer on behalf of U.S. Legal
16 Support. The court reporter is Susan
17 Ashe, also on behalf of U.S. Legal
18 Support.
19 Will counsel please state their
20 appearances for the record, then the court
21 reporter will swear in the witness.
22 MR. KUSHAN: Jeff Kushan, from
23 Sidley Austin, for the Petitioner. With
24 me is Amit Bhatla, Chelsea Himes, and
25 Brian Goldberg of Dechert.

1 DR. KHANDURI: This is Pratibha
2 Khanduri, from Sterne Kessler, on behalf
3 of patent owner Halozyme. Also in the
4 room for Halozyme are Eldora Ellison,
5 Ralph Powers, III, from Sterne Kessler;
6 Nancy Zhang and Elliot Choi from Quinn
7 Emanuel; and attending remotely are Josh
8 Mack and Aubrey Haddach from Halozyme.
9 Whereupon,
10 JAMES J. MOON, PH.D.
11 having been first duly sworn, was examined
12 and testified as follows:
13 EXAMINATION
14 BY MR. KUSHAN:
15 Q. Good morning. Could you state your name
16 for the record.
17 A. I'm James Moon.
18 Q. And where do you reside?
19 A. I reside in Ann Arbor, Michigan.
20 Q. Have you ever been deposed before?
21 A. Yes, I have been deposed before.
22 Q. How many times?
23 A. I've been deposed twice before.
24 Q. Okay. Were you a patent expert in that
25 role?

1 A. Yes. I served as a patent expert in those
2 two depositions.
3 Q. Okay. Were those in connection with court
4 proceedings?
5 (No audible response.)
6 Q. Let me start with this -- let me give you
7 a little bit of background.
8 A. Yes.
9 Q. So you've been deposed. You know the
10 process. I will ask you questions, and you have to
11 respond to my questions.
12 A. Right. Right.
13 Q. Okay? Your counsel may have -- make
14 objections. Once she's finished the objection,
15 proceed to answer my question, unless you've been
16 instructed not to answer. Okay?
17 (No audible response.)
18 Q. If you don't understand a question I've
19 presented to you, please let me know, and I'll try
20 to give you a better question. Okay?
21 A. Okay. I understand.
22 Q. If you need a break, just let me know.
23 Generally, we'll finish the answer to your question
24 before we break, but I'll try to always take a break
25 when you ask me for a break. Okay?

1 A. Okay. Thank you.
2 Q. If I need to have a conversation with your
3 counsel, sometimes I may excuse you from the room.
4 I'll just let you know. Okay?
5 A. Okay. Thank you.
6 Q. So you understand you're under oath today?
7 A. Yes, I understand that.
8 Q. And you have to provide truthful testimony
9 in response to the questions I pose to you.
10 Do you understand that?
11 A. Yes, I understand that.
12 Q. Is there any reason you cannot testify
13 truthfully today?
14 A. I will always truthfully testify.
15 Q. When were you retained by Halozyme or by
16 Sterne Kess- -- well, actually, who retained you?
17 A. I was contacted by my counsel, Pratibha.
18 Q. When was that?
19 A. I don't know the exact date, but it was a
20 few months ago. Sometime early 2025, this year.
21 Q. Do you think it was in the summer of this
22 year?
23 A. I don't know the exact date, but summer of
24 this year -- between summer and fall of this year,
25 yeah.

1 Q. Okay. If you had to give me an estimate
2 of how many hours you've worked on the matter for
3 this proceeding, how many hours would that be?
4 A. I don't remember the exact hours, but I
5 can give you a range.
6 I would say less than 100 hours, between
7 50 to 100-ish hours.
8 Q. Okay.
9 A. Yeah.
10 Q. What did you do to prepare for today's
11 deposition? Just give me a general description of
12 that.
13 A. To prepare for the deposition today?
14 Q. Yes.
15 A. I reviewed the literature. I reviewed the
16 exhibits that I cited in the declaration. I met and
17 discussed these with my counsel.
18 Q. Is the literature that you reviewed
19 limited to the literature that you had cited in your
20 declarations?
21 DR. KHANDURI: Dr. Moon, I would
22 caution you to not divulge the substance
23 of communication with counsel.
24 To the extent you can answer the
25 question without revealing substance or

1 communications with counsel, you can do
2 so.
3 A. So I read many papers. That's part of my
4 daily job.
5 And then I also reviewed the exhibits that
6 I listed in my declaration. And they form the basis
7 of my opinion.
8 Q. I just want to understand: The literature
9 that you reviewed recently in connection with
10 preparing for this deposition, were all the papers
11 and other materials the ones that are on your
12 exhibit list on your declarations?
13 A. Once again, I read the many papers, but
14 the papers that I rely on for forming opinions
15 related to this matter are stated in the exhibit
16 list.
17 MR. KUSHAN: I'm going to
18 introduce....
19 (Whereupon, Halozyme Exhibit 2074,
20 previously marked, was presented to the witness.)
21 DR. KHANDURI: Thank you.
22 Q. This is your -- either four --
23 MR. KUSHAN: Yeah, I just want
24 the four declarations. Can I just have
25 them. Okay.

1 Q. So the first one was your declaration in
2 PGR2025-0003. It's this one.
3 The second one is your declaration -- your
4 second one, this is the -- let's try this again.
5 That declaration is your declaration in
6 the second proceeding, the -0004 proceeding.
7 DR. KHANDURI: Counsel, Dr. Moon
8 has copies of his declaration. And I
9 represent they are -- these are clean
10 copies. Do you mind if we use that?
11 MR. KUSHAN: That's fine with
12 me. And do you need copies --
13 DR. KHANDURI: You can take the
14 file.
15 MR. KUSHAN: All right.
16 Perfect. That saves a lot of time.
17 Q. All right. So you have before you --
18 A. Thank you.
19 MR. POWERS: Yes.
20 Q. You have before you the four declarations
21 you have prepared in connection with the proceedings
22 we're addressing today. Right?
23 That's the 2025-0003, -0004, -0006, and
24 -0009 proceedings. Correct?
25 A. Yes. I have my declarations here.

1 Q. And those are the declarations you
2 prepared and signed in each of these proceedings.
3 Correct?
4 A. Yes, I prepared and signed those
5 declarations.
6 Q. Before you signed each of those
7 declarations, did you review each carefully?
8 A. Yes, I -- I prepared and reviewed them
9 carefully before signing them.
10 Q. And are there any errors in the four
11 declarations, to your knowledge?
12 A. To my knowledge, there are no errors in
13 any of these declarations.
14 Q. All right. During the course of the
15 deposition today, I'm going to ask you questions,
16 and I'll reference the declaration in the -0003
17 proceeding.
18 If any of your answers with regard to the
19 other declarations would be different, please let me
20 know. Otherwise, I'm going to assume that your
21 answer with respect to the 0003 proceeding will
22 apply to all four of the declarations you filed.
23 Is that fair?
24 A. Yes, I understand that.
25 Q. Okay. So, if you could, go to Page 5 of

1 your declaration in the 0003 proceeding.
2 And do you see, at the bottom of that page
3 is a -- it goes to the next page. You'll see a list
4 of all the materials you say that you've reviewed in
5 the declaration?
6 A. Yes. I see the list of documents
7 considered.
8 Q. You reviewed each of the documents that
9 list -- that is listed in that section of your
10 declaration. Right?
11 A. Yes. I reviewed each of the documents
12 cited here.
13 Q. And again, were there any other documents
14 that you reviewed in connection with forming your
15 opinions in this declaration and the other three
16 declarations that are not listed on that list of
17 exhibits?
18 A. Once again, I read many papers as part of
19 my job. And all the papers that I read that allowed
20 me to form the opinions in this declaration are
21 listed here.
22 Q. And do you recall any specific papers that
23 are not on that list that you reviewed between the
24 sign -- time you signed your declaration and now
25 that relate to the opinions that you're providing

1 today?
2 A. I don't recall any other papers that are
3 not cited here that I can think of.
4 Q. Okay. If you look at the list of
5 exhibits, there's no exhibit with the number EX0-~--
6 1001. Is that right?
7 A. I don't see that number in the exhibit
8 list.
9 Q. Do you understand that the four
10 proceedings that you provided declarations in relate
11 to four different patents owned by Halozyme?
12 A. I understand there are four different
13 patents that are in discussion today, yes.
14 Q. Have you reviewed those four different
15 patents in connection with preparing your opinions
16 in these four proceedings?
17 A. No, I have not reviewed the patents.
18 Q. Have you been given any information about
19 what is in, or described in, the four patents that
20 are the subject of these four proceedings?
21 DR. KHANDURI: Objection; form.
22 A. No. I was not given any information on
23 these patents, and I have not reviewed them.
24 Q. So it's correct that none of the opinions
25 you're expressing in your four declarations concerns

1 information that's actually in any of those four
2 patents that are the subject of these four
3 proceedings. Is that right?
4 DR. KHANDURI: Objection; form.
5 A. I was asked by my counsel to opine
6 whether:
7 ...polyclonal antibodies
8 generated in human females
9 against any of the modified
10 PH20 polypeptides to bind to
11 wild-type human PH20
12 polypeptide in vivo.
13 And that's what I opined on in my
14 declaration.
15 Q. So you limited your opinions to that
16 question in your declaration.
17 And I'll also point out you have other
18 statements following that one on Paragraph 15,
19 other --
20 DR. KHANDURI: Objection --
21 Q. With respect to the questions that you
22 framed in your declaration that you were asked to
23 address, that's the basis of your opinions. Right?
24 DR. KHANDURI: Objection; form.
25 A. In addition to what I stated earlier and

1 also in Paragraph 14, I have been asked to consider
2 and opine whether...polyclonal antibodies generated
3 in non-human female mammals against any of the
4 modified PH20 polypeptides to bind to wild-type PH20
5 polypeptide in vivo, as stated in Paragraph 15.
6 And also, I've been asked to opine whether
7 a POSA would have expected successful delivery of
8 monoclonal antibodies to the vaginal cavity of human
9 females.
10 So I reviewed the literature, formed my
11 opinions, and prepared these four declarations.
12 Q. So you don't know whether any of the
13 opinions you're providing in your four declarations
14 concern any information that is in the four patents
15 in the four proceedings. Is that right?
16 DR. KHANDURI: Objection; form.
17 A. Once again, I've been asked by my counsel
18 these three main questions that I mentioned earlier,
19 as stated in Paragraph 14, 15, and 16 of my
20 declaration, and I rendered my opinions in my
21 declaration.
22 I have not had a chance to review the four
23 patents you mentioned.
24 Q. Okay. Did you review any documents titled
25 "Institution Decisions" that were in the records of

1 the four proceedings that you're providing testimony
2 in?
3 A. Could you repeat the question?
4 Q. Sure. Did you review any documents that
5 have the title "Institution Decision" in any of the
6 four proceedings that you're providing testimony?
7 A. I did not review those documents that you
8 mentioned.
9 Q. Okay. Did you review any declarations
10 that were prepared by an individual named
11 Dr. Michael Hecht?
12 A. No, I have not reviewed any declaration
13 that you mentioned.
14 Q. Did you review any declarations from a
15 person named Dr. Sheldon Park?
16 A. No, I have not reviewed that.
17 Q. Did you review a declaration from an
18 individual named Dr. Gary Cherr?
19 A. No, I have not reviewed them.
20 Q. Do you know who Dr. Cherr is?
21 A. I don't know that person.
22 Q. Have you ever heard his name?
23 A. I don't recall that name.
24 Q. You've never spoken to Dr. Cherr?
25 A. I don't recall speaking to Dr. Cherr.

1 Q. Do you recall speaking to any scientist in
2 connection with these proceedings who is not
3 counsel?
4 DR. KHANDURI: Objection; form.
5 A. No. I only discussed these matters with
6 the counsel here.
7 Q. And just to confirm, you did not review a
8 declaration from an individual named Gregory Petsko?
9 A. I did not review declarations of that
10 individual.
11 Q. Do you know who Dr. Petsko is?
12 A. I do not know Dr. Petsko.
13 Q. Have you ever heard his name?
14 A. I don't recall his name.
15 Q. And you haven't reviewed a declaration
16 from Dr. Melanie Simpson. Is that right?
17 A. I have not reviewed declarations of that
18 individual.
19 Q. And you've never -- have you ever heard
20 her name?
21 A. I don't recall her name.
22 Q. Okay. All right. So I want to go over
23 your educational and training background.
24 A. Um-hum.
25 Q. You have an undergraduate degree in

1 bioengineering from UC Berkeley?
2 A. Yes, I have an undergraduate degree from
3 UC Berkeley in bioengineering.
4 Q. And was that -- so that program, what was
5 that focused on?
6 A. The bioengineering program at UC Berkeley
7 focuses on different ways to come up with novel
8 therapeutics, different ways to come up with
9 preventive therapeutics against many different
10 diseases.
11 And I was trained to develop new
12 engineering tools to improve human health.
13 Q. Did you have any particular focus in your
14 undergraduate work?
15 A. During my undergrad studies, I performed
16 the research in a laboratory that studies
17 endothelial cells in blood vessels.
18 Q. Endothelial cells in what?
19 A. In blood vessels.
20 Q. In blood vessels. Okay.
21 And then, I'm going to actually give you
22 your CV while I have it. This is Exhibit 2075.
23 Just confirm that is your CV.
24 (Whereupon, Halozyme Exhibit 2075,
25 previously marked, was presented to the witness.)

1 DR. KHANDURI: Thank you.
2 A. Yes, this is my CV.
3 Q. Okay.
4 A. Exhibit No. 2075.
5 Q. All right. And you got your Ph.D. at
6 Rice --
7 A. Yes.
8 Q. -- in 2008. Is that right?
9 A. Yes, I obtained my Ph.D. from Rice
10 University in 2008.
11 Q. Okay. And it says that your dissertation
12 was directed to synthesis of biomimetic hydrogels
13 for neovascularization in vivo.
14 That's the focus you had in your
15 dissertation. Is that right?
16 A. Yes. My dissertation was on synthesis of
17 biomimetic hydrogels for neovascularization in vivo.
18 Q. What are the hydrogels made out of?
19 A. In my own work, we used a polymer called
20 polyethylene glycol to form hydrogels.
21 Q. Okay. And these hydrogels, do they have a
22 medical application?
23 A. Yes. These hydrogels have many potential
24 biomedical applications.
25 In my own work, we use those hydrogels to

1 promote new blood vessel formation.
2 Q. Okay. And then in 2008 -- from 2008 to
3 2012, you were a postdoctoral associate at MIT in
4 the lab of Dr. Darrell Irvine. Is that right?
5 A. Yes. I was a postdoctoral associate in
6 the laboratory of Dr. Darrell Irvine at MIT.
7 Q. And that was for a four-year postdoc?
8 A. It was roughly four and a half years of
9 postdoc training.
10 Q. And your focus -- what was your focus in
11 your postdoctoral work?
12 A. My postdoctoral work focused on vaccine
13 development and vaccine delivery.
14 Q. Before you got to MIT in 2008, had you
15 take -- had you taken courses in immunology?
16 A. Yes, I took courses in immunology.
17 Q. Was that in your postdoctoral work -- I'm
18 sorry, in your doctoral work or in your
19 undergraduate work?
20 A. I took courses in immunology in undergrad
21 at UC Berkeley.
22 I also took courses on biomaterials,
23 how -- and how they impact host systems, including
24 immune system, during my Ph.D. work at Rice
25 University.

1 I took courses in cell biology in
2 undergrad as well as in grad education.
3 Q. Did you take any coursework during your
4 time in your postdoctoral work?
5 A. I attended workshops. I may have sat in a
6 few courses during my postdoctoral work, but I did
7 not take formal classes for credit.
8 Q. Were any of those courses in the field of
9 immunology?
10 A. Most workshops and seminars that I
11 attended during my postdoctoral training were
12 related to immunology and vaccinology.
13 Q. And that was in that period 2008 to 2012.
14 Right?
15 A. That's correct. I took those workshops
16 and seminars between that time frame.
17 MR. KUSHAN: I'm going to
18 introduce a new exhibit. This will be
19 Exhibit 1118.
20 COURT REPORTER: Do you want me
21 to put a sticker on it?
22 MR. KUSHAN: Yes, please.
23 (Whereupon, Exhibit 1118 was marked for
24 identification.)
25 WITNESS: Thank you.

1 Q. This is a paper entitled "Engineering
2 Nano- and Microparticles to Tune Immunity,"
3 published in "Advanced Materials," Vol. 24,
4 Pages 3724 to 3746, in 2012. First author, James J.
5 Moon.
6 Is this a paper you authored, Dr. Moon?
7 A. Yes, I authored this paper in this
8 exhibit. Yeah.
9 Q. Does this exhibit describe the work that
10 you did during your postdoctoral period?
11 DR. KHANDURI: Objection; form.
12 A. I haven't reviewed this article for many
13 years. This was published in 2012.
14 Q. And I'm just getting -- does this
15 generally -- generally relate to the work that you
16 were doing in your postdoctoral work?
17 A. Oh, as the title suggests, we focused on
18 engineering nano- and microparticles to tune immune
19 responses in this review article.
20 And I believe we covered many topics
21 related to immunology and vaccine development in
22 this review article.
23 Q. So the nanoparticles and microparticles
24 you were developing were physical materials that
25 might be included in a vaccine. Is that right?

1 A. In general, in my own postdoctoral work,
2 we developed nano- and microparticles to deliver
3 vaccine components to improve vaccine responses.
4 Q. And what kinds of immunogens were you
5 delivering in these vaccines on those particles?
6 A. We delivered a variety of agents,
7 including vaccine antigens, adjuvant molecules, to
8 boost immune responses.
9 Q. Were any of the immunogens proteins?
10 A. Yes. I worked with protein antigens
11 during my postdoctoral training.
12 Q. What kind of proteins were they? Were
13 they from humans or viruses, or what -- just give me
14 a sense of what kind of proteins you were working
15 with.
16 DR. KHANDURI: Objection; form.
17 A. We used the proteins from a variety of
18 sources. One example is a protein from a infectious
19 pathogen to boost immune responses.
20 Q. And those would be viral pathogens?
21 A. We used viral pathogens, as one of the
22 example, for protein-based vaccines.
23 Q. Right. So none of your degrees are in
24 immunology. Right?
25 A. My degrees are in bioengineering.

1 But we use the principles of engineering
2 to improve immune responses and use that as a basis
3 for vaccine development.
4 Q. Do you believe that in December of 2012
5 you were an expert in -- on the human immune system?
6 DR. KHANDURI: Objection; form.
7 Relevance.
8 A. As part of my postdoctoral training, we
9 studied how to optimize and develop vaccines for
10 potential applications in humans.
11 Q. Do you think that the education and
12 training you obtained by December of 2012 made you
13 an expert in the human immune system?
14 DR. KHANDURI: Objection;
15 relevance.
16 A. As I mentioned, during my education and my
17 postdoctoral training, I applied principles of
18 engineering -- in particular, biomedical
19 engineering -- to develop better vaccines.
20 And we do that for the purpose of
21 developing vaccines in humans.
22 So whenever we design these vaccines, we
23 have that in mind, that we want to apply our
24 technologies to improve human health.
25 And I --

1 Q. I'm sorry.
2 A. And I --
3 Q. Go ahead.
4 A. And I meet at least the qualifications of
5 a POSA, as I stated in the declaration.
6 Q. Let's go to the declaration and look at
7 that paragraph.
8 So do you see, at Paragraph 18, you state:
9 I have been asked to apply
10 the following definition of a
11 POSA for purposes of my
12 analysis provided here.
13 And then that is:
14 A person of ordinary skill
15 in the art would have had an
16 undergraduate degree, a Ph.D.,
17 and post-doctoral experience in
18 scientific fields relevant to
19 study of protein structure and
20 function, such as chemistry,
21 biochemistry, biology,
22 biophysics.
23 So none of your degrees are in chemistry,
24 biochemistry, biology, or biophysics, are they?
25 DR. KHANDURI: Objection; form.

1 A. Bioengineering is a very interdisciplinary
2 field. It applies principles of chemistry,
3 biochemistry, biology, and biophysics to study
4 protein structure and function.
5 And in my own studies, we used principles
6 of biochemistry -- biochemistry, biology, and
7 biophysics, and immunology to come up with better
8 vaccines.
9 Therefore, I meet at least the
10 qualifications of a POSA as it's stated here.
11 Q. So if you look at the remainder of that
12 explanation in Paragraph 18, are -- in 2012, in
13 December of 2012, were you familiar with factors
14 that influence protein structure, folding, and
15 activity?
16 DR. KHANDURI: Objection; form,
17 relevance.
18 A. Yes.
19 Whether it's by 2012, you mentioned --
20 yes, I was familiar with the factors influencing
21 protein structure, folding, and activity.
22 And we use these principles to develop
23 vaccines.
24 Q. So the materials that you were developing
25 were not proteins. Right?

1 A. The materials we developed were designed
2 to contain and deliver antigens, including protein
3 antigens, for vaccine applications.
4 Q. Do you recall the biggest protein that you
5 used in one of your experimental efforts to produce
6 a vaccine during the period before December of 2012?
7 DR. KHANDURI: Objection; form.
8 A. I used many different protein antigens as
9 a vaccine component during my postdoctoral training.
10 One antigen that can -- I can think of is
11 ovalbumin as a model antigen.
12 Q. Were any of the protein antigens you
13 investigated during your work prior to December of
14 2012 a human protein?
15 A. I primarily used -- well, one of the
16 examples that I used were infectious
17 pathogen-derived viral antigens for vaccine
18 applications.
19 I may have used a human protein in some of
20 the studies, but I don't recall specific protein at
21 this point.
22 Q. Okay. In your work before 2000- -- sorry.
23 When I say "2012," let's just assume it's
24 going to be December of 2012, if I don't state that
25 explicitly.

1 So by December of 2012, had you used
2 protein homology models in your work?
3 A. Yes. I used protein homology models, such
4 as UniProt, prior to 2012.
5 Q. UniProt is the website that houses data
6 about protein sequences. Right?
7 A. Using UniProt, one can study the sequence
8 identity between different proteins.
9 Q. Had you used a protein structural model
10 produced using a service such as SWISS-MODEL?
11 DR. KHANDURI: Objection; form.
12 Q. By December 2000- and -- December of 2012?
13 DR. KHANDURI: Objection; form.
14 A. I was in a disciplinary team,
15 multidisciplinary team, that developed vaccines.
16 And there were other members who were
17 using SWISS-MODELs for protein antigens. And I
18 interacted with them to design vaccines.
19 Q. But you didn't ever personally create the
20 models, the protein models, using SWISS-MODEL before
21 December of 2012. Right?
22 DR. KHANDURI: Objection; form.
23 A. I did not use SWISS-MODELs personally, but
24 I was in a multidisciplinary team.
25 They used SWISS-MODELs and other softwares

1 to study protein structure with respect to protein
2 antigens for vaccine applications.
3 Q. And I'm asking primarily about your
4 personal experiences.
5 Based on your personal experiences, had
6 you ever studied a protein structure created in
7 SWISS-MODEL using a tool such as PyMOL or another
8 visualization tool?
9 DR. KHANDURI: Objection; form.
10 A. Once again, I was in a multidisciplinary
11 team, and I interacted with other researchers who
12 are using these models, including SWISS-MODEL, to
13 study antigen structure for vaccine applications.
14 And I basically perform this research in
15 collaboration with other individuals in the
16 multidisciplinary team.
17 Q. Okay. Again, just to be clear, I'm trying
18 to understand: You were not the person doing the
19 visualization of the protein structure with a tool
20 like PyMOL in these teams. That was somebody else.
21 Is that right?
22 DR. KHANDURI: Objection; form.
23 A. I mean, we, as a team, analyze the protein
24 structure with respect to protein antigens.
25 I did not personally use SWISS-MODEL. But

1 I was in a multidisciplinary team that used protein
2 modeling softwares to better design vaccines.
3 Q. Do you know what PyMOL is?
4 A. I understand there are many models for
5 protein modeling software.
6 Q. Do you recall if you had used, personally,
7 PyMOL to inspect or study a protein structure before
8 December of 2012?
9 DR. KHANDURI: Objection; form.
10 A. I -- once again, I did not personally use
11 PyMOL, but I was in a multidisciplinary team that
12 used protein modeling software to study protein
13 antigens.
14 Q. Before December -- or by December of 2012,
15 had you ever performed sequence alignments of two
16 proteins?
17 A. Yes. By 2012, I performed the sequence
18 alignment of proteins.
19 Q. Okay. By December of 2012 -- well, have
20 you ever -- by December of 2012, had you ever --
21 had -- try that one again.
22 By December of 2012, had you ever
23 produced, through expression techniques, a protein
24 that incorporated mutations into it?
25 DR. KHANDURI: Objection; form.

1 A. So I was in a multidisciplinary team that
2 developed the vaccines.
3 And, for example, one of the antigens we
4 focused on was HIV. So our team would make
5 mutations to the antigen to better deliver the HIV
6 antigens.
7 Q. Were you the person who personally
8 produced those proteins with mutations in it -- in
9 the protein?
10 DR. KHANDURI: Objection; form.
11 A. I worked with proteins that were mutated
12 for HIV vaccine applications.
13 I did not personally produce mutated
14 proteins, but I closely worked in a
15 multidisciplinary team to design and develop mutated
16 antigens for vaccine applications.
17 Q. Was that in the period of your
18 postdoctoral work?
19 A. Yes. I worked on HIV vaccines during my
20 postdoctoral work.
21 Q. By December of 2012, had you personally
22 performed experiments where you denatured or
23 refolded proteins?
24 A. Yes. By 2012, I did denatured proteins
25 and refolded proteins.

1 Q. By December of 2012, had you ever
2 personally done work to map epitopes on a protein
3 structure using a protein structural model?
4 DR. KHANDURI: Objection; form.
5 A. Once again, I was in a multidisciplinary
6 team that worked on vaccine development.
7 Other researchers were using protein
8 modeling softwares to study protein structures
9 within the team.
10 And together, we studied how antibodies
11 are binding to epitopes to target antigens.
12 Q. So somebody on the team may have done the
13 work to determine where the epitopes on the protein
14 structure were, and then you would discuss that
15 within this team. Is that right?
16 DR. KHANDURI: Objection; form.
17 A. So once again, I was in a
18 multidisciplinary team. There were researchers in
19 the team that were primarily responsible for the
20 modeling of software. And together with the team,
21 we studied antibody epitope interactions.
22 I also studied protein epitope
23 interactions using other tools, including ELISA.
24 Q. These are -- so you would test binding of
25 antibodies to the protein using the ELISA technique?

1 A. Yes. We would use ELISA as one of the
2 techniques.
3 Q. And you would -- you personally performed
4 that work, that experimental work?
5 A. Yes, I personally performed ELISA.
6 Q. And again, this was in the postdoctoral
7 period of your career. Right?
8 A. Yes. It's during the postdoctoral period
9 of my training.
10 Q. By December of 2012, had you ever
11 identified a linear epitope on a protein structure?
12 A. Yes, I worked with linear epitopes in a
13 protein structure by 2012.
14 Q. And to be clear, I'm asking if you had
15 identified the -- let me -- I'll make it a better
16 question.
17 By December of 2012, had you identified
18 the location of a linear epitope on a protein
19 structure?
20 A. Yes. By 2012, I'd identified and worked
21 with linear epitopes in a protein structure.
22 Q. How did you do -- how did you do that
23 work? How did you determine the linear epitope's
24 location in the protein?
25 A. For example, you can study linear epitopes

1 using ELISA.
2 Q. Is that how you did it?
3 A. I personally performed the ELISA to study
4 linear epitopes.
5 I also collaborated with other researchers
6 working on protein modeling to study linear
7 epitopes.
8 Q. When you did that work, were you working
9 with an enzymatic digest of the protein to identify
10 fragments that the antibodies might bind to?
11 DR. KHANDURI: Objection; form.
12 A. Could you repeat the question?
13 Q. Sure. I'm trying to understand how you --
14 what the experimental technique was that you used to
15 identify the linear epitopes.
16 My question was: Did you identify the
17 linear epitopes by reacting the antibodies with
18 fragments of the protein antigen?
19 A. Yes. You can study linear epitope
20 protein -- linear epitope of a protein interacting
21 with antibodies using fragmented protein.
22 Q. And just to be clear, I'm asking you: Is
23 that how you did it back before 2012, in your
24 experimental work?
25 A. In my own experiments, we do use peptide

1 sequences responsible for the linear epitopes and
2 use that as a substrate for ELISA using the
3 antibody.
4 Q. Okay. How did you identify the peptides
5 you selected to screen with in the ELISA, in your
6 own work?
7 A. I first review the literature, and then
8 study linear epitopes that have been identified in
9 the past by other researchers, and then design
10 peptide epitopes around those reported epitopes, and
11 then perform ELISA.
12 Q. Okay. Before December of 2012, had you
13 ever characterized the antibody repertoire created
14 in a polyclonal response in a mammal?
15 DR. KHANDURI: Objection; form.
16 A. Yes. I studied protein repertoire of
17 polyclonal antibodies by 2012.
18 Q. And to make sure I -- my question is
19 clear, when I use the word "repertoire," I'm using
20 it in connection with the set of antibodies produced
21 by the polyclonal anti- -- the polyclonal response.
22 Is that the meaning you understood in my
23 last question?
24 DR. KHANDURI: Objection; form.
25 Also, Counsel, do you mind

1 speaking a bit louder?
2 MR. KUSHAN: Sure.
3 DR. KHANDURI: I'm having a hard
4 time.
5 A. Could you repeat the question?
6 Q. Of course.
7 A. Yeah.
8 Q. In the last question, I asked you -- or
9 the -- I had asked about the repertoire of
10 antibodies produced by a polyclonal response, and
11 your answer used the word "polypeptide" -- or
12 "protein."
13 I just want to make sure that you
14 understood my question.
15 I was asking if you would characterize the
16 set of antibodies produced in the mammal in response
17 to the immunization, that -- that polyclonal sera,
18 did you characterize antibodies in that polyclonal
19 response?
20 DR. KHANDURI: Objection; form.
21 A. Yes, I characterized polyclonal antibodies
22 in sera.
23 Q. And that was before December of 2012?
24 A. Yes, that's right, before December 2012.
25 Q. Okay. And had you compare -- did you

1 compare the diversity of the antibodies within the
2 polyclonal sera one to the other for their ability
3 to bind to the target protein?
4 DR. KHANDURI: Objection; form.
5 A. I characterized polyclonal antibodies
6 developed in sera and compared polyclonal epitopes
7 from different sera.
8 Q. So you were screening the collection of
9 antibodies against, for example, an antigen that had
10 been immobilized. Is that one --
11 DR. KHANDURI: Objection; form.
12 A. I would have study/studied how polyclonal
13 antibodies in sera were to bind to target protein
14 antigen.
15 Q. All right. Before 2013 -- by December of
16 2012, had you done experimental work where you had
17 induced a polyclonal response to a mutated form of a
18 protein?
19 DR. KHANDURI: Objection; form.
20 A. By 2012, I studied how mutated form of
21 antigens affect polyclonal antibody responses.
22 Q. By December of 2012, had you performed any
23 research that investigated the effects of
24 immunization of an individual or a mammal as to the
25 effects of the antibody production within the

1 reproductive tract of the animal?
2 DR. KHANDURI: Objection; form.
3 A. Yes, I studied how vaccine can induce
4 antibody responses in vaginal tract in animals, by
5 2012.
6 Q. All right. Do you have any medical
7 training?
8 DR. KHANDURI: Objection; form.
9 A. I have my degree in bioengineering in
10 undergrad and Ph.D. And that's interdisciplinary
11 major that trains engineers in biomedical
12 applications.
13 Q. Before this case, had you ever
14 investigated the PH20 polypeptide?
15 A. I have not performed any research on PH20
16 polypeptide.
17 Q. Had you performed any research on any
18 enzymes?
19 A. Yes, I performed research on enzymes
20 before 2012.
21 Q. Did you perform research on enzymes that
22 had been mutated before 2012?
23 A. I don't recall if I worked with mutated
24 enzymes before 2012. I worked with mutated antigens
25 before 2012.

1 Q. And just to reiterate, do you believe that
2 you are a person of ordinary skill in the art as of
3 December of 2012, according to this set of patents?
4 DR. KHANDURI: Objection; form.
5 A. Yeah. As I stated in Paragraph 19 in my
6 declaration, I had a list of qualifications of a
7 POSA by December 2012.
8 MR. KUSHAN: We've been going
9 for about an hour. Do you want to take a
10 break?
11 WITNESS: Sure.
12 MR. KUSHAN: Okay. We can
13 just -- five minutes or so?
14 WITNESS: Yeah.
15 DR. KHANDURI: Sure.
16 WITNESS: Thank you.
17 VIDEOGRAPHER: We're off the
18 record at 9:37 a.m.
19 (Whereupon, a recess was taken.)
20 VIDEOGRAPHER: We are going back
21 on the record at 9:55 a.m.
22 BY MR. KUSHAN:
23 Q. Dr. Moon, during the break, did you speak
24 with anybody?
25 A. Yeah. During the break, I spoke with

1 counsel, a few members of the counsel.
2 Q. What did you speak about?
3 A. We spoke about matters not related to the
4 case.
5 Q. What was that?
6 A. We talked about life extension. Yeah.
7 Q. Before the break, we were discussing some
8 of your work with identification of linear epitopes.
9 Were there any other techniques you can
10 recall using, before December of 2012, to identify
11 or characterize linear epitopes on protein?
12 A. Do you mean, other than protein modeling
13 in ELISA, what other technique's available?
14 Q. Correct.
15 A. There are approaches to study peptide
16 epitopes. And one of the techniques would be
17 something called "ELISpots."
18 It's a variation of ELISA that
19 immunologists use to study peptide linear epitopes
20 in B lymphocytes and other lymphocytes.
21 Q. And did you use those techniques,
22 personally, before December of 2012?
23 A. Yes, I used those techniques before 2012.
24 Q. That was the -- I'm sorry. Could you
25 spell the technique?

1 A. "ELISpot" is spelled E-L-I-S-p-o-t.
2 Q. And that was done with peptides that were
3 synthesized?
4 A. Yes. ELISpots can be done using peptides,
5 as well as the whole protein as well.
6 Q. How were the peptides selected for those
7 experiments?
8 A. As we discussed before, these linear
9 epitopes, as well as peptides used by ELISpots, can
10 be selected based on prior work done in the
11 literature, as well as other techniques where those
12 linear epitopes are varied and synthesized and
13 tested using ELISpot or ELISA.
14 Q. And I'm interested in understanding how
15 the particular sequence of the peptide was selected
16 that would be then used and made and tested.
17 DR. KHANDURI: Objection; form.
18 Q. Could you just explain that?
19 DR. KHANDURI: Objection; form.
20 A. So, in general, immunologists and
21 vaccinologists would fragment proteins into smaller
22 domains and incubate B cells or T cells using those
23 fragments, and then study cytokine production.
24 And once you find the specific fragments
25 that are inducing cytokine production, you can dig

1 deeper into smaller and smaller fragments until you
2 find those linear epitopes.
3 Q. So that technique involves basically
4 making enzymatic -- enzymatic fragments of the
5 protein, and then that would be the starting point
6 for that line of investigation?
7 DR. KHANDURI: Objection; form.
8 A. Yes, you can use enzymatic degradation of
9 a protein to arrive at fragmented proteins for those
10 experiments.
11 Q. And in the work that you did before
12 December of 2012, did you use any computational
13 techniques to identify linear epitopes that you
14 would then study?
15 A. As I mentioned before, I was in a
16 multidisciplinary team of vaccine development, and
17 we, as a team, used protein modeling software and
18 use that to find epitopes that are bound by
19 antibodies.
20 Q. How did you find the epitopes using
21 computational methods in the -- in your -- in that
22 work that you just described?
23 A. For example, you could perform docking
24 experiments to see how specific antibody is binding
25 to specific domains with -- within the target

1 antigen.
2 Q. Is that a computational method?
3 A. That's a --
4 DR. KHANDURI: Objection; form.
5 A. That's a computationally based protein
6 modeling approach where antibodies docking to a
7 specific protein antigen can be studied.
8 But as I mentioned, there are other tools
9 available to study, including ELISA and ELISpots.
10 Q. Okay. In that answer you just provided, I
11 just want to make sure that you understood my
12 question, which was: Did you use, personally, those
13 techniques, such as the docking technique that you
14 just mentioned, in your work before 2012?
15 A. As I mentioned before, I did not
16 personally perform protein modeling or
17 computationally based docking experiments in silico.
18 But I was in a team that performed these
19 studies, and I would follow up their results using
20 ELISA and ELISpot.
21 Q. All right. Could I ask you -- that you
22 pick up your declaration in the 600- -- in the 6- --
23 sorry, -0003 proceeding, and go to Paragraph 14.
24 And do you see, at the bottom of Page 4,
25 in Paragraph 14, there's a statement:

1 Throughout, I use the
2 phrase "modified PH20
3 polypeptides" to refer to
4 polypeptides comprising an
5 amino acid sequence that is at
6 least 95% identical to the
7 amino acid sequence of any one
8 of SEQ ID NO: 3 and 32-66, and
9 include a modification at
10 position 320 such that D is
11 replaced by [sic] H, K, R, or
12 S.
13 So this is defining a set of modified PH20
14 polypeptides that can have different amino acid
15 sequences. Right?
16 A. Yes. This is referring to modify the
17 polypeptide PH20 with different peptide sequences.
18 Q. Do you know how many changes to the amino
19 acid sequence are permitted by the language that you
20 have used to associate with the phrase "modified
21 PH20 polypeptides"?
22 DR. KHANDURI: Objection; form.
23 A. I understand the phrase "modified PH20
24 polypeptides" refer to polypeptides comprising an
25 amino acid sequence that is at least 95% identical

1 to the amino acid sequence of any one of Sequence
2 ID 3 and 32-66, and include modification at
3 position 320, such that these replaced with H, K, R,
4 or S.
5 And based on this description, as long as
6 there is modification at position 320 and potential
7 modifications so that at least 95% is identical to
8 the Sequence ID 3 and 32-66, that would meet the
9 definition of modified polypeptide PH20.
10 Q. So in that set of modified PH20
11 polypeptides, what is the maximum number of amino
12 acid changes that are permitted to the -- any
13 individual PH20 polypeptide?
14 DR. KHANDURI: Objection; form.
15 A. I have not calculated the maximum number
16 of mutations allowed to meet the definition of
17 modified PH20 polypeptides.
18 But I -- I can go through calculations, if
19 I'm given enough information and time.
20 Q. So before you signed your declarations,
21 you had not performed that calculation?
22 A. I have not calculated the maximum number
23 of mutations allowed under this definition.
24 Q. Do you know or have an understanding of
25 how many different amino acid sequences are captured

1 by the definition of the modified poly- -- PH20
2 polypeptides that you use in your declaration?
3 A. I know the Sequence ID No. 3 and 32-66
4 comprise at least 430 amino acid long sequences.
5 And as long as modified PH20 polypeptide
6 meet the definition of 95% sequence identity and
7 modification at position 320, that would meet the
8 definition of modified PH20.
9 Q. Right. My question was a little bit
10 different.
11 I'm asking if you know how many different
12 polypeptide sequences will satisfy those parameters
13 that you've set forth in the definition of modified
14 PH20 polypeptides.
15 A. Once again, I have not calculated the
16 maximum number of mutations or different variations
17 of modified PH20 that meet the definition.
18 Q. Do you understand that the modifications
19 that may be covered by this language include
20 additional amino acid substitutions in the sequence?
21 DR. KHANDURI: Objection; form.
22 Q. Besides the one at position 320, for
23 example?
24 A. As long as there are at least 95% sequence
25 identity and position modification at 320, that

1 would meet the definition of modified PH20.
2 Q. So amino -- other amino acid substitutions
3 would be permitted, then. Right?
4 (No audible response.)
5 Q. Other positions in the protein sequence?
6 A. Under this definition, of course I would
7 understand amino acid substitutions.
8 Q. And other kinds of modifications could
9 include a deletion of amino acids from the amino
10 acid sequence. Is that right?
11 A. Deletions -- of course I would understand
12 amino acid modifications or deletions are allowed
13 under modified PH20 polypeptide definition, as long
14 as there is 95% sequence identity and modification
15 at 320.
16 Q. And the amino acid substitutions that
17 would be covered by this language would include a
18 change from the wild-type amino acid at any position
19 to any of the other 19 amino acids. Correct?
20 DR. KHANDURI: Objection; form.
21 A. Yeah. Of course, I would expect modified
22 PH20 with amino acid substitutions would meet the
23 definition of modified PH20, as long as there is 95%
24 sequence identity and modification at position 320.
25 Q. In your other three declarations, you use

1 a similar definition of modified PH20 polypeptides.
2 But those refer to other specific positions, such as
3 313, 317, and 312. Correct?
4 DR. KHANDURI: Objection; form,
5 foundation.
6 Q. They're all in Paragraph 14 of each
7 declaration.
8 A. In the case -004, in Paragraph 14, I
9 understand "modified PH20 polypeptide" refers to
10 polypeptides comprising of an amino acid sequence
11 that is at least 95% identical to the amino acid
12 sequence of any of Sequence ID No. 3, 32-66, and
13 include the modification of position 313 selected
14 from A, H, K, L, P, R, and Y.
15 In the case of -006, in Paragraph 14, I
16 understand the "modified PH20 polypeptide" refers to
17 polypeptides comprising of an amino acid sequence
18 that is at least 95% identical to the amino acid
19 sequence of any of Sequence ID No. 3, 32-66, and
20 include a modification at position 317 selected from
21 H, I, K, M, Q, R, and S.
22 In the case of -009, in Paragraph 14, I
23 understand "modified PH20 polypeptide" refers to
24 polypeptides comprising of an amino acid sequence
25 that is at least 91% identical to the amino acid

1 sequence of any one of Sequence ID No. 3, 7, and
2 32-66, and include a modification at position 312
3 selected from G, K, L, N, and T.
4 So those are the differences in those four
5 cases.
6 Q. Based on your understanding of those four
7 definitions, do you believe that the size of the set
8 of modified PH20 polypeptides covered by the phrase
9 "modified PH polypeptides" is different in a
10 meaningful way?
11 DR. KHANDURI: Objection; form.
12 A. I understand, in those four cases, the
13 specific amino acid modifications required are
14 different.
15 In particular, the single amino acid
16 mutation position is different from one to another,
17 and the sequence identity percentage allowed is also
18 different.
19 Q. But it's a similar size, 95, 91 --
20 DR. KHANDURI: Objection; form,
21 foundation.
22 A. The ranges are different from at least 91%
23 to 95%, and specific amino acid modification
24 positions are also different in four cases.
25 Q. Would it surprise you to learn that the

1 number of distinct polypeptide sequences within each
2 of these sets that are modified PH20 polypeptides is
3 on the scale of 1049 or higher sequences?
4 A. I have not done the --
5 DR. KHANDURI: Form --
6 A. -- calculations.
7 DR. KHANDURI: Sorry.
8 Objection; form.
9 Q. When you formed your opinions, were you
10 visualizing the set of modified PH polypeptides to
11 have that many different polypeptide sequences in
12 each set?
13 DR. KHANDURI: Objection; form.
14 A. I didn't personally calculate the number
15 of mutations allowed.
16 But I understood this definition allows
17 many different variations of modified PH20, and I
18 used that definition to form the basis of my
19 opinion.
20 Q. But you didn't have a specific number of
21 different amino acid sequences in the set of
22 modified PH20 polypeptides in mind when you were
23 forming your opinions?
24 DR. KHANDURI: Objection; form.
25 A. I applied the definitions of modified PH20

1 given by my counsel. And I understood there are
2 many variants of modified PH20 in each case.
3 And I factored that into forming my
4 opinions.
5 Q. When you formed your opinions in the four
6 declarations, did you contemplate any particular
7 modified PH20 polypeptide that included 15 or more
8 substitutions, additions, or deletions to the amino
9 acid sequence?
10 DR. KHANDURI: Objection; form.
11 A. So in each of these four cases, modified
12 PH20 allows for single epitope mutations at a
13 specified position, with sequence identity ranging
14 from 91 to 95%.
15 Q. All right. Dr. Moon, I was asking you a
16 little bit different question.
17 So I'm asking you to tell me: When you
18 were considering the effect of changes to this set
19 of polypeptide sequences, did you contemplate one
20 example of a PH20 polypeptide that incorporated, in
21 addition to one of those single mutations at
22 positions 3, 23, 13, 317, or 312, addition --
23 15 additional changes to the protein sequence?
24 That's what I'm asking.
25 Did you consider --

1 DR. KHANDURI: Objection --
2 MR. KUSHAN: Sorry.
3 Q. I want you to consider -- like I want you
4 to -- I want you to tell me whether you had
5 visualized in your mind that particular type of
6 modification to the modified PH20 polypeptide when
7 you were forming your opinions --
8 DR. KHANDURI: Object --
9 Q. -- 15 additional substitutions besides the
10 one that's specified.
11 DR. KHANDURI: Objection; form.
12 A. It's my understanding that addition of
13 15 additional amino acid sequences into definition
14 of PH- -- modified PH20 would still meet the
15 definition of modified PH20, as long as there is the
16 sequence identity ranging from 91 to 95% and amino
17 acid modifications and specify the location.
18 So 15 amino acid modifications would still
19 meet the definition of modified polypeptide PH20
20 under each case.
21 Q. All right. Let me try this again.
22 Go back to the time before you signed your
23 declaration.
24 At that point in time, when you signed
25 your declaration, had you evaluated any single

1 modified PH20 polypeptide that incorporated a
2 substitution at position 320 and also imported --
3 incorporated 15 or more additional substitutions
4 into the amino acid sequence?
5 DR. KHANDURI: Objection; form.
6 A. It's my understanding that the structure
7 you described meet the definition of modified PH20
8 polypeptide.
9 Q. Do you understand my question is asking
10 you about whether you considered that specific
11 example of a PH20 polypeptide before you signed your
12 declaration?
13 DR. KHANDURI: Objection; form.
14 A. I mean, I considered many different
15 variations of modified PH20. And as long as you
16 meet the definition outlined in Paragraph 14,
17 that -- that is what I used to form the opinions of
18 my declaration.
19 Whether I specifically imagined 15 amino
20 acid modifications -- 15 amino acid modifications
21 would fall within the range of modifications I would
22 have considered.
23 Q. I'm asking you a slightly different
24 question. I'm only asking you what you did back
25 then before you signed your declaration, not whether

1 it is possible that one that has 15 additional
2 changes meet the definition.
3 What specific examples of modified PH20
4 polypeptides did you consider before you signed your
5 declaration when you were forming your opinions?
6 DR. KHANDURI: Objection; form.
7 A. I considered many different variations of
8 modified PH20. I considered, for example, adding a
9 PADRE peptide, as an example.
10 I also considered deletion of specific
11 amino acid, as that meets the definition of modified
12 PH20.
13 So I considered many possibilities of
14 modified PH20.
15 Q. So in the example where you're adding the
16 PADRE sequence, what was the sequence that you were
17 adding to the starting PH20 polypeptide sequence?
18 If you want to look at Paragraph 32 of
19 your declaration, that's where you discussed the
20 PADRE.
21 A. Thank you.
22 Could you repeat your question?
23 Q. I'm asking: So you mentioned a specific
24 example where you added a PADRE sequence to the
25 amino acid sequence of PH20.

1 Was this inserted into the middle of the
2 sequence, or was it put at the end, either end, of
3 the PH20 sequence? Which -- what was the addition?
4 DR. KHANDURI: Objection; form.
5 A. PADRE is known as a pan-DR binding epitope
6 peptide, a strong helper T cell epitope peptide.
7 So the location of PADRE within
8 polypeptide would not matter that much, if that --
9 that's what you're asking.
10 Q. No. Let me try my question again.
11 You mentioned -- you indicated that you
12 had considered, before you signed your declarations,
13 an example of a PH polypeptide that you had added
14 the -- a PADRE sequence to.
15 And I'm just trying to understand: What
16 was that example that you were discussing?
17 Was the PADRE sequence added at the end,
18 or C-terminus, of the protein, or was it inserted
19 into the sequence?
20 Just explain what the example was.
21 DR. KHANDURI: Objection; form.
22 A. I don't recall the exact locations of
23 where PADRE was inserted in this particular exhibit.
24 But I, as well as a POSA, would
25 understand, regardless of location of where PADRE

1 was inserted -- either at N-terminus or in the
2 middle or at C-terminus -- having PADRE would result
3 in antibody responses to the antigen.
4 Q. Again, my question is about the example
5 that you mentioned that you had considered, not
6 possible changes.
7 So for the example that you considered
8 before you signed your declaration, how many amino
9 acid sequences were in the PADRE sequence that you
10 added to the PH20 polypeptide?
11 DR. KHANDURI: Objection; form,
12 foundation.
13 A. I don't recall the exact amino acid length
14 of the PADRE. I think it ranges from 10 -- amino
15 acid sequence 10 to 20.
16 And I considered adding PADRE to various
17 locations within modified PH20 and still meet the
18 definitions of modified PH20 specified in
19 Paragraph 14.
20 Q. And what -- would it be -- what -- those
21 locations, were they all just an insert of the PADRE
22 sequence into the PH20 sequence?
23 DR. KHANDURI: Objection; form.
24 A. I considered the insertion of PADRE into
25 N-terminus or at C-terminus or in the middle of

1 modified PH20.
2 I also considered replacing specific amino
3 acids within PH20 with the PADRE sequences; hence,
4 to meet the definition of modified PH20 outlined in
5 Paragraph 14.
6 And that's what I went -- what I
7 considered when I formed my opinions.
8 Q. Do you recall if you had kind of
9 constructed the sequence of all these different
10 examples in order to evaluate each one?
11 DR. KHANDURI: Objection; form.
12 Q. And -- sorry. Let me clarify my question.
13 I assume you didn't synthesize the
14 polypeptide. But I want to understand if you
15 created a digital listing of the amino acid
16 sequences of all these examples that you considered.
17 DR. KHANDURI: Objection; form.
18 A. Could you repeat the question?
19 Q. Sure. I'm just trying to understand:
20 When you did this, you made these sequences that you
21 referred to, did you type them up to have the
22 sequence on your computer of the three or four
23 examples that you just mentioned?
24 DR. KHANDURI: Objection; form.
25 A. I pictured them in my mind rather than

1 using computer.
2 Q. So you --
3 A. I pictured introducing PADRE into modified
4 PH20.
5 Q. Was there a particular PADRE sequence that
6 you were picturing in your mind being added into the
7 PH20 sequence?
8 DR. KHANDURI: Objection; form.
9 A. PADRE is a well-known peptide sequence
10 with ability to bind to helper T cell epitopes.
11 I don't recall the exact amino acid
12 sequence, but that's just an example of potential
13 modifications to modified PH20.
14 Q. Did you construct a structural model of
15 the PH20 polypeptide which incorporated the PADRE
16 sequence in it?
17 DR. KHANDURI: Objection; form.
18 A. I did not use any computational modeling
19 software to study modified PH20 containing PADRE
20 sequence.
21 But I basically pictured modified PH20
22 containing PADRE sequence and how that would
23 generate polyclonal antibody responses.
24 Q. In the example that you mentioned of
25 inserting the sequence within the middle of -- or

1 inside of the sequence of PH20, do you remember
2 where you would have positioned the PADRE sequence
3 in the overall PH20 sequence?
4 DR. KHANDURI: Objection; form.
5 A. As I mentioned, as long as there's a PADRE
6 sequence within any locations within modified PH20,
7 that would result in very strong antibody responses.
8 So I pictured inserting PADRE into --
9 either at N-terminus, C-terminus, or anywhere along
10 the internal residues of modified PH20.
11 Q. But am I correct in understanding that you
12 created no written or digital records of the
13 sequences that you were contemplating as part of
14 this assessment of the PADRE sequence in the PH20
15 sequence?
16 DR. KHANDURI: Objection; form.
17 A. Once again, I pictured inserting PADRE
18 sequences to any locations within at least 430 amino
19 acid long modified PH20.
20 I did not write them down or recorded them
21 in my computer.
22 Q. Did you consider, in the course of your
23 work in this case, sequences -- starting PH20
24 polypeptide sequences other than the one that
25 terminates at position 430?

1 DR. KHANDURI: Objection; form.
2 A. My understanding is Sequence ID No. 3 and
3 Sequence ID 32-66 describe polypeptides that are at
4 least 430 amino acid long -- at least 430 amino acid
5 long.
6 Q. Was there a maximum length of the sequence
7 in -- in the PH20 polypeptide that you considered?
8 A. It's my understanding that Sequence ID
9 No. 7 is the longer version of PH20.
10 Q. Do you know whether SEQ ID 7 contains the
11 GPI anchor sequence of PH20?
12 DR. KHANDURI: Objection; form.
13 A. I do not know that.
14 Q. Did you consider each of those sequences
15 that you just listed -- 3 and 32-66 -- individually
16 when you were forming your opinions in this case?
17 A. When I formed my opinions in this case, I
18 examined all the sequences listed in the exhibit,
19 including Sequence ID No. 3, 7, and 32-66.
20 Q. So using, for example, the 95% sequence
21 identity boundary, do you understand that
22 accommodates up to 22 changes to the starting
23 polypeptide sequence?
24 DR. KHANDURI: Objection; form.
25 A. I need to do the calculations to arrive at

1 maximum number of allowed modifications that still
2 meet the definition of modified PH20.
3 Q. Okay. But I'm -- am I correct in
4 understanding that in the work that you did to
5 prepare your opinions, you did not write out a
6 series of amino acid sequences that incorporated
7 one, two, five, 10, or more discrete changes within
8 the amino acid sequence of the PH20 polypeptide?
9 DR. KHANDURI: Objection; form.
10 A. Once again, I mentally pictured making
11 modifications to PH20. I did not write down all the
12 possible sequence variations of modified PH20.
13 Q. If you were a person of ordinary skill
14 working in a lab, and you were asked in December of
15 2012 to identify a PH20 polypeptide that would
16 tolerate 20 changes to it that could be used as an
17 immunogen in a vaccine, would you only evaluate that
18 in your mind?
19 DR. KHANDURI: Objection; form,
20 relevance.
21 A. Could you repeat the question?
22 Q. Sure. So if you were a person of skill in
23 the art --
24 A. Um-hum.
25 Q. -- and you were asked to devise a modified

1 PH20 polypeptide with 20 changes in it in order to
2 evaluate whether that modified PH20 polypeptide
3 would be a suitable immunogen in a vaccine, would
4 you only consider the changes to that polypeptide
5 sequence in your mind?
6 DR. KHANDURI: Objection; form,
7 relevance.
8 A. As I mentioned in Paragraph 14, a POSA
9 would have expected that polyclonal antibodies
10 generated in human females against any one of the --
11 any of the modified PH20 polypeptides would bind to
12 the wild-type human PH20 polypeptide in vivo.
13 And looking at potential modifications of
14 PH20 to meet the definition of modified PH20
15 polypeptides, a POSA would have expected to generate
16 polyclonal antibodies using all the variations
17 allowed under the definition of modified PH20.
18 Q. So, Dr. Moon, I was asking you a very
19 different question than the one you just answered.
20 My question was: In how you would go
21 about identifying modified PH20 polypeptides that
22 have up to, let's say, 20 changes in the sequence,
23 in December of 2012, as a person of ordinary skill
24 in the art, in order to evaluate those modified PH20
25 polypeptides as candidates for a potential vaccine,

1 you certainly wouldn't have only considered these
2 possible changes to the sequence in your mind.
3 Right?
4 DR. KHANDURI: Objection; form,
5 relevance.
6 A. As I mentioned before, a POSA would expect
7 to generate polyclonal antibodies using a --
8 Q. I'm sorry. I'm going to interrupt you
9 because you're --
10 A. Yeah.
11 Q. -- not answering the question I'm
12 presenting to you. And I'd like you to understand
13 my question.
14 So I'm asking -- my question is --
15 DR. KHANDURI: Counsel, please
16 let --
17 MR. KUSHAN: Yeah.
18 Q. My question was -- I -- my question was
19 asking you about how you would go about designing
20 and evaluating a particular modified PH20
21 polypeptide, in December of 2012, that incorporated
22 up to 15 or 20 changes to the amino acid sequence.
23 I was asking how you would go about that
24 process, and whether you would only consider the
25 sequence in your mind as far as the change sequence.

1 That's the question I'm asking.
2 Do you understand that question?
3 DR. KHANDURI: Objection; form.
4 And, Counsel, please do not
5 interrupt the witness.
6 MR. KUSHAN: Counsel, you've
7 done it to our witnesses, and we don't
8 want to waste time.
9 I understand you wanted to start
10 early, so I'm to get an efficient
11 examination conducted. So if he's
12 answering a question I didn't ask, I'm
13 going to ask him to answer the question I
14 asked.
15 Q. So, Dr. Moon, I just want to understand:
16 If you were going about the process of considering a
17 modified PH20 polypeptide that had 15 changes in it,
18 in December of 2012, as a person of ordinary skill
19 in the art, as to whether that modified PH20
20 polypeptide would be a suitable immunogen in a
21 vaccine, would you only consider the sequence of
22 that change -- protein in your mind?
23 DR. KHANDURI: Objection; form,
24 relevance.
25 A. I mean, as I outlined and written in my

1 declaration, so modified PH20 can generate
2 polyclonal antibodies. And there are many tools
3 available for a POSA to generate polyclonal
4 antibodies using modified PH20.
5 And PADRE is just one example where short
6 amino acid sequences are introduced in modified PH20
7 to generate polyclonal antibody responses.
8 So there is a reasonable expectation that
9 a POSA would have that all modified PH20 that meet
10 the definition of Paragraph 14 would generate
11 polyclonal antibody responses.
12 Q. Dr. Moon, what did you understand my last
13 question to be asking you?
14 DR. KHANDURI: Objection; form.
15 A. I think you are asking whether modified
16 PH20 would generate antibody responses.
17 Q. See, that's where we may have a
18 disconnect. That was not what I was asking.
19 I was asking about a person of skill in
20 the art, in 2012, trying to figure out which changes
21 to a modified PH20 could be made that would render
22 it suitable as an immunogen in a vaccine.
23 And my focus was the methodology you would
24 follow to devise those amino acid sequences.
25 I wanted to confirm, if you're a person of

1 skill in the art being asked to devise a new PH20
2 polypeptide sequence with 15 changes to it, in
3 December of 2012, you would not do all that work in
4 your mind. You would create the sequence and you
5 would evaluate the sequence using your computer and
6 other tools.
7 Is that fair?
8 DR. KHANDURI: Objection; form,
9 relevance.
10 A. I understand your question, yes. Yes. So
11 let me answer that. Yeah?
12 Q. Sure.
13 A. Yeah. So as of 2012, a POSA would have
14 understood modified PH20 that meet the definition of
15 that shown in Paragraph 14 would all generate
16 polyclonal antibodies.
17 If your question is how to choose the best
18 candidate for vaccine applications, a POSA would
19 have tested them.
20 But if you are asking -- but you are not
21 asking, what's the best candidate antigen. Right?
22 You are asking whether making these modifications --
23 oh, no. I take that back.
24 The question you are asking is: How to
25 choose the best candidate antigen that generates

1 strongest antibody responses?
2 If that's the question, a POSA would run
3 the study.
4 But as I understand, modified PH20 that
5 meet the definition shown in Paragraph 14 would be
6 expected to generate polyclonal antibodies after
7 vaccination.
8 Q. So, Dr. Moon, I -- there's a significant
9 disconnect between what I'm saying and what you're
10 understanding. And I want to work through this so
11 we can have a more efficient deposition.
12 What I'm asking about is the procedures a
13 person of skill would have followed in evaluating a
14 possible change to the PH20 polypeptide; not whether
15 it would cause an effect as an immunogen in the
16 future, as to the process they go about to evaluate
17 a modified PH20 polypeptide sequence.
18 I'm asking you, very simply: Would they
19 have written out a variety of different possible
20 amino acid sequences and considered those individual
21 sequences as to the impact those changes would have
22 on the PH20, just as a methodology to consider the
23 sequences?
24 DR. KHANDURI: Objection; form,
25 relevance.

1 A. I was asked by my counsel to opine whether
2 modified PH20 would generate polyclonal antibodies
3 in human female tract.
4 And it's my opinion that -- and also a
5 POSA would agree that modified PH20 polypeptides
6 would generate polyclonal antibodies in human female
7 reproductive tract.
8 We are not asking what is the best
9 candidate antigen among all these variations.
10 I think your question is whether -- which
11 one is the best candidate antigen? In that case,
12 you could write down the sequences and perform
13 studies.
14 But a POSA would expect all modified
15 version of PH20 would generate polyclonal antibodies
16 in human female tract, as outlined in the
17 declaration.
18 Q. And when you say "all" modified PH20
19 polypeptides in that answer you just provided,
20 you're speaking of the 1049 different amino acid
21 sequences that meet the requirements of the modified
22 PH20 polypeptides in Paragraph 14 of your
23 declarations. Right?
24 DR. KHANDURI: Objection; form,
25 foundation.

1 A. I have not done calculations to variations
2 of modified PH20.
3 But it's my opinion that all the modified
4 PH20 polypeptides that meet the definition as
5 outlined in Paragraph 14 would generate polyclonal
6 antibodies.
7 Q. And it's your opinion that if that set of
8 modified PH20 polypeptides includes 1049 different
9 polypeptide sequences, every one of those
10 polypeptide sequences, when administered to a
11 mammal, will induce antibodies that binds to the
12 wild-type PH20.
13 Is that your testimony?
14 DR. KHANDURI: Objection; form.
15 A. Once again, I have not calculated the
16 number of potential mutations and variations of
17 modified PH20.
18 But it's my opinion that all the allowed
19 modifications to PH20, as outlined in 14, would
20 result in polyclonal antibodies generated in female
21 mammals against any of the modified PH20
22 polypeptides, would bind to the wild-type PH20
23 polypeptide in vivo.
24 DR. KHANDURI: Counsel, it's
25 been about an hour. Can we take a break

1 soon?
2 MR. KUSHAN: Would you like to
3 take a break?
4 WITNESS: Yes.
5 MR. KUSHAN: Okay. We'll take a
6 break.
7 VIDEOGRAPHER: Off the record at
8 10:52 a.m.
9 (Whereupon, a recess was taken.)
10 VIDEOGRAPHER: We are going back
11 on the record at 11:18 a.m.
12 BY MR. KUSHAN:
13 Q. So, Dr. Moon, did you speak to anybody
14 over the break?
15 A. Yes. I talked briefly with my counsel
16 during the break.
17 Q. What did you talk about?
18 A. We continued to talk about lifespan
19 extension, yeah. Nothing related to the cases.
20 Q. All right. So do you remember earlier, at
21 the beginning of the deposition today, I told you
22 that, in the deposition, I ask you a question and
23 you have to answer the question I put to you.
24 Do you understand that?
25 A. Yes, I understand that.

1 Q. All right. And you understand that over
2 the last session of questions and answers, there was
3 a disconnect between the questions I put to you and
4 the answers you were providing to me. You were not
5 answering my questions.
6 Do you appreciate that?
7 DR. KHANDURI: Objection; form,
8 foundation.
9 A. I think I answered your question during
10 the last session.
11 Q. So do you recall I asked you one question
12 about the methodology someone might use in
13 evaluating a mutated poly- -- PH20 polypeptide, and
14 your understanding of my question seemed to be,
15 would I -- how do I find the best version of a PH20
16 polypeptide to use as a vaccine? And that's a
17 disconnect.
18 So I'd like you to please listen carefully
19 to the question that I present to you and answer the
20 question that I present to you directly.
21 If you don't understand the question I've
22 presented to you, tell me you don't understand it,
23 and I'll try to give you a better question.
24 If we go through the day today and you
25 cannot answer the question that I'm asking you, we

1 may need to have another deposition.
2 So I wanted you to understand that you
3 have to -- we're entitled to ask you questions, and
4 we're entitled to get your answers to my questions
5 that I've put to you.
6 Do you understand that?
7 DR. KHANDURI: Objection; form.
8 A. I understand that.
9 Q. Great. Could you go to your declaration
10 and go to Page 12 and look at Paragraph 22.
11 A. This is Case -0004?
12 Q. -0003.
13 A. -3?
14 Q. Yes. Do you have the -0003?
15 A. I used to have. Wait.
16 Q. Did you put those back?
17 A. Yeah.
18 MR. KUSHAN: Could you go look
19 and see if there's a -000- --
20 DR. KHANDURI: Oh. You want me
21 to take....
22 MR. BHATLA: -- -03 is down
23 there.
24 COURT REPORTER: I'm sorry.
25 MR. BHATLA: Six.

1 WITNESS: Thank you.
2 MR. KUSHAN: It's always
3 important to have the same document.
4 WITNESS: Yeah.
5 DR. KHANDURI: Counsel, could
6 you give all four declarations to the
7 witness, please.
8 (Exhibits handed to the witness.)
9 DR. KHANDURI: Thank you.
10 BY MR. KUSHAN:
11 Q. All right. So go to Page 12,
12 Paragraph 22.
13 A. Yes. I'm looking at Paragraph 22.
14 Q. All right. Do you see there's a figure
15 above Paragraph 22?
16 A. Yes, I see the figure.
17 Q. Okay. And it's illustrating different --
18 different antibodies, each binding to a distinct
19 epitope on the antigen, as it's depicted in the
20 picture -- figure. Right?
21 A. The figures are showing monoclonal
22 antibodies, the antigen with the different epitopes,
23 and polyclonal antibodies.
24 Q. Okay. So when you immunize a subject with
25 an antigen, you'll produce B cells that each

1 individually produce one antibody. Right?
2 A. Each B cell produces one type of
3 monoclonal antibody.
4 Q. Okay. And using the illustration you have
5 on Page 12, different B cells will be the source of
6 each of the different antibodies binding to a
7 different epitope on the antigen. Right?
8 DR. KHANDURI: Objection; form.
9 A. Yes. In general, B cells produce
10 monoclonal antibodies to each epitope. And when you
11 have a collection of B cells, they would cover
12 polyclonal antibodies.
13 Q. Okay. So if I have immunized a mammal
14 with an antigen and there's polyclonal antibody
15 response to that immunization, it creates a
16 repertoire of B cells that produce, each of them, a
17 different antibody that collectively make up the
18 antibodies in the polyclonal antisera.
19 Is that a fair statement?
20 DR. KHANDURI: Objection; form.
21 A. After vaccination, each B cell will
22 produce monoclonal antibody, and collection of the
23 B cells will produce polyclonal antibodies with a
24 diverse repertoire.
25 Q. Okay. Now, if you go to Paragraph 42 of

1 your declaration. This is on Page 24.
2 Do you see, in the middle -- in the second
3 sentence, you state:
4 ...POSAs would have
5 expected that each of these
6 polypeptides would present
7 numerous epitopes to the host's
8 immune system when administered
9 as a vaccine to a human female.
10 And that's referencing the set of modified
11 PH20 polypeptides -- well, sorry, the set -- that's
12 referring to the set of wild-type polypeptides that
13 are in SEQ ID 3 and 32-66. Right?
14 (Witness reading.)
15 A. I see the sentence in Paragraph 42.
16 Q. And you understand -- and your testimony
17 there is that a POSA would have expected that the
18 different polypeptides in that set would each
19 present numerous epitopes to the host's immune
20 system when that polypeptide was administered as a
21 vaccine to a human female. Right?
22 A. In Paragraph 42:
23 PH20 polypeptide with
24 amino acid sequence of any of
25 Sequence ID No. 3 and 32 and --

1 to 66 are at least 430 amino
2 acids long. Thus, POSA would
3 have expected that each of
4 these polypeptides would
5 present numerous epitopes to
6 the host's immune system when
7 administered as a vaccine to a
8 human female.
9 Q. Okay. So when a mammal is immunized with
10 one of those PH20 polypeptides, will antibodies to
11 every one of the epitopes on the modified PH20
12 polypeptide be produced during that polyclonal
13 antibody response?
14 DR. KHANDURI: Objection; form.
15 A. As I mentioned earlier, modified PH20
16 polypeptides will generate polyclonal antibody
17 responses.
18 And every one of modified PH20 would be
19 expected to generate polyclonal antibody responses.
20 Q. And my question was: Would the
21 immunization with the PH20 polypeptide cause the
22 mammal to produce antibodies to every epitope on the
23 PH20 polypeptide?
24 Do you understand my question?
25 A. I understand your question.

1 Q. Could you answer my question now?
2 A. When you perform immunizations with
3 polypeptides with multiple epitopes, as in PH20, you
4 expect to get polyclonal antibody responses to
5 multiple epitopes within that polypeptide.
6 There may be some epitopes that may not
7 generate antibody response. But, collectively, the
8 polypeptide has numerous multi-epitopes. Therefore,
9 a POSA would expect to get polyclonal antibody
10 responses covering a multitude of epitopes.
11 Q. What types of epitopes on the PH20 would
12 not induce production of antibodies against them?
13 DR. KHANDURI: Objection; form.
14 A. In general, when there are multiple
15 epitopes present in an antigen, they will generate
16 polyclonal antibodies against the multiple epitopes.
17 There may be some epitopes that do not
18 generate antibody response, but the majority of
19 epitopes found within the polypeptide will generate
20 antibody responses.
21 And we are focused on the mixture of
22 antibodies within the polyclonal repertoire. So you
23 anticipate generating polyclonal antibodies covering
24 the majority of epitopes found within that
25 polypeptide.

1 Q. Okay. And my question, again, is focused
2 on -- not the majority of the epitopes being bound
3 by the antibodies in the polyclonal.
4 I'm speaking to the -- what you
5 acknowledge, there are some epitopes that may not
6 induce production of an antibody against those
7 epitopes. I'm asking you about those epitopes.
8 And then, my specific question is: What
9 might cause the immune system to not produce
10 antibodies against those epitopes?
11 Do you understand my question?
12 A. Yes, I understand your question. Yeah.
13 Q. So please answer my question.
14 A. In general, there are multiple epitopes
15 present within polypeptide.
16 And when you vaccinate individual, they
17 will generate polyclonal antibodies covering a
18 multitude of epitopes within the polypeptide.
19 And there are many research tools
20 available that a POSA would use to generate
21 polyclonal antibody responses to even broader number
22 of epitopes present within that polypeptide
23 structures.
24 Q. So that answer does not an- -- that does
25 not answer the question I asked.

1 I was asking you about the epitopes on the
2 PH20 polypeptide that may not induce production of
3 an antibody response against those particular
4 epitopes.
5 And I'm asking you: What are the reasons
6 why the immune system might not produce antibodies
7 against certain of those epitopes on the PH20
8 polypeptide?
9 DR. KHANDURI: Objection; form.
10 A. There are some epitopes that could
11 generate high antibody response with high affinity.
12 There are some epitopes that could generate lower
13 affinity response.
14 But, collectively, these are still
15 polyclonal antibodies that are binding to multitude
16 of epitopes available in polypeptides.
17 Q. So is one of the reasons why the immune
18 system may not produce, in the polyclonal response,
19 antibodies to certain epitopes that the antibodies
20 don't form with sufficient affinity to the epitope?
21 DR. KHANDURI: Objection; form.
22 A. There may be certain epitopes that
23 generate lower affinity antibody response.
24 But, collectively, when you look at large
25 complex antigens, such as PH20, they present

1 multiple epitopes.
2 And, collectively, there are whole
3 polyclonal repertoires that will allow binding to
4 PH20.
5 Q. Dr. Moon, I want to make sure you
6 understand: I wasn't asking you about the majority
7 of the epitopes. I wasn't asking about the
8 collective response. My questions are pretty
9 narrow.
10 I'm only asking about the epitopes that do
11 not induce formation of antibodies within the
12 polyclonal antibody response.
13 So one reason may be that the antibodies
14 that are -- the B cells produced have insufficient
15 affinity.
16 That's one reason. Is that right?
17 DR. KHANDURI: Objection; form.
18 A. Once again, there may be some epitopes
19 that generate low affinity response.
20 But, collectively, there are multiple
21 epitopes in PH20 that would allow generation of
22 polyclonal antibodies.
23 Q. Dr. Moon --
24 MR. KUSHAN: All right. I'm
25 going to move to strike.

1 Q. The last answer just illustrates that I
2 didn't -- I explicitly asked you to focus on not the
3 collective response, but the particular epitopes
4 that are not inducing a response.
5 And I just want you to focus on the
6 questions I'm presenting and answer those, if you
7 could.
8 If you can't answer the question, you can
9 tell me that, but I need you to answer the question
10 that I'm presenting to you.
11 So are there any other reasons why the
12 immune system will not produce an antibody to an
13 epitope on the PH20 protein when the PH20 protein is
14 used in a vaccine?
15 DR. KHANDURI: Objection; form.
16 A. I gave you my response, that there may be
17 some epitopes that generates low affinity antibody
18 response.
19 Q. Have you ever heard of the concept of
20 "immune tolerance"?
21 A. Yes.
22 Q. What is immune tolerance in the context of
23 the polyclonal antibody response?
24 A. In Paragraph 32, I stated:
25 The "immune system is

1 trained not to respond to self
2 molecules (in order to avoid
3 autoimmunity)." However, under
4 certain conditions, an antibody
5 response against self-antigens
6 is desired to counter
7 overexpression of the
8 self-antigen in a disease (such
9 as, TNF-alpha overexpression
10 causing chronic inflammation in
11 cachexia, Crohn's disease, and
12 rheumatoid arthritis).
13 And:
14 By December 2021 [sic], a
15 POSA would have known of
16 techniques to elicit a
17 polyclonal antibody response
18 against a self-antigen.
19 Q. Dr. Moon, is it your understanding that
20 the human PH20 protein is a self-antigen in humans?
21 A. I understand PH20 is a sperm-associated
22 protein.
23 Q. Dr. Moon, my question was: Do you
24 understand that the PH20 -- human PH20 protein is a
25 self-antigen in humans?

1 Can you answer that question.
2 DR. KHANDURI: Objection; form.
3 A. I understand PH20 is a sperm-associated
4 protein.
5 As for whether it's expressed in females,
6 I do not know.
7 Q. Did you investigate whether the human PH20
8 protein is expressed in females before you prepared
9 your opinions?
10 A. I understand PH20 is a sperm-associated
11 protein.
12 I do not know whether PH20 is expressed in
13 females.
14 But my opinions stay the same, that
15 modified PH20 will generate polyclonal antibody
16 responses.
17 Q. Do you know if the PH20 protein is on the
18 Y chromosome of human males?
19 That's -- sorry.
20 Do you know if the PH20 gene is on the
21 Y chromosome in humans?
22 A. I do not know that.
23 Q. Do you know what chromosome the human PH20
24 gene is located on in humans?
25 A. I do not know that.

1 MR. KUSHAN: I'm going to mark
2 as Exhibit 1119 a paper in the journal
3 "Matrix Biology," Vol. 20, Pages 499 to
4 508, 2001; the first author Csoka,
5 C-s-o-k-a.
6 (Whereupon, Exhibit 1119 was marked for
7 identification.)
8 Q. If you could, Dr. Moon, review the first
9 portion of the abstract of this paper.
10 And once -- and I'm going to ask you, as
11 you read that: Does this give you information about
12 where -- what chromosomes the genes of the PH20 --
13 encodes the PH20 protein are located on?
14 (Witness reading.)
15 Q. Dr. Moon, have you determined if this
16 information in Exhibit 1119 identifies the
17 chromosome on which the PH20 gene is located?
18 DR. KHANDURI: Objection; form.
19 A. This is first time I'm seeing this
20 document, so I'd like to finish reading it.
21 Q. So you're incapable of reading the
22 sentence and understanding in the abstract:
23 Three genes (HYAL1, HYAL2
24 and HYAL3) are clustered on
25 chromosome 3p21.3, and another

1 two genes (HYAL4 and
2 PH-20/SPAM1) and one expressed
3 pseudogene (HYALP1) are
4 similarly clustered on
5 chromosome 7q31.3.
6 DR. KHANDURI: Objection; form.
7 Q. That information is insufficient to tell
8 you what gene -- or what chromosome the PH20 gene is
9 located on in the human?
10 DR. KHANDURI: Objection; form.
11 A. I see that sentence in the abstract.
12 Q. Do you have reason --
13 A. But before I can give my opinions, I'd
14 like to read the paper.
15 Q. So you have not previously investigated
16 whether the PH20 gene is expressed in human females.
17 Right?
18 DR. KHANDURI: Objection; form.
19 A. Once again, I have not seen this document
20 before. So I do not know whether PH20 is expressed
21 in females or not.
22 Q. All right. Let's move on.
23 So, before, we were speaking of the
24 polyclonal antibody response to the PH20 protein and
25 whether antibodies will form in that polyclonal

1 response against every epitope on the PH20 protein.
2 Is it true that in a polyclonal antibody
3 response, some epitopes will induce a stronger
4 immune response than other epitopes on the protein?
5 DR. KHANDURI: Objection; form.
6 A. In a protein antigen, there are multiple
7 epitopes. And a complex antigen, including PH20,
8 would also have multiple epitopes that may have
9 higher -- that may generate high antibody affinity
10 monoclonals or lower affinity monoclonals.
11 But, collectively, a complex antigen like
12 PH20 will generate polyclonal antibodies.
13 Q. In the -- in that response, the epitopes
14 that induced the stronger responses, do those have a
15 term that's used in connection with those epitopes
16 in immunology?
17 A. Immunol- -- in immunological terms, people
18 generally refer to them as immunodominant epitopes.
19 Q. "Immunodominant epitopes." Okay.
20 If you immunize a mammal with a mutated
21 form of PH20, are the epitopes associated with the
22 locations of mutations in the PH20 protein typically
23 the immunodominant epitopes?
24 DR. KHANDURI: Objection; form.
25 A. Could you repeat the question?

1 Q. Sure. If you're immunizing a mammal with
2 a mutated form of the PH20 protein, is it true that
3 the epitopes that are associated with the sites of
4 mutation on the structure of the PH20 protein are
5 the immunodominant epitopes in a polyclonal
6 response?
7 A. So there are multiple epitopes in a large
8 complex protein like PH20. And when you introduce
9 mutations, as specified in Paragraph 14, that will
10 generate polyclonal antibody responses.
11 There may be some epitopes that are
12 immunodominant. There may be epitopes that are less
13 immunodominant.
14 But, collectively, you still get
15 polyclonal antibodies that will bind to wild-type
16 PH20.
17 Q. Dr. Moon, that didn't answer my question.
18 I was asking you whether the sites of the
19 mutations on the modified PH20 polypeptide are the
20 locations where the -- those epitopes associated
21 with those modified structures are typically the
22 immunodominant epitopes in a polyclonal antibody
23 response.
24 Can you answer that question.
25 DR. KHANDURI: Objection; form.

1 A. Once again, when you immunize someone with
2 a large, complex antigen like PH20, there are
3 multiple epitopes that are present.
4 And there are epitopes that may generate
5 high affinity antibodies. There are epitopes that
6 may generate a bit lower affinity antibodies.
7 But, collectively, the polyclonal
8 antibodies will cover multiple epitopes.
9 So even if you make mutations that are
10 less immunodominant, they would still generate
11 antibody responses covering multiple epitopes within
12 PH20.
13 Q. Dr. Moon, that's the second time I asked
14 you the question, and you've still not answered my
15 question.
16 So my question is asking whether the sites
17 of the mutations of the modified PH20 create
18 epitopes that are immunodominant epitopes in a
19 polyclonal antibody response.
20 Are you able to answer that question,
21 please?
22 DR. KHANDURI: Objection; form.
23 A. As I responded before, there are multiple
24 epitopes in PH20.
25 There are epitopes that are -- that may

1 generate high affinity. There are epitopes that are
2 less immunodominant and generate less affinities.
3 But, collectively, these mutated, modified
4 PH20 would contain multiple epitopes. And even if
5 the mutations are less immunodominant, the modified
6 PH20 would generate polyclonal antibodies that cover
7 multiple epitopes in multi- -- in wild-type PH20.
8 Q. So that is the third time I've asked you
9 the question, and you've still not answered the
10 question I presented to you.
11 I want you to just tell me: Are you able
12 to answer the question whether epitopes associated
13 with the modifications made to a modified PH20
14 polypeptide are usually the immunodominant epitopes
15 on a modified PH20 polypeptide when it's used as the
16 immunogen in a polyclonal antibody response?
17 Can you answer that question.
18 DR. KHANDURI: Objection; form.
19 A. I think I answered your question already.
20 It's my opinion that there are multiple
21 epitopes present in PH20.
22 And even if you make mutations in
23 immunodominant epitope or less immunodominant
24 epitope, the resulting polypeptide will generate
25 polyclonal antibody responses.

1 Q. And that -- for the fourth time, that is
2 not my question.
3 I'm asking you: So -- do you understand
4 that I'm asking you about an epitope that is
5 associated with the mutation made to the PH20
6 polypeptide?
7 Do you understand that is part of my
8 question being put to you?
9 A. Yes, I understand that.
10 Q. Okay. So I'm asking whether that epitope
11 associated with a muta- -- with the mutation in the
12 PH20 protein is typically an immunodominant epitope
13 when you use the PH20 as an immunogen to raise a
14 polyclonal antibody response.
15 Do you understand the question?
16 A. Yes.
17 Q. Okay. Please answer that question.
18 DR. KHANDURI: Objection; form.
19 A. I'll give you the same answer: Regardless
20 of whether mutated position reside within --
21 Q. I'm going to interrupt you, because
22 that -- you've -- you just told me you're going to
23 give me the same answer, and I've told you before
24 that's not responding to my question.
25 My question is asking you whether you know

1 that a site of a mutation that gives rise to an
2 epitope -- so this is the epitope associated with
3 the site of the mutation in the PH20 polypeptide --
4 is that epitope associated with the mutation,
5 typically an immunodominant epitope, if you use the
6 protein, the PH20 protein, as the immunogen?
7 Can you answer that question.
8 DR. KHANDURI: Objection; form.
9 Counsel, this is the second time
10 you have interrupted the witness. He's
11 answering the question the best he can.
12 Please let him complete his answer.
13 Q. So go ahead. Can you answer my question.
14 A. So going back to Paragraph 14 --
15 Q. Okay.
16 MR. KUSHAN: I'm going to --
17 Counsel, I'm going to -- I'm
18 going to ask the witness again to answer
19 the question I put to him. And ask him --
20 Q. Are you able to answer the question
21 whether the -- an epitope associated with the site
22 of a mutation on the PH20 protein is typically an
23 immunodominant epitope when the modified PH20 is
24 used as an immunogen to raise a polyclonal antibody
25 response?

1 Do you understand my question to you?
2 DR. KHANDURI: Objection; form.
3 Please, Counsel, for the third
4 time, do not interrupt the witness. Let
5 him complete his answer.
6 MR. KUSHAN: We're going to
7 recall the witness if he refuses to answer
8 questions. I just want to put you on
9 notice.
10 DR. KHANDURI: He is answering
11 the question --
12 MR. KUSHAN: No, he's not.
13 DR. KHANDURI: -- the best he
14 can.
15 MR. KUSHAN: So I'm going to
16 excuse the witness. We're going to go on
17 the record.
18 Can you step out of the room,
19 please.
20 WITNESS: Sure.
21 MR. KUSHAN: Thank you,
22 Dr. Moon.
23 (Witness leaves the conference room.)
24 MR. KUSHAN: We're going to ask
25 for another deposition of this witness if

1 he refuses to answer the questions we're
2 putting to him.
3 You can tell me he's answering
4 the question, but you know absolutely that
5 every single answer he gives me is
6 ignoring the question I'm putting to him.
7 He's refusing to answer
8 literally every question I'm asking.
9 So I'm putting you on notice
10 that this is not an acceptable behavior
11 for a witness in a deposition.
12 And we will reserve our right to
13 recall the witness for an additional
14 deposition if he refuses to -- continues
15 to refuse to answer our questions.
16 DR. KHANDURI: We disagree.
17 He's answering the question the
18 way you are presenting him.
19 Ask clearer questions, and
20 hopefully you'll get the answer that
21 you're hoping for.
22 He's answering that -- he's
23 answering the best he can.
24 MR. KUSHAN: He's refusing to
25 answer.

1 DR. KHANDURI: We disagree.
2 MR. KUSHAN: Recall your
3 witness.
4 DR. KHANDURI: Are you ready?
5 MR. KUSHAN: Yeah.
6 (Pause.)
7 BY MR. KUSHAN:
8 Q. Dr. Moon, when you were retrieved, did
9 your counsel give you any instructions?
10 A. No.
11 Q. Any -- did she say anything to you?
12 A. No.
13 Q. All right. So if I introduce a mutation
14 into the PH20 polypeptide, an amino acid
15 substitution, or a series of them, I can alter the
16 structure of the protein. Is that correct?
17 A. I assume, depending on where you introduce
18 mutations, you could alter the structure of the
19 resulting protein.
20 Q. And that structure may be a structure not
21 present in the wild-type PH20 protein. Correct?
22 DR. KHANDURI: Objection; form.
23 A. Depending on where you introduce
24 mutations, the resulting structure may be similar
25 or -- similar to PH20 or not. Yes.

1 Q. So in the scenario where the structure is
2 not similar to the corresponding structure, in the
3 wild-type protein, can that structure, that modified
4 structure, become an epitope recognized by an
5 antibody if you use that modified PH20 protein as an
6 immunogen?
7 A. Could you repeat the question?
8 Q. So in the scenario where the structure
9 that has been introduced with the mutation is not a
10 structure found in the wild-type protein, could that
11 modified structure become an epitope recognized by
12 an antibody if you used the modified PH20 protein as
13 the immunogen?
14 DR. KHANDURI: Objection; form.
15 A. Yes. If you introduce any mutation and
16 the resulting structures are different from
17 wild-type PH20, that can be used to generate
18 antibody responses.
19 Q. And the epitope, the new epitope that
20 we've been discussing, the one that's associated
21 with the modified structure, could that epitope be
22 an immunodominant epitope?
23 DR. KHANDURI: Objection; form.
24 A. The mutations could be an immunodominant
25 epitope or not, as I mentioned before. And that

1 doesn't matter whether it generates polyclonal
2 antibody responses or not.
3 Q. Do you know whether changed structures on
4 a modified PH20 polypeptide are typically
5 immunodominant relative to the native structure or
6 structures on the PH20 polypeptide?
7 DR. KHANDURI: Objection; form.
8 A. When you introduce a mutation to a
9 protein, regardless of where the mutation occurs, a
10 POSA would find ways to generate polyclonal antibody
11 responses.
12 Q. So my question was whether the changed
13 structures associated with the mutation tend to be
14 immunodominant epitopes on the immunogen.
15 Can you answer that question.
16 A. Could you repeat the question again?
17 Q. Sure. Is it typical that the changed
18 structure on a protein like PH20 that is associated
19 with the mutation -- those changed structures, do
20 they tend to be immunodominant epitopes when you use
21 the mutated protein as an immunogen compared to the
22 wild-type structure?
23 DR. KHANDURI: Objection; form.
24 A. When you introduce mutations to a protein,
25 in general, and if that results in changes in the

1 structure, that mutated protein will generate
2 polyclonal antibody responses.
3 Q. Right. And I'm asking if the responses --
4 well, I'm asking you if the changed structure is
5 an -- typically an immunodominant epitope in that
6 response.
7 DR. KHANDURI: Objection; form.
8 A. If the mutation results in protein
9 structures that are distinct from the wild-type
10 protein, regardless of where the mutation occurs,
11 whether it's an immunodominant or less
12 immunodominant epitope, that will result in
13 polyclonal antibody responses.
14 Q. Right. And I'm asking if responses -- I'm
15 asking you if the changed structure is an --
16 typically an immunodominant epitope in that
17 response.
18 DR. KHANDURI: Objection; form.
19 A. If the mutation results in protein
20 structures that are distinct from the wild-type
21 protein, regardless of where the mutation occurs,
22 whether it's an immunodominant or less
23 immunodominant epitope, that will result in
24 polyclonal antibody responses.
25 Q. Right. And that does not answer my

1 question, again.
2 I'm asking whether the changed structure
3 typically is an immunodominant epitope.
4 DR. KHANDURI: Objection; form.
5 A. Could you repeat the question again?
6 Q. Yes. So we were referring to the changed
7 structure on the protein.
8 A. Right.
9 Q. You're with me. Right?
10 A. Right.
11 Q. Okay. I'm asking if that changed
12 structure is typically an immunodominant epitope.
13 DR. KHANDURI: Objection; form.
14 A. If a mutation introduced the protein
15 results and changed the structure, in general, that
16 changed structure will trigger more antibody
17 responses.
18 Q. So it would be an immunodominant epitope?
19 DR. KHANDURI: Objection; form.
20 A. There are multiple epitopes within a given
21 protein.
22 And to say a specific domain is an
23 immunodominant epitope, you will need to test other
24 epitopes and compare.
25 Q. So you --

A. I --
Q. Are you finished?
A. Yes. Yes.
Q. So you would have to test each mutated PH20 protein to know what kind of repertoire the body would produce in the polyclonal antibody response.
Is that fair?
DR. KHANDURI: Objection; form, foundation.
A. As I mentioned, each of the modified PH20 will generate polyclonal antibody responses.
Q. But you would not know what antibodies are in the polyclonal antibody repertoire unless you tested it, the mutated protein?
DR. KHANDURI: Objection; form.
A. Mutated protein will generate polyclonal antibody responses that are binding to multiple epitopes within the target protein.
Q. So you don't know one way or another -- sorry.
So I asked you:
Would you have to test each mutated PH20 protein to know what kind of repertoire of

1 antibodies in the body --
2 Sorry.
3 You would have to test
4 each mutated PH20 protein to
5 know what kind of repertoire
6 the body would produce in the
7 polyclonal antibody response.
8 Is that fair?
9 And your answer was:
10 As I mentioned, each of
11 the modified PH20 polypeptides
12 would generate a polyclonal
13 antibody response.
14 So I was asking whether you would need to
15 test the particular modified PH20 polypeptide to
16 understand what the particular antibody repertoire
17 was in the polyclonal response. And you gave me a
18 general answer.
19 I'm just wondering -- or, can you answer
20 the question I put to you.
21 DR. KHANDURI: Objection; form.
22 A. If your scientific question is whether
23 each antibody binds to specific domains in the
24 target protein -- and there are ways to test them.
25 But what I'm saying is: All modified

1 version of PH20 will generate polyclonal antibodies
2 that will bind to wild-type PH20.
3 Q. Dr. Moon, are you familiar with vaccines
4 against the human papillomavirus?
5 A. In general, I'm familiar with vaccine
6 efforts against papillomavirus.
7 Q. Okay. And there's an FDA-approved vaccine
8 available for the HPV virus. Right?
9 A. Yes. There's an FDA-approved vaccine
10 product against HPV.
11 Q. Do you know what it's called?
12 A. I believe it's called Gardasil.
13 Q. Have you studied the Gardasil vaccine or
14 its behavior as a vaccine previously in your
15 professional work?
16 DR. KHANDURI: Objection; form.
17 A. I have not studied Gardasil vaccine
18 specifically in the past.
19 Q. Do you know how Gardasil is administered
20 to patients?
21 A. It's my understanding that it's
22 administered parenterally.
23 Q. Where does the virus associated with HPV
24 manifest itself in the human body?
25 A. It's my understanding that HPV infection

1 can occur in many parts in the body, including
2 reproductive tract.
3 Q. Does that include the reproductive tract
4 in females?
5 A. Yes. I understand HPV infection can occur
6 in female reproductive tract.
7 MR. KUSHAN: I'm going to
8 introduce an exhibit, which is 1120.
9 (Whereupon, Exhibit 1120 was marked for
10 identification.)
11 DR. KHANDURI: You can drop it.
12 Thank you.
13 WITNESS: Thank you.
14 BY MR. KUSHAN:
15 Q. This is a paper in PL- -- the journal
16 "PLOS," first author Huo, H-u-o, Vol. 7, Issue 3.
17 Page e33736 is the first page. March of 2012.
18 This paper is reporting on a comparison of
19 administration of HPV antigens to human subjects by
20 a sublingual route and by an intramuscular route.
21 Dr. Moon, a sublingual route is a mucosal
22 administration route. Right?
23 A. Sublingual route is considered a mucosal
24 route.
25 Q. Okay. And an intramuscular is an

1 intra- -- is a systemic exposure of the antigen.
2 Right?
3 A. Intramuscular is considered a systemic
4 exposure.
5 Q. All right. Could you go to Page e33736.
6 And do you see there's a figure, Figure 2,
7 on the top half of this page.
8 And I'll just walk you through this. On
9 the -- in Panel -- are you there?
10 A. Figure 2?
11 Q. Figure 2, yeah.
12 A. Yes, I'm looking at Figure 2.
13 Q. And it's Figure 2.
14 And Panel A is showing responses of
15 subjects immunized intramuscularly.
16 And Panel B is showing responses of
17 subjects immunized sublingually.
18 And it's showing the frequency -- all
19 these bars are showing the frequency of antibody
20 secreting cells in the assay.
21 Is this kind of data something that you
22 are familiar with, generally, in your work?
23 DR. KHANDURI: Objection; form.
24 A. Yes. In my lab, we study similar results
25 in vaccine studies.

1 Q. And so, the responses being shown are over
2 a 20-day period with different -- with the vaccine,
3 with different -- different formulation of the
4 HPV16 VLP.
5 And, just generally, does the response
6 seen with the intramuscular administration appear to
7 be at or above the level of the response observed
8 with the sublingual administration of the vaccines?
9 DR. KHANDURI: Objection; scope.
10 (Witness reading.)
11 A. In general, the data points associated
12 with the intramuscular in Panel A seem to be higher
13 than what's shown in Panel B with the sublingual
14 route.
15 Q. Look at the paragraph on the right column,
16 at the bottom of the page, that starts, "One of the
17 potential translational advantages...."
18 Do you see that paragraph?
19 A. Yes, I see that paragraph.
20 Q. And there's a statement in there. It
21 says:
22 ...while intramuscular
23 immunization was capable of
24 inducing measurable virus
25 neutralizing activity in

1 cervical and/or vaginal
2 secretions in 3/6 subjects
3 (concomitant with high serum
4 neutralizing titers suggesting
5 transudation of serum IgG)....
6 Do you know what "transudation of serum
7 IgG" is referring to?
8 A. I assume it refers to translocation from
9 serum to cervical and/or vaginal sites, in this
10 sentence.
11 Q. Okay. So that's one way antibodies in the
12 circulation that result from a systemic immunization
13 can get into the mucosal compartment within the
14 reproductive tract of human females. Right?
15 DR. KHANDURI: Objection; form,
16 scope.
17 A. In general, serum IgG can translocate to
18 reproductive tract.
19 Q. If you could go to the next page, and
20 there's a figure there, Figure 3.
21 And again, it's comparing the effects of
22 immunization by the intramuscular route -- those are
23 the three graphs on the left side -- and sublingual
24 immunization on the right side.
25 And in this graph, "A" refers to the

1 response in the serum of the antibodies.
2 In the "B" segment, that's labeled as
3 being antibody in the cervical secretions.
4 And in "C," it's antibody in vaginal
5 secretions.
6 Do you see that?
7 A. I see that -- I see that in Figure
8 Caption 3.
9 Q. Okay. And look at the scales of the plots
10 on the left side, associated with intramuscular
11 administration, as compared to the scales of the
12 sublingual administration.
13 Do the responses of the Ig [sic] measured
14 in serum cervical secretions and vaginal
15 secretions -- are those higher than the levels
16 observed for sublingual administration in those
17 three locations?
18 DR. KHANDURI: Objection; form,
19 scope.
20 A. I see that, in general, in Figure 3, the
21 values shown on the left column is higher than the
22 values shown on the right column.
23 Q. So do you see any impediments of systemic
24 administration of the immunogen in this HPV vaccine
25 at creating sufficient levels of IgG in the female

1 reproductive tract?
2 DR. KHANDURI: Objection;
3 form -- objection; form.
4 A. This is first time I see this document.
5 But I see, in the case of this particular
6 immunogen, Gardasil, the figures in 3 show
7 intramuscular immunization has high antibody titers
8 compared with the sublingual.
9 Q. There's high antibody titers in the female
10 reproductive tract. Right?
11 A. In this particular data set, they show
12 higher antibody IgG responses in serum, cervical,
13 and vaginal sites for intramuscular sites, in
14 this -- in this particular assay.
15 Q. Have you -- are you familiar with the term
16 "transcytosis"?
17 A. Yes. In general, I'm familiar with the
18 term "transcytosis."
19 Q. What is "transcytosis"?
20 A. That usually refers to a cell that's
21 binding to a protein or target agent and shuttling
22 it to the other side of the cell body.
23 Q. Is transcytosis a mechanism that can
24 transport immun- -- immunoglobulin G in the
25 circulatory system into the human female

1 reproductive tract?
2 DR. KHANDURI: Objection; form.
3 A. In general, transcytosis can be used to
4 shuttle antibodies from one site to another across
5 the cell membrane.
6 Q. Do you know how that occurs?
7 A. I'm generally familiar with the process of
8 transcytosis.
9 Q. How does that -- how does transcytosis
10 move immunoglobulin from the circulatory system into
11 the human female reproductive tract?
12 A. Once again, I'm generally familiar with
13 the term "transcytosis."
14 And antibodies can bind to Fc receptors on
15 cell membrane, resulting in transcytosis.
16 MR. KUSHAN: Okay. I'm going to
17 introduce Exhibit 1121. This is a paper
18 published in "PNAS," Vol. 108, No. 11,
19 Pages 4388 to 4393, March 15, 2011. First
20 author is Li.
21 (Whereupon, Exhibit 1121 was marked for
22 identification.)
23 Q. And if you want to look at -- just look at
24 the abstract of this paper.
25 Is this referring -- this is referring to

1 the role of FcRn in mediating transcytosis of IgG.
2 Just read the abstract and then let me
3 know if that's generally what this paper is
4 addressing.
5 DR. KHANDURI: Objection; scope.
6 (Witness reading.)
7 A. Okay. I read the abstract.
8 Q. So you see, in the middle of the abstract,
9 about halfway down, it says:
10 Furthermore, endosomal
11 acidification appears to be a
12 prerequisite for FcRn-mediated
13 IgG transcytosis; IgG
14 transcytosis was demonstrated
15 in vivo by translocation of
16 systemically administered IgG
17 into the genital lumen in
18 wild-type but not FcRn-KO -- or
19 knockout -- mice.
20 Is that point consistent with the
21 explanation you provided a bit ago about how
22 transcytosis works using the FcRn receptor?
23 DR. KHANDURI: Objection; form,
24 scope.
25 A. I see that sentence in the abstract. This

1 is first time I'm seeing this document.
2 But, in general, FcRn is involved in IgG
3 transcytosis.
4 Q. Okay.
5 DR. KHANDURI: Counsel, is this
6 a good time to take a break?
7 MR. KUSHAN: I was just thinking
8 that.
9 DR. KHANDURI: Okay.
10 MR. KUSHAN: Would this be a
11 good time for you, Dr. Moon, for lunch?
12 WITNESS: Yes.
13 MR. KUSHAN: Okay. Why don't we
14 break for lunch.
15 DR. KHANDURI: Half an hour?
16 MR. KUSHAN: That's fine.
17 VIDEOGRAPHER: Going off the
18 record at 12:28 p.m.
19 (Whereupon, a recess was taken for lunch
20 at 12:28 p.m.)
21 - - -
22
23
24
25

1 A F T E R N O O N S E S S I O N
2 (Time noted: 1:13 p.m.)
3 VIDEOGRAPHER: We are going back
4 on the record at 1:13 p.m.
5 BY MR. KUSHAN:
6 Q. Dr. Moon, did you speak with anybody over
7 the break, lunch break?
8 A. I spoke with counsel about the lunch menu.
9 Other than that, we didn't discuss any cases.
10 Q. If you could turn to Page 19 of your
11 declaration, Paragraph 32. I think we discussed
12 this a bit earlier today.
13 A. So Case No. -003?
14 Q. Yeah, we'll go with -0003.
15 A. Page 19?
16 Q. 19. Paragraph 32.
17 A. Okay.
18 Q. So this is where you're discussing immune
19 tolerance. Correct?
20 A. In this paragraph, I discuss self
21 molecules and how to generate immune responses.
22 Q. In the normal functioning of the immune
23 system, immune tolerance functions to prevent the
24 immune system from mounting immune responses against
25 the host's own proteins. Right?

A. As I wrote in Paragraph 32:

The "immune system is trained not to respond to self molecules...."

Q. And is it fair to say that the immune tolerance mechanisms in the body function to prevent the survival and activation of B cells that would produce antibodies against self-antigens?

DR. KHANDURI: Objection; form.

A. Could you repeat the question.

Q. Is it fair to say that the immune tolerance mechanisms in the body function to prevent the survival and activation of B cells that produce antibodies that bind to self-antigens?

DR. KHANDURI: Objection; form.

A. So, in general, the immune system is trained not to respond to self molecules, as I stated in Paragraph 32.

Q. And my question was: There are mechanisms in the immune system that implement immune tolerance. Right?

DR. KHANDURI: Objection; form.

A. There are mechanisms in place related to immune tolerance.

Q. And some of those mechanisms function to

1 remove B cells that produce antibodies that bind to
2 self-antigens. Right?
3 A. There are mechanisms that can remove
4 T cells responding to self-antigens.
5 Q. And these immune tolerance mechanisms are
6 both in central and peripheral tolerance immune
7 systems. Right?
8 DR. KHANDURI: Objection; form.
9 A. There are multiple mechanisms in place.
10 And central and peripheral tolerance are
11 involved in immune tolerance.
12 Q. Immune tolerance mechanisms operate both
13 in the mucosal and systemic immune responses.
14 Right?
15 A. Both the mucosal and cell compartments are
16 involved in immune tolerance.
17 Q. Would you agree that immune tolerance
18 mechanisms can alter the populations of both
19 long-lived plasma cells and memory B cells?
20 DR. KHANDURI: Objection; form.
21 A. There are mechanisms involved in
22 regulation of long-lived plasma and memory B cells.
23 Q. So is it fair to say that immune tolerance
24 mechanisms can influence the antibodies that are
25 within the antibody repertoire produced by a

1 polyclonal response to the PH20 protein?
2 DR. KHANDURI: Objection; form.
3 A. There are mechanisms involved in self
4 tolerance to self-proteins, but I do not know
5 whether PH20 is a self-protein or not in females.
6 Q. But, just generally -- not just for PH20,
7 but just generally, if someone is attempting to
8 vaccinate somebody with a self-protein and there are
9 not efforts made to overcome immune tolerance, the
10 body will not produce antibodies to the
11 self-protein.
12 Is that how self- -- is that how immune
13 tolerance works?
14 DR. KHANDURI: Objection; form.
15 A. In general, there are mechanisms in place
16 to control and modulate induction of antibodies to
17 self molecules.
18 But as I stated in Paragraph 32, under
19 certain conditions, an antibody response to
20 self-antigen can be induced and sometimes desired.
21 And there are multiple ways that a POSA
22 could have used to induce polyclonal antibody
23 responses against the multitude of antigens,
24 including a self-antigen.
25 Q. If I administered a self-protein to a

1 human in saline -- without adjuvants, without other
2 things in the composition -- would you expect the
3 human immune system to produce a polyclonal antibody
4 response against that self-protein?
5 DR. KHANDURI: Objection; form.
6 A. So, in general, there are mechanisms in
7 place to limit induction of antibody responses to
8 self molecules.
9 But as I mentioned, there are multiple
10 ways that a POSA could have used to induce
11 polyclonal antibody responses to protein antigens,
12 including a self-antigen.
13 Q. And to be clear, if they -- if the POSA
14 did not use those additional ways to overcome immune
15 tolerance, the human body would not mount a
16 polyclonal antibody response to that self-antigen.
17 Right?
18 A. In general, if you inject self-protein
19 into an individual, you don't expect to generate
20 antibody responses to the self-antigen.
21 Q. If I take a human prot- -- a human
22 self-protein that is found in other animals in
23 the -- well, sorry. Let me try that one again.
24 So if I have two species, and they have --
25 they both make the same protein, but they're

1 different species' versions of each protein -- in
2 that hypothetical -- kind of like PH20. There's a
3 human PH20. There's a mouse PH20. There are other
4 species of PH20.
5 If the two proteins, like the two PH20s,
6 mouse and human, have common epitopes in their
7 native wild-type form, would you expect antibodies
8 in the mouse to form against that common epitope if
9 you inject the human protein into the mouse?
10 DR. KHANDURI: Objection --
11 Q. Do you understand my question?
12 DR. KHANDURI: Objection; form.
13 A. If you inject proteins from different
14 species with 100% sequence identity, a POSA would
15 think injection of unmodified protein in saline
16 would not generate strong antibody responses.
17 But in most cases, proteins in different
18 species have less than 100% sequence identity. So
19 in those cases, you expect to get antibody
20 responses.
21 Q. If there is an epitope shared between the
22 human and mouse species of the native protein, would
23 the antibody -- antibodies in the mouse not be
24 produced against that epitope, which is shared
25 between the two species as a self epitope?

1 DR. KHANDURI: Objection; form.
2 A. Could you repeat the question?
3 Q. Of course. It's a complicated question,
4 so let me break it up for you.
5 So there could be, on two species of a
6 protein, a common epitope found on both species of
7 protein. Right?
8 A. Okay.
9 Q. And in each mammal, they could have an
10 antibody form -- or an antibody could recognize that
11 epitope as a self epitope. Right? Theoretically?
12 DR. KHANDURI: Objection; form.
13 A. So as long as there is a single epitope
14 mutation in those two proteins, a POSA would expect
15 to see generation of antibody responses.
16 Q. So if you mutate the common epitope shared
17 by the two proteins, that will induce production of
18 antibodies when you take one species' protein and
19 inject it in the other mammal?
20 DR. KHANDURI: Objection; form.
21 A. Oh, that's not what I stated.
22 Q. Okay.
23 A. I stated that as long as there is a single
24 epitope mutation anywhere within the protein --
25 Q. So --

1 A. -- that may -- that single mutation would
2 allow induction of antibodies to "multi" epitopes.
3 Q. So that would override immune tolerance
4 against the shared epitope between the two species?
5 DR. KHANDURI: Objection; form.
6 A. Once again, there's -- as long as there is
7 one single epitope, a single amino acid mutation in
8 the proteins, anywhere in the protein, that will
9 result in antibody responses spreading to multiple
10 epitopes found in the protein.
11 Q. So T cells and -- where do T cells and
12 B cells originate?
13 A. T cells are known to generate in --
14 T cells and B cells are known to generate in bone
15 marrow.
16 Q. And are both T cells and B cells trained
17 by the immune system?
18 DR. KHANDURI: Objection; form.
19 A. Both T cells and B cells are trained and
20 interact with immune systems.
21 Q. Does that training occur before T cells
22 and B cells migrate into the mucosal immune system?
23 A. Generally, T cells and B cells can be
24 trained in different parts of the body, including
25 bone marrow, thymus, spleen, and potentially mucosal

1 tissues, too.
2 Q. So you would expect immune tolerance to
3 function in mucosal -- in mucosal environment as
4 well. Right?
5 DR. KHANDURI: Objection; form.
6 A. There are mechanisms in place to maintain
7 immune tolerance in various tissues, including
8 mucosal compartments.
9 Q. Would you agree, in general, that most
10 proteins are poorly immunogenic or nonimmunogenic
11 when administered by themselves?
12 DR. KHANDURI: Objection; form.
13 A. Could you repeat the question?
14 Q. Sure. Would you agree with the statement
15 that most proteins are poorly immunogenic or
16 nonimmunogenic when administered by themselves?
17 A. I think this depends on the protein.
18 If you are injecting self-antigen protein,
19 without any modification, by itself, it may not
20 generate strong antibody responses, due to
21 mechanisms of immune tolerance.
22 But as long as there is a single epitope
23 mutation, of course I would find good ways to induce
24 antibody responses.
25 Q. Do you commonly try to overcome immune

1 tolerance using an adjuvant when you administer the
2 protein?
3 A. Yes. Adjuvants are used to induce
4 antibody responses with protein antigens.
5 Q. Can adjuvants have varying degrees of
6 impact on the magnitude of the immune response
7 against a protein?
8 DR. KHANDURI: Objection; form.
9 A. In general, adjuvants are used to induce
10 higher antibody titers, together with protein
11 antigens.
12 Q. Can you use, in a vaccine in a human, a
13 highly potent adjuvant?
14 DR. KHANDURI: Objection; form.
15 Q. And to be clear, something that would
16 overcome immune tolerance to the injected protein.
17 DR. KHANDURI: Objection; form.
18 A. There are strong adjuvants that are well
19 reported in the literature.
20 Q. Are there any risks of using a strong
21 adjuvant in a vaccine for a human?
22 A. There are adjuvants that are known to
23 cause injection inflammation.
24 So, in those cases, researchers have to be
25 cautious on selection of adjuvants.

1 Q. Can you induce autoimmunity to a
2 self-protein that is other than the one being
3 injected, if you use a powerful adjuvant, in a
4 human?
5 DR. KHANDURI: Objection; form.
6 A. When you use a very strong adjuvant, there
7 is concern of potential side effects, including
8 inflammation and induction of antibodies to other
9 proteins.
10 Q. So does that limit the choices for
11 adjuvants that could be used in human vaccines?
12 A. There are many choices of adjuvants that
13 are in development. And many, but not all, can be
14 used in humans.
15 Q. Could you go to Paragraph 23 of your
16 declaration on Page 12.
17 A. Paragraph 22?
18 Q. 23.
19 A. 23? Okay.
20 Q. You make a reference at the bottom of that
21 paragraph to epitopes that are linear?
22 A. Yes, I mentioned linear epitopes here.
23 Q. What do you mean by "linear" epitope?
24 A. What I mean by "linear" is that these are
25 contiguous amino acid sequences within the antigen.

1 Q. And those are -- there's another kind of
2 epitope called "conformational" epitope. Right?
3 A. Yes. Conformational epitope is another
4 kind of epitope in an antigen.
5 Q. And what's the difference between a linear
6 epitope and a conformational epitope?
7 A. Linear epitopes refer to contiguous domain
8 of antigen that -- that will induce antibody
9 responses.
10 Configuration -- configurational epitopes
11 refer to epitopes that are formed by
12 three-dimensional structure of the antigen inducing
13 antibody responses.
14 Q. Will conformational epitopes in a protein
15 be preserved in a protein that has been denatured?
16 A. Some conformational epitopes in a protein
17 can still be maintained after denaturization.
18 Q. Would you say the majority of the
19 conformational epitopes will be maintained in a
20 denatured protein?
21 DR. KHANDURI: Objection; form.
22 A. I think it depends on the method of
23 denaturization. There are some techniques that will
24 disrupt more conformational epitopes compared with
25 others.

1 Q. Is it fair to say that the -- a disruption
2 of the structure of the protein can destroy
3 conformational epitopes?
4 A. If you denature a protein, you could
5 disrupt conformational epitopes of a certain region.
6 And once again, depending on the
7 techniques of denaturization, the extent to have
8 disruption in conformational epitopes may be
9 different.
10 Q. So the number of antibodies that might
11 form to a denatured PH20 protein may be different
12 than the number of antibodies that would form to the
13 undenatured wild-type PH20 protein?
14 DR. KHANDURI: Objection; form.
15 A. Once again, depending on the method of
16 denaturization, number of epitopes in one form of
17 antigen versus other may be different, the number of
18 configuration of epitopes.
19 Q. If you could look at Paragraph 22 of your
20 declaration, also on Page 12.
21 No. I'm sorry. Hold on one second.
22 This always happens in depositions, where
23 your pages become disordered. Just bear with me.
24 (Pause.)
25 Q. All right. If I could have you do this:

1 Go to Page 25 and look at Paragraph 44.
2 A. Okay. I'm looking at Paragraph 44.
3 Q. Okay. Do you see, about five or six lines
4 down, there's -- you say:
5 ...or the modified PH20
6 polypeptide underwent a
7 conformational change (e.g.,
8 due to intentional
9 denaturation)....
10 Do you see that?
11 A. Yes, I see that.
12 Q. I see that word -- those two words being
13 used together at several places in your declaration,
14 "intentional denaturation."
15 What do you mean by the words "intentional
16 denaturation," as you're using it in your
17 declaration?
18 A. In vaccine studies, researchers could
19 intentionally denature a given protein for vaccine
20 applications as well.
21 So researchers could use undisrupted
22 antigen or antigen that is intentionally disrupted
23 or intentionally denatured to generate antibody
24 responses.
25 And as I mentioned, there are many

1 techniques available to achieve denaturization of a
2 protein.
3 Q. Can mutations into -- introduced into the
4 amino acid sequence of a protein cause denaturation
5 of the protein?
6 A. I would assume some amino acid
7 modifications to a protein can result in unfolding
8 or denaturization of the antigen.
9 Q. And if those amino acid mutations caused
10 unfolding or denaturation of the protein, would the
11 denatured or unfolded protein have a different
12 number of epitopes on it compared to the wild-type
13 protein?
14 DR. KHANDURI: Objection; form.
15 A. As I mentioned in Paragraph 44, even if
16 you intentionally denature a protein, the vast
17 majority of the epitopes would be still present for
18 induction of antibody responses.
19 Q. Are the majority of epitopes on a protein
20 like PH20 linear epitopes or conformational
21 epitopes?
22 A. In general, large complex proteins like
23 PH20 have both conformational and linear epitopes.
24 Q. Do you know whether there are more
25 conformational epitopes than linear epitopes, or

1 vice versa, on the PH20 protein?
2 A. I do not know, for the case of specific
3 PH20, whether there are more configurational or
4 linear epitopes.
5 Q. Did you investigate the epitopes that are
6 present on the human PH20 protein as part of your
7 preparation of your declaration -- of your
8 declaration here?
9 DR. KHANDURI: Objection; form.
10 A. PH20 is a large, complex protein.
11 So, in general, those complex proteins
12 have multiple epitopes, including linear and
13 configurational epitopes.
14 As for the number of epitopes on PH20, I
15 didn't look into number of epitopes.
16 But I understand there are multiple
17 epitopes that can serve as both configurational and
18 linear epitopes.
19 Q. If you intentionally denature a protein
20 antigen like PH20, can you refold the protein by
21 removing or changing the conditions in which it's
22 found?
23 DR. KHANDURI: Objection; form.
24 A. I think it -- I think it depends on the
25 method of denaturization, whether you can refold

1 disrupted protein or not.
2 Q. Have you personally refolded proteins that
3 have been denatured?
4 A. I have not personally refolded proteins
5 that were denatured.
6 But I examined literature. I worked in a
7 multidisciplinary research lab that worked on
8 protein antigens.
9 Q. Can a denatured modified PH20 protein form
10 aggregates?
11 DR. KHANDURI: Objection; form.
12 A. In general, denatured proteins could or
13 could not result in aggregation.
14 Q. Can mutations introduced into the PH20
15 protein induce the protein to form aggregates?
16 DR. KHANDURI: Objection; form.
17 A. In general, mutations in any given protein
18 could result in protein aggregation.
19 Q. Do aggregated proteins present different
20 epitopes relative to the native, properly folded
21 protein; for example, in PH20?
22 DR. KHANDURI: Exam- -- excuse
23 me. Objection; form.
24 A. Once again, large proteins have multiple
25 epitopes. And that will be the same for PH20.

1 Q. Do you know how protein aggregates form?
2 A. In general, when hydrophobic domains are
3 exposed to external surface, that can result in
4 protein aggregation.
5 Q. And those can -- those hydrophobic
6 portions that get exposed can form complexes between
7 multiple molecules of the protein in a random way.
8 Right?
9 A. There may be some proteins that aggregate,
10 resulting in some changes.
11 But, in general, even after protein
12 aggregation, the aggregated proteins will still
13 present epitopes that will induce polyclonal
14 antibody responses to the parent protein.
15 Q. Can an aggregated protein present new
16 epitopes not originally present on the wild-type
17 protein?
18 A. In some cases, aggregated proteins could
19 present some new configurational epitopes.
20 Q. Could you look at Paragraph 44 again.
21 A. Okay.
22 Q. Do you see, in the first sentence, you
23 state:
24 Moreover, given the high
25 degree of amino acid sequence

1 identity (at least 95%) between
2 the administered modified PH20
3 polypeptides and the wild-type
4 human PH [sic] polypeptide
5 (SEQ ID 7), even if some
6 epitopes on the modified PH20
7 polypeptide were changed or
8 disrupted....
9 And then you continue on.
10 When you were forming your opinions, did
11 you consider the modified PH20 polypeptides that you
12 were addressing to be those that were 95% sequence
13 identity with SEQ ID 7?
14 DR. KHANDURI: Objection; form.
15 (Witness reading.)
16 A. I understand the modified PH20
17 polypeptides have the definitions given in
18 Paragraph 14.
19 Q. So you're referring to proteins that have
20 95% sequence identity that are admin- -- sorry.
21 You're speaking of proteins being
22 administered, which are the modified PH20
23 polypeptides.
24 And you're saying those, in this sentence,
25 are those with 95% sequence identity with the

1 wild-type PH20 polypeptide SEQ ID 7. Right?
2 DR. KHANDURI: Objection; form.
3 A. I understand polypeptides shown in
4 Sequence No. 3 and 32-66 are truncated version of
5 PH20 found in human sperm, which is indicated by
6 Sequence ID No. 7.
7 And I understand there's a high degree of
8 amino acid sequence identity, at least 95%, between
9 modified PH20 polypeptides and wild-type human PH20
10 polypeptide, as shown in ID No. 7.
11 But, by extension, because Sequence ID
12 No. 3 and 32-66 are truncated version of Sequence ID
13 No. 7, there would be also high degree of amino acid
14 sequence identity between modified PH20 and PH20
15 shown in Sequence 3 and 32-66.
16 Q. But in Paragraph 44 in your declaration,
17 you're referring to modified PH20 polypeptides that
18 have 95% sequence identity to SEQ ID 7. Right?
19 (Witness reading.)
20 A. I understand there is a high degree of
21 sequence identity between modified PH20 and
22 wild-type human PH20 polypeptide sequence shown in
23 7, as well as truncated version of wild-type human
24 PH20 shown in Sequence No. 3 and 32-66.
25 And by that extension, a POSA would think

1 the vast majority of the epitopes on the modified
2 PH20 polypeptides to be the same or similar to those
3 on the wild-type human PH20 polypeptide shown in
4 Sequence No. 7, as well as the truncated version,
5 Sequence No. 3, and 20, 32-66.
6 Q. So just to be clear, what you're
7 addressing in Paragraph 44 is the set of modified
8 PH20 polypeptides that are 95% identical to
9 SEQ ID 7.
10 And you also believe that polypeptides
11 that are 95% sequence identity with SEQ ID 3 and
12 32-66 also would induce antibodies that bind to the
13 wild-type PH20.
14 Is that what you're saying?
15 DR. KHANDURI: Objection; form.
16 A. Could you repeat the question.
17 Q. So --
18 A. Yeah.
19 Q. -- what's -- so what's written in
20 Paragraph 44 is addressing modified PH20
21 polypeptides that are 95% sequence identity -- or
22 have 95% sequence identity with SEQ ID 7. Right?
23 (Witness reading.)
24 A. There is a high degree of amino acid
25 sequence identity between modified PH20 and

1 wild-type human PH20 shown in Sequence No. 7, but --
2 in addition, not "but" -- in addition, there's high
3 degree of sequence identity between modified PH20
4 and wild-type PH20 polypeptide shown in Sequence
5 No. 3 and 32-66.
6 Q. Okay. Do you know if SEQ ID 7 is a
7 soluble form of human PH20?
8 A. I do not know whether it's a soluble form.
9 Q. Did you investigate how many of the
10 modified PH20 polypeptides that you described in
11 Paragraph 14 will become denatured because of the
12 changes to the protein?
13 DR. KHANDURI: Objection; form.
14 A. I do not know how many of the modified
15 PH20, as described in Paragraph 14, are in soluble
16 form.
17 Q. Did you investigate how many of the
18 modified PH20 polypeptides you defined in
19 Paragraph 14 that will become aggregated?
20 A. I do not know how many of those variants
21 described in Paragraph 14 will result in protein
22 aggregation.
23 Q. Did you investigate how many of the
24 modified PH20 polypeptides in the set defined in
25 Paragraph 14 will become misfolded because of the

1 mutations made to them?
2 DR. KHANDURI: Objection; form.
3 A. I do not know how many of the modified
4 PH20 will result in disruption or misfolding.
5 Q. But it's your testimony that regardless of
6 that uncertainty, every single modified PH20
7 polypeptide within the definition in Paragraph 4 --
8 14 will cause production of polyclonal antibodies in
9 a human that bind to the wild-type PH20 on sperm?
10 DR. KHANDURI: Objection; form.
11 A. It's my opinion that modified PH20
12 polypeptide, as defined in Paragraph 14, will result
13 in polyclonal antibodies that will bind to wild-type
14 human PH20 polypeptide in vivo.
15 Q. So if you look in Paragraph 45, please.
16 And just....
17 If you can look, there's -- you say
18 "irrespective of," and then you list three
19 conditions:
20 ...the location of an
21 amino acid difference on any of
22 the admin- -- on any of the
23 administered modified PH20
24 polypeptides relative to the
25 wild-type, whether any of the

1 administered PH20 polypeptides
2 are enzymatically active, or
3 whether the administered
4 modified PH20 polypeptide has a
5 conformational change (such as
6 due to intentional
7 denaturation)....
8 So you're saying, regardless of those
9 three things happening when you make mutations to
10 the PH20 protein, you believe administering any of
11 the PH20 polypeptides within the scope of what you
12 say in Paragraph 14 will raise antibodies that bind
13 to the wild-type PH20 on human sperm?
14 DR. KHANDURI: Objection; form.
15 A. It is my opinion that a POSA would have
16 expected the polyclonal antibodies generated against
17 the administered modified PH20 polypeptides,
18 regardless of the three conditions I listed in
19 Paragraph 45, will result in antibodies that bind to
20 wild-type PH20 polypeptide.
21 Q. Do you also personally believe that to be
22 true?
23 DR. KHANDURI: Objection; form.
24 A. This is my personal opinion that I stated
25 in the declaration.

1 Q. And just to be clear, I'm just confirming
2 that you're not telling -- you're not just saying
3 your opinion is that the POSA would believe it.
4 I just -- I'm asking: You personally
5 believe it, regardless of whether a POSA believes
6 it?
7 A. I personally believe this as well.
8 Q. Did you evaluate any structural models of
9 the PH20 protein in forming your opinions in your
10 declarations?
11 DR. KHANDURI: Objection; form.
12 A. As I mentioned, modified PH20 will have
13 multiple epitopes. And even after denaturation, the
14 modified PH20 will have multiple epitopes that will
15 generate polyclonal antibody responses.
16 Therefore, the structure of modified PH20
17 does not play a major role in forming my opinions.
18 A POSA would have used modified PH20 as --
19 without further modification.
20 What I mean by is that a POSA would have
21 used a denatured or nondenatured modified PH20 to
22 generate polyclonal antibody responses.
23 Q. Does it matter to you how many, or the
24 locations of amino acid modifications, are in the
25 modified PH20 in -- as to the ability of the

1 modified PH20 to create antibodies and a polyclonal
2 response against the wild-type protein?
3 DR. KHANDURI: Objection; form.
4 A. As I mentioned in Paragraph 14, as long as
5 there is single epitope amino acid modification, a
6 modified PH20, all the variations of that would
7 result in polyclonal antibody responses.
8 Q. So your opinion is: As long as the PH20
9 in that -- sorry.
10 As you just said -- strike that.
11 So you just stated that as long as there
12 is the one amino acid substitution in the modified
13 PH20 being used.
14 Are you assuming that the modified PH20
15 that's being administered in your example to the
16 human has only one amino acid substitution in it?
17 DR. KHANDURI: Objection; form.
18 A. Regardless of number of mutations, as long
19 as it meets the definition stated in Paragraph 14,
20 it's my -- it's my opinion that modified PH20
21 injected into human females will result in
22 polyclonal antibody responses.
23 Q. So just to be clear, are you saying that
24 your opinions are based on a modified PH20
25 polypeptide that has only the one identified change

1 at position 320 in it?
2 DR. KHANDURI: Objection; form.
3 A. My opinion stays the same, whether
4 modified PH20 has only one modification at
5 position 320 or many modifications, so that up to
6 95% is identical to the Sequence ID No. 3 and 32-66.
7 All these variants would be expected to
8 generate polyclonal antibody responses.
9 Q. Is it your opinion that any sequence --
10 any contiguous sequence of amino acids within the
11 PH20 protein sequence can be a linear epitope?
12 DR. KHANDURI: Objection; form.
13 A. Any potential linear contiguous sequences
14 in a given protein could be a linear epitope.
15 And, same thing can be generally said to
16 PH20 as well.
17 Q. So anywhere in the -- so if I pick any
18 stretch of contiguous amino acids within the PH20,
19 the native PH20 polypeptide sequence, any stretch of
20 amino acids will be a linear epitope, as we've --
21 DR. KHANDURI: Object --
22 Q. -- been using that term in the -- in your
23 declarations?
24 DR. KHANDURI: Objection; form.
25 A. There are multiple linear and

1 configurational epitopes in any given protein.
2 Q. I'm just trying to clarify.
3 Are there a smaller number of linear
4 epitopes on the modified -- or in the native PH20
5 polypeptide than as many as you can derive from just
6 picking any stretch of the amino acid sequence?
7 That's a bad question. Let me try it
8 again.
9 In order to be a B cell epitope, does the
10 linear sequence have to be bound by a B cell?
11 DR. KHANDURI: Objection; form.
12 A. In general, B cells need to bind to their
13 target epitope to generate antibody responses.
14 Q. So not every -- not any sequence within
15 the PH20 sequence will provide that as a place where
16 a B cell can bind. Right?
17 DR. KHANDURI: Objection; form.
18 A. So again, there are multiple epitopes in a
19 complex protein. There are multiple linear epitopes
20 that B cells can bind to.
21 Q. Let me try a better question.
22 Do you agree that in order for antibodies
23 specific to a linear epitope on PH20 to be produced,
24 the B cells must recognize the linear epitope
25 through their BCR?

1 DR. KHANDURI: Objection; form.
2 A. In general, BCR on B cells need to bind to
3 an epitope to generate antibody responses.
4 Q. Do you know how many linear B-cell
5 epitopes are on the PH20 wild-type protein sequence?
6 DR. KHANDURI: Objection; form.
7 A. I don't know how many B-cell epitopes
8 there are in wild-type PH20, but I understand there
9 are many potential epitopes.
10 Q. In December of 2012, could a person of
11 ordinary skill have determined how many B-cell
12 epitopes are present on the wild-type PH20 sequence?
13 I'm sorry.
14 In December 2012, could a person of
15 ordinary skill have determined how many linear
16 B-cell epitopes are present on the wild-type PH20
17 sequence?
18 A. All the linear epitopes within a given
19 protein could serve as a B-cell epitope.
20 Q. Could linear sequences of amino acids
21 buried within the protein interior function as a
22 linear B-cell epitope on the human PH20 protein?
23 DR. KHANDURI: Objection; form.
24 A. Even if you have linear epitopes buried in
25 3D structure of a protein, if you denature the

1 protein and expose the linear epitope, that will
2 serve as a linear B-cell epitope.
3 Q. Will the antibody that forms against that
4 buried linear epitope bind to the native wild-type
5 PH20 on sperm?
6 DR. KHANDURI: Objection; form.
7 A. Could you repeat the question?
8 Q. Yes. You gave me an example of forming an
9 antibody to a linear B-cell epitope on the interior
10 of the protein where you used the denatured form of
11 the protein.
12 And my question is whether that antibody
13 that binds to the linear B-cell epitope that is on
14 the denatured form, but in the folded protein, is on
15 the interior of the protein -- I'm asking if that
16 antibody will bind to the native PH20 protein on
17 sperm.
18 A. So once you denature a protein and expose
19 internal linear epitopes, that can generate antibody
20 responses to that epitope. And that can trigger
21 subsequent immune responses to other domains found
22 in that antigen, resulting in polyclonal antibody
23 responses to multiple other epitopes.
24 So if you were to use modified PH20 and
25 denature it, it will generate antibody responses

1 that will trigger subsequent polyclonal antibodies
2 that bind to wild-type PH20 bound -- found in sperm.
3 Q. But the antibody that binds to the linear
4 B-cell epitope that's ordinarily in a buried site
5 will not bind to the native structure found on --
6 PH20 found on sperm. Right?
7 DR. KHANDURI: Objection; form.
8 A. As I mentioned, when you denature a
9 protein, that can result in internal domains to be
10 exposed, resulting in B-cell responses, then that
11 will trigger other B-cell activations that result in
12 polyclonal antibodies against the multiple epitopes.
13 Q. All right. Let's take --
14 A. And I can see the similar conditions can
15 occur in the case of a modified PH20.
16 Q. But I'm trying to just -- let's take the
17 other antibodies that might also form off the table
18 for a minute.
19 I'm just asking about the antibody that
20 you referred to that formed to the linear B-cell
21 epitope on the interior of the protein that was made
22 with the denatured PH20.
23 That antibody will not bind to the folded
24 PH20 protein on sperm. Right?
25 DR. KHANDURI: Objection; form.

1 A. I do not know enough about biology or PH20
2 in sperm to answer that particular hypothetical
3 question.
4 DR. KHANDURI: Counsel, can we
5 take a break soon?
6 MR. KUSHAN: I have just one or
7 two more questions, then we can take a
8 break.
9 Q. Do you -- so did you investigate whether
10 PH20 on sperm, after it enters the reproductive
11 tract until it fertilizes the egg, undergoes any
12 kind of structural change?
13 DR. KHANDURI: Objection; form.
14 A. I just know PH20 is a sperm-associated
15 protein.
16 Q. So you don't know whether the protein
17 itself undergoes structural changes to its sequence
18 between the time it enters the reproductive tract
19 until it fertilizes the egg?
20 A. I did not study the structure of PH20 in
21 human female reproductive tract.
22 But it's my opinion that regardless of the
23 sequence variance within modified PH20, those would
24 serve as antigens that will generate polyclonal
25 antibodies that will bind to wild-type PH20

1 associated with sperm.
2 MR. KUSHAN: Do you want to take
3 a break?
4 WITNESS: Sure.
5 MR. KUSHAN: Okay.
6 VIDEOGRAPHER: Off the record at
7 2:21 p.m.
8 (Whereupon, a recess was taken.)
9 VIDEOGRAPHER: We are going back
10 on the record at 2:54 p.m.
11 BY MR. KUSHAN:
12 Q. Dr. Moon, did you speak with counsel
13 during the break?
14 A. No, I did not.
15 Q. To prepare your declarations in this
16 case -- I just want to confirm a couple of your
17 answers from before.
18 One question I asked you is whether you
19 had looked at a PH20 homology model as part of the
20 work that you did to prepare your declarations.
21 Did you look at a PH20 homology model?
22 DR. KHANDURI: Objection; form.
23 A. Could you clarify the question?
24 Q. Right. So, you know, proteins exist in
25 three dimensions. Right?

1 A. Proteins exist in three-dimensional
2 structure.
3 Q. And so, if you did a X-ray crystallography
4 study of the protein, you could get information that
5 is used to create a three-dimensional image of the
6 protein. Right?
7 DR. KHANDURI: Objection; form.
8 A. You can study 3D structure of a protein
9 using crystallography.
10 Q. Right. And you can use SWISS-MODEL to
11 also create a model of a protein structure using its
12 amino acid sequence. Right?
13 DR. KHANDURI: Objection; form.
14 A. That's another method of looking at
15 protein structure.
16 Q. So all I'm asking is: Did you look at one
17 of those PH20 structural models in the course of
18 preparing your opinions in this case?
19 DR. KHANDURI: Objection; form.
20 A. I did not need to look into structure of
21 PH20 to arrive at my opinion that I stated in the
22 declaration that modified PH20 will generate
23 polyclonal antibody responses that will bind to
24 wild-type human PH20 polypeptide.
25 Q. So, Dr. Moon, my question wasn't whether

1 you had an opinion about this, but my question was
2 just a question about whether you did something.
3 And I asked -- and it's very simple: Did
4 you look at a PH20 homology model in the course of
5 preparing your opinions in this case?
6 DR. KHANDURI: Objection; form.
7 A. I used the UniProt to look at sequence
8 identity between modified PH20 polypeptides and
9 other sequences listed in my declaration.
10 Q. But you --
11 A. I did not use crystallography or
12 SWISS-MODEL to examine PH20 during preparation of
13 this declaration.
14 Q. And you didn't view a PH20 model --
15 sorry.
16 You did not view a structural model of
17 PH20 in forming your opinions in the declaration.
18 Is that right?
19 DR. KHANDURI: Objection; form.
20 (Witness reading.)
21 A. I did not use SWISS-MODEL or
22 crystallography model to study PH20 in order to form
23 my opinion that modified PH20 polypeptide will
24 generate polyclonal antibodies that will bind to
25 wild-type human PH20.

1 Q. So at the very beginning of the deposition
2 today, you explained that in your -- some of the
3 work that you did during your postdoc phase, that
4 you investigated the location of linear epitopes.
5 Do you remember that explanation you gave
6 us?
7 A. I remember our exchange.
8 Q. And that involves making fragments of the
9 protein that you were trying to locate the linear
10 epitopes in. Right?
11 DR. KHANDURI: Objection; form.
12 A. In the postdoctoral training time, I used
13 fragmented proteins for vaccine applications.
14 Q. So in February -- I'm sorry.
15 In December of 2012, a POSA could have
16 used other techniques to locate linear B-cell
17 epitopes on the surface of the human PH20 protein.
18 Right?
19 DR. KHANDURI: Objection; form.
20 A. There are tools available to study
21 epitopes in any given protein.
22 Q. Are those computational tools?
23 A. Those tools would include the
24 computational tools.
25 Q. So a person of skill in the art could have

1 used computational tools in 2012 to locate the
2 positions of linear B-cell epitopes on the PH20
3 protein that are on the surface of the protein.
4 Right?
5 DR. KHANDURI: Objection; form.
6 A. Computational tools can be used to study
7 structure of a protein, including PH20.
8 Q. And also to find the locations of the
9 B-cell epitopes on the surface of the protein.
10 Right?
11 A. Computational tools can be used to study
12 structure of a protein, as well as epitopes in a
13 given protein.
14 Q. And the location of the epitopes as well.
15 Right?
16 A. Computational tools can be used to study
17 structure of a protein and potential epitopes.
18 But as I mentioned in my declaration,
19 modified PH20 polypeptide will degenerate
20 polypeptides that will bind to wild-type human PH20.
21 And I did not need to examine
22 computational models to arrive at this opinion.
23 Q. As part of your work in this case forming
24 opinions about linear epitopes that give rise to
25 B cells -- sorry. Try that one again.

1 As part of your work in this case, did you
2 look for any reports of investigations into the
3 locations of B-cell epitopes on the human PH20
4 protein?
5 DR. KHANDURI: Objection; form.
6 A. PH20, I understand, is a large protein
7 with multiple epitopes. And modified PH20 also has
8 multiple epitopes that will induce polyclonal
9 antibody responses.
10 And I didn't need to use computational
11 tools to arrive at my opinion that modified PH20
12 polypeptides will induce polyclonal antibodies
13 against the wild-type human PH20.
14 Q. So, Dr. Moon, my question is much simpler,
15 and you don't need to repeat what you already have
16 said many times today.
17 I'm just asking about what you did to
18 prepare these declarations. And one thing -- I'm
19 asking a very specific thing.
20 Did you look for information published in
21 the literature that describe the location of B-cell
22 epitopes on the human PH20 protein?
23 DR. KHANDURI: Objection; form.
24 A. I did not look into published epitopes
25 within PH20.

1 Q. Okay.
2 A. But I understand there are multiple
3 epitopes in PH20 that can serve as epitopes for
4 generating polyclonal antibody responses.
5 MR. KUSHAN: We're going to mark
6 Exhibit 1122.
7 (Whereupon, Exhibit 1122 was marked for
8 identification.)
9 MR. KUSHAN: Sorry.
10 DR. KHANDURI: Thank you.
11 MR. KUSHAN: This is a paper
12 published in the "AAPS Journal,"
13 Vol. 24 -- numbered 110, starting at
14 Page 109, published in 2022, first author
15 Marie Printz.
16 BY MR. KUSHAN:
17 Q. Dr. Moon, could you look down at the left
18 corner of the paper and tell me what affiliation --
19 what company affiliation Marie Printz has?
20 A. I see Halozyme Therapeutics as an author
21 affiliation for Dr. Marie Printz.
22 Q. Halozyme owns the patents that are the
23 subject of these proceedings. Right?
24 A. I understand Halozyme is the owner of the
25 patent that I -- the case, -0003.

1 Q. Look in the abstract, and do you see that
2 the authors reported that they had identified -- or
3 they stated:
4 Fifteen epitopes in the
5 rHuPH20 --
6 That's the recombinant human PH20.
7 -- sequence had the
8 potential to cross-react with
9 B cells.
10 Do you see that?
11 (No audible response.)
12 Q. It's about four lines from the bottom of
13 the paragraph, left column.
14 A. I see the sentence:
15 Fifteen epitopes in the
16 rHuPH20 sequence had the
17 potential to cross-react to
18 B cells.
19 But this is the first time I'm seeing this
20 document.
21 Q. Okay. Could you turn to Page 110. I just
22 want to focus you on -- in the left column of
23 Page 110, under the heading "B Cell Epitope
24 Prediction."
25 A. Which page, please?

1 Q. Page 110. The page number is in the top
2 right corner.
3 A. They're all 110.
4 Q. Oh, wait. That's right.
5 There it is, Page 5 of 15.
6 Do you see that?
7 A. Okay.
8 Q. And in the left column, they're talking
9 about B Cell Epitope Prediction and B Cell Epitope
10 Mapping.
11 And about halfway down the paragraph of
12 the B Cell Epitope Prediction paragraph, in the
13 middle of the page, it says:
14 Potential antigenic
15 epitopes for rHuPH20 were
16 identified by employing a model
17 of the 3D crystal structure of
18 recombinant human PH20, which
19 was based on the crystal
20 structure of HYAL1....
21 Do you see that?
22 (Witness reading.)
23 A. Yes, I see that sentence.
24 Q. And that's performing an inspection of a
25 PH20 homology model that we were talking about a

1 couple minutes ago. Right?
2 DR. KHANDURI: Objection; form.
3 (Witness reading.)
4 A. I see here that they used a model of the
5 3D crystal structure of rHuPH20.
6 Q. And do you see that the crystal structure
7 model was based on the crystal structure of the
8 HYAL1 protein?
9 That's the clause -- that's the part of
10 the sentence after that parenthetical. The part
11 that says "which was based on the crystal structure
12 of HYAL1."
13 DR. KHANDURI: Objection; form,
14 relevance.
15 A. I see the sentence. It reads, "which was
16 based on the crystal structure of HYAL1 using amino
17 acids 2-403 of rHuPH20."
18 Q. Okay. And then, in the next sentence,
19 they said:
20 Potential epitopes were
21 identified on the basis of
22 structure and solvent
23 accessibility....
24 In February of 20- -- I'm sorry.
25 In December of 2012, could a POSA have

1 performed these steps of inspecting the PH20 model
2 in evaluating structure and solvent accessibility of
3 the protein to identify linear B-cell epitopes?
4 DR. KHANDURI: Objection; form,
5 scope.
6 (Witness reading.)
7 Q. Dr. Moon, I want to make sure you
8 understood -- I'm just asking a simpler question:
9 In December of 2012, could a person of skill in the
10 art have used a PH20 homology model and inspected
11 the structure and solvent accessibility of the
12 protein to identify linear B-cell epitopes on the
13 human PH20 protein?
14 DR. KHANDURI: Objection; form,
15 scope, relevance.
16 (Witness reading.)
17 Q. Dr. Moon, my -- the answer to my question,
18 I don't believe, is in this paper. I'm asking -- I
19 want to make sure you understood my question.
20 Can you tell me what my question was?
21 DR. KHANDURI: Objection; form.
22 A. Could you repeat your question?
23 Q. Sure.
24 A. Yeah.
25 Q. I just want to know if a person of skill

1 in the art, a POSA, in December of 2012 could have
2 used a PH20 homology model, and by inspecting the
3 structure and solvent accessibility of the protein,
4 they could have identified the linear B-cell
5 epitopes on the surface of the human PH20 protein.
6 DR. KHANDURI: Objection; form,
7 scope, relevance.
8 (Witness reading.)
9 A. Can I spend more time to read this paper?
10 Q. I don't believe that's necessary. I just
11 want to know --
12 A. Okay.
13 Q. -- were -- you were a person of skill in
14 the art in 20- -- December 2012. Right?
15 A. Yes.
16 Q. If you look at that description, I'm
17 asking -- I'm only asking you: As a person skilled
18 in the art, could you have performed those steps
19 that are listed in the bottom half of the paragraph
20 under B-cell epitope prediction in February of
21 20- -- in December of 2012?
22 DR. KHANDURI: Objection; form,
23 scope, relevance.
24 A. I think I need to read the whole paper.
25 Q. So you're -- so do you know -- are you

1 aware of any reason why a POSA could not have
2 performed these steps of using a PH20 homology model
3 and looking at the structure and solvent
4 accessibility of the protein to identify the linear
5 B-cell epitopes on PH20, on its surface?
6 DR. KHANDURI: Objection; form,
7 scope, relevance.
8 A. This is the first time I'm looking at this
9 particular document, and I'd like to read it through
10 before answering your questions related to this
11 document.
12 Q. So I'm allowed to ask you questions about
13 what you believe. And my questions are focused on
14 the capabilities of a POSA in December of 2012 --
15 which you say you were, right? -- that -- you're
16 maintaining you're a person of skill in the art in
17 2012?
18 DR. KHANDURI: Objection; form.
19 A. I meet at least the qualifications of a
20 POSA.
21 Q. And so, I'm asking you if you could have
22 performed those steps that are described in that one
23 paragraph to identify the linear B-cell epitopes on
24 PH20. Yes or no, could you have done that?
25 DR. KHANDURI: Objection; form,

1 scope.
2 A. Yeah, I'll need to read the entire
3 document before --
4 Q. Why?
5 A. -- answering that.
6 DR. KHANDURI: Objection; form.
7 Q. Why do you need to read the other -- the
8 rest of the document to answer my question?
9 DR. KHANDURI: Objection; form,
10 scope.
11 Q. Let me help you.
12 Were -- was it possible to inspect a model
13 of the 3D crystal structure of PH20, based on the
14 crystal structure of HYAL1 in December of 2012 --
15 DR. KHANDURI: Objection; form,
16 scope.
17 Q. -- based on your knowledge and
18 understanding as a POSA in December of 2012?
19 DR. KHANDURI: Objection; form,
20 scope.
21 A. I'd like to read the document before --
22 Q. Dr. Park [sic] --
23 A. -- answering.
24 Q. -- let me ask -- I'm -- you're avoiding
25 answering the question.

1 MR. KUSHAN: It's not funny.
2 Okay? Just --
3 MS. ZHANG: You got his name
4 wrong.
5 MR. CHOI: His name's not
6 "Dr.~Park."
7 MR. KUSHAN: Sorry. I
8 apologize. I'll withdraw that.
9 Q. Dr. Moon, if you could just listen very
10 carefully. My question is asking whether you, as a
11 person skilled in the art, could have performed
12 these steps in December of 2012.
13 DR. KHANDURI: Objection; form,
14 scope.
15 A. I would like to read the entire document
16 before answering the question.
17 Q. So you're unable to answer that question
18 without reading the entire document. That's your
19 testimony?
20 DR. KHANDURI: Objection; form.
21 Q. About something you would know in December
22 of 2012.
23 DR. KHANDURI: Objection; form.
24 A. I would like to read the entire document
25 before answering specific questions.

1 Q. I'll take that as a you cannot answer my
2 question based on knowledge you had in December of
3 2012.
4 DR. KHANDURI: Objection; form.
5 Q. Is that fair?
6 DR. KHANDURI: Objection; form.
7 A. Once again, you're asking about a specific
8 experiment described in one paragraph out of
9 15 pages of document. And I'd like to read the
10 entire document before answering your question.
11 Q. So I'm not asking you about the results at
12 this point. What I'm asking you, if you're familiar
13 with the tools that were used and referenced in that
14 paragraph.
15 Do you know what a homology model is,
16 Dr. Moon?
17 DR. KHANDURI: Objection; form,
18 foundation.
19 (Witness reading.)
20 A. Where does it say "homology model"?
21 Q. It says that:
22 Potential antigenic
23 epitopes for recombinant human
24 PH20 were identified by
25 employing a model of the 3D

1 crystal structure of rHuPH20,
2 which was based on the crystal
3 structure of HYAL1 using amino
4 acids 2-403....
5 Do you understand that to be describing a
6 homology model that is based on the crystal
7 structure of HYAL1?
8 DR. KHANDURI: Objection; form,
9 scope.
10 A. It doesn't say "homology model" in the
11 document.
12 Q. So you don't recognize, from that
13 description, that they're referring to a PH20
14 homology model. Is that right?
15 DR. KHANDURI: Objection; form,
16 scope.
17 A. Before answering particular question about
18 this document, I would like to read the whole
19 document.
20 Q. All right. So I'm going to take your
21 answer -- you are refusing to answer my question or
22 you do not know the answer to my question. And I
23 will take that as your testimony.
24 DR. KHANDURI: Objection; form.
25 A. The document -- paragraph you mention

1 doesn't mention "homology model."
2 Q. Do you know what a homology model is and
3 how they're prepared?
4 A. So I would like to read the whole document
5 before I answer --
6 Q. No, no. My --
7 A. -- that question.
8 Q. Dr. Moon, my question was: Do you know
9 what a homology model based on a crystal structure
10 is?
11 DR. KHANDURI: Objection; form.
12 A. I would like to read the whole document
13 before answering any --
14 Q. Dr. -- Dr. Moon, I'm not asking -- this is
15 a question that's not based on this document. This
16 is a question based on your knowledge.
17 Do you know what a homology model is?
18 A. Are you referring to sequence alignment
19 models --
20 Q. No.
21 A. -- used in UniProt?
22 Q. No. I'm referring to a model that is
23 produced by SWISS-MODEL based on an amino acid
24 sequence and the structure -- the crystal structure
25 of HYAL1, which produces a model of the PH20

1 protein.
2 DR. KHANDURI: Objection; form,
3 scope.
4 Q. Do you know what that is?
5 A. Before answering specific questions, I
6 would like to read this whole document.
7 Q. Is it your testimony that in December of
8 2012, a POSA would not know what a homology model
9 is?
10 DR. KHANDURI: Objection; form.
11 (Witness reading.)
12 Q. Just to be clear, my question that's
13 pending right now is based on your personal
14 knowledge and not anything on a piece of paper in
15 front of you.
16 My question is: Do you know what a
17 homology model is, Dr. Moon?
18 DR. KHANDURI: Objection; form,
19 scope.
20 A. As I mentioned, as of 2012, I used many
21 different tools to analyze protein structure,
22 looking at sequence searching and alignments,
23 protein modeling software, and etc.
24 Q. So --
25 A. And I was in a part of multidisciplinary

1 team that examined protein modeling softwares to
2 design vaccine antigens.
3 Q. Have you ever used a software program
4 called PyMOL?
5 A. Could you repeat that?
6 Q. Have you ever used a software program
7 called PyMOL?
8 A. I have not used PyMOL --
9 Q. Have you used --
10 A. -- personally.
11 Q. Have you ever used any software program to
12 view a protein structural model?
13 DR. KHANDURI: Objection; form.
14 A. I was in a multidisciplinary research
15 group, as of 2012, to study protein structure using
16 modeling softwares.
17 But I have not personally used
18 three-dimensional structure models.
19 Q. All right. So if you could go to
20 Paragraph 36 of your declaration.
21 Sorry. Let's go back a couple of
22 paragraphs.
23 If you look at Paragraph 34 that's on
24 Page 20, and you're discussing in this paragraph and
25 two paragraphs that follow it:

1 ...polyclonal antibodies
2 generated against a polypeptide
3 antigen were known to
4 cross-react with another
5 polypeptide having as low as
6 ~46 – 49% sequence identity to
7 the stimulating polypeptide,
8 irrespective of whether the
9 polypeptides are from a
10 different animal species.
11 Do you see what --
12 A. Yes, I see that sentence.
13 Q. All right. And then, if you could go to
14 Paragraph 55, referring back to that Section VI:
15 ...polyclonal
16 antibodies --
17 This is what you state in Paragraph 55:
18 ...polyclonal --
19 polyclonal antibodies were
20 known to cross-react with a
21 polypeptide having as low as
22 ~46 – 49% sequence identity
23 with the polypeptide that
24 stimulated the polyclonal
25 antibody response.

1 A. Yes, I see that sentence.
2 Q. All right. So an antibody that binds to
3 two proteins, two different proteins, you're
4 referring to that as a cross-reactive antibody.
5 Right?
6 DR. KHANDURI: Objection; form.
7 A. "Cross-reactive antibody" generally refers
8 to antibodies that bind to two different proteins.
9 Q. So the one antibody is recognizing two --
10 the same antigenic determinant on two different
11 proteins.
12 Is that fair?
13 DR. KHANDURI: Objection; form.
14 A. "Cross-reactive antibody" generally refers
15 to antibodies that bind to two different proteins.
16 Q. And it's able to bind to two different
17 proteins because the same epitope is present on both
18 proteins. Right?
19 A. In general, cross-reactive antibodies bind
20 to similar or the same domains found within two
21 different proteins.
22 Q. Is it your opinion that any pair of
23 proteins that share 46% sequence identity will
24 induce production of cross-reactive antibodies that
25 bind to both proteins?

1 DR. KHANDURI: Objection; form.
2 A. I listed multiple examples where
3 polyclonal antibodies were known to cross-react with
4 other proteins in my declaration. And polyclonal
5 antibodies were known to cross-react to the
6 polypeptide having as low as about 46 to 49%
7 sequence identity with a polypeptide that stimulated
8 the polyclonal antibody response.
9 Q. So could you also ask -- answer my
10 question?
11 DR. KHANDURI: Objection; form.
12 A. Could you repeat your question?
13 Q. Yes. So you -- your answer to my last
14 question was explaining that you had found some
15 examples of proteins that induce production of
16 cross-reactive antibodies. Right?
17 A. There are examples that I listed in my
18 declaration.
19 Q. Right. And so, my question was actually
20 different. My question was: Is it your opinion
21 that any pair of two proteins that share 46%
22 sequence identity will induce production of
23 cross-reactive antibodies that bind to both
24 proteins?
25 That's my question. Could you please

1 answer that question.
2 DR. KHANDURI: Objection; form,
3 scope.
4 A. It is my opinion that proteins with a
5 sequence homology as low as about 46% sequence
6 identity will generate polyclonal antibodies that
7 cross-react with the other protein.
8 Q. So you list three examples of those types
9 of pairs of proteins that produced cross-reactive
10 antibodies in your declaration. Right?
11 DR. KHANDURI: Objection; form.
12 A. I listed three different examples where
13 antibodies generated cross-reactive polyclonal
14 antibody responses.
15 Q. How did you find the example of the
16 proteins that had 46% sequence identity?
17 DR. KHANDURI: Objection; form.
18 And I would caution Dr. Moon to
19 not divulge the substance of communication
20 with the counsel.
21 To the extent you can answer the
22 question without revealing the substance
23 of communications with counsel, you can do
24 so.
25 A. I searched the literature to find examples

1 where antibodies having various sequence identity
2 generates cross-reactive antibody responses.
3 Q. Did you find any other examples of two
4 proteins that had 46% sequence identity that induced
5 production of cross-reactive antibodies?
6 DR. KHANDURI: Dr. Moon, I will
7 caution you to not divulge the substance
8 of any --
9 MR. KUSHAN: Wait, wait, wait,
10 wait. He was describing his -- he said he
11 did a search, and I'm asking about his
12 search.
13 I'm not asking about his
14 conversations with you. So --
15 DR. KHANDURI: Yeah. Let me put
16 what I want to say on record. Okay?
17 MR. KUSHAN: I -- go ahead.
18 DR. KHANDURI: Dr. Moon, I will
19 caution you to not divulge the substance
20 of communication with counsel.
21 To the extent you can answer the
22 question without revealing the substance
23 of communications, you can do so.
24 BY MR. KUSHAN:
25 Q. And I'm clarifying: My question is about

1 what you did, Dr. Moon.
2 So based on your last answer, you said you
3 performed a search of the literature, looking for
4 examples of production of cross-reactive epitopes.
5 Right?
6 DR. KHANDURI: Objection; form.
7 A. I reviewed the literature where
8 cross-reactive antibody responses were generated.
9 Q. Dr. Moon, let me just clarify: Did you
10 perform a search of the literature to look for
11 examples of two proteins that share sequence
12 identity and produce cross-reactive antibodies?
13 DR. KHANDURI: Objection; form.
14 A. Could you repeat your question?
15 Q. Yeah, sure. I just want to know: Did you
16 do a literature search yourself to look for examples
17 of proteins from different sources that produced
18 cross-reactive antibodies?
19 DR. KHANDURI: Objection; form.
20 A. I did a literature search myself to look
21 for cases and examples where polyclonal antibodies
22 were generated.
23 Q. And you found three examples?
24 DR. KHANDURI: Objection; form.
25 A. I found at least three examples that I

1 listed in the declaration.
2 Q. Did you find any examples, other than the
3 one you list, where the sequence identity was
4 between 46 and 49% of the two proteins?
5 DR. KHANDURI: Objection; form.
6 A. There may be -- there may have been more
7 examples like this. But in my declaration, I put
8 one example where polypeptides having as low as 46
9 to 49 sequence identity generating polyclonal
10 cross-reactive antibody responses.
11 Q. Dr. Moon, did you find any other papers,
12 besides the three that you list in your declaration,
13 that reported results, from testing of two different
14 proteins, a capability to produce cross-reactive
15 epitopes that you did not include in your
16 declaration?
17 DR. KHANDURI: Objection; form.
18 A. There may have been other examples. But I
19 don't recall a specific example at the moment.
20 Q. Did you find any examples of two proteins
21 that had 90% sequence identity which failed to
22 produce cross-reactive antibodies?
23 (Witness reading.)
24 A. As I wrote in Paragraph 35, this is an
25 example where proteins with a 90% sequence identity

1 between mouse MOG domain and human MOG domain
2 generating polyclonal cross-reactive antibody
3 responses.
4 I also list another example in
5 Paragraph 36, where a protein with a sequence
6 homology -- sequence identity at 90%, 95%, or 98%
7 with a chicken, human, and rat type II collagen
8 inducing cross-reactive antibody responses --
9 Q. You did not --
10 A. -- in this --
11 Q. -- identify any examples other than these
12 three. Right?
13 DR. KHANDURI: Objection; form.
14 A. There may have been other examples like
15 this, but I don't recall the specific examples.
16 Q. Why did you not include them in your
17 declaration?
18 DR. KHANDURI: Objection; form.
19 (Witness reading.)
20 A. Once again, I may have seen other examples
21 in the literature. But I provided three concrete
22 examples in my declaration.
23 Q. Right. My question was trying to
24 understand why, if you saw other examples that
25 supported this idea that two proteins with 46%

1 sequence identity will induce production of
2 cross-reactive epitopes, why did you not include
3 those other examples in your declaration?
4 (Witness reading.)
5 A. Once again, I may have seen other
6 examples, other than those three cases, during my
7 search, but these three cases were sufficient to
8 help me form my opinions outlined in this
9 declaration.
10 Q. Are you speculating that there might have
11 been other examples that you could find, or are you
12 telling us under oath that you found other examples
13 besides these three and you chose not to discuss
14 them?
15 Which of those two situations are you
16 describing to us?
17 DR. KHANDURI: Objection; form.
18 A. Could you repeat the question?
19 Q. Yes. I'm trying to determine if you are
20 speculating if you -- there might be additional
21 examples that could be found, as opposed to you
22 found other examples of two proteins with 46% or
23 higher sequence identity producing cross-reactive
24 epitopes.
25 I'm trying to figure out: Which scenario

1 are we speaking of? You did -- you might find more,
2 or you did find more examples in your search?
3 DR. KHANDURI: Objection; form.
4 (Pause.)
5 A. So these three examples allowed me to form
6 opinions outlined in this declaration.
7 There may have been other examples. But I
8 don't recall the specific example at the moment,
9 sitting here today.
10 Q. And it's your opinion that any two
11 proteins that have at least 46% sequence identity
12 will induce production of cross-reactive epitopes
13 when you immunize a mammal with those two different
14 antigens?
15 DR. KHANDURI: Objection; form.
16 Q. Sorry. Let me strike that question.
17 (Pause.)
18 Q. Could you confirm that after performing
19 your literature search, you found no publications or
20 other information indicating that antibodies raised
21 against one species of PH20 induced production of
22 any antibody that bound to another species like
23 PH20?
24 DR. KHANDURI: Objection; form.
25 A. I didn't look into specific examples of

1 PH20 injected into animals to form my opinions that
2 proteins with a sequence identity greater than at
3 least 46% will generate cross-reactive polyclonal
4 antibody responses.
5 Modified -- based on these, modified PH20
6 would be expected to generate polyclonal antibody
7 responses that will bind to wild-type PH20.
8 Q. Are you aware of any examples of PH20
9 proteins from different species producing
10 cross-reactive antibodies through immunization of a
11 mammal?
12 A. Once again, I didn't look into specific
13 examples of PH20 generating antibody responses in
14 animals.
15 But reviewing the literature, I found at
16 least three examples, outlined here, showing that
17 protein with a sequence homology of at least 46%
18 would generate cross-reactive antibody responses.
19 And those three examples allowed me to
20 form the opinion that modified PH20 will generate
21 polyclonal antibody responses that will bind to
22 wild-type PH20 when injected in human females, as
23 well as in other --
24 Q. All right.
25 A. -- female mammals.

1 MR. KUSHAN: Why don't we take a
2 break?
3 VIDEOGRAPHER: We'll go off?
4 MR. KUSHAN: Yeah.
5 VIDEOGRAPHER: Off the record at
6 3:53 p.m.
7 (Whereupon, a recess was taken.)
8 VIDEOGRAPHER: We are going back
9 on the record at 4:27 p.m.
10 BY MR. KUSHAN:
11 Q. Dr. Moon, I'm going to hand you an exhibit
12 that's already been marked Exhibit EX2153.
13 (Whereupon, Halozyme Exhibit EX2153,
14 previously marked, was presented to the witness.)
15 DR. KHANDURI: Thank you.
16 Q. I believe this is the paper that you rely
17 on in Paragraph 34 of your declaration. Is that
18 right?
19 A. Exhibit 2153 is one of the exhibits that I
20 reviewed.
21 Q. So you relied on the information in
22 Exhibit 2153 to support your opinions in your
23 declaration. Right?
24 A. Exhibit 2153 is one of the exhibits that I
25 used to form my opinions.

1 Q. Okay. Now, this is a very simple
2 question: Did you find this paper, or was this
3 paper provided to you?
4 DR. KHANDURI: Dr. Moon, I will
5 caution you not to divulge the substance
6 of communication with counsel.
7 To the extent you can answer the
8 question without revealing the substance
9 of communications with the counsel, you
10 can do so.
11 MR. KUSHAN: Sorry. Are you
12 alleging there is a privilege basis
13 relating to my question?
14 DR. KHANDURI: Could be.
15 MR. KUSHAN: Could you step out,
16 Dr. Park -- I'm sorry. I'm so sorry.
17 Dr. Moon, could you please step
18 out of the room for one minute? And I
19 just have to talk to your counsel.
20 (Witness leaves the conference
21 room.)
22 MR. KUSHAN: I just want to
23 understand, get it on the record, why you
24 believe there could be an assertion of
25 privilege of work product relating to the

1 question I asked, which was: How did he
2 get this paper?
3 DR. KHANDURI: I'm just
4 cautioning the witness --
5 MR. KUSHAN: No --
6 DR. KHANDURI: -- do not divulge
7 the substance of communication. That's
8 all.
9 MR. KUSHAN: You're signaling to
10 the witness that there may be privilege.
11 And I want to understand the basis that
12 you have for privilege to that statement.
13 DR. KHANDURI: Yeah. I want to
14 make sure Dr. Moon understands the bounds
15 of the answer that he -- he should give in
16 response to your question. That's all.
17 MR. KUSHAN: So my question is
18 not very complicated. It's: Where did he
19 get the paper?
20 And there's no basis of --
21 there's no theory of privilege that would
22 suggest that is privileged.
23 DR. KHANDURI: I asserted my --
24 I stated my caution to Dr. Moon on record.
25 It's on record.

1 And I think we can move on.
2 MR. KUSHAN: I'm asking you to
3 not say it again, because you're coaching
4 your witness. And I'm just --
5 DR. KHANDURI: I'm not --
6 MR. KUSHAN: There's no --
7 there's no conceivable basis of privilege
8 in the source of the document that he's
9 using to support his opinions in this
10 proceeding. That's my point.
11 And by you saying -- cautioning
12 him not to reveal privilege, you're
13 coaching him. And I believe that's
14 improper, and I would just ask that you
15 not do that anymore.
16 DR. KHANDURI: I disagree. It's
17 fully appropriate, I think.
18 MR. KUSHAN: All right.
19 DR. KHANDURI: Let's just move
20 on.
21 MR. KUSHAN: But you've not
22 identified -- there's no theory you have
23 why his answer could be privileged.
24 DR. KHANDURI: I'm cautioning
25 the witness to be aware that his

1 answers -- in case his answers lead to
2 communications with counsel, he should be
3 aware of that. That's all.
4 MR. KUSHAN: Well, if you hear
5 him say that in his answer, you can
6 intervene.
7 DR. KHANDURI: So --
8 MR. KUSHAN: That's the proper
9 way.
10 DR. KHANDURI: -- let's just
11 move on --
12 MR. KUSHAN: That's the -- no.
13 That's the proper way to deal with it. If
14 you sense that he's going to start
15 revealing privileged communications, you
16 can interrupt the witness and instruct me
17 [sic] not to answer. Okay?
18 DR. KHANDURI: It would be too
19 late by then.
20 MR. KUSHAN: No. It's not.
21 You -- you can jump in. It's not --
22 DR. KHANDURI: It could be too
23 late by then. Let's just move on.
24 I've made my point.
25 MR. KUSHAN: Can you go get --

1 DR. KHANDURI: Yep.
2 MR. KUSHAN: -- your witness.
3 (Witness returns to the
4 conference room.)
5 DR. KHANDURI: Thank you.
6 BY MR. KUSHAN:
7 Q. Dr. Moon, do you recall the question I
8 asked you before the break? Or --
9 A. Could you --
10 Q. -- just before you left?
11 A. Could you repeat the question?
12 Q. Yes. The question is: Did you find
13 Exhibit 2153 yourself, or was Exhibit 2153 provided
14 to you?
15 DR. KHANDURI: Dr. Moon, the
16 same caution.
17 (Witness reading.)
18 A. I believe this is one of the papers I
19 found during the literature search.
20 Q. And do you have any recollection of
21 finding any other paper, besides this and the other
22 two papers that are cited in your declaration, that
23 showed that two different proteins with less than
24 90% sequence identity generated cross-reactive
25 antibodies?

1 DR. KHANDURI: Objection; form.
2 (Pause.)
3 Q. I'm going to read the question again to be
4 clear.
5 Do you have any recollection of -- other
6 than Exhibit 2153 and the other two papers cited in
7 your declaration, of a paper that you found in your
8 search that had less than 90% sequence identity --
9 sorry.
10 MR. KUSHAN: Yeah, (sotto voce)
11 we lost antibodies.
12 Q. Yeah. All right. So let's try it one
13 more time.
14 So, Dr. Moon, you performed a search for
15 literature that resulted in you finding, as you just
16 testified, Exhibit 2153. Right?
17 A. Yes. I did a literature search, and I
18 believe this is one of the papers I found during the
19 literature search.
20 MR. KUSHAN: And I'm going to
21 hand you Exhibit 2154.
22 (Whereupon, Halozyme Exhibit EX2154,
23 previously marked, was presented to the witness.)
24 DR. KHANDURI: Thanks.
25 Q. This is another one of the papers that is

1 cited in your declaration. And you addressed this
2 one in Paragraph 35. Right?
3 This is the same paper that you cited in
4 Paragraph 35. Right?
5 A. I cited this paper in Paragraph 35.
6 Q. And you relied on this paper to support
7 your opinion that two proteins with 90% sequence
8 identity or higher will generate cross-reactive --
9 cross-reactive antibodies. Correct?
10 (Pause.)
11 DR. KHANDURI: Objection; form.
12 A. I cited, in Paragraph 35, this paper,
13 2154, showed that two proteins with a sequence
14 identity of about 90% is generating cross-reactive
15 antibody responses.
16 Q. And so, you relied on the information in
17 Exhibit 2154 to support your opinions in your
18 declaration. Correct?
19 A. Exhibit 2154 is one of the documents that
20 I relied on to prepare my declaration.
21 And as outlined in Paragraph 35, this
22 exhibit showed that proteins with about 90% sequence
23 identity generates cross-reactive antibody
24 responses.
25 Q. Dr. Moon, did you find Exhibit 2154, or

1 was it provided to you?
2 (Witness reading.)
3 A. I believe this is one of the papers I
4 found during my literature search.
5 MR. KUSHAN: Okay. I'm going to
6 hand you another exhibit. This is
7 Exhibit 2155.
8 (Whereupon, Halozyme Exhibit EX2155,
9 previously marked, was presented to the witness.)
10 Q. And I believe this is the paper by
11 Trentham that is addressed in Paragraph 36 of your
12 declaration.
13 Did you rely on Exhibit 2155 to support
14 your opinions in your declaration?
15 (Witness reading.)
16 A. I relied on many papers to prepare my
17 declaration, and this is one of the papers that I
18 used.
19 Q. Dr. Moon, did you find Exhibit 2155, or
20 was Exhibit 2155 provided to you?
21 (Witness reading.)
22 A. I believe this is one of the papers that I
23 found during the literature search that allowed me
24 to form the opinions outlined in the declaration.
25 Q. And to be clear: As you sit here today,

1 you have no recollection of any other paper that
2 shows two proteins with a low 90% sequence identity
3 generating cross-reactive antibodies?
4 DR. KHANDURI: Objection; form.
5 A. Well, Exhibit 2153 shows proteins with --
6 MR. KUSHAN: I apologize. I'll
7 withdraw that question. That was
8 certainly imprecise.
9 Q. Other than the three papers that you cite
10 in your declaration, you cannot identify any other
11 paper, after you performed your search, that shows
12 two proteins with sequence identity of 46% to 90%
13 that generated cross-reactive antibodies.
14 DR. KHANDURI: Objection; form.
15 Q. Is that right?
16 DR. KHANDURI: Objection; form.
17 A. During my search, I may have found other
18 examples like these, but I don't recall the specific
19 reports at the moment.
20 Q. Can you -- do you recall what proteins --
21 what kind of proteins they were, if you remember a
22 paper?
23 (Witness reading.)
24 A. I may have seen other papers along these
25 line performed in mice, but I do not recall what

1 specific protein was used in those examples.
2 Q. If you could go to Exhibit 2153, which is
3 the heat shock protein paper.
4 Do you have that?
5 A. Yes, I have that.
6 Q. When you prepared your opinions in your
7 declaration, did you compare the proteins that were
8 discussed in Exhibit 2153 to PH20 proteins?
9 DR. KHANDURI: Objection; form.
10 A. Could you repeat the question?
11 (Pause.)
12 Q. Okay. My question was: When you formed
13 your opinions in your declaration about this topic
14 we've been discussing, did you compare the proteins
15 that were discussed in Exhibit 2153 in any way to
16 the PH20 proteins?
17 DR. KHANDURI: Objection; form.
18 A. Could you be more specific -- by
19 comparison?
20 Q. Sure. Did you -- did you see if they
21 were -- these proteins were enzymes like the PH20
22 proteins?
23 A. These studies are about use of proteins
24 for vaccine applications, how proteins of different
25 sequence identity are inducing cross-reactive

1 antibody responses.
2 Q. Were the heat shock proteins being used
3 as -- in a vaccine, or were they just being studied
4 because people had observed autoantibodies to be
5 produced against them?
6 DR. KHANDURI: Objection; form.
7 (Witness reading.)
8 A. In this particular report, the researchers
9 were studying heat shock protein in the setting of
10 infection with microbes.
11 And they are reporting mice can generate
12 antibody responses to heat shock protein.
13 Q. Dr. Moon, did you compare the length of
14 the protein sequences being discussed in the
15 Exhibit 23- -- 2153 paper to the length of the PH20
16 proteins as part of your analysis?
17 (Witness reading.)
18 A. I did not directly compare the length of
19 the heat shock protein to PH20 to arrive at my
20 opinions outlined in the declaration.
21 What this paper is showing is that, as
22 long as proteins have sequence identity as low as
23 46%, these antigens can generate cross-reactive
24 antibody responses.
25 And similar principles can be applied to

1 modify the PH20.
2 Q. And under the same reasoning, any two
3 proteins that have 46% sequence identity would also
4 generate cross-reactive antibodies. Correct?
5 DR. KHANDURI: Objection; form.
6 A. This paper clearly reported that proteins
7 with a sequence identity as low as 46% can generate
8 cross-reactive antibody responses.
9 Q. And I'm just exploring your reasoning why
10 that suggests that PH20 proteins with 46% sequence
11 identity to other proteins will generate
12 cross-reactive antibodies that bind to other PH20
13 proteins.
14 Why?
15 DR. KHANDURI: Objection; form.
16 A. Basically, these three papers, including
17 Exhibit 2153, are showing that when you use proteins
18 with sequence homology ranging from as low as 46% to
19 90% and higher, they are generating cross-reactive
20 antibody responses.
21 So the same principles could be expected
22 to work for modified PH20.
23 Q. Now, you're saying that because the two
24 proteins have 46% sequence identity or because
25 they're homologous proteins that have 46% sequence

1 identity?
2 DR. KHANDURI: Objection; form.
3 Q. I think, in your declarations, you just
4 refer to "sequence identity." Right?
5 (No audible response.)
6 Q. So if you look at Paragraph 34, you say:
7 ...polyclonal antibodies
8 generated against a polypeptide
9 antigen were known to
10 cross-react with another
11 polypeptide having as low as
12 ~46 – 49% sequence identity to
13 the stimulating polypeptide,
14 irrespective of whether the
15 polypeptides are from a
16 different animal species.
17 Right?
18 So that's sequence identity you're
19 referring to. Correct?
20 A. I'm referring to the sequence identity in
21 that statement.
22 Q. Right. And then, in the Oliver paper,
23 which is Exhibit 2154, you're referring to the
24 existence of 90% sequence identity between the mouse
25 and human MOG proteins. Right?

1 Again, it was the sequence identity that
2 you were pointing to to support your opinion that
3 the two proteins would generate cross-reactive
4 antibodies. Right?
5 A. In this exhibit, they used mouse MOG
6 protein and human MOG protein with a sequence
7 identity of about 90% to show cross-reactivity.
8 Q. And in Paragraph 36, regarding the
9 Exhibit 2155, which is the Trentham paper, again,
10 you're using sequence identities as a basis for your
11 opinion that the three proteins will generate
12 cross-reactive antibodies. Right?
13 A. This paper, 2155, showed that proteins
14 with a sequence identity 90%, 95%, or 98% generate
15 cross-reactive antibody responses.
16 Q. So again, your opinions are based on
17 sequence identity as the critical question above
18 46%?
19 DR. KHANDURI: Objection --
20 objection; form.
21 A. As I stated in Paragraph 37, based on
22 these reports:
23 ...POSA would have
24 expected that polyclonal
25 antibodies generated in a

1 subject against a polypeptide
2 would cross-react with
3 polypeptides having as low as
4 ~46 – 49% sequence identity....
5 Q. And that's true for any polypeptide that
6 meets that threshold of 46 to 49% sequence identity.
7 Right?
8 DR. KHANDURI: Objection; form.
9 A. (Reading):
10 ...POSA would have
11 expected that polyclonal
12 antibodies generated in a
13 subject against a polypeptide
14 would cross-react with
15 polypeptides having as low as
16 ~46 – 49% sequence identity....
17 Q. Okay. Now, we talked a bit earlier about
18 the alignments that you -- are in your declaration
19 in the appendix.
20 I just want to ask: Did you prepare the
21 alignments that are reported in Appendix B and
22 Appendix -- yeah.
23 So there are three alignments in
24 Appendix B. And did you prepare all these
25 alignments yourself?

1 (Witness reading.)
2 A. Yes, I recall I prepared the alignments
3 myself.
4 DR. KHANDURI: All right. Why
5 don't we take about a five-ish minute
6 break.
7 VIDEOGRAPHER: We're going off
8 the record --
9 DR. KHANDURI: Okay.
10 VIDEOGRAPHER: -- at 4:58 p.m.
11 (Whereupon, a recess was taken.)
12 VIDEOGRAPHER: We are going back
13 on the record at 5:13 p.m.
14 BY MR. KUSHAN:
15 Q. Dr. Moon, did you speak with anybody on
16 the break?
17 A. No.
18 MR. KUSHAN: Okay. I'm going to
19 mark as Exhibit 1123 an excerpt from a
20 textbook by Janeway -- Janeway's,
21 consisting of Chapters 8, 10, 12, 15, and
22 Appendix I.
23 (Whereupon, Exhibit 1123 was marked for
24 identification.)
25 Q. This is the 8th Edition of Janeway's

1 "Immunobiology," published in 2011 -- 2012, by
2 Garland Science.
3 Yes. There are portions of Chapters 8,
4 10, 12, 15, and Appendix I.
5 Dr. Park [sic], are you familiar with the
6 Janeway's Immunobiology textbook?
7 A. By the way, I'm Dr. Moon.
8 Q. I'm sorry. I'm so --
9 A. Yeah.
10 Q. I -- sorry. I've said that a couple times
11 today. I wanted to apologize.
12 A. Okay.
13 Q. Dr. Moon, can I just clarify: Have you
14 seen or are you familiar with this Immunobiology
15 textbook from Janeway's?
16 A. I may have read this a long time ago.
17 Q. Would this have been one of the textbooks
18 you might have used in the 2008 to 2012 time frame,
19 or earlier versions of it?
20 A. I don't --
21 DR. KHANDURI: Objection; form.
22 A. -- recall the exact text, but I may have
23 seen this long, long time ago.
24 Q. Okay. Could I ask that you go to the very
25 back, Page 721. And if you need to -- you can take

1 the paper -- the clip off.
2 I'm just going to ask you a couple
3 questions about the table that -- I'm sorry.
4 In the directory, it's --
5 A. What page?
6 Q. -- Page 719. It's Figure A.2.
7 A. So Figure A.2.
8 Figure A.2. Yeah, I'm looking at that.
9 Q. And this is a table that compiles "Factors
10 that influence the immunogenicity of proteins."
11 And I just want to go over some of these
12 characteristics and see if they are consistent with
13 your familiarity of this phenomenon of
14 immunogenicity of proteins. Okay?
15 (No audible response.)
16 Q. Do you agree, as it's being represented in
17 Figure A.2, that the size of a protein can influence
18 the immunogenicity of the protein?
19 (Witness reading.)
20 A. In general, size of antigen may affect
21 immunogenicity.
22 Q. Okay. And larger proteins are labeled
23 "increased immunogenicity."
24 Is that consistent with your experience?
25 (Witness reading.)

1 A. Could you repeat the question?
2 Q. Sure. Is it consistent with your
3 experiences in the field of immunology that larger
4 proteins are generally more immunogenic -- more --
5 more immunogenic than smaller proteins?
6 A. In general, larger proteins are more
7 immunogenic than smaller proteins.
8 Q. Okay. If you go a few rows down, there's
9 a row called "Form," and it has four boxes.
10 "Particulate" is described as being
11 increased immunogenicity compared to "soluble," as
12 to the -- I'm sorry -- yeah, particularly as
13 compared -- let me start over.
14 The table is describing proteins that are
15 in particulate form to be -- to have increased
16 immunogenicity relative to proteins that are
17 soluble. Is that right?
18 A. In general, particulate form of antigens
19 are known to be more immunogenic than soluble
20 proteins.
21 Q. And similarly, denatured forms of proteins
22 are known to be more immunogenic -- more immunogenic
23 than the native form of the protein. Correct?
24 A. In general, denatured proteins are more
25 immunogenic than native proteins.

1 Q. Okay. And the next row is describing
2 similarity to self-protein.
3 That's addressing the self-protein
4 questions we were discussing earlier today. Right?
5 A. I see that row, "Similarity to self
6 protein."
7 Q. And it's reporting that where a protein
8 has multiple differences relative to a self-protein,
9 that's increased immunogenic -- it has increased
10 immunogenicity. Correct?
11 A. It's been generally known that proteins
12 with multiple differences are more immunogenic.
13 Q. And proteins that have fewer differences
14 and are more similar to the native wild-type protein
15 have decreased immunogenicity. Right?
16 A. So this is a very general table that
17 describes immunogenicity of proteins.
18 The proteins with multiple differences are
19 known to be more immunogenic. A POSA would have
20 used proteins with fewer differences as an effective
21 antigen using different approaches that I outlined
22 in the declaration.
23 Q. And is it correct that these are
24 principles that someone who was a POSA in 2012 would
25 have been familiar with?

1 A. These are general concepts in immunology.
2 MR. KUSHAN: Okay. I have no
3 further questions.
4 DR. KHANDURI: We'll take --
5 we'll take a break.
6 Let's go off record.
7 VIDEOGRAPHER: Going off the
8 record at 5:23 p.m.
9 (Whereupon, a recess was taken.)
10 VIDEOGRAPHER: We are going back
11 on the record at 5:29 p.m.
12 DR. KHANDURI: Thank you,
13 Dr. Moon, for your time. We don't have
14 any questions for you. We invoke the
15 witness's right to read and sign.
16 MR. KUSHAN: Okay.
17 DR. KHANDURI: Thank you.
18 VIDEOGRAPHER: We are going off
19 the record --
20 DR. KHANDURI: We're off.
21 MR. KUSHAN: Yeah.
22 VIDEOGRAPHER: -- off the record
23 at 5:29 p.m.
24 (Whereupon the deposition concluded at
25 5:29 p.m.)

1 DEPONENT'S SIGNATURE

2

3 Please be advised I have read the

4 foregoing deposition, pages 1 through 201,

5 inclusive. I hereby state there are:

6 (Check one)

7 _____ No corrections

8

9 _____ Corrections per attached

10

11

12 _____

13 JAMES J. MOON, PH.D.

14

15 (X) Reading and signing was requested.

16 ( ) Reading and signing was waived.

17 ( ) Reading and signing was not requested.

18

19

20 Should the signature of the witness not

21 be affixed to the deposition, the witness shall not

22 have availed himself of the opportunity to sign or

23 the signature has been waived.

24

25 --oOo--

1 ERRATA SHEET

2 NAME OF CASE: Merck Sharp & Dohme LLC v.

3 Halozyme, Inc.

4 DATE OF DEPOSITION: November 18, 2025

5 NAME OF WITNESS: JAMES J. MOON, PH.D.

6 Reason Codes:

7 1: To clarify the record.

8 2: To conform to the facts.

9 3: To correct transcription error.

10 Page _____ Line _____ Reason _____

11 From _____ to _____

12 Page _____ Line _____ Reason _____

13 From _____ to _____

14 Page _____ Line _____ Reason _____

15 From _____ to _____

16 Page _____ Line _____ Reason _____

17 From _____ to _____

18 Page _____ Line _____ Reason _____

19 From _____ to _____

20 Page _____ Line _____ Reason _____

21 From _____ to _____

22 Page _____ Line _____ Reason _____

23 From _____ to _____

24 _____ _____

25 JAMES J. MOON, PH.D. DATE

1 DECLARATION UNDER PENALTY OF PERJURY
2 I am the witness in the foregoing
3 deposition.
4 I have read the foregoing deposition or
5 have had read to me the foregoing deposition, and
6 having made such changes and corrections as I
7 desired, I certify that the same is true in my own
8 knowledge.
9 I hereby declare under penalty of perjury
10 that the foregoing is true and correct.
11 In witness whereof, I hereby subscribe my
12 name this _____ day of _____, 2025.
13
14 _____
15 JAMES J. MOON, PH.D.
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CERTIFICATE

I, SUSAN ASHE, a Registered Merit Reporter and Notary Public, hereby certify that the foregoing is a true and accurate transcript of the deposition of said witness, who was first duly sworn by me on the date and place hereinbefore set forth.

I FURTHER CERTIFY that I am neither attorney nor counsel, nor related to or 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 in this action, nor am I financially interested in this case.

Dated this 24th day of November 2025.

Susan Ashe, Notary Public
of the District of Columbia

My commission expires: May 14, 2028.

Exhibits

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EX 1119 James J. Moon, Ph. D. 111825
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EX 1120 James J. Moon, Ph. D. 111825
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EX 1121 James J. Moon, Ph. D. 111825
6:21 114:17, 21
EX 1122 James J. Moon, Ph. D. 111825
7:4 155:6,7
EX 1123 James J. Moon, Ph. D. 111825
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