

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

BIONTECH SE and PFIZER INC.,
Petitioner

v.

MODERNATX, INC.,
Patent Owner.

IPR2023-01358 (Patent 10,702,600 B1)
IPR2023-01359 (Patent 10,933,127 B2)

Record of Oral Hearing
Held: December 10, 2024

Before SHERIDAN K. SNEDDEN, TIMOTHY G. MAJORS, and
DAVID COTTA, Administrative Patent Judges.

APPEARANCES:

ON BEHALF OF THE PETITIONER:

NAVEEN MODI, ESQ.
Paul Hastings, LLP
2050 M Street, N.W.
Washington, D.C. 20036
202-551-1990
naveenmodi@paulhastings.com

DAVID KRINSKY, ESQ.
Williams & Connolly, LLP
680 Maine Ave S.W.
Washington, D.C. 20024
202-434-5338
dkrinsky@wc.com

ON BEHALF OF THE PATENT OWNER:

KEVIN PRUSSIA, ESQ.
ANNALEIGH CURTIS, ESQ.
Wilmer Cutler Pickering Hale and Dorr, LLP
60 State Street
Boston, Massachusetts 02109
617-526-6243
kevin.prussia@wilmerhale.com
Annaleigh.curtis@wilmerhale.com

The above-entitled matter came on for hearing Tuesday, December 10, 2024, commencing at 9:00 a.m. EST, at the U.S. Patent and Trademark Office, 600 Dulany Street, Alexandria, Virginia.

P-R-O-C-E-E-D-I-N-G-S

(9:02 a.m.)

JUDGE COTTA: All right. Good morning. This is the final hearing in IPR 2023-01358 and IPR 2023-01359 regarding U.S. Patent Nos. 10,702,600 and 10,933,127. The Petitioners are Pfizer, Inc. and BioNTech SE. The patent owner is Moderna TX Inc. This hearing is open to the public and a full transcript of the hearing will be made part of the record. I'm Judge Cotta and with me in the hearing room is Judge Majors, appearing remotely is Judge Snedden. Counsel for Petitioner, could you please identify yourself and your colleagues for the record?

MR. MODI: Good morning, Your Honors. Naveen Modi from Paul Hastings. I'm here on behalf of Petitioner BioNTech. With me, I have my colleague Ryan Meuth.

MR. KRINSKY: My name's David Krinsky. I'm here on behalf of Petitioner Pfizer, with the Board's permission, Mr. Modi and I will be splitting up the argument. And with me, well, I won't recognize absolutely everyone, but I do want to recognize that Nina Holloway, my client, is here.

JUDGE COTTA: Thank you. And counsel for Patent Owner, could you please identify yourself and your colleagues?

MR. PRUSSIA: Good morning, Your Honor, Kevin Prussia on behalf of the Patent Owner. I will be splitting the argument with Annaleigh Curtis, also from my firm, Wilmer Hale. With us on behalf of Moderna is Kelli Powell, who is director of patent litigation, and Dr. Jacob Moore, who is senior counsel of intellectual property.

JUDGE COTTA: Very good. We look forward to the parties' presentations today. But before we get there, there are a few points that I

1 would like to cover. First of all this hearing is open to the public, but there
2 have been some submissions in this case that were filed under seal.

3 We understand from an email that we received that neither party
4 expects their presentations will require closing the courtroom to maintain
5 confidentiality. We share the parties' expectation that the hearing will not
6 require either party to divulge confidential information.

7 That said, if the argument today does take an unexpected turn, such
8 that either party feels the need to discuss confidential information, please let
9 us know and we will take appropriate steps to ensure that you can present
10 the argument that you would like to make without compromising
11 confidentiality.

12 And we would most likely do that by allowing time at the end of the
13 hearing to address confidential issues. In that circumstance, we don't expect
14 that we would give you additional time to discuss the confidential issues. It
15 would come out of the total time that we've already allocated for the parties'
16 presentations.

17 Finally, with respect to confidentiality, this is a very voluminous
18 record. There's a lot to keep track of. If we, the judges, should inadvertently
19 ask a question that starts to reveal confidential information or that requires
20 confidential information to answer, I don't expect that to happen, but if it
21 does, please feel free to interrupt and caution us so that we avoid inadvertent
22 disclosure.

23 Secondly, we have access to the entire record, including
24 demonstratives, so when referring to each demonstrative, paper, or exhibit,
25 please do so by slide or page number, and then pause a few seconds to allow
26 us time to find it.

1 During yesterday, we received objections to demonstratives. We're
2 not going to rule on those objections now. Demonstratives are not evidence.
3 But if the parties wish to use the time that they've been allotted to argue their
4 objections, they should feel free to do so.

5 I will maintain a clock. And I will give each party a five-minute
6 warning during their opening argument and appropriate warning near the
7 end of any reserved rebuttal time. Our hearing room has a timer and we set
8 it with enough for each party the requested time allotment. The light on the
9 clock will change to yellow when you are nearing the end of your time,
10 whether that's opening or rebuttal. And when the light is red, you will have
11 run out of time.

12 As far as hearing order, Petitioner, you have 90 minutes total for
13 argument. Would you like to reserve any time for rebuttal?

14 MR. MODI: Yes, Your Honor. I'd like to reserve 20 minutes.

15 JUDGE COTTA: 20 minutes.

16 MR. MODI: Thank you.

17 JUDGE COTTA: And Patent Owner, we received a request for Ms.
18 Annaleigh Curtis to participate under our LEAP practitioner program, and I
19 understand that she will present at least a portion of your argument, and that
20 entitles you to an additional 15 minutes.

21 We remind Patent Owner that the LEAP practitioner must have a
22 meaningful and substantive opportunity to argue during the hearing today.
23 So with that said, you will have a total of 105 minutes. Would you like to
24 reserve any rebuttal time?

25 MR. PRUSSIA: Yes, Your Honor, with the panel's permission, we'd
26 like to reserve 15 minutes.

1 JUDGE COTTA: 15 minutes. Okay. Petitioner you will go first as
2 you have the burden of showing unpatentability of the challenged claims.
3 You can begin whenever you are ready.

4 MR. MODI: Thank you, Your Honor. Your Honor, we have a copy
5 of our demonstratives, can we pass those to you?

6 JUDGE COTTA: Well, we have an electronic copy, so it's not
7 necessary. You're welcome to, and I don't know if it might benefit the court
8 reporter if you give a copy to the court reporter. Okay. So we're all set.

9 MR. MODI: Your Honors, are you ready?

10 JUDGE COTTA: Yes, please begin. Oh, let me set the time. All
11 right. You're on the clock.

12 MR. MODI: Good morning, Your Honors. May it please the Board.
13 Based on the petitions and supporting evidence, the Board is to conduct
14 trials in these IPRs. The record now includes even more evidence than
15 before that supports unpatentability.

16 JUDGE COTTA: Can I pause for one second?

17 MR. MODI: Sure, Your Honor.

18 JUDGE COTTA: I just received a notice that we have more people
19 that would like to come in, so why don't we just let them in, since you're
20 only 46 seconds, 14 seconds in?

21 MR. MODI: Sure.

22 MR. PRUSSIA: I will let him have his 14 seconds.

23 MR. MODI: As you can tell, this is why we needed a bigger hearing
24 room.

25 JUDGE COTTA: So I appreciate that.

1 MR. MODI: Thank you for accommodating us. Okay. I will just
2 restart.

3 Good morning, again, Your Honors. May it please the Board. Based
4 on the petition and supporting evidence, the Board is to conduct the trials in
5 these IPRs. The record now includes even more evidence than before that
6 supports unpatentability.

7 Now, as Your Honor noted, the record here is large. And while Patent
8 Owner, Moderna, tries to muddy the waters, the issues are simple. We
9 request that the Board hold the challenged claims unpatentable and let me
10 explain why. Can we go to Slide 2.

11 So we're going to divide our opening presentation into three parts
12 today. I will begin by providing an overview of the challenged patents, the
13 prior art, and each of the grounds, then I will address the anticipation ground
14 based on Schrum. Finally, I will turn it over to my colleague, Mr. Krinsky,
15 who will address the obviousness-based grounds.

16 Of course, we're here to answer your questions, and I'm happy to
17 focus on anything that Your Honors would like us to focus on. With that,
18 let's go to Slide 3, please.

19 As the Board appreciates, the breadth of the challenged claims and the
20 teachings of the prior art will inform the discussion today. So I meant to
21 spend a few minutes just setting the stage. If we go to Slide 4?

22 So I mean, as both of the IPRs here involve the '600 and '127 patents.
23 Both patents were filed during the height of the COVID-19 pandemic on
24 February 28th, and May 21st, 2020, respectively. Both patents claim
25 priority to provisional applications going back to October of 2015. Now if
26 we go to Slide 5, I think we should start with what the patents tell us. So

1 here we have the summary of the invention, a snapshot from that summary
2 of the invention section.

3 And this is what the summary tells us, and this is again, from the
4 challenged patents. It says, "Provided herein are RNA vaccines that build on
5 the knowledge that RNA can safely direct the body's cellular machinery to
6 produce nearly any protein of interest."

7 So let's stand back. What is the patent telling us here? They are
8 telling us that they have not discovered that mRNA can code and actually
9 produce a protein. And why could they? That was well-established back in
10 2015. Instead, they claim that the patents are directed to vaccines using
11 mRNA technology. But as we discussed, they run right into the prior art
12 with the broad patent claims that they have here.

13 And let's start with those claims. Let's go to Slide 14, please. So if
14 you look at the challenged claims, you have Claim 1 of the '127 patent, oh,
15 sorry, the '600 patent on the top left, Claim 1 of the '127 patent here on the
16 bottom left. So what do these claims cover?

17 They are really broad. So if we start with the '600 patent, you can see
18 it covers an mRNA encoding a protein, then the mRNA is formulated in a
19 lipid nanoparticle. From there the mRNA encoded protein is a
20 betacoronavirus S protein. That's it, Your Honors. This is a really broad
21 claim.

22 And then what does the '127 patent do? The only thing it adds is the
23 language that deals with inducing an immune response. Let's go to Slide 16,
24 please.

25 So again, I want to step back. And really, I want to sort of stress how
26 important it is that these challenged claims do not recite any specific

1 vaccine, they recite generic concepts. For instance, Patent Owner is trying
2 to cover previous patents, mRNA is a broad structural components, where
3 emerging COVID-19 was, as well as any other BetaCoV that might come
4 into existence.

5 What else? It's any lipid nanoparticle delivery system using the broad
6 four categories of lipids at times, and use a S protein encoding mRNA. And
7 finally for the '127, it's inducing any level of immune response, right.

8 So again, these patents are really broad, so they run right into the prior
9 art. And if we could go to Slide 17. The Board's aware of the grounds here
10 of both IPRs involved, anticipation by Schrum, and then obviousness over
11 Schrum and Geall, Yang, or Altmeyer. And like I said, I'm going to focus
12 on the anticipation ground. So let's go to Slide 6, please.

13 So let's start with Schrum. While it's important to remember, Schrum
14 is a Moderna application, Patent Owner's application, that was published in
15 October of 2013, more than two years before the provisional applications to
16 which the challenged patents claimed priority. Let's go to Slide 7.

17 What is interesting, Your Honors, is that Moderna actually explicitly
18 abandoned Schrum. And that was done in August 2015. There was no prior
19 art rejection in that application, but they still abandoned it. And what did
20 they do after that? Just two months later, they start filing the provisional
21 applications that the challenged patents claim priority to.

22 And if you look at the provisional applications, they name countless
23 immunogens, with no actual vaccines or data. What's also interesting is in
24 the challenged patents, the challenged patents similarly recite countless
25 immunogens and have a broad disclosure. They actually include either
26 identical or essentially identical passages from Schrum. I want to repeat

1 that. The challenged patents here, include either identical or essentially
2 identical passages from Schrum, and I'll show you a couple of those later.

3 And they try to capture what was already disclosed, and in fact,
4 claimed in Schrum, at least partly. So let's go to Slide 8. And I want to
5 spend a little bit more time on Schrum and looking at it in detail. So if you
6 look at Schrum, in the first few paragraphs of Schrum, Your Honors, this is,
7 if you look on the slide, it's Paragraphs 4 through 8. Schrum comes out and
8 tells us that it teaches a composition comprising a modified mRNA,
9 encoding a protein formulated in a four-component lipid nanoparticle. You
10 can see that here in Paragraph 8.

11 So again, let's pause for a second. What have we learned so far? It is
12 undisputed that mRNA encodes a protein and produces a protein, right.
13 That's in the challenged patents themselves. It is also known that the
14 specific protein dictates the application of the mRNA composition. So the
15 question here becomes then, what do you do with the teachings of Schrum,
16 and what protein do you encode? Well, Schrum also answers that question.
17 So if you go to Slide 9.

18 So if we look at Slide 9, this is from Schrum where it has a section,
19 entire section on vaccines. And what does it tell us? It tells us that you can
20 use the mRNA formulations here as a vaccine, where they can encode for an
21 immunogen, right. You see that here. Let's go to Slide 10.

22 What's more in that same section that we were just looking at, what
23 does Schrum tell us? It incorporates Geall in its entirety. Again, and what
24 does Geall provide? It provides better known immunogens that Schrum's
25 mRNA and vaccine can encode. And as we have discussed, one of those is
26 the BetaCoV, SARS CoV, spike protein.

1 Now I want to pause for a second again. If you look at the breadth of
2 the challenged patents here, it's very similar to Schrum and Geall. In fact,
3 the challenged patents include disclosure, again, I will say that's either
4 identical or essentially identical to Schrum, and I will give you examples of
5 those in a minute.

6 And then what the challenged patents do is recite infectious disease
7 immunogens of Geall expressly rather than through incorporation, which is
8 what Schrum does. So they are no different from our perspective, which is
9 why Schrum anticipates. We'll go to Slide 11.

10 Now I think it's important to note that Schrum's teachings are all
11 related. And you don't have to take my word for it, I actually just showed
12 you some of the teachings of Schrum. But let's take a look at the deposition
13 testimony from our expert, Dr. Griffin, that Patent Owner elicited during this
14 proceeding.

15 This is what Dr. Griffin had to say when he was asked about Schrum's
16 disclosure. He says, "I started reading Schrum. And I'm reading the
17 beginning of Schrum where I get an overview. Then, I move onto where I
18 am taught about modified mRNA. I am taught about delivery systems,
19 including LNP. Then, after a very long section on the nucleotide
20 modifications, when I'm wondering what I'm going to do with this
21 technology."

22 What happens? "I then come across a section that starts bottom of the
23 right page, just right above paragraph 340, where I am now taught that I can
24 use this technology to make a vaccine." What's more, he says, "I am
25 directed to reference Geall, which is incorporated in its reference as if it
26 were stapled to the back of Schrum. There's a list of pathogens for which I

1 can use this technology to make a vaccine. And in the list of pathogens is
2 coronavirus, which is in the list of top ten pathogens of emerging pathogens
3 of pandemic potential in 2015."

4 So what he is telling us there is that some -- Geall teaches us the top
5 ten pathogens that were a problem, and that was a known problem in 2015.
6 And then he says, "As I'm reading this as a person of ordinary skill, I see
7 only a coronavirus mentioned on the bottom of page 19, but specifically the
8 S protein is called out as a protein that I can make with this technology in
9 vaccine design."

10 So I want to pause there for a minute. This is testimony from one of
11 skill in the art, Dr. Griffin. And if the Board may recall, the person of
12 ordinary skill is remarkably educated and experienced, regardless of whose
13 definition the Board uses. In fact, it's a team that's the person of ordinary
14 skill in the art. So it's incredible for Moderna to come here and say the
15 claims are unanticipated or rendered obvious in light of the skill of the
16 person of ordinary skill in the art. If we go to Slide 12.

17 There's more than Schrum, Your Honors. So this is Paragraph 397
18 from Schrum, and what does this teach us? In Paragraph 397, in one place it
19 teaches us the user of -- encoding mRNA formulated in a lipid nanoparticle
20 as a vaccine used to elicit an immune response. Now they have some
21 arguments on Paragraph 397, they're trying to parse it, they're like no, it only
22 refers to modified mRNA, not modified mRNA, but as we will discuss, it
23 clearly does. Again, all of the teachings of Schrum are related.

24 But here's the interesting point. Remember I kept saying that they
25 take passages of Schrum, they have been put into the '600 and '127 patent.
26 I'd actually like to show you that they have a copy of 397 that's essentially

1 identical to what's in Schrum. Can we pull up Column 85 of the '127 patent,
2 please?

3 And while Ryan is pulling that up, Your Honors, it's interesting to
4 note, right, today they want Your Honors to say, well, 397 is not related to
5 the intervention of Schrum, it's different. But like I said, an essentially
6 identical version of that paragraph is in the '600 and '127 patents. And why
7 is that important?

8 It's important because it tells us that Paragraph 397 is a disclosure of
9 an mRNA LNP vaccine, and that the challenged patents are not directed to
10 anything new. What's more, they actually cited to this paragraph of Schrum
11 as support in response to a rejection under Section 112 in the '127 patent,
12 Your Honors. And you can find that, that's at Exhibit 1008 at 488. And
13 Ryan can you zoom in to Column 85, Lines 47 to 58, please? So you can
14 see it right there, Your Honors.

15 This is again, the '127 patent, Column 85, Lines 47 to 58. What does
16 the '127 patent give you? An identical copy of Paragraph 397. In some
17 embodiments an immune response may be elicited by delivering a lipid
18 nanoparticle which may include an immunogen, and then it says, it tells each
19 of which may be incorporated by reference in their entirety. The polymer
20 may encapsulate the nanospecies or partially encapsulate the nanospecies.
21 The immunogen may be --

22 JUDGE COTTA: I'd like to interrupt for a second.

23 MR. MODI: Sure, Your Honor.

24 JUDGE COTTA: This is all new argument, isn't it?

25 MR. MODI: So, Your Honor, this is in response to their argument
26 and their sur reply, which we didn't get a chance to respond to, where they

1 argued that 397 doesn't disclose modified mRNA. And from our
2 perspective, this is certainly part of the record, and it shows that why
3 paragraph 397 here does tie everything together. And even if you don't look
4 it together, we still win. I just think it's telling that they have paragraphs like
5 this incorporated in the '600 and '127 patents.

6 JUDGE COTTA: And looking just at Schrum, what does Schrum tell
7 us in terms of this being mRNA?

8 MR. MODI: Sure, Your Honor. And we can actually jump to that.
9 So if you can go to Slide, let's go to Slide 54, please. So if you look at 54,
10 what we have here is Paragraphs 340, which is the vaccine fraction on the
11 left. You have Paragraph 378, which is the section that deals with the lipid
12 nanoparticles. And then we have Paragraph 397. So we get to the mRNA
13 encoding vaccines in Schrum in two ways, so the mRNA encoding the
14 immunogen in two ways, at least two ways, I would say.

15 The first is you have Section 340, right, which is a vaccine section.
16 And that tells us that you have mRNA molecules may be used to elicit or
17 provoke an immune response. And then Paragraph 342 is not here, but 342
18 also tells us that may be the modified mRNA. And then what does Schrum
19 tell us a few pages later? It gives us Paragraph 378. And what does 378
20 say? It says the modified nucleic acid molecules and mRNA of the
21 invention can be formulated using one or more liposomes, lipoplexes, or
22 lipid nanoparticles. So that's one way how we get to the mRNA encoding an
23 immunogen.

24 The second way to get to it is through Paragraph 397, again, in one
25 place. So if you look at Paragraph 397, it's in the same section where
26 Paragraph 378 is, right. And what does it tell us? It says, "Like Paragraph

1 340, it tells us in one embodiment you have an immune response, may be
2 elicited by delivering in lipid nanoparticle which may include a nanospecies,
3 a polymer, and an immunogen". It doesn't stop there. It goes on and says,
4 "The immunogen may be a modified RNA as described herein". And of
5 course, that talks about a modified RNA described therein, it's talking about,
6 for example, the modified RNA that we have in Section 342 and 340.

7 JUDGE COTTA: Is there anything else that a modified mRNA, I'm
8 sorry, a modified RNA as described herein could refer to other than mRNA?

9 MR. MODI: So two responses to that, Your Honor. First is that,
10 Moderna, it's in Patent Owner's response, and I'm going to give you the cite
11 to this. They actually agreed with us that this paragraph does refer to
12 mRNA. And that's at Patent Owner Response 22.

13 What they said there was one -- so remember they are saying 397 has
14 two embodiments. And they say, well, the first one includes a vaccine, but
15 no mRNA, the second includes mRNA but no vaccine. Right. That's what
16 they said in their Patent Owner response. But in their sur reply, they were
17 obviously saying something different.

18 So from our perspective, Your Honor, this paragraph, and it talks
19 about modified RNA, it is talking about modified mRNA. And like I said, if
20 you look, just compare the two patents next to each other. It uses very
21 similar language.

22 And then the second point that I wanted to make was, if you look at
23 some of the other things that they're pointing to for modified RNA, right.
24 They're pointing to things like siRNA, and they are saying RNAi, but those
25 don't encode proteins, they in fact, inhibit expression. So their argument just
26 doesn't hold water.

1 And then like I said, at the end of the day, the problem that they have
2 is all of these teachings of Schrum are inter-related. And once I note again,
3 with respect to Paragraph 378, that we just looked at, that's actually on the
4 slide, on 54. Again, I think, Your Honor, it's telling. They today, want to
5 run away from their disclosure of Schrum. But if you actually look at their
6 own disclosure, again, Paragraph 378 also exists in essentially identical form
7 in their own disclosure.

8 And that's at, for example '127 patent, Column 76, Lines 27 to 47. So
9 from our perspective, it's all the, it's in one place, Schrum clearly teaches the
10 mRNA that's encoding an immunogen for a vaccine in one place.

11 JUDGE MAJORS: Mr. Modi, Patent Owner cites some testimony
12 from your expert, Dr. Moon. The Patent Owner says to the effect that
13 Paragraph 397 disclosed multiple embodiments, not one embodiment in
14 there. What's your response to that?

15 MR. MODI: We disagree, Your Honor. And I think we actually have
16 testimony from Dr. Moon that that's one of the slides, so why don't we look
17 at it. So if you go to Slide 55. So this is testimony from Dr. Moon. And
18 you can see that this is what he said in Paragraph 35 of Exhibit 1161.

19 He said, "A person of ordinary skill would have readily understood
20 that Schrum's disclosure that 'an immune response may be elicited by
21 delivering a lipid nanoparticle' refers to a lipid nanoparticle-based vaccine
22 composition. In fact, Schrum uses nearly identical language in its discussion
23 of mRNA vaccines. Under the heading, 'Activation of the Immune
24 Response: Vaccines,' Schrum teaches that '[i]n one embodiment of the
25 present invention, mRNA molecules may be used to elicit or provoke an
26 immune response in an organism.' Moreover, under the same 'Vaccines'

1 heading, Schrum also explains that the mRNA vaccines can 'encode an
2 immunogen,' consistent with paragraph 397's reference to a modified mRNA
3 immunogen".

4 And if we go to Slide 56, there is more there, Your Honor. And I
5 think it's actually telling, and I know Your Honors will do this, when we
6 look at the testimony of our experts and their experts, for example, Dr. Chan,
7 he was trying parse Paragraph 397, and he was contradicting himself. He
8 said well, you know, it refers to the lipid nanoparticle and that's magic and
9 then, right. But I think from our perspective, it's their reading of 397 when it
10 refers to the lipid nanoparticle, if you can go back onto the previous slide.
11 All it says is the lipid nanoparticle may be formulated.

12 And of course, it's the lipid nanoparticle that's referenced in the first
13 sentence of 397. But again, I think the Board can lose sight of the fact, these
14 teachings are all related, Judge Majors. And if you go back to Slide 58, 56,
15 sorry. We have more testimony from Dr. Moon here, which again shows
16 why Paragraph 397 in one place discloses what's claimed.

17 JUDGE MAJORS: Before we move off this topic, with respect to the
18 method claims, can you help me understand where in Schrum there's a
19 disclosure of the neutralizing antibody response that's recited in Claim 3?

20 MR. MODI: I'm happy to, Your Honor. I'm happy to. So if you
21 could go to Slide 34, please. So if we look at, we have a couple of
22 arguments here, Your Honor, on Claim 3, right. I think that is the claim you
23 were directing, you were referring to. Again, it's a very broad claim. All it
24 says is "The method of claim 2, beyond the immune response is a
25 neutralizing antibody response specific to the BetaCoV S protein".

1 So two arguments in response to this claim. One is, we believe this is
2 -- all this is claiming is an intended result. And as Your Honors know, that's
3 black letter law, it's not patentable. Go to Slide 35. We actually made this
4 argument in our petition, you can see that here.

5 We have not received a response from Moderna to this day to this
6 argument. So for this reason alone, we think that Claim 3 is unpatentable.
7 And if you actually look at the testimony we have from the expert, from
8 their expert, Dr. Fuller, and within that deposition that whether a vaccine's in
9 use and immune response just depends on the entity they're expressing. And
10 that's Exhibit 1104, 52, 10 through 13.

11 And so of course, she's explaining that again, this is just an intended
12 result, right. And then if you go to Slide 36, again, black letter federal
13 circuit law claiming results is simply not patentable, the *Allergen* case tells
14 us that it cites to average lots, and it tells us that. But even if this Board
15 were to give this claim weight, let's go to Slide 37 and then we address,
16 Judge Majors, of how we get to neutralizing antibodies, if you were to give
17 this claim weight.

18 So again, let's go back to Schrum, let's start with Schrum. What does
19 Schrum teach us? It says, "In one embodiment of the present invention,
20 mRNA molecules may be used to elicit or provoke an immune response in
21 an organism. The mRNA molecules to be delivered may encode an
22 immunogen peptide or polypeptide." It doesn't stop there.

23 Item 342 tells us, "the modified nucleic acid molecules and/or
24 mmRNA of the invention may encode an immunogen." What else does it
25 tells us? I think this is the language that is fatal to that, their argument here.
26 It says, "the modified nucleic acid molecules and mmRNA of the present

1 invention encoding an immunogen may be delivered to a vertebrate in a dose
2 amount large enough to be immunogenic to the vertebrate." Right?

3 Obviously, once by definition immunogenic, what does that mean?
4 Well, it's inducing an immune -- a response. And what Schrum is doing
5 right there, is incorporating by reference Geall. So let's take a look at Geall's
6 teachings and what does Geall tell us? So if you go to Slide 38, what does
7 Geall tell us? It says that you have anticipation of the RNA, the immunogen
8 is transmitted *in vivo*, and can elicit an immune response in the recipient.

9 And goes on to say the immunogen may elicit an immune response
10 against a virus and of course, that's BetaCoV, as one example. And it goes
11 on and says, "the immune response may comprise an antibody response,"
12 right. And what else does it teach? It says, "the immune response is
13 preferably protective and preferably involves antibodies."

14 Now, let us step back for a minute. Why does then Schrum and Geall
15 teach us this? Well, because we have testimony from both experts here,
16 Your Honors, that says the protected immune response encompasses a
17 neutralizing antibodies response. I don't have the testimony on the slides,
18 but I will give you the cites.

19 So Exhibit 1104, Page 60, Lines 10 through 16. Their expert, Dr.
20 Fuller, testified that in the context of SARS-CoV, protection is taught to be
21 mediated by neutralizing antibodies against the S protein, because the
22 antibody framework against the S protein is taught to interfere with the
23 ability of the virus to attach to and infect the cells. So their own expert
24 admitted that when you have the S protein, there will be neutralizing
25 antibodies.

1 And then of course, our expert agrees. And that's Exhibit 1002, that's
2 Dr. Griffin's direct testimony, Paragraphs 86 to 87. And I think if you step
3 back and just think about what are we talking about in terms of neutralizing
4 antibodies, they -- that's how vaccines protect against a virus. They
5 neutralize the virus, thereby affording protection. So when you look at the
6 combined teachings of Schrum and Geall, coupled with that with the
7 testimony we have both experts, we believe that more than satisfies Claim 3.

8 So if I could go back, Your Honors, and just one last point on this.
9 Go to Slide 39. You know, one of their mantra in their papers is, "we don't
10 have any data". Well, data is not required for anticipation. And Mr. Krinsky
11 will address that point for obviousness. But from our perspective, the prior
12 art teachings are very clear and leads to anticipation in their obviousness
13 here.

14 But if I could back to slide 15, I just want to make a couple of points
15 on Schrum. Because I do think, Your Honors, this case is simple. I want to
16 come back to why this case is simple. So Slide 15 shows you the claims of
17 Schrum compared to the claims of the challenged patents. And I think you
18 can learn a lot from this comparison.

19 So if you look, and so again, they try to claim this in Schrum and
20 exclusively abandon Schrum, right. So what do they claim? They said you
21 have a formulation comprising a modified mRNA encoding the polypeptide
22 of interest, right.

23 And then in Claim 12, they give you the full component of the
24 nanoparticle composition. Now let's compare to the '600 and '127, and you
25 can see between the color coding, it matches up. What is the difference?

1 The only difference, Your Honors, is they explicitly cite in the '600 and '127
2 patent the BetaCoV S protein. That's the difference.

3 And how do we get to that? This comes back to why this case is
4 simple. For anticipation, all the Board needs to decide is that Schrum,
5 through its incorporation by reference, discloses that SARS-CoV S protein
6 as the immunogen to be encoded.

7 And for obviousness, again, it's simple. Do the Geall, when going to
8 the references teach the SARS-CoV S protein as a vaccine immunogen that
9 may be encoded by Schrum's mRNA vaccine? And that a person of
10 ordinary skill would have reasons to combine with an expectation of
11 success? The answer to both of those questions is a resounding yes.

12 So if I could go to, I want to address a couple of their other arguments
13 here. One is this incorporation by reference argument. So if we could go to
14 Slide 23. So if you look at Slide 23, again, Schrum incorporates Geall in its
15 entirety by reference. And if you go to Slide 24, of course Geall discloses
16 the spike polypeptide, right. So there may be a couple of arguments, first on
17 incorporation and then on the S protein. So I'd like to address those.

18 So if you could go to Slide 25. This is a simple case on incorporation,
19 Your Honors. They try to make hay out of this, it is simple. What does
20 Slide 25 show us? The federal circuit's case law on incorporation and
21 reference requires only two things, where the incorporating material is
22 found, and what this material incorporates. Here Schrum tells us it's Geall
23 and it's in its entirety. And if you go to Slide 26, we actually have the *Paice*
24 case here.

25 And if you look at the *Paice* case, what did the federal circuit find in
26 the *Paice* case? It said the first sentence of the passage is broad and

1 unambiguous. It states, "Severinsky 'is', without qualification,
2 incorporated", such language is plainly sufficient to incorporation
3 Severinsky in its entirety. Well, we have more in Schrum. Schrum has us
4 incorporate the reference in its entirety. So this case could not be a clearer
5 case of incorporation of reference of Geall's teachings in its entirety.

6 And if the Board had any doubt, there are other cases, for example,
7 and I want to maybe preface this comment with, it's telling that even in their
8 sur reply, they still are disputing that the disclosure is incorporated in its
9 entirety. And two responses, Your Honor, this is again in the Moderna
10 application that they abandoned. Right. They're running away from their
11 own disclosure.

12 Second part is, there are cases out there, for example, there's the *TQ*
13 *Delta vs. ADTRAN* case from Delaware where Judge Andrews found that in
14 its entirety language does plainly teach that the entire reference teachings are
15 incorporated. And the cite for that case is 2021 Westlaw 1203, 998.

16 So from our perspective, there shouldn't really be an issue with respect
17 to incorporation by reference, but let me quickly address the one argument
18 that they make on incorporation. So they come back, right. So if you go
19 past the legal argument that we have, we went under the legal argument,
20 they say, well, factually all Schrum does is it incorporates only the doses,
21 not the immunogen. That makes no sense, Your Honor. Think about it.

22 If you had a bottle of aspirin with 81 milligrams, let's say, is the dose,
23 and if I say, oh, here's a dose of 81 milligram, you're going to say, well, what
24 is the -- what's the dose? What is this dose for? It's for aspirin.

25 And that's precisely what we have in Geall, it tells us that
26 immunogens, right, and they're tied to the doses so they can't really separate

1 the two. And I want to show you some testimony that we have on that point.
2 So if we could go to, let's go to Slide -- oh, you already have it here, so Slide
3 43, Your Honors.

4 So this is from their expert, Dr. Fuller, she admitted that some
5 immunogens are more immunogenic than others, right. Why is that? And
6 that's obviously again, black letter sort of science, right. And of course,
7 then, the bases are going to affect the immunogen you give. And then what
8 did Dr. Griffin testify? We can see his testimony at the bottom.

9 He says, "A POSA would not consider Geall's teachings or dosage
10 levels without also considering its discussion of immunogens, particularly
11 here where Geall is expressly incorporated in its entirety." So we think
12 again, whether you look at it from a legal perspective or you look at it from a
13 science perspective, the reference is incorporated in its entirety. Now, let me
14 address quickly --

15 JUDGE MAJORS: Mr. Modi, what should we make of the argument,
16 however, that the Geall reference is allegedly focused on the self-amplifying
17 variety of RNA, and the doses that are referenced in that disclosure are
18 specific to that construct, not mRNA of the non-self-amplifying?

19 MR. MODI: Right. So Your Honor, a couple responses to that, and I
20 believe the Board actually said this in its Institution Decision, too. Of
21 course, Geall says it's preferred, saRNA is preferred, it doesn't limit to
22 saRNA.

23 The second is, we don't believe that they're trying to construe the
24 claim here to include that the mRNA is somehow limited. We think they
25 have a high burden on disclaimer here. And if you look at that section, all

1 it's saying is, you don't necessarily need the saRNA, right. That's all they're
2 saying.

3 And of course, the claim's bound to recite mRNA. And then this is
4 the key here, Your Honors, that Geall reference, right, where they keep on
5 saying Geall is self-amplifying RNA and not mRNA, if you go to their own
6 disclosure, Your Honor, it actually incorporates a section from Geall, or
7 actually Geall in its entirety, this is the Geall 2012 publication. So can you
8 pull that up, Ryan? If you could go back to the '127 patent? And I think
9 again, this is fatal, Your Honor, to a lot of their arguments here today.

10 Like they say, well, Geall is self-amplifying on RNA so it's not
11 mRNA. So if we could go to, this is '127 patent, I will give you the cite, I'll
12 read it into the record, it's Column 83, Lines 42 to 48. So here, at the
13 bottom, Your Honor, you can see, this is again, in their own patent, they are
14 saying as another limiting example, the LNP formulation may contain, and
15 then it gives you the LNP formulation, in a molar ratio 2:40:10:48, see e.g.,
16 Geall et al., Nonviral delivery of self-amplifying RNA eg mRNA vaccines.
17 This is the 2012 paper, that's Exhibit 2021 in this case. We think that's fatal
18 to their argument here that the mRNA is limited to non-self-amplifying
19 RNAs.

20 And then of course, as Your Honors know, I'm not going into the
21 details, when they wanted to rely on these self-amplifying disclosures, they
22 did. They relied on it in their submissions to the FDA, right. And then
23 again, at the end of the day, we have to kind of look back and see what
24 they're trying to do. They're trying to run away from their own disclosures
25 where Schrum incorporates Geall by reference and their own patent
26 incorporates Geall by reference.

1 And then the last point I will make is, Your Honors, and I'm glad you
2 asked me that question, because that same passage of Geall that you referred
3 to, this same, precise passage, actually also appears in Paragraph 346 of the
4 Schrum publication.

5 And the Board actually noted as much in its decision in institution and
6 that's how we get to the -- 346 basically provides another example of how
7 we get to the LNP composition, I mean, that's in the vaccine section. And if
8 you look at Paragraph 346, again, it incorporates by reference this very same
9 disclosure. So their arguments are an mRNA, not including self-amplifying
10 mRNA, just don't hold water.

11 I see I'm running out of time, I want to be sure I leave enough time
12 Mr. Krinsky, so I just want to quickly touch on the S protein point. So if
13 you go to Slide 44, please. And I will just try to get to this very quickly.

14 So what did they do, one of their other arguments is well, the S
15 protein that's taught in the '127 is somehow limited to a full-length S protein
16 and we think this analysis is incredible. If you look at Geall, what does it
17 teach us? It says the coronavirus immunogen may be a spike polypeptide.

18 It's essentially the same language that's used in their patent. It just
19 can't hold water, their arguments can't hold water. But let's take a look
20 quickly, why. So if you go to Slide 45, they're essentially arguing for a
21 lexicography here, and they're saying that their patent uses the S protein, it's
22 a full-length S protein. That is not true. Let's go to Slide 46. Again,
23 lexicography is a high bar.

24 This specification again uses S protein at least three different ways.
25 The examples of full-length S protein are given that. But if you look at
26 Column 7, Lines 27 through 30, Column 8, Lines 6 through 9, and Column

1 8, Lines 41 through 44, data filtering immunogenic fragment of S protein.

2 That's a truncated version of the S protein. And I'm actually going to show
3 you that. So if you could go to Slide 44, please.

4 It's not highlighted on Slide 44, but if you look, it's the sentence right
5 under the arrow. What does it tell us? It says, "In some embodiments, at
6 least one antigenic polypeptide ... may be a spike protein or an
7 immunogenic fragment thereof."

8 So they clearly have disclosed truncated S proteins. And it's actually
9 incredible again, they go to length saying their disclosure doesn't have it.
10 That's at their sur reply at 5. Simply not true, I just showed it to you. And
11 then finally, of course, when it refers to the subunits, it says the S protein
12 includes S, S1, and S2. So their argument just doesn't make sense.

13 And at the end of the day, yes, we agree the claim does recite the
14 subunit language, but when it recites the S protein language, it covers two
15 things, full-length and truncated versions. So their claim for such an
16 argument, is just, it doesn't hold water. And if you go to Slide 47, we have
17 Dr. Fuller recognized herself that you have truncated versions of S proteins.

18 And then if you go to Slide 48. Slide 48 talks about why the Geall
19 discloses a full-length spike protein. I'm not going to read the testimony to
20 you, you have it on Slide 48. But I will say Dr. Griffin explained it in detail
21 why you get to the full-length spike polypeptide in Geall. But that's
22 consistent with the prior art, Your Honors. Yang and Du that you can see on
23 Slide 48, they disclose full-length S proteins, but don't actually call them
24 full-length. So their argument just doesn't hold water.

25 And they point to some statements in Geall, if you go to Slide 49, that
26 are F proteins, it doesn't matter, because Geall also refers to them as full-

1 length. And from our perspective the question is whether it be for patent, for
2 patent and prior art, you know, what the PT is post-polypeptide. And at the
3 end of the day on this issue, Your Honors, I will leave you with this, they
4 can't have it both ways. Either the prior art and the patent refer to a full-
5 length S protein, or their patent is just broader.

6 And then finally, on forming a spike issue, just a couple points, the
7 claims don't require forming a spike. The Board actually recognized as
8 much. There's a lot of hay that they make, oh, the district court used to
9 forming a spike language.

10 But if you actually look at the district court's decision, it's Exhibit
11 1035, I believe it's Pages 10 through 13, I invite the Board to read that
12 decision. The district court was very, very careful in saying I am not
13 importing any functional limitation.

14 And as the Board recognized, at least in the '600 Institution Decision,
15 that -- when you talked about forming a spike, is this only to the S protein as
16 opposed to the other proteins that are a part of the betacoronavirus?

17 So unless Your Honors have any other questions, I will conclude my
18 opening presentation by saying the claims are anticipated. At a minimum,
19 Your Honors, they're obvious. With that, I'm going to turn it over to Mr.
20 Krinsky. Thank you.

21 MR. KRINSKY: Thank you, Your Honor. David Krinsky from
22 Williams & Connolly on behalf of Pfizer, but the Petitioners collectively
23 here.

24 I want to focus my presentation on obviousness that are Grounds 2 to
25 4. As Mr. Modi explained, we believe these claims are anticipated, but to
26 the extent the Board has any difficulty with any of the anticipation

1 arguments, you know, there were some references in the Institution Decision
2 that question of whether there was too much picking and choosing.

3 It's just not a close question on obviousness. This is a case where,
4 when you step back and look back both motivation and reasonable
5 expectation of success, the Board, in our view, correctly found in a
6 preliminary stage, that there were compelling merits on obviousness, and the
7 record has only gotten stronger for us since then, as you'll see.

8 So just to give a quick overview, as the Board will recall, each of our
9 obviousness grounds begins with Schrum, which teaches the entirety of an
10 mRNA and LNP formulation into which the person of ordinary skill could
11 insert the antigen of choice. That's what Schrum teaches.

12 Schrum, as Mr. Modi indicated, incorporates Geall which lists a
13 number of such antigens that at a bare minimum, are antigens that can be
14 used with Schrum. But independently of Geall, both the Yang and the
15 Altmeyer references teach that the coronavirus, betacoronavirus S protein,
16 would in particular, have been an antigen of interest. And the record is
17 replete with different vaccine types that use that antigen and would be
18 natural and there would have been a strong motivation to use with Schrum.

19 As mentioned, we need to show that, and we believe we have shown,
20 that Schrum, together with these secondary references teaches each of the
21 limitations of the claim, that there would have been a motivation to combine
22 and that there would have been reasonable expectation of success in
23 practicing the claim. And the reason I emphasize this hornbook law, is that
24 the structure of Moderna's response here is largely to raise a number of
25 concerns and reasons for skepticism rather than to engage directly on these
26 points.

1 I don't think -- it could hardly be clearer that Schrum itself provides a
2 motivation to use this vaccine. And that each of these references, Geall,
3 Yang, and Altmeyer, gives a reason to use this particular antigen on
4 reasonable expectation of success.

5 It's all but undisputed that there would have been an expectation that
6 you would see some expression upon administering this vaccine and that
7 upon seeing some expression, there would be an immune response. That's
8 all the claims require.

9 The questions beyond that of like, could you reach FDA approval,
10 would it have been, you know, an effective vaccine to the point of being able
11 to prevent a particular disease, none of that is required by these claims,
12 unlike a lot of the case law Moderna cites. So that is an overview.

13 Let me jump back to Slide 15, please. So I just wanted to put up the
14 claims, because I think that's probably the clearest explication of how all
15 these limitations are taught and also of the structure and the motivation here.
16 Mr. Modi walked you through it, I don't want to belabor the point.

17 But the -- there really isn't a dispute in the papers that Schrum, from
18 an obviousness perspective, teaches each and every one of the limitations
19 with the exception of the box, you know. We have this question of
20 incorporation and how you use Geall, but the box betacoronavirus BetaCoV
21 S protein is the antigen that is selected and inserted into this mRNA plus
22 LNP formulation.

23 The arguments on motivation all go to, well, you know, wouldn't there
24 have been some reason to use some other possible formulation, some other
25 way of delivering a BetaCoV antigen. We would submit that's just simply

1 the wrong test. There is a strong reason to use this one. And Schrum
2 teaches that directly. If we look at Slide 64, please.

3 You looked at these passages, this is Paragraph 340 of Schrum and
4 Paragraph 397 of Schrum with Mr. Modi, I don't want to belabor them. But
5 it is expressly teaching that mRNA molecules may be used to elicit or
6 provoke an immune response, and it's teaching that those mRNA molecules
7 are delivered by including them in a lipid nanoparticle. That's simply what
8 the claims recite. And then you can select an immunogen to encode in that
9 lipid nanoparticle, mRNA.

10 The context of the art here was one of intense enthusiasm for this type
11 of vaccine. On Slide 65, I have the Kallen 2014 reference, which is Exhibit
12 1020, and the Schlake 2012 reference, which is Exhibit 1019. And each of
13 these show great enthusiasm for and recognize the great promise of mRNA
14 vaccines.

15 Kallen says that, "Recent advances strongly suggest that mRNA rather
16 than DNA will be the nucleotide basis for a new class of vaccines and
17 drugs." It talks about how they represent the truly disruptive technology that
18 may start the revolution in medicine.

19 And then Schlake goes on to talk about how their, you know, they
20 have desirable immunological properties with an outstanding safety profile
21 and specifically calling out the fact that you can express from mRNA any
22 protein you like without a need to adjust the production process that's
23 highlighted in the middle of the box at right in Schlake 2012.

24 So the context here, before you get to any of these concerns, the
25 POSA would have been interested in and very enthusiastic about this
26 technology. And there, you know, it could hardly be -- not only is this a

1 strong reason on it's own, but Moderna, we submit has a pretty high burden
2 to meet to suggest that the POSA would be so discouraged by any of the
3 things they raise. That some of the POSA would overlook these, and say,
4 no, no, we're going to use some other technology exclusively, walk away
5 from mRNA, that's just not where the art was going.

6 JUDGE COTTA: Could you address some of the concerns, and
7 specifically the extent to which they would relate to a betacoronavirus?

8 MR. KRINSKY: Sure. I have a slide where I sort of pick through the
9 concerns. I think, I don't think any of their concerns are really specific to
10 betacoronaviruses. Let's go to Slide 80, 80? I'm sorry, next one, 81. My
11 apologies, Your Honor.

12 The, you know, the alleged failures they point to, let me pick through
13 the list here. And skepticism I've already addressed, in the sense that there
14 were strong reasons to favor mRNA. And the references I pointed to earlier
15 were in fact ones that had been cited by Moderna as skepticism references.
16 Nothing there was specific to betacoronaviruses. None of the alleged
17 failures in the prior art were failures, but also none of them were
18 betacoronaviruses, you know, they point -- Slide 90, they point to this HIV-1
19 and rabies vaccine.

20 Again, neither is a coronavirus, but more importantly, neither is a
21 failure. Each of the rabies vaccine, this is in the lead reference, Exhibit
22 1119, they cite in their sur reply, the Auberer reference, Exhibit 2486, they
23 also cite in their sur reply. They each had immune responses, you know.
24 These are mRNA vaccines that upon delivery, but for the fact that they are
25 not coronaviruses, would have met the limitations of the claim.

1 JUDGE COTTA: So are those two trials that you are referring to, are
2 those two of the seven mRNA trials that Patent Owner has identified as --

3 MR. KRINSKY: Candidly, I'm not entirely sure how they're
4 counting. But there is no instance, to answer the question Your Honor posed
5 a moment ago, there is no instance of somebody trying to and failing to
6 administer, get an immune response from an mRNA. I mean, the failures
7 are towards this higher bar that we don't need to meet of, do you get FDA
8 approval? Do you establish sufficient efficacy?

9 JUDGE COTTA: Are there any instances of failure with respect to
10 the S protein?

11 MR. KRINSKY: There are not. And that's a critical point. Dr. Fuller
12 testified, let me see if I can find the exact quote, at any rate, there were --
13 well, if we go to Slide 77, you know. We have instance after instance, the
14 Du 2009 reference, the Buchholz 2004 reference for administrations of S
15 protein as a protein. And then the Yang, next slide, Yang 2004 reference,
16 this is Slide 78, and Wang 2015 reference were S protein administered as
17 DNA, so we've made a nucleic acid vaccine. They all induced an immune
18 response and they all have neutralizing antibodies.

19 So there really isn't any reason to think there wouldn't be an
20 expression or wouldn't be an immune response specific to the coronaviruses.
21 This is a general purpose tool and the record would suggest it'll work just as
22 well for BetaCoVs as anything else. They raise, sort of the next category of
23 concerns they raise over ADE.

24 JUDGE MAJORS: Just before you hit the ADE thing, there's a lot of
25 argument on Patent Owner's part to the effect that Petitioner's proofs are

1 lacking in any pre-priority date successes with mRNA vaccines, putting
2 aside the S protein for the moment.

3 Can you help us understand what's their -- I recognize the citation you
4 gave before with Kallen, et cetera, but where somebody was, it could have
5 been preclinical testing, but where they're actually testing mRNA to encode
6 an immunogen and there was success exhibited?

7 MR. KRINSKY: So I think the -- so the answer is yes. But I want to
8 break that down into a few pieces, because Schrum itself shows that there
9 would have been success in expression. I don't think there's going to be a
10 serious debate that when you insert a protein into the -- when you insert a
11 polypeptide encoding a protein into mRNA, the reasonable expectation is
12 that you will get expression of that protein.

13 JUDGE MAJORS: Right. Schrum made that. It was a blood factor,
14 right?

15 MR. KRINSKY: Correct. And if we go to Slide 73, Dr. Fuller
16 admitted this was a general concept, you know, we can design an mRNA or
17 a DNA molecule to prompt the person's cells to start making a protein and
18 then that'll get expressed.

19 She then also admitted, and this is Slide 75, and this is why I said that
20 it is practically undisputed that there would have been a reasonable
21 expectation of success here. Once you know that the spike protein is
22 expressing, that is, once you do get expression of that protein, you would
23 expect that the vaccine candidate would induce an immune response. And
24 the answer is yes. So what we have here, we do not have a betacoronavirus
25 being expressed in an mRNA. Having put aside, so if it's not quite true,
26 Geall 2013 is further evidence that it's a SR -- SRN.

1 PARTICIPANT: But is it --

2 MR. KRINSKY: Sorry, I thought there might be a question from
3 Judge Snedden, I apologize?

4 JUDGE MAJORS: And I should qualify my earlier question.

5 PARTICIPANT: No, I couldn't -- actually on my phone, and I -- I
6 don't know if --

7 JUDGE COTTA: -- listening wise, how is that opening. It seems to
8 have stopped, should we just continue?

9 MR. KRINSKY: Sure.

10 JUDGE COTTA: I'm very sorry for the interruption, I don't know
11 what that was.

12 MR. KRINSKY: No problem, Your Honor.

13 JUDGE MAJORS: So I was just going to say, I should qualify my
14 prior question. I'm accepting for arguments sake, that there is a distinction
15 between the mRNA and the amplifying, because I recognize their argument
16 that they want the finding to be what everybody was focused on is saRNA,
17 DNA and viral constructs and not just mRNA. So I'm just trying to see, is
18 there a specific clinical or even pre-clinical study that we should look at, and
19 I recognize this point about Schrum and expressing protein, but where they
20 were actually using the mRNA construct for a vaccine of any immunogen?

21 MR. KRINSKY: So there were -- I mean, I think -- so certainly Geall
22 teaches that this is, you know, a possibility. Altmeyer includes a teaching of
23 RNA. I don't believe that we have data for a betacoronavirus in a non-self-
24 amplifying mRNA vaccine. But, you know, that sort of data wouldn't be
25 required for anticipation level and for obviousness.

1 JUDGE MAJORS: No. And I understand your point on that. I was
2 simply asking for any immunogen, putting aside betacoronavirus S protein,
3 it could be some other viral protein that's being used, mRNA, using it for
4 purposes of expressing the immunogen?

5 MR. KRINSKY: I mean, I think Exhibit 1010, which is Geall has,
6 and any use of that. But there also was use of mRNA to inoculate against
7 influenza back in the 1990s. And my colleague may be able to get the
8 reference for that if we pass notes here. Exhibit 2025, I'm told, is an
9 example of that.

10 But with respect, Your Honor, I don't think, the critical point here is
11 that the undisputed record would suggest you can express any antigen you
12 like, that's what Schrum expressly teaches, and that's what Dr. Fuller appears
13 to agree.

14 And then you have multiple instances of S protein being used as an
15 antigen and actually eliciting an immune response, again in the Du reference
16 and in the, even right up to the priority date in the Wang 2015 paper, you
17 have a DNA vaccine using S protein. And they all elicit neutralizing
18 antibodies, they all elicit immune responses. There's no instance here of
19 failure.

20 Also worth noting the DNA is upstream biologically of RNA, you
21 know. So in order for a DNA virus to be working, it has to be yielding
22 mRNA which then expresses in the cells and elicits a [inaudible] which gets
23 an immune response.

24 JUDGE COTTA: Okay. Can you address Patent Owner's point that
25 there's a difference between a therapeutic and a vaccine? And in order to
26 trigger an immune response in some cases, you may need an adjuvant or

1 something, there may be some characteristic of the vaccine that's necessary
2 beyond just the proteins, that you get the immune response?

3 MR. KRINSKY: So first let me say, there's nothing in these claims
4 that forbid the use of an adjuvant or the like. So that would still fall within
5 the scope of the claims and would be perhaps a routine way of increasing an
6 immune response if need be.

7 But even before you get to that point, the record here is if there is any
8 expression of protein, there is going to be some degree of immune response.
9 Now whether immune response is large enough to get the desired degree of
10 immunization that you want is a matter of routine experimentation, perhaps
11 a matter of additional work to be done that might even be non-routine in
12 certain vaccines.

13 But in here, there would have been a reasonable expectation that you
14 would achieve some immune response based on Dr. Fuller's testimony and
15 based on the consistent experience with any S proteins. The closest they
16 come to a failure in this regard is the Brito reference, where they have a 50
17 microgram dose of -- and you'll see some slides on this from them, I'm sure,
18 a 50 microgram dose of non-self-amplifying mRNA.

19 Brito itself says, well, that just wasn't enough, you know. We would
20 expect that the reason why we didn't see much of any immune response was
21 non-self-amplifying mRNA was the dose in that instance. That's as close as
22 the record reflects to a failure.

23 There would have been a reasonable expectation, you know, we don't
24 have to show absolute certainty here. There wasn't a reasonable expectation
25 in the general case, which we have multiple instances of and which was the
26 whole point of Schrum, you would get an immune response.

1 Let me turn briefly to ADE, because I think that's something that
2 Moderna has talked a lot about, and with respect, ADE is just a red herring.
3 And the reason it's a red herring, is twofold. One, it is -- it doesn't have a
4 reasonable expectation, I mean, the claims don't require no ADE ever.

5 They don't speak to the level of risk or the level of safety. It's a
6 motivation point, fairly construed. And they don't come close to
7 establishing the ADE was such a significant concern or such a significant for
8 betacoronaviruses in particular, that the POSA would not have followed the
9 motivation of our principal references, you know.

10 The starting point being the, as I said, the excitement in this field, the
11 excitement of mRNA vaccines. And by the way, it's uncontested that
12 betacoronavirus was a pathogen of interest. So you have a motivation, this
13 is Slide 68, you know, Dr. Krause, this is Patent Owner's declarant at
14 Paragraph 170, is talking about the latent need for a betacoronavirus vaccine
15 and how it existed, even though the SARS and MERS outbreaks had been
16 controlled.

17 So the question is, in the case of that need, would ADE been such a
18 concern that you would have abandoned the project or gone in some other
19 direction than the S protein that is of interest? And I submit that the answer
20 is no, the POSA would not have been deterred.

21 The Bucholz reference in 2004, down, this is at Slide 93, please.
22 Bucholz tested intra-nasal immunization with S protein as well as several
23 other SARS-CoV antigens, found that the S protein was highly
24 immunogenic and protective.

25 And unlike the other antigens the S protein led to in neutralizing
26 response, but it -- none of these proteins led to antibody mediated

1 enhancement of exception, you know. The experience in the S protein field
2 was, you know, this is a concern that could arise in general with vaccines,
3 but it's fine, you know.

4 They cite the Vennema reference from 1990, that's an old reference
5 that preceded all this work in the field that no one was, in fact, deterred
6 from. But in any event, was attributed by, among others, the Yang reference
7 to the specificities of that feline vaccine. I have here on Slide 99, discussion
8 of Vennema in both Yang and Bucholz.

9 And they, you know, they don't dismiss the problem. They say, well,
10 this is something that could arise, it's a concern that might, the POSA might
11 have. But, you know, they attribute it to feline infectious peritonitis virus.
12 And they themselves were not deterred, and they don't suggest that this is
13 somehow a blind alley that would defeat a motivation or teach away from
14 the use of betacoronavirus S protein.

15 They also cite to, and I'm sure you'll hear about the Jaume reference
16 which, you know, all of this was addressed in the Institution Decision. And
17 really, the record hasn't changed in Moderna's favor at all. Jaume was an *in*
18 *vitro* study, you know, where there was some entry of virus into cells that,
19 you know, was seen as a potential marker of ADE.

20 Notwithstanding that, S protein has never been shown to elicit ADE in
21 an actual mammal. I mean, this was an *in vitro* experiment where the
22 question was could you find some viral infection of cells in the test tube
23 when you expose -- when you expose them to virus after exposing them to
24 antibodies that were elicited in an amount. And, you know, that again,
25 would not have deterred the POSA, particularly in the face of the other
26 evidence that *in vivo*, this just hasn't been seen.

1 The final note I'd like to make on ADE, you know, we have
2 consistently maintained that the claims encompass both full-length and non-
3 full-length S protein. But they use this as sort of a reason why, you know,
4 perhaps the POSA would worry about full-length. But the record shows
5 exactly the opposite if we go to Slide 96, you know.

6 Dr. Fuller explained about how, you know, the full-length S protein
7 will let more epitopes and more neutralizing antibody, that's a reason to use
8 full-length S protein. But the record similarly reflects that full-length S
9 protein would have been thought to be, because it elicits more neutralizing
10 antibodies, would have been less likely to ADE, so if anything, ADE is a
11 motivation to use full-length S protein rather than something else.

12 JUDGE COTTA: If we could, I would like to switch topics a little bit.

13 MR. KRINSKY: Sure.

14 JUDGE COTTA: I was hoping you could address commercial
15 success. And with respect to commercial success, partially to avoid
16 confidential information, but also I think the bigger issue that we're most
17 concerned about is first, nexus.

18 And then second, the extent to which you make the argument that a lot
19 of this is already in the art, so, you know, any success that they have is
20 attributable to what's already known. If you could address both of those
21 points, that would be --

22 MR. KRINSKY: Sure. And I don't think confidential information is
23 going to be a big problem here. We could go to Slide 128. As Mr. Modi
24 explained, these are really fairly broad or perhaps, these are fairly general
25 claims, you know. They're directed to the idea effectively of using mRNA
26 encapsulated in LNP to encode any coronavirus S protein.

1 And the priority date here is years before the SARS-CoV 2 pandemic,
2 and years before anyone knew this particular coronavirus or the sequence for
3 this particular coronavirus. And so, you know, given that and given all of
4 the many details of a particular vaccine formulation that are not spelled out
5 in these claims, we would submit, there isn't even that serious of challenge
6 to the notion, there isn't really a presumption of nexus here.

7 But the commercial products, Pfizer BioNTech's Comirnaty, and
8 Moderna's Spikevax, are just, you know, particular embodiments that are not
9 commensurate with this broad claim.

10 JUDGE COTTA: So there's no dispute that the commercial products
11 embody the claim?

12 MR. KRINSKY: There is a dispute on that. There's actually a, I
13 mean, we're contesting infringement in district court. We believe they
14 haven't shown --

15 JUDGE COTTA: For purposes of this proceeding, is there a dispute?

16 MR. KRINSKY: There is a dispute, I mean, we would say that, you
17 know, they have not met the burden to show that, they -- but even if they're
18 taken --

19 JUDGE COTTA: Is that something that's raised in your pleadings?
20 My recollection is that there was deposition testimony cited from your
21 expert where the expert did not identify anything that was missing?

22 MR. KRINSKY: I think the question is whether the sequences of
23 those, which are not native, I mean, they have mutations, they're modified.
24 This is actually effectively genetically engineered sequences are coronavirus
25 spike proteins. I mean they're, those are not, you know, they're not the same
26 as what you see in an actual --

1 JUDGE COTTA: I'm just, virus -- from our perspective is there
2 anywhere where that's called out in the pleadings or?

3 MR. KRINSKY: I would point to our reply, I don't know that I have
4 the page number, but --

5 JUDGE COTTA: Maybe when you come back, you could point us to
6 that?

7 MR. KRINSKY: Sure. But even if you take them as embodiments,
8 even if we do assume for purposes of this record that they are embodiments,
9 they're not on all fours with these claims, you know. There is undisputedly a
10 lot of additional work that went into turning these into viable vaccines.
11 They're much more specific. And they include, in addition to a mutated
12 sequence, and that I do have, is Dr., excuse me, Dr. Griffin in Exhibit 1159,
13 two paragraphs.

14 JUDGE COTTA: I'm sorry, I'm very sorry to interrupt. Can you
15 pause for a second. I've just been told that we've lost Judge Snedden.

16 MR. KRINSKY: Oh.

17 JUDGE COTTA: I'm sorry.

18 MR. KRINSKY: No problem.

19 JUDGE COTTA: I will give you a little extra time to kind of --

20 MR. KRINSKY: I appreciate that.

21 JUDGE COTTA: -- do yours. Sorry.

22 MR. KRINSKY: No problem.

23 (Pause.)

24 JUDGE COTTA: You are welcome to take a seat if you want while
25 you wait.

26 MR. KRINSKY: It's nice to stand. But thank you, Your Honor.

1 (Pause.)

2 IT STAFF: Please stand by, I'm going to call Judge Snedden.

3 (Pause.)

4 IT STAFF: Hello, Judge Snedden are you there?

5 JUDGE SNEDDEN: Yes, I'm here now.

6 IT STAFF: Oh, okay. Let me just pause these three.

7 JUDGE SNEDDEN: Okay. Thank you.

8 JUDGE COTTA: All right. If we're past our technical --

9 JUDGE SNEDDEN: I just want to make sure --

10 JUDGE COTTA: Glad to have you back. All right. Get started, I'll
11 let you run for a little while to sort of cover the pause.

12 MR. KRINSKY: Okay. Thank you, very much. Just to finish
13 answering that question, you know. Comirnaty and Spikevax vaccines each
14 have different mRNA sequences from just the plain, natural coronavirus
15 spike protein. And this is called out in our reply at Page 26, citing Dr.
16 Griffin, 1159, Exhibit 1159, Paragraphs 457 to 64.

17 You know, they have, not only do they have this 2P mutation intended
18 to help the stability of the protein, but they have 5 prem caps, 5 prem and 3
19 prem untranslated regions and various codon optimizations. All of those,
20 number one, I think, that is the answer to the question of why we don't think
21 they've shown that this is, these are embodiments.

22 But even if you assume for purposes of this proceeding that they are
23 embodiments, that's a lot of detail that helped contribute to their ultimate
24 success, which is not mentioned anywhere in the '600 or '127 patents, it's not
25 mentioned anywhere in the claims. These are additional features that need
26 elucidating.

1 And I think, help defeat a showing of nexus and a showing of
2 commensurateness. Nothing about this record tells you that these successes
3 somehow are attributable to anything novel in the patent. I think you asked
4 the question of the prior art, you know. I mean, our -- I believe we've amply
5 shown that, you know, the idea of LNP encapsulated mRNA, and the idea of
6 using those to encapsulate a coronavirus spike protein was all in the art.

7 That's all that the --

8 JUDGE COTTA: To what extent does that depend on us finding
9 anticipation? For example, the argument you just made, seems to be calling
10 Schrum into play --

11 MR. KRINSKY: So either --

12 JUDGE COTTA: And if we don't find anticipation, are those still in
13 the art?

14 MR. KRINSKY: So certainly those components are in the art. And I
15 think the key point on nexus is that even if you don't find anticipation, we
16 believe there's a strong case of prima facie obviousness here.

17 They have no way to show that the success of Comirnaty and
18 Spikevax are attributable to any novelty of the combination that they purport
19 to have put in the '600 and '127 patents, rather than the prior art disclosures
20 of the Moderna LNP rather than the selection of this particular antigen,
21 which is all over the art, rather than the 11 other patents that they claim
22 covered their formulation.

23 It's just an insufficient tie to this particular set of features that's called
24 out in this claim to say that Comirnaty and Spikevax's success somehow tells
25 you that this would have been non-obvious, you know. We have here an
26 unusual fact pattern with a later arising pandemic, you know. There's no

1 way to know whether, looking backwards from the pandemic, there's no way
2 to know whether the, you know, any success that -- oh, I think we may have
3 lost Judge Snedden again. Judge Snedden, can you hear me?

4 JUDGE COTTA: Sometimes the video --

5 MR. KRINSKY: You just seemed awfully still.

6 JUDGE COTTA: Just while we're off the record, the little lights seem
7 not to be working, the green, yellow, red.

8 (Whereupon, the foregoing matter went off the record at 10:25 a.m.
9 and went back on the record at 10:26 a.m.)

10 MR. KRINSKY: Just to finish the thought, you know. Given the gap
11 in time that we have temporally here, and given the comparative threat of
12 these claims relative to a specific drug product, there's just no way for the
13 Board to take the success of Comirnaty and Spikevax and say, aha, that is
14 attributable to the 2015 Moderna patents that are being challenged, rather
15 than the prior art features, which even if you don't find anticipation, you
16 know, they're not even disputing that this particular set of LNP components,
17 for example, the formulation of the LNP itself, is taught expressly in
18 Schrum. And they don't dispute that. So how can you, you know, attribute
19 success to this invention rather than to that, for example, or for any of
20 Moderna's other patents.

21 And even if there were a nexus here, the prima facie case is unusually
22 strong. I mean, we have here an express teaching, you know, to use this
23 vaccine vehicle to deliver antigens and an express teaching that this is a
24 desirable antigen.

25 It's a strong motivation to combine. It's a strong, reasonable
26 expectation of success, because as I said, there's really no dispute that you

1 would get some degree of immune response and reasonably expect to get
2 some degree of immune response. And so, singularly, they should have to
3 overcome that prima facie case. Under the best of circumstances, it remains
4 compelling.

5 To circle back, I know I'm about to go into my rebuttal time, but I just
6 want to address a question that had been raised earlier. Judge Majors'
7 question about examples in the art, and I apologize for having gotten a little,
8 my wires slightly crossed.

9 The Geall 2012 reference is a, excuse me, Geall 2013 reference,
10 taught an RSV vaccine that was successful that was self-amplifying. If you
11 want to look to non-self-amplifying, I would point Your Honors to the
12 CureVac demonstrations discussed in the Petsch 2012 reference, that's
13 Exhibit 2025 at 1210.

14 I believe it was also discussed in the Institution Decision, but we have
15 it at our Slide 84. You know this is an animal model where they showed,
16 they say they validated the mRNA vaccine approach for a B-cell dependent
17 mode of protection against influenza.

18 So this we would highlight as an example of a non-self-amplifying
19 mRNA vaccine that was in the prior art as, you know, working as a vaccine,
20 as well as just simply getting some degree of measured immune response.

21 So with that, unless there are further questions, I will save the rest of
22 my time for rebuttal, other than, I think I've hit all of Moderna's big -- sorry,
23 stop the clock. I think I've hit all of Moderna's big road blocks. But the
24 headline point I want Your Honors to just take away from this is that the art
25 would have, there would have been a strong motivation towards this

1 combination, and none of those roadblocks come close to a teach away,
2 which is really what they need.

3 MR. PRUSSIA: Your Honor, I'm happy to jump right into or we
4 could take a brief break?

5 JUDGE COTTA: I'm happy to continue, just kind of everybody else
6 happy to continue, Judge Majors, Judge Snedden?

7 MR. PRUSSIA: Actually, I've had a request from my team, could we
8 take a brief break?

9 JUDGE COTTA: Sure. Let's take a five-minute break.

10 MR. PRUSSIA: Okay. Thank you.

11 (Whereupon, the foregoing matter went off the record at 10:29 a.m.
12 and went back on the record at 10:37 a.m.)

13 JUDGE COTTA: Do we have Judge Snedden?

14 MR. PRUSSIA: Your Honor, I think we're at 90 minutes for our
15 presentation.

16 JUDGE COTTA: Oh, I'm sorry, I forgot the extra time.

17 MR. PRUSSIA: That's quite all right.

18 JUDGE COTTA: I'm told that Judge Snedden is on the line but not
19 visible, which is fine.

20 MR. PRUSSIA: Okay. May it please the Court, may I proceed?

21 JUDGE COTTA: Yes. We're on the record and you may begin.

22 MR. PRUSSIA: Thank you, Your Honors. Kevin Prussia for Patent
23 Owner Moderna. I will start our presentation focusing on the anticipation
24 and obviousness arguments asserted in the grounds. And then I'll pass to
25 Ms. Curtis who will address objective indicia of non-obviousness.

1 Let me start by saying this. Moderna was the first in the world to
2 disclose mRNA/LNP compositions for infectious disease. The inventions
3 covered by the challenged claims reflect a platform technology that enabled
4 the creation of first in class vaccines that were developed in record time and
5 changed the trajectory of the global pandemic caused by SARS-CoV-2.
6 Now they do not dispute that the COVID-19 vaccines are covered by the
7 challenged claims.

8 There was some confusion about that this morning, but Your Honor,
9 Judge Cotta, is correct. There's nothing in the record disputing that the
10 vaccines are covered by the claims. And those claims should be upheld over
11 the prior art setting the grounds. With respect to Ground 1, it fails because
12 Schrum and Geall do not disclose all of the claim limitations.

13 And we do dispute that whether the claim limitations are in the prior
14 art, because not all of them are. And the disclosures in those references are
15 too numerous and too disparate to clearly and unequivocally anticipate the
16 claims. And that's what the law requires.

17 As to Ground 2, and 3 and 4, they all fail because the field of mRNA
18 vaccines was too nascent and too unpredictable to have a reasonable
19 expectation of success, especially given the nature of the grounds here.

20 All of the asserted grounds require extrapolating results from non-
21 mRNA nucleic acid technologies and non-LNP delivery methods. Now as
22 of the priority date, there was a lot in the literature about betacoronaviruses.
23 And a lot of work has been done with respect to mRNA. But despite all that,
24 there isn't a single reference that taught or suggests an mRNA vaccine for a
25 betacoronavirus.

1 And there's good reason for that, and we'll talk about that this
2 morning. Before I get into that, I just want to hit two things that are really
3 important that came up in Mr. Krinsky's presentation.

4 The first, they say that there's no evidence of mRNA failing to
5 generate an immune response. That's false. And I'll walk through that this
6 morning. They also say that there's no evidence that the S protein would not
7 work, that's a new argument. But it's also incorrect. And I'll walk through
8 that this morning.

9 JUDGE COTTA: I'm sorry. I have to pause you. Apparently, we've
10 lost Judge Snedden again. Can we go off the record for a second, maybe we
11 just use a call-in line?

12 (Whereupon, the foregoing matter went off the record at 10:41 a.m.
13 and went back on the record at 10:43 a.m.)

14 JUDGE COTTA: Yes. We're back on the record and Judge Snedden,
15 with no objection from the parties, is participating by phone.

16 MR. PRUSSIA: Thank you. Let's start with Slide 4, please. So in
17 my presentation this morning, I'm going to focus on Claim 3 of the '127
18 patent. Of course, I'm happy to answer any questions the panel may have
19 regarding any challenged claim. But let's take a closer look at the limitations
20 of Claim 3. We'll go to Slide 6. There are five key limitations. There's the
21 claimed mRNA, which we have annotated in purple on the screen.

22 There is the limitation requiring the betacoronavirus S protein, that's
23 in yellow. There is a limitation requiring it to be formulated in LNP, we
24 have that in blue. And then there are two key limitations, there are two
25 functional limitations that are key.

1 The first that the composition is administered in an effective amount
2 to induce an immune response to the BetaCoV S protein, that's in green.
3 And then that the generated immune response is a neutralizing antibody
4 response that's specific to the S protein, and that's in salmon.

5 Now the reason why I want to focus on Claim 3 this morning, is
6 because it best illustrates the critical deficiencies in the petition, in particular
7 those last two limitations, the functional limitations that I focused on. And
8 that's because none of the grounds involve immune results obtained with an
9 mRNA/LNP composition. Schrum does not include any immune response
10 data at all. And each of the other references in the grounds involve immune
11 results obtained using non-mRNA and non-LNP technologies.

12 There simply is no disclosure anywhere in the grounds of an
13 mRNA/LNP composition that induced an immune response to anything at
14 all, let alone betacoronavirus S protein.

15 JUDGE COTTA: Can you respond to Patent Owner's argument that
16 Claim 3 is not entitled to patentability?

17 MR. PRUSSIA: Yes, I can, Your Honor. And first, let me say that
18 while it is, there is a sentence in the petition, I do consider this to be new
19 argument. You can look throughout the briefing, there's no real discussion
20 of this anywhere in the briefing.

21 But it is entitled to patentable weight, for a few reasons. First of all,
22 the case that they cite on that slide they show you, Slide 36 from the
23 *Allergan* case, that's from the dissent, the quote that they showed you. The
24 majority actually set forth the right standard. And you'll see that at footnote
25 1 of the decision at 726 F.3d 1286, page 1294.

1 What the majority said in that case, the evidence of record does not
2 establish that the claim limitation at issue there is an inherent property or
3 necessary result of the administration of the claim composition.

4 They aren't saying these words, but what they're arguing essentially, is
5 that Claim 3 is the inherent result of the composition when it's administered.
6 And that's just not true. All the record evidence establishes that.

7 First of all, the claim is written in functional terms and it requires an
8 immune result. And we know that a vaccine can generate an immune result,
9 no result at all. Dr. Fuller has explained that there are several types of
10 immune results. There are, immune responses, I should say. There's a
11 cellular immune response, there's a humeral immune response. She explains
12 that during her deposition, Exhibit 1104 at Pages 51, Line 22, to 5213, and
13 Page 269, Line 17 to Page 217, Line 9.

14 And Dr. Griffin agrees, he agrees, his deposition, Exhibit 2253, Page
15 129, Line 14 to Page 133, Line 8. So there are different types of immune
16 results, immune responses that can be generated from administering a
17 composition like that claimed here.

18 And the claimed antibodies -- the claimed neutralizing antibodies that
19 are recited in Claim 3, are a specific type of immune response that can
20 provide protection in the case of a betacoronavirus. And the claim
21 specifically requires an effective amount to induce a neutralizing antibody
22 response.

23 And that effective amount will vary depending on the vaccine
24 technology, the delivery method and the like. And we explain this in our sur
25 reply at Pages 13 and 16. So these are functional limitations of the claim,

1 they are not inherent. They are not something that is necessary or not the
2 natural result of administering the compound.

3 And it's a critical aspect of the invention. And it's consistent with the
4 disclosure in the patent. For example, if we go to Example 24 in the patent,
5 which I'll show in a minute, a little bit later in this presentation, you see it in
6 the explicit disclosure of this mRNA/LNP composition that's encoded for a
7 full-length spike protein. And it results in complete protection and
8 significant neutralizing antibodies.

9 So this is not a situation like we have in the *Allergan*, that they're
10 trying to characterize, where the claim is not a step of the method, it is an
11 active step of the method. Or, where the claim covers something that is
12 inherent.

13 So if we go to Slide 7, the consequence of all this, and the reason why
14 they're focusing, so far they're trying to get Claim 3 to not have any weight
15 is because, it again, it really illustrates the deficiencies in the grounds.

16 And there is no anticipation because there's no prior art disclosing the
17 required neutralizing antibody response. And there's no obviousness
18 because each of the grounds involve different nucleic acid technologies and
19 different delivery vehicles.

20 And I'm going to walk through this. Before I do, I just want to say
21 one thing briefly on Dr. Griffin, if I may. And I'm going to focus on this
22 because they don't have any example in the literature, where a person of skill
23 in the art did what they theorize would have been done in the petition.

24 There is no example where a person of skill in the art looked at results
25 with a different nucleic acid technology and a different delivery method and
26 tried to make some predictions about what you would obtain with mRNA.

1 And so the only evidence they have is the test that's the unsupportive
2 testimony of their expert, Dr. Griffin. And that's fine. He fits within the
3 POSA definition as an infectious disease physician. But they're relying on
4 his testimony as a nucleic acid scientist, and he is not that.

5 He admitted during his deposition that none of his research involved
6 delivery mRNA to cells. He admitted during his deposition that he had done
7 no work with mRNA vaccines or any other nucleic acid vaccine. None of
8 his research involved delivery of any nucleic acid encoding a pathogenic
9 protein to cells. And we discuss this at our sur reply at Page 3.

10 So I mention this, Your Honor, we didn't move to exclude his
11 testimony, right. This is a credibility determination. And where they have
12 nothing in the prior art supporting their arguments, and they're only relying
13 on an expert, you have to ask the question, is he qualified to offer the
14 opinions that he's offering? And he's not a nucleic acid scientist.

15 If you go to Slide 8, his expertise stands in stark contrast to Dr. Fuller,
16 who we submit is the only nucleic acid scientist who is a declarant in this
17 proceeding. She has extensive experience in this space, over three decades
18 of experience. She's taken nucleic acid vaccines from the bench to the
19 clinic.

20 She has the ability to testify about what a nucleic scientist would be
21 motivated to do, and the expectations that they would have had in the field at
22 the time, because she was in the field. She was the only declarant who was
23 working in this field at the time.

24 JUDGE COTTA: Could you address the point that some testimony
25 from Dr. Fuller that suggested she may have looked to other vaccine types,
26 DNA, RNA, saRNA, to inform her testing on this?

1 MR. PRUSSIA: Yes.

2 JUDGE COTTA: How should we look at that as a --

3 MR. PRUSSIA: Thank you, Your Honor. And I was going to get this
4 later, but I'll answer your question now. That testimony is post-priority.
5 They were asking about her research, and I believe in 2020 time frame,
6 about work that she was doing to develop one of her vaccine candidates.

7 And all she said was, if you look at the literature, she never said that
8 you would look at that literature with respect to non-mRNA vaccine
9 technologies to try and make how to draw some inference or make a
10 prediction about what you would get with mRNA. In fact, when she was
11 asked that question specifically during her deposition, she said you cannot
12 do that. And we cite that deposition testimony in our papers.

13 JUDGE MAJORS: Question, Mr. Prussia. Doesn't the Schrum
14 reference, in as much as it encompasses or incorporates Geall, I know you
15 dispute that, but if Geall is focused on the self-amplifying RNA but it is
16 described, I might say interchangeably with mRNA in the context of those
17 vaccine disclosures around Paragraph 340, et cetera, I didn't see anywhere in
18 Schrum where they're saying, you know, this applies for mRNA, but not for
19 saRNA or vice versa.

20 And I'm troubled a little bit with this idea of a skilled person wouldn't
21 look to other vaccine platforms. Again, accepting that saRNA, mRNA
22 aren't the same, but they wouldn't look to one or the other when they are
23 trying to decide what is relevant technology for designing a particular, again,
24 mRNA or saRNA. Is that, does that make sense, my question?

25 MR. PRUSSIA: I believe it does, Your Honor. So there's the
26 anticipation issue, which I'll get to in a moment. But on this question as to

1 what would a person of skill look at, a person of skill would consider all of
2 the teachings in the art, of course.

3 But the question that's being asked by their petition, is in a situation
4 where you have literally no data at all with respect to an mRNA/LNP
5 composition in terms of a vaccine, there's no data at all in the prior art,
6 would you have a reasonable expectation of success based on results that
7 were obtained with DNA vaccines, or saRNA vaccines? That in some cases
8 were encoding entirely different proteins, like in the saRNA context, it was
9 an RSVF protein.

10 Or in the context of DNA, not a full-length spike protein, they were
11 in, the teachings in Yang is with respect to truncated spike proteins. And
12 that situation, would a person of skill in the art be able to have a reasonable
13 expectation of what you would be able to achieve with an untested platform
14 in the vaccine space? And the answer to that question has to be no.

15 When you jump from one platform to another, you're going to get,
16 you're going to expect different results. These are different biological
17 pathways with respect to these different nucleic acid technologies. And
18 these carriers have different chemical compositions. Of course, they're
19 going to have an impact on the results that you're going to achieve.

20 And we'll get to Brito later, but Brito was the only example in the
21 record, in this entire proceeding, a very voluminous one, Your Honor, it's the
22 only example in the record where there's a head-to-head comparison. Where
23 you hold everything constant except for the vaccine technology. And what
24 do we see in Brito? We see that you cannot make any prediction at all.

25 So let's get to the anticipation grounds if I can. And let's go to Slide
26 19. And as Your Honors know, we make three primary arguments. And I'm

1 not going to go through all three, I'm going to focus on the third one,
2 because even if you assume that Geall is incorporated for its immunogens,
3 and even if you assume that the combination of Geall and Schrum discloses
4 all the limitations, which to be clear, we do dispute that, you still don't get to
5 anticipation because the disclosures are too numerous, they're requires too
6 much picking and choosing to meet the standard for anticipation under the
7 law.

8 JUDGE COTTA: So how do you address the *Gleave* case?

9 MR. PRUSSIA: Well, *Gleave* is completely inapplicable, Your
10 Honor. *Gleave* was a situation where there was a long list, 1,400 entries, it
11 was a single list. Every one of those entries were just all oligo nucleotide
12 sequences of the same gene.

13 It's like taking the spike polypeptide here and taking one version of
14 the spike polypeptide and having 1,400 different, a listing of 1,400 different
15 variations of the all oligo nucleotide sequences of that single spike
16 polypeptide.

17 But you don't, this is not that. Here you have to make a selection, first
18 of all, to arrive at an mRNA/LNP composition, which as I will explain to
19 you in a minute, there is no single embodiment disclosure of that in Schrum.

20 But even if you do assume that there's a single embodiment disclosure
21 in Schrum and they're going mRNA/LNP, you still have to pick the
22 immunogen, and there's over 500 immunogens that are listed in Geall, none
23 of which are connected to each other.

24 They cover all kinds of things, 21 different biofamilies, and there's no
25 teaching in Geall that sets one over the other. So it's not a *Gleave* situation
26 at all. It is more like the cases that we cite, including *Arkley* and the like.

1 And if we go to Slide 29, *Arkley* again sets out the standard.
2 Anticipation requires clear and unequivocal disclosure. And there is no
3 anticipation if the art requires picking and choosing from a multitude of
4 different options, and that's what we have here. Slide 31, please.

5 This is just a cartoon to exemplify conservative estimate of the
6 amount of combinations that are disclosed in Schrum. Now our view is that
7 there's way more than that. But just under their theory, if you go to the
8 vaccine section of Schrum alone, and you focus on that, there are at least
9 3,000 different options.

10 And I just want to pause on this for a minute, because we think that
11 they should be held to their petition. If you look at the petition, Your Honor,
12 there is nothing on this. There is a single statement that you all, I think,
13 correctly identify in the ID, with respect to this opinion from Dr. Griffin that
14 a person of skill in the art would look at Schrum and Geall and arrive at the
15 claimed invention. But there's no analysis. This is all an attempt to backfill.
16 And so we don't think it should be credited, but even if you do look at it, it
17 fails.

18 Let me start by this, you heard a suggestion that we're running away
19 from the disclosures in Schrum, that's not true. The fact is simply, we
20 dedicated Schrum to the public, but it's a different disclosure. The
21 disclosure in Schrum and Geall are very different from the challenged
22 claims.

23 As a reminder, Schrum was submitted during prosecution and it
24 discloses a number of different types of nucleic acids. We see that at
25 Paragraph 21, which I'll show on the screen in a minute, and over a dozen

1 different delivery vehicles. It does discuss vaccines, we're not disputing
2 that, of course. But the disclosure is very brief and it's highly generalized.

3 It's just 11 paragraphs in over 1,300 and it doesn't disclose any viral
4 immunogen specifically. It does not suggest a specific type of immunogen,
5 for example, it doesn't say bio immunogens over bacteria or fungi or
6 something like that. And it, Schrum itself, the whole disclosure doesn't
7 include any working example of any mRNA composition encoded for an
8 immunogen. And Geall --

9 JUDGE COTTA: Doesn't the absence of the immunogen disclosed in
10 Schrum for that reason to look to Geall for that?

11 MR. PRUSSIA: We'll give you that, and we'll say go to Geall. But
12 Geall discloses over 500-plus immunogens. And again, it's a complete
13 scattershot list. There's no direction toward any particular type of
14 immunogen. This is again, not a *Gleave* situation at all.

15 There's no connection at all in Geall's lists. Twenty-one different
16 virus families, no specific direction to a respiratory illness, no specific
17 direction to a betacoronavirus. There's no reference to that testimony that
18 you saw from Griffin that, you know, a betacoronavirus is the top ten
19 pathogen. There's no direction at all in Geall. The amount of selection that
20 you have to do to arrive at a betacoronavirus is too much to meet the
21 standard that the federal circuit has set out for us.

22 And even if you do get there, Your Honors, remember the disclosure
23 in Geall is to a spike polypeptide. That's a genus that encompasses any kind
24 of spike polypeptide. Spike was a very large polypeptide.

25 JUDGE COTTA: Doesn't that mirror the language in the claim of S
26 protein?

1 MR. PRUSSIA: No. S protein is a very specific thing. And I can
2 track back to the plain construction, if it would be helpful. But an S protein
3 is a full-length spike protein. And we know that --

4 JUDGE COTTA: But how is that different from spike polypeptide?

5 MR. PRUSSIA: Well, an S protein is a specific thing. It's a specific
6 construct, a full-length protein. A spike polypeptide includes anything, any
7 variation of a spike polypeptide. A spike polypeptide can include the
8 subunits as we see in our claims. It can include in fragments. It can include
9 truncated versions as we see in the prior art.

10 And that's what they're saying as to how an S protein should be
11 construed in this proceeding. But we know that the plain and ordinary
12 meaning, we go to their Slide 48. Their expert, focus on the red box at the
13 bottom, has offered the opinion that a person of skill in the art would
14 understand that spike protein refers to the full-length spike protein. We
15 agree. That's the plain and ordinary meaning of the term.

16 And if we go to Slide 13, let's look at the claims. The way in which S
17 protein is used in the claims and throughout the specification is consistent
18 with that plain and ordinary meaning. We are not arguing for lexicography,
19 I don't know where that came from. There's no lexicography argument on
20 our side. We're arguing the plain and ordinary meaning.

21 And if you look at the claims, S protein under a construction world
22 would include everything, like a spike polypeptide that's disclosed in Geall.
23 It would render superfluous the S protein subunit limitation.

24 Because if an S protein is the same thing as a spike polypeptide and
25 can include fragments and the like, then it would encompass an S protein
26 subunit. And what has the federal circuit told us about constructions that

1 would render other limitations superfluous? They're presumptively
2 incorrect.

3 So we have an undisputed plain and ordinary meaning that has protein
4 as a full-length spike protein, and we have the claims that set out S protein
5 subunit as being two different things. And every single disclosure in the
6 specification of the challenged patents, refers to either a full-length spike
7 protein or a subunit. All of the working examples, all of the nucleic acid
8 sequences, all of the amino acid sequences, they all encompass or relate to a
9 full-length spike protein.

10 Now you saw them show you a passage earlier today, I can't
11 remember where it was in the spec. It was on their slide and made reference
12 to fragments thereof. And they try to suggest, well that means that S protein
13 must include fragments.

14 Well, what's in the claim? The claim doesn't say or fragments thereof,
15 the claim says S protein. That further illustrates that the way it's used in the
16 patent is consistent with the plain and ordinary meaning.

17 So let's go back to Geall if we can. And that contrast with the
18 disclosure in Geall of a spike polypeptide, which is of course broader than
19 just the specific full-length S protein, and encompasses a genus of spike
20 polypeptides. There's nothing in Geall that says, that directs you to a claim
21 S protein or S protein subunit.

22 So let's go to their Slide 54 to address the argument that they made to
23 Your Honors this morning that Schrum somehow discloses a single
24 bodiment mRNA/LNP vaccine. It does not. And you can see that just by
25 looking at the paragraph numbers on their own slide. Okay. That these are
26 different disclosures in different sections of Schrum.

1 First, you have to make a decision. You have to make a selection to
2 go to the vaccine section of Schrum which, again, is just 11 paragraphs in
3 the disclosure, right. So you've got to make that choice first.

4 But you get to the vaccine section, and you read the whole thing, the
5 11 paragraphs. And there's nothing in that section that directs you to the
6 lipid carrier section that they have at the bottom lefthand screen. There's
7 nothing in that vaccine section that says you should go to lipid carrier
8 section.

9 So you have to make an independent selection as a POSA to go to that
10 section independently. So that's another choice you have to make. And
11 even once you arrive at that lipid carrier section, you need to make a further
12 selection to arrive at the LNP disclosure in Paragraph 397.

13 And they already explained to you why that you would go to 397 over
14 all of the other paragraphs in that portion of Schrum that also disclose
15 delivery of an immunogen. For example, Paragraph 434, which discusses
16 synthetic nanocarriers in delivery of immunogen. Paragraph 381 which
17 discusses cationic emulsions in delivery of --

18 JUDGE COTTA: If I could interrupt you for a second, just looking at
19 Paragraph 397, and I think I asked the same question of the Petitioner, but it
20 uses the phrase "a modified RNA-described herein", what does that refer to
21 if not mRNA?

22 MR. PRUSSIA: Let's go to my slide 43, please. Modified mRNA,
23 modified RNA is not the same thing as messenger RNA. And we know that
24 just by looking at Schrum itself. This is a side-by-side of Paragraph 397
25 with Paragraph 22 from Schrum.

1 And we have highlighted on the right, that when Schrum, we don't
2 need to put their slide back on the screen, but if you go back to their slide,
3 when Schrum wanted to refer to modified or rather, messenger RNA,
4 mRNA, it knew how to do so. It made specific reference to mRNA, it does
5 that throughout their slide.

6 And you see that in our slide on calling out Paragraph 22, where
7 there's a specific reference to messenger RNA, mRNA. What precedes that?
8 A reference to RNA. So Schrum sets out RNA and messenger RNA as
9 being two different things. And that's consistent with how a person of
10 ordinary skill in the art would understand it as well.

11 JUDGE MAJORS: Now the reference in Schrum to modified RNA is
12 at least arguably related to modifying the nucleosides, not necessarily that it
13 be mRNA or self-amplifying, for example?

14 MR. PRUSSIA: I think that's a fair reading, Your Honor. But it's not
15 a specific direction to an mRNA encapsulated in an LNP, which is what
16 they're trying to argue.

17 JUDGE MAJORS: But why would the skilled person not read it as
18 encompassing both? So they're saying modified RNA molecules here can be
19 encapsulated in an LNP. Why doesn't that disclosure there in 397
20 encompass both readings?

21 MR. PRUSSIA: Even if you consider RNA to be some sort of
22 umbrella genus term that would encompass all types of RNA, you still have
23 to make a selection, Your Honor. The law requires clear and unequivocal
24 disclosure.

25 And that isn't present in 397, because there is no reference to
26 messenger RNA in 397. And with respect to that last sentence, which is

1 what they use to tie it all together, right. We asked Dr. Moon about this
2 during his deposition, and Judge Majors, you pointed this out, and he
3 couldn't even answer the question. He said he couldn't offer an opinion as to
4 what that last sentence meant.

5 Now they showed you some further testimony afterwards, of course,
6 when the attorneys who get involved to draft the declaration where he said
7 something different. But he was asked the question during his deposition
8 and he couldn't answer it. And we think that's reflective of the record in this
9 proceeding.

10 JUDGE COTTA: Not to beat a dead horse, but can you give me the
11 example? Like, what specific types of modified RNA could paragraph 397
12 be referring to that are disclosed somewhere in Schrum?

13 MR. PRUSSIA: Yes. So, Your Honor, there is nothing in the record
14 on that. There is nothing in the record identifying what modified RNA, to
15 answer your question, I would -- I would be making it up, I couldn't point
16 you to anything on the record on that.

17 JUDGE COTTA: Okay.

18 JUDGE MAJORS: Mr. Prussia, what do you make of the argument
19 earlier that some of the claims of the Schrum reference package together the
20 different elements of the challenged claims, sort of, except for the
21 immunogen --

22 MR. PRUSSIA: So that's a new argument, as Your Honor, I think
23 correctly pointed out earlier. And I don't have that slide in front of me. If
24 someone maybe has it, maybe they could pull it up. But my recollection of
25 that slide is it doesn't even, again, it doesn't even again, specifically disclose
26 mRNA in an LNP.

1 So it doesn't disclose the immunogen, that's for sure. But it includes, I
2 believe, LNPs in a long list of other carriers. So you have to make a further
3 selection to get to an mRNA/LNP. The bottom line is, Your -- and so the
4 bottom line is, Your Honor, there is no single embodiment disclosure
5 anywhere in Schrum of an mRNA in an LNP.

6 You have to make all sorts of selections to arrive there. And even
7 once you do, even if you do say that there is a disclosure of an mRNA/LNP
8 composition, including for an immunogen in Schrum, you still have to get to
9 the immunogen. You have to get to Geall. And the disclosures in Geall are
10 too disparate, they are not interconnected. Too much picking and choosing
11 to meet the federal circuit standard under *Arkley* and the like.

12 Briefly on the question of data and the role that it plays in
13 anticipation. They showed you on their Slide 39, the *BMS* case, which they
14 cite for the proposition that anticipation does not require actual performance
15 of suggestions in a disclosure. That's a correct statement of the law. Of
16 course, we're not going to dispute that.

17 But it doesn't apply here for a few reasons. First, if you go to look at
18 the *BMS* case, the claim in that case required premedicating. And the
19 dispute in that case was whether the prior art anticipated where the reference
20 itself expressly disclosed premedicating, it used those words.

21 But it didn't actually show administration of premedication in the
22 study. And so, the question was, was that necessary? And the federal circuit
23 said no, there was disclosure of the premedicating, and so there was no need
24 to actually show the data resulting from the premedicating.

25 That's not the situation here. There's no disclosure of the step that's in
26 our claims of the method that requires providing an effective amount to

1 induce an immune response. There's no disclosure of that in Schrum.
2 There's no disclosure of that in Geall. There is no disclosure of an effective
3 amount of the betacoronavirus S protein in an mRNA/LNP composition
4 period.

5 What they do is they take the generic statement in Schrum with
6 respect to an immune response and try to apply that to Geall's immunogen.
7 But Geall's immunogen is in the context of a laundry list. And the only
8 information, the only example of eliciting an immune response in Geall, is
9 with respect to the RSV F protein, not the betacoronavirus spike protein.

10 So I went a little bit out of order. But I do want to, if I can, just go
11 back to claim construction.

12 JUDGE COTTA: I just wanted to ask a question and just to follow up
13 on your no data point. And maybe you could tie that a little bit to the
14 breadth of the claims, which don't require any particular level of immune
15 response. It seems to me if you get any immune response whatsoever, for
16 any degree of those neutralizing antibody response, then that would meet the
17 claim. Can you address your no data argument as it relates to that specific
18 point?

19 MR. PRUSSIA: Yes, I can, Your Honor. First of all, there is, if we
20 go to Slide 28, there is testimony in the record that was elicited from
21 Petitioners that the, I'm trying to find it, I thought I had it at my fingertips.
22 Let me just get it, Your Honor. Give me a minute, I'm sorry.

23 It's at Exhibit 1104, Page 255, Line 18 to 257 to Page 10. During her
24 deposition, Petitioners asked Dr. Fuller for her understanding of what the
25 immune results limitations required. And she testified that a person of skill

1 in the art reading the patent, would understand that the claimed invention
2 results in a new result that is protected.

3 And she said that's consistent with the disclosures in the patent
4 specification. We have here, for example, in Example 24, which explicitly
5 describes the administration, an *in vivo* administration of the claimed
6 mRNA/LNP composition occurring for a full-length spike protein.

7 And the inventors report that the administration resulted in complete
8 protection in the throat and induced significant amount of neutralizing
9 antibodies. And Dr. Fuller's testimony as a person of skill in the art, just
10 based on their own experience and understanding in combination with the
11 disclosures and the patent would understand that it's not any immune
12 response. That would sort of run counter to the utility of what's being
13 claimed here.

14 Specifically, in the context of Claim 3 which specifically requires a
15 neutralizing antibody response, which a person of skill in the art would
16 understand is something that provides protection against infection.

17 JUDGE COTTA: But you haven't argued that the claims require any
18 particular claim construction on that point?

19 MR. PRUSSIA: No, that's the plain and ordinary meaning, Your
20 Honor. And that's testimony they elicited during her deposition.

21 So I just wanted to briefly hit the mRNA construction, Slide 12.
22 There is a clear and unmistakable disclaimer that the mRNA of the invention
23 does not include self-replicating RNA and does not include the components
24 necessary for viral replication. So this disclaimer is clear, it's unmistakable,
25 and it's dispositive. And it should be applied here.

26 JUDGE COTTA: How is that dispositive?

1 MR. PRUSSIA: Well, in terms of the meaning of the mRNA in the
2 claim is. I think they ultimately in terms of --

3 JUDGE COTTA: Assume we agree with your claim construction
4 point, how is that dispositive? Or how does that influence the case?

5 MR. PRUSSIA: Oh, well, thank you, Your Honor. It does, well,
6 there's one of two ways in which -- there's two different ways to get to the
7 same result.

8 So we think the claims, the specification makes clear that it does not
9 encompass self-replicating RNA, either through this disclaimer or through
10 their own admissions that we think are clear now through the papers that we
11 submitted and the reply briefing, which make clear that they are no longer
12 arguing that Geall, for example, discloses replicating the claimed mRNA.

13 So I don't think there's a dispute between the parties on this point, but
14 to the extent they are still holding onto an argument that Geall discloses the
15 claimed mRNA, then we think this disclaimer is dispositive of that issue.

16 Now they are -- I understand their argument to be that they are not
17 relying on Geall for teaching the claimed mRNA, they are only relying on
18 Geall for disclosure of immunogens. That's what I understand their position
19 to be.

20 But in the petition, they make arguments suggesting otherwise, and so
21 that's the reason why we've asserted and argued for this claim construction.
22 But if the record is clear that that's not what Geall is being used for, there is
23 no real need to get to the claim construction issue.

24 So if I can, let me go to obviousness. And before I get into motivation
25 -- we can take that down. Before I get to motivation and reasonable
26 expectation of success, let me just briefly respond to the suggestion that the

1 prior art discloses all of the claim limitations. That is demonstrably
2 incorrect. None of the prior art in the grounds discloses an mRNA/LNP
3 vaccine generating an immune response to an immunogen, let alone the
4 betacoronavirus S protein.

5 And all of the responses they showed you are resulting from different
6 nucleic acid technologies and different delivery vehicles. And none of the
7 grounds disclose immune responses from a nucleic acid vaccine to a full-
8 length S protein.

9 Let's tick through it quickly. Slide 42, we'll start with Geall. Again,
10 Geall was submitted during prosecution. Geall never refers to mRNA. And
11 as we just discussed, Petitioners no longer assert that Geall discloses the
12 claimed mRNA or mRNA formulated in an LNP.

13 It does not disclose the claimed full-length S protein. There is this
14 reference to a spike polypeptide, that's not the same thing. Go to Slide 43,
15 Yang. And before we put it up, Geall also doesn't disclose neutralizing
16 antibodies to the claimed full-length S protein. Go to Slide 43, Yang.

17 It discloses DNA, of course, not mRNA. It discloses naked delivery,
18 not LNP, and it discloses truncated spike proteins, not the claimed full-
19 length spike protein. And of course, it doesn't disclose any immune data to
20 the claimed full-length S protein.

21 Altmeyer, Slide 44. Again, does not disclose mRNA vaccines.
22 There's this reference to the spike, the SFV spike RNA vaccine. I think the
23 parties agree that's not the claimed mRNA, it's a nucleic acid technology
24 with no one, to be honest, quite knows what exactly it is.

25 In terms of delivery, it does not disclose an LNP, it discloses
26 aluminum adjuvant or naked delivery. And it doesn't disclose any

1 initializing antibodies to the full-length S protein. To be clear, there are
2 references to making a full-length S protein in Altmeyer, but the data that's
3 in the Example 5 in Altmeyer, that's not attributable to the S protein that is
4 encoded by the nucleic acid vaccine. Altmeyer involved a prime and then
5 several boosters and the data is reported with respect to the booster vaccine
6 as a whole.

7 So let's talk about motivation, Slide 45. And I'm not going to spend
8 time on motivation except on the disease enhancement part. But I think it's
9 important that we think about what the prior art looked like at the time. And
10 the reason for that is because mRNA was known to have significant
11 challenges to work the exogenous mRNA needed to survive in the body so
12 that it could get to the cellular system.

13 And then once it got to the cells, it needs to get into the cells to access
14 the ribosome in a cellular machinery. But that, of course, had been proven
15 to be exceptionally difficult to do, because mRNA was unstable and it was
16 known to not produce a sufficient adaptive immune response. Let's go to
17 Slide 39, please.

18 So as a result the field had almost uniformly moved on to investigate
19 other nucleic acid technologies. And just to illustrate this, I'm not going to
20 dwell on it. But of all the clinical trials that were active for infectious
21 diseases, involving infectious diseases at the time, only .3 percent of them
22 involved mRNA. And all of them ultimately failed.

23 And to Your Honor's question about was any of this specific to the
24 betacoronavirus, of course. And the reason for that is there were unique
25 concerns about the S protein, and I'm going to get to that in a minute. But

1 there were also concerns -- the concerns were only limited to disease
2 enhancement, that was a big concern.

3 But in terms of just the mechanics of what we're talking about here
4 itself, the S protein is exceptionally large, it's around 1,400 amino acids.
5 There was no demonstration anywhere in the prior art of successfully
6 encoding, delivering an mRNA that encoded for a protein as large as the S
7 protein. So if given the known concerns about the stability of mRNA, there
8 would have been even further concern in the specific context of a
9 betacoronavirus S protein, just given the nature of this particular target.

10 So and just briefly before I go into disease enhancement, the reason
11 why the field was -- if we go to Slide 48, was focused on these other
12 technologies, is because of the known advantages of DNA vaccines and of
13 viral vector vaccines and saRNA vaccines.

14 DNA vaccines were known to be more stable and less immunogenic
15 than mRNA. There was at least a decade as of the priority date, at least a
16 decade of literature describing DNA vaccine platforms.

17 Viral vector vaccines were also known to have advantages with
18 respect to the means for getting the nucleic acids into the cell. And saRNA,
19 which was a newer platform that is disclosed in Geall and the like, was
20 known to have, and we can go to Slide 51, specific advantages that were
21 designed to overcome the potency issues that were associated with mRNA.
22 And that's due to the ability for the saRNA to self-replicate in the cell and
23 amplify the amount of protein expressed.

24 JUDGE COTTA: If I could interrupt you and it was related to this
25 topic, but there's statements in the '600 patent and the '127 patent as well, I
26 believe, and in Schrum, suggesting that you can use mRNA with a liposome

1 to express a therapeutic. Can you address why that doesn't translate to a
2 vaccine?

3 MR. PRUSSIA: Sure, Your Honor. Two things. Expression does not
4 equal an immune response. And this is for a few reasons. First of all, take a
5 step back, the examples in Schrum of the reporter proteins and the other
6 proteins that are exemplified in Schrum, that are directed towards protein
7 expression and reducing the immune response, those proteins are different in
8 kind from the betacoronavirus S protein as I mentioned before. Significantly
9 smaller proteins, not as long as the S protein.

10 Why does that matter? Well, the testimony in this record is that the
11 longer the protein, so intuitively, the more opportunities there are for
12 translation error. And Dr. Griffin admitted that when there is a potential for
13 a mis-folding, and if you do that, you're not going to produce an immune
14 response, let alone a neutralizing antibody response. And that's at Exhibit
15 2253, Page 48.

16 JUDGE COTTA: So is it your position that if a protein doesn't fold,
17 there will be no immune response whatsoever?

18 MR. PRUSSIA: Yes, Your Honor. That's testimony in the record.
19 And you'll see that at 2253, Page 48, Lines 4 to 16, Page 49, Lines 2 to 12,
20 Page 68, Line 4 to Page 69, Line 1. If we go to Slide 24.

21 We also see that here from this testimony from Dr. Griffin, again in
22 Exhibit 2253, Page 47, 15 to 19, expression of a protein by itself does not
23 necessarily lead to production of neutralizing antibodies. So the record is
24 very clear on this, Your Honor, a few things.

25 One, that expression does not equal an immune response. And two, as
26 I also just articulated that when you have a protein as long and as large as

1 the S protein, you introduce more opportunities for error. So Schrum's
2 disclosure is very useful with respect to therapeutics and the purpose of that
3 disclosure is primarily directed towards that. Protein expression, of course,
4 is relevant to a vaccine as well. But one doesn't necessarily equate to the
5 other.

6 JUDGE MAJORS: Is expression even required for the composition
7 claims of the '600 patent?

8 MR. PRUSSIA: Yes, so it's a great question, Your Honor. Now we
9 do cite, you're right that there is no -- unlike the '127 claims, there is no
10 specific limitation requiring a specific immune result, one of them, let alone
11 the neutralizing antibodies that are required by Claim 3.

12 But we do cite the end, so there's no additional step in the claim, right.
13 But we do think that the, when it comes to considerations of what a person
14 of skill would have been motivated to do and whether a person of skill in the
15 art would have had in particular, a reasonable expectation of success, the
16 *Yamamuchi* case that we cite in our papers is particularly relevant there.

17 Because it's a composition claim, but when you're considering
18 whether a person of skill in the art would have had a reasonable expectation
19 of success at arriving at an mRNA/LNP composition encoded for the S
20 protein, you do have to consider things like would the POSA had a
21 reasonable expectation of generating, expressing it -- of expressing the
22 protein and generating an immune response. Because if you look at the '600
23 patent, it is directed towards a vaccine.

24 JUDGE MAJORS: Well, I think the law is to the effect you have to
25 have a reasonable expectation of what's claimed. For a composition claim,

1 this is what I struggle with a little bit, you might simply want to make it
2 simply to test it.

3 Whether it folds or not, figure that out in subsequent testing. So I'm
4 struggling with that on, particularly the composition claims and all the
5 arguments around it, it has to form a spike, all of that. In my thinking, I
6 don't see why that's required for claims that aren't method claims?

7 MR. PRUSSIA: Yes. Again, it's a great question, Your Honor. And
8 I do think, there is a distinction for sure. And that's the reason why I'm
9 focusing on Claim 3, for that reason in particular. But I still do think the
10 composition claims get the benefit of the utility of the disclosure.

11 And the utility in the 600 patent, if you look at the title of the patent
12 itself, it's abstract, it makes reference to a vaccine. That is not in the claim,
13 for sure. The claim only requires a composition that's encoded for the
14 protein.

15 But in asking the question of whether a person of skill in the art would
16 have had a reasonable expectation at arriving at that composition, the
17 considerations come into that are whether, or for what purpose, this
18 composition is being used for. And that's discussed in *Yamamuchi*. So there
19 is a distinction.

20 And I'll concede the fact that there is a difference between the, in
21 terms of the claim scope and the patentability of, the additional patentability
22 of those immune result limitations that we think is why Claim 3 is different
23 and why I'm focusing on it this morning.

24 So the field, go to Slide 52, was skeptical of mRNA vaccines for
25 infectious disease. Now, we mentioned that the .3 percent of clinical trials
26 that were ongoing at the time, none of them used LNP, right.

1 We all want to talk this morning about mRNA, but we have to remind
2 ourselves, the claim is towards an mRNA/LNP composition. It's the
3 combination, they're both together. And none of the clinical trials at issue at
4 the time involved LNP. None of them used a protein that was as large as a
5 full-length protein, and all of them ultimately failed. Go to Slide 53.

6 Petitioners suggests that the clinical trial failure rate is irrelevant. And
7 that's wrong, federal circuit has told us that explicitly in OSI that we can
8 consider the failure rate in the field, the clinical trial failure rate as being
9 relevant. There is no track record of success with respect to mRNA.

10 JUDGE COTTA: Do you agree that, even for the '127 patent, the
11 claims do not require as high a threshold of therapeutic effectiveness as
12 might be required in a clinical trial?

13 MR. PRUSSIA: It does. Your Honor is correct, it doesn't require
14 vaccine efficacy of 97 percent. It requires the showing of protect -- with
15 respect to Claim 3, neutralizing antibodies, which a person of skill in the art
16 would understand to be protected.

17 And if we look at the literature, they suggested earlier that there's no
18 example in the prior art of there being an mRNA vaccine that didn't work.
19 Well, I'll direct you to Exhibit 2046.

20 This is with respect to the rabies vaccine that was in clinical trials.
21 They found with respect to the intramuscular injection, and I'm quoting, "It
22 was ineffective", this is on Page 1 of the paper, "... with only one participant
23 showing a detectable immune response". For the HIV vaccine, Exhibit 2044
24 at Page 2, explicit disclosure, "We were not able to demonstrate
25 immunogenic effects of the vaccine". That's a direct quote.

1 JUDGE COTTA: It was from my understanding, I think, Petitioner is
2 arguing that, okay, these were not successful trials but they did show an
3 immune response.

4 MR. PRUSSIA: I just read from the paper, "We were not able to
5 demonstrate immunogenic effects of the vaccine". That's Exhibit 2044 at
6 Page 2.

7 JUDGE MAJORS: Mr. Prussia, Exhibit 2046, that published in 2017,
8 so how is that relevant to the skilled person's knowledge in 2015?

9 MR. PRUSSIA: Yes. That clinical trial was ongoing as of the
10 priority date. It was one of the seven clinical trials that we made reference
11 to. And the result of that trial was that. So there were failures.

12 JUDGE MAJORS: And the failures before October of 2015 that we
13 should be looking at?

14 MR. PRUSSIA: There was zero reports with respect -- zero reports of
15 success prior to the -- as of the priority date that we're applying in this trial.

16 JUDGE MAJORS: One might however argue that --

17 MR. PRUSSIA: -- in this proceeding. Sorry.

18 JUDGE MAJORS: I'm sorry to interrupt you.

19 MR. PRUSSIA: No, no. Sorry.

20 JUDGE MAJORS: One might however, say that the fact that they
21 were moving forward into clinical trials is some indication that these were
22 doing clinical trials, right?

23 MR. PRUSSIA: Sure, yes.

24 JUDGE MAJORS: That there was some indication that there would
25 be success, even if they later failed. So what's Patent Owner's position on
26 that?

1 MR. PRUSSIA: I think that's a fair suggestion, Your Honor. But
2 again, the claims are toward an mRNA/LNP. So we don't, just to be very
3 clear, we're not saying that a person skilled in the art as of 2015, that mRNA
4 was like DOA, right. I mean, because we have disclosures in Kalen, and
5 Schlake and Petsch of there being some observation of success.

6 Our position is you have to take the, the person of skill in the art, as
7 the Federal Circuit has told us repeatedly, has the benefit of all the teachings
8 in the art. And there's a long history with mRNA. And that history includes
9 lots of examples of failures, it includes examples, you know, around the
10 priority date, there is disclosures in Kalen, Schlake and Petsch, where people
11 were able to observe success.

12 But if you look at the nature of the disclosure in those papers, for
13 example, in Petsch, which Your Honor cited in the Institution Decision, it
14 was quite clear that the success that they observed, as they say, and I'm
15 reading at Exhibit 2025 at 1215, Petsch notes that an independent group
16 recently detected no humoral immunity after vaccination with conventional
17 mRNA and concluded that protamine complexation, which was the delivery
18 vehicle they used in Petsch, was in their words, necessary for protective
19 immunity.

20 So there was disclosure, for sure, with mRNA, right. But it was
21 limited. And you have disclosures in Petsch that is repeated in Kalen, and
22 Schlake that was reflective of the thinking at the time that you needed
23 protamine as a delivery mechanism for an mRNA to work.

24 JUDGE MAJORS: Well, let me move on to what Geall says, in fact,
25 have it here, but I'm looking at the 2013 Geall reference, and they seem to

1 say that there were two delivery strategies that emerged, by protamine and
2 LNPs.

3 MR. PRUSSIA: Yes.

4 JUDGE MAJORS: So I will tell you I struggle with this from a
5 motivation standpoint. And you might say that mRNA was the disfavored
6 option or LNP the disfavored option. But we have teachings and multiple
7 references as you just acknowledged, to say LNPs are an option to deliver
8 these RNAs into the cell.

9 MR. PRUSSIA: So I think what Geall identifies, as it's proof of
10 concept, to the right, at Page 154 of the reference, is a specific reference to
11 Petsch and the two-component mRNA with the protamine complex. And
12 then with respect to LNPs, a self-amplifying RNA system. So there is no
13 disclosure in Geall of the claimed mRNA/LNP. And that's the point we're
14 making.

15 JUDGE MAJORS: Well, I recognize that, but then if you look again
16 at the proof of concept just to the left of where you were reading, they say,
17 RNA vaccines "both mRNA and replicons are effective at eliciting antigen
18 specific humoral and cellular immune responses in animal models of
19 infectious and non-infectious diseases". So it feels like we're parsing the
20 disclosure so fine to say well, they referenced LNPs here but that was only
21 in the context of saRNAs, not in a broader role, not using it for mRNAs.

22 MR. PRUSSIA: Yes. I, Your Honor, I think if you look at the
23 references that are cited in the notes, and then you've got to read that, the
24 whole section, and the only disclosure of mRNAs with respect to --

25 JUDGE MAJORS: This part you mean?

1 MR. PRUSSIA: -- yes. And when you go to Petsch, Petsch explicitly
2 notes that another group had, and I lost the quote now, was shown no
3 humoral immunity with respect to conventional mRNA and they opine and
4 talk of worlds that protamine was in their words, necessary for it to get the
5 results that they observed.

6 So it may feel like we're parsing, but that's what a POSA would do. A
7 POSA would look at the statement, look at the references that are being
8 cited, look at what's actually disclosed in those papers and see, oh, okay,
9 Petsch is talking about mRNA with protamine, and Petsch tells me that you
10 need protamine.

11 And then go look at not just Petsch, but also Schlake and Kalen and
12 see that they did the exact same thing. So you wouldn't walk away from
13 those disclosures and say to yourself, you know what, mRNA/LNP, that's
14 the way to go. There was no disclosure of mRNA and LNP.

15 And then if I can, I want to spend the remaining of my time talking
16 about two things. One, disease enhancement and then second, what we call
17 for shorthand, lack of interchangeability. So first, with respect to Slide 54,
18 let's talk about disease enhancement.

19 This was an established concern. Dr. Fuller provides testimony about
20 that as we said on the screen, with Slide 55. The prior art was replete with
21 teachings regarding disease enhancement concerns with spike protein. It
22 starts with Vennema, but it doesn't end there, it goes on. Yang 2004, which
23 is in the grounds, discusses the possible immune potentiation of the disease.
24 Yang 2005, a year later, Exhibit 2137, showed enhanced entry. We're going
25 to take a closer look at Yang, show that the full-length spike protein
26 demonstrated -- strike that.

1 They observed that the full-length spike protein showed enhanced
2 entry in the presence of certain antibodies. Du 2009, Exhibit 1031, also
3 reports that the full-length S protein induced, enhanced infection even
4 though it also induced neutralizing antibodies. And Jaume, which we're also
5 going to take a look at, reported that the full-length spike protein triggered
6 infection.

7 So the prior art was replete with specific teachings that the full-length
8 spike protein could cause disease enhancement. If you go to Slide 56, I have
9 excerpts from Du and Yang on the screen on the left, is Du at Pages 229 to
10 230 of Exhibit 1031.

11 And I have it on the screen, Your Honors, because you heard a lot
12 from them, we saw in their papers a suggestion that, well, you know, this S
13 protein enhanced infection thing, it wouldn't be a concern because once you
14 see neutralizing antibodies, you know you're not going to see disease
15 enhancement.

16 And Du says exactly the opposite. Du says that although the full-
17 length S protein base vaccines can induce neutralizing antibodies, they may
18 also induce harmful immune responses that enhanced infection.

19 And Yang, which is the Yang that is in the grounds, also reports on
20 immune potentiation. And let's just drill down on Yang for a minute,
21 because that research group, I think is highly relevant to the considerations
22 here. So we go to Slide 57.

23 Yang's research group confirmed that there were disease enhancement
24 concerns with the full-length spike protein. What I have on the screen are a
25 couple of different excerpts from Yang. On the left, Figure 1b, I'll start
26 there, is an experiment where they tested, they introduced pseudo viruses

1 after administration of a DNA vaccine with a full-length SARS-CoV protein.
2 And they observed antibody dependent enhancement of S entry.

3 You see that in the graph there, the further down on the Y axis you go,
4 that means the more disease enhancement you observe. And Yang in its
5 abstract, I don't have it on the slide, but if you go to the abstract of Yang, it
6 describes this finding as being unexpected, those are the words of Yang.

7 So what did Yang do? Yang did decide to take that full-length S
8 protein into the clinic. Yang decided, if we look at the top righthand corner,
9 that it was necessary to investigate whether it was possible to modify the S
10 immunogen to avoid antibody dependent enhancement of entry.

11 So what did they do? They came up with a construct that was not a
12 full-length spike, but a version of the spike that had the transmembrane
13 portion deleted. And they tested it. What did they find? They found that it
14 induced neutralizing antibodies.

15 So it's not a full-length spike, it's a construct that is shorter than the
16 full-length spike. It was successful in neutralizing antibodies and failed to
17 cause antibody enhancement of entry. Why is this important? If we pull up
18 Exhibit 2138.

19 So ultimately Yang's group took this DNA vaccine construct into the
20 clinic. The only example of a betacoronavirus vaccine that was tested in
21 humans as of the priority date, is this construct from Yang's group. Okay.

22 And Yang's group did not take a full-length spike protein into the
23 clinic. Why? Because they saw disease enhancement. You just saw in the
24 prior exhibit, in 2137, they specifically took the truncated spike, as we'll see
25 in a minute, the same truncated spike that's reported into the grounds, into

1 the clinic. Precisely because it didn't cause disease enhancement and
2 induced neutralizing antibodies.

3 So we have on the screen, Exhibit 2138, this is the Martin 2008 paper.
4 And you'll see, you won't see Yang's name on this paper, so you're
5 wondering, how's it connected to Yang? Well, Gary Nabel, he's a senior
6 author, if you go back to Exhibit 1101, which I believe is the Yang reference
7 in the grounds and also the prior Yang that we looked at, 2137, Nabel was an
8 author. He was the senior author on those papers.

9 And so this report on the SARS DNA vaccine that went into Phase 1
10 clinical trials. Again, this is the only example of a betacoronavirus vaccine
11 that went into clinical trials. Okay. And if you look under methods, it
12 makes reference to a single plasmid DNA vaccine encoding the spike
13 glycoprotein.

14 Let's see what it is. If you go to Page 2, which is at Page 6339 of the
15 exhibit, and focus on the righthand column, we see a sentence, the plasmid
16 was constructed to produce a deletion mutant of the SARS spike
17 glycoprotein with the pseudoplasmic domain truncated. You see a
18 reference, Reference 9.

19 If you go to see what Reference 9 is, it's the Yang paper that's in
20 Ground 3, Yang 2004. And if you go to Page 5 of the PDF, the preceding
21 page, what does Yang and Nabel's group report about this construct, this
22 construct, this truncated spike construct in clinical trials?

23 That it was well-tolerated, produced cellular immune responses and
24 neutralizing antibodies, and they suggested it should be further considered
25 for evaluation for potential future SARS outbreaks. So this is the only
26 evidence in the record of a betacoronavirus vaccine that had been tested in

1 humans, as of 2015. And it involved a truncated spike, it has generated
2 neutralizing antibodies, did not cause disease enhancement. And it's from
3 the same group who specifically considered a full-length spike and went the
4 other way, precisely because of disease enhancement.

5 JUDGE MAJORS: Can I ask a follow-up question to that?

6 MR. PRUSSIA: Yes.

7 JUDGE MAJORS: Do you agree that the claims don't require that the
8 subject be a human, right? It could be any animal?

9 MR. PRUSSIA: The claims are not specifically directed towards a
10 human. That's right.

11 JUDGE MAJORS: And are you familiar with the, I think it's Exhibit
12 1011, the Wang reference?

13 MR. PRUSSIA: Yes, sir.

14 JUDGE MAJORS: I believe that also involved some of the same
15 group of researchers, Wang, Yang, and --

16 MR. PRUSSIA: I believe that's right, yes, sure. Yes.

17 JUDGE MAJORS: Now they were testing, as I read the reference,
18 they were testing in 2015, a full-length S protein in mice and non-human
19 primates.

20 MR. PRUSSIA: Yes, sir.

21 JUDGE MAJORS: So we have contemporaneous evidence, while
22 you might have one arm of the research moving forward in human clinical
23 trials where they're using a truncation, we have another arm of these
24 researchers continuing to do testing with the full S protein --

25 MR. PRUSSIA: Yes.

1 JUDGE MAJORS: -- in other animals. So this gets us into the realm
2 of okay, maybe somebody might have thought that there were advantages of
3 the truncations relative to disease enhancement. But skilled people at the
4 time continued to test the full S --

5 MR. PRUSSIA: Yes.

6 JUDGE MAJORS: -- in animal models.

7 MR. PRUSSIA: Yes.

8 JUDGE MAJORS: And report neutralizing antibodies.

9 MR. PRUSSIA: Two quick points on that, Your Honor. Well, one
10 quick and the second one will be longer, because I'm going to drill down
11 into it, because I think you're highlighting something that's really important.

12 The first is, when you look at Wang, this actually is the evidence of an
13 S protein that was, that failed to induce an immune response. Remember
14 Wang is the one where they do a prime and then they follow it up with
15 boosts. And they report on the prime that it elicited no detectable or very
16 low antibodies. That's the whole reason why they're investigating the boost.
17 So I just wanted to make that quick point.

18 But the second point, Your Honor, getting to what I actually think
19 really supports our position. If we go to Slide 58. This is where Jaume
20 really comes into play. And that's because the results that were observed in
21 the prior art with respect to disease enhancement, they were entirely
22 unpredictable.

23 And Jaume summarizes this quite nicely, where they report that
24 different SARS vaccine candidates elicit sera that differ in their capacity to
25 induce ADE. So and the reason for this, is because it was entirely
26 unpredictable.

1 Jaume reports that there was a novel cell entry mechanism that was
2 responsible for disease enhancement in the betacoronavirus context. So this
3 is why their assertion that, hey, you know, everyone's concern, every
4 vaccine researcher is concerned about disease enhancement, doesn't, that
5 argument does not fly in the context of the record of this proceeding.

6 Because the specific record here is that as evidenced by Jaume, is that
7 this was a novel mechanism with respect to betacoronaviruses. And it was a
8 particular concern because of the fact that different vaccine candidates
9 elicited sera that differ in their capacity to induce ADE. So you couldn't
10 predict whether, will a Yang DNA construct would be okay, versus a
11 different construct.

12 And that's what is reported in Jaume. And this is in 2011. So this is
13 just a few years before the date that we're all working with in terms of the
14 priority date in this proceeding.

15 So you know, Petitioners showed you a slide this morning that sort of
16 suggested that, you know, this finding in Jaume wasn't really conclusive.
17 But if we go to the paper itself, Exhibit 2030, and we go to 1590, Jaume
18 tested a lot of different things.

19 I mean, if you go through the whole paper, there's lots of different
20 experiments that they did. And their conclusion couldn't have been any
21 clearer. And this is at Page 10,590 on the righthand column that we have
22 highlighted. Our experiments conclusively demonstrate with several lines of
23 evidence that you would see, that they observed disease enhancement with
24 the spike immunogen.

25 JUDGE MAJORS: So can I ask you one question?

26 MR. PRUSSIA: Yes, sir.

1 JUDGE MAJORS: Disease enhancement, is that an immune response
2 to the spike?

3 MR. PRUSSIA: What's the best way to answer that, guys? I don't
4 think so. I mean, I think that what happens is the -- I'm actually, to make
5 sure I answer your question the right way, Your Honor.

6 JUDGE MAJORS: If you want to confer, that's okay.

7 MR. PRUSSIA: Okay. Can I ask for it when I stand back up, is that
8 all right? Okay.

9 One other thing about Jaume, if I could, if we go to Slide 59. Just to
10 illustrate how unpredictable this was, what we have, this is something that
11 we put together comparing Yang's truncated spike, this is the one that went
12 into the clinic, it's in the middle. DNA vaccine, no disease enhancement.

13 Jaume's truncated spike reported in its paper, which only differs by
14 three amino acids, as compared to the Yang spike that did not show disease
15 enhancement, so one, and Jaume found that it did observe disease
16 enhancement with that construct that it tested. Yang did not.

17 So here we have two almost identical spike protein constructs,
18 truncated spikes. One, no disease enhancement in DNA, one, disease
19 enhancement in a different vaccine technology. So this just shows the
20 unpredictability in the field at the time.

21 So if I can. So what's the point of all this? The point is that, if you go
22 to Slide 65, unlike contrary to what they're asserting, a person of skill in the
23 art would not have been laser-focused on the spike protein.

24 There were other targets that were demonstrated to generate
25 neutralizing antibodies like Jaime and Yang. And there was teaching in the

1 art that they could be a good candidate because they don't induce early death
2 after challenge. The field was unpredictable.

3 And there was demonstrated evidence that the S protein could cause
4 disease enhancement. But no one really understood why. And no one could
5 design a vaccine that was predicted to not cause disease enhancement a
6 priori.

7 And the only example of the vaccine construct that went into the
8 clinic, did not include a full-length spike protein and it was reported that the
9 reason they went with that construct was to avoid disease enhancement.

10 So let me now turn to Slide 40. And I'm going to drill down on Point
11 2 on this slide, that results from different nucleic acid vaccines, different
12 engines, and different delivery methods, yield different an unpredictable
13 results. Slide 69, please.

14 Vaccine technology is not and was not interchangeable, as Dr. Fuller
15 put it. And again, just to re-emphasize where I started, she's the only nucleic
16 acid scientist in this proceeding. She testified, and we have Page 552 from
17 her 2199 -- sorry, Page 552, Paragraph 552, from Exhibit 2199, where she
18 says, "It was not possible to assume that a POSA would obtain the same (or
19 similar) results with different vaccine technologies, e.g., saRNA versus
20 mRNA. Instead, at that time, there was evidence of lack of
21 interchangeability. Choosing the same protein with different vaccine
22 technology resulted in different outcomes."

23 So this is her testimony. But it's not just her testimony. Go to Slide
24 70. Her testimony is based on the explicit disclosures in the prior art. So
25 Slide 70 shows two figures from the Brito paper, and there's a type, it's Brito

1 study was not in 2005, Brito study was in 2014. So this is a year before the
2 date we're all operating with, it's Exhibit 2005.

3 So the year before the date we're working with here, Brito reports, and
4 just, I'll pause. The senior author in Brito is Geall, the same Geall in the
5 grounds, right. So Geall's group is reporting in 2014, that vaccine
6 technology is not interchangeable.

7 So what they did was, they compared saRNA, mRNA, and DNA
8 vaccines. They were all encoded for the RSVF protein, and they were all
9 formulated in the same thing, this cationic nano emulsion system.

10 So everything was held constant, except for the vaccine technology.
11 And you can see the SAM, which is the saRNA, with respect to just the
12 antibody titers generally, and the neutralizing antibody titers, they were
13 detectable, and they were significant.

14 With respect to mRNA, did not generate anything. And with respect
15 to DNA, sort of inconsistent results. Now, they try and say that, and by the
16 way, this phenomenon was reported not only for RSV, but it was also
17 reported for HIV by Geall and Brito.

18 Now they try to say, they try to discount this by saying it was all about
19 the dose. But when we asked Dr. Griffin about that during his deposition, he
20 admitted that that statement, or that suggestion that it was because of the
21 dose was pure speculation. And if you go to Slide 71, Dr. Fuller explained
22 why.

23 So this is from her declaration at Paragraph 557. She explained that
24 the mRNA that was administered in Brito, it's 15 microgram dose, it's a
25 1,000 times higher than the saRNA dose of .015 microgram. There was no
26 teaching in the art, they won't show you any teaching in the art that

1 suggested that you would need a 1,000 times more mRNA than saRNA to
2 elicit an immune response.

3 Quite the contrary, Dr. Fuller testified that 15 micrograms is already
4 above the upper limit of what a POSA would expect to see in a mouse model
5 like that. As she put it, the upper limit is about 10 micrograms. And so any
6 response, any additional dose after that you would expect to see negligible,
7 if any effect.

8 JUDGE COTTA: Can you address or help me to harmonize that
9 testimony with the examples in the record, including, I think Petsch, that use
10 a dose that's well above 15 micrograms?

11 MR. PRUSSIA: Yes. They use 80 micrograms. All right. So just for
12 a couple things. One, the 15 micrograms that's in Brito is already more than
13 the 10 micrograms that's disclosed in our patents, in Example 23, and a very
14 similar mouse model. Okay.

15 Brito used 80 micrograms and they were able to see response in the
16 context of the influenza vaccine that they were testing in that particular
17 model. But that's already an exceptionally high dose. And it doesn't in any
18 way suggest that if you were to administer 80 micrograms in the context of
19 this RSV, that you would see the same thing. Because as Dr. Fuller put it, in
20 this model, a POSA would not expect to see a dose response above 10
21 micrograms.

22 So if we go to Slide 80, the third point on Brito then, Your Honor, is
23 well, it's -- it feels as though they're putting the burden on us to show that
24 these vaccine technologies are not interchangeable. It should go without
25 saying, but I have it on the screen to remind all of us that this is their burden.

1 They're theory of the petition, they're the master of their petition.
2 They're theory is that a person of skill in the art would look at these non-
3 mRNA, non-LNP technologies and have a reasonable expectation of
4 success. That's their theory they went with, where is their evidence? What
5 document do they show you to support that a POSA could do that?

6 Instead, they try to shift the burden on us. But you know what? Brito
7 is the only evidence in the record that these technologies are not
8 interchangeable. It's their burden. And the Federal Circuit has told us that
9 unpredictability results equates more with non-obviousness than
10 obviousness. And what we see here throughout the prior art, is evidence of
11 unpredictability.

12 And let me just, if I can, point out one more thing about Brito. They
13 held the delivery vehicle constant. The other thing about the grounds, is that
14 they all rely on different delivery vehicles. And we know from Dr. Chan,
15 Slide 75, the choice of delivery system matters. And that just makes sense.

16 I mean, these different delivery systems, they have different
17 chemistries, and this idea that you can just swap out results that you
18 observed with Dr. Geall's cationic nano emulsion and get the same thing that
19 Petsch got in protamine, and apply that to LNPs, that just doesn't -- that's not
20 valid in any science, and again, they don't come forward with any actual
21 evidence that establishes that for you. Go to Slide 77.

22 Again, this is their burden. They chose to come forward with this
23 theory of the petition. Where is the evidence that you can jump from DNA
24 to saRNA and have an expectation? We asked their expert. Okay. We
25 asked them, what's your best evidence, give me a piece of paper, give me
26 something. And the only thing he responded was, it's a concept. A concept

1 is not evidence. Dr. Griffin has never studied this. He's not a nucleic acid
2 scientist. Go to Slide 78.

3 Dr. Fuller is the only one who has experience in this space. She's
4 done head-to-head studies. And just like Brito, she reached the conclusion
5 that they are not interchangeable. And what I'd like to do if I can is pass to
6 Ms. Curtis, unless there's any additional questions on anticipation or
7 obviousness?

8 JUDGE COTTA: Yes, go ahead, please.

9 MR. PRUSSIA: Thank you.

10 MS. CURTIS: Thank you. And may it please the Board, Annaleigh
11 Curtis for Patent Owner, Moderna. I will be addressing objective indicia of
12 non-obviousness. And if I could have Slide 102 on the screen. If there were
13 ever a case where objective indicia can and should be dispositive, it is this
14 case.

15 I want to spend the bulk of my time today on nexus, since that's where
16 Petitioners have focused. But I would also like to address Mr. Krinsky's
17 suggestion in his argument that there's a dispute about whether the vaccines
18 at issue here embody the claims.

19 I would also like to address his argument that the elements of the
20 claims were known in the art. And then, if I have time at the end, to discuss
21 the evidence of objective indicia that has gone largely un rebutted.

22 But just before I get into nexus, I do want to briefly summarize the
23 un rebutted evidence of objective indicia. There's no dispute here, as we'll
24 discuss, that SpikeVax and Comirnaty do embody the claimed
25 betacoronavirus vaccine platform, that they're highly advocacies, that they
26 together dominate the market for COVID-19 vaccines. And that they

1 changed the trajectory of the global COVID-19 pandemic on an
2 unprecedented timetable, despite intense competition from other vaccine
3 makers, going from sequencing to authorization in less than one year.

4 But as to nexus, Petitioners focus in their reply on co-extensiveness.
5 But that's not required, as you know, for a finding of nexus. And to simplify
6 the issues for the Board, Moderna is relying now only on reasonable
7 commensurateness and the unique characteristics of the claimed invention,
8 neither of which are rebutted.

9 JUDGE COTTA: So just to be clear, you're not relying on
10 presumption?

11 MS. CURTIS: That's right.

12 Starting with reasonable commensurateness, if I could have Slide 104
13 on the screen. The Federal Circuit has explained that objective indicia need
14 only be reasonably commensurate with the scope of the claims. And it has
15 been clear that patentees do not need to show evidence regarding every
16 single embodiment of the claims.

17 Dr. Krause explained in his declaration that one of the chief benefits
18 of the claimed invention is that it can be used across different
19 betacoronaviruses. So the argument that Petitioners make about SARS-
20 CoV-2 didn't exist at the time of 2015, that's the whole point of having a
21 pandemic preparedness vaccine platform, you can not always anticipate
22 what new viruses are going to come about. But with this platform, you are
23 able to very quickly generate a vaccine against newly arising
24 betacoronaviruses, the viruses that come out.

25 And the evidence of record here bears that out. The claimed vaccine
26 platform has been quite successful even when specific formulation, protein

1 choice, and other unclaimed details are changed. And to talk through how
2 that's the case, I'd like to have Petitioner Slide 129 pulled up.

3 Now, I do want to note we've objected to this slide, this is all entirely
4 new argument by Petitioners, but I'll address it in discussing through why
5 commensurateness is one path to nexus here.

6 So Petitioners have said there's no evidence of objective indicia type
7 of certain aspects of the claimed invention. And I just want to rebut that,
8 because they're actually dead wrong on each of these points.

9 On the first point, the evidence of record is that the invention works
10 not just against SARS-CoV-2, but also against MERS. We know that from
11 the example, in the patent examples, 23 and 24. That's in our Patent Owner's
12 Response at 64 and 67 to 68.

13 It's also worked against the initial strain of COVID-19 despite
14 differences in formulation between SpikeVax and Comirnaty. That's in our
15 Response at 63. And has worked in successive iterations of those vaccines
16 that are targeted at seasonal variants. We argued that at 63 of the Response.
17 And Dr. Krause discusses that Paragraph 228 of his declaration, which is
18 Exhibit 2200. So we have here a multitude of examples of the claimed
19 platform working.

20 On the second point, again, the evidence in the patent itself, in
21 Example 23, shows that the claim combination worked encoding for the S2
22 subunit of MERS, so we don't just have evidence for the full-length spike
23 protein.

24 On the third point, there's evidence in the record on vaccines that use
25 unmodified mRNA that showed immune response generation. And that's at
26 Exhibit 2184 and we discussed that in the response at 63.

1 On the fourth point, Comirnaty and SpikeVax, as Petitioners
2 acknowledge, each have different LNP formulations, mRNA sequences, and
3 code on optimizations from each other. The parties agree on that.

4 So to the extent the Petitioner's fourth bullet here is meant to imply
5 that Comirnaty and SpikeVax each use the same structure as each other and
6 that that is the only structure that will work, that's incorrect.

7 And then finally, with respect to the last point regarding the fact that
8 the vaccines are developed in response to an unprecedented global
9 pandemic, those same factors were at play. There was a pandemic for all of
10 the 200-plus vaccine manufacturers, research institutions who were trying to
11 develop a COVID-19 vaccine.

12 Yet, the two that were able to do so most successfully, fastest, with
13 the highest efficacy, practiced the challenged claims. We argue that in the
14 sur reply at 27, and that's in Mr. Malakowski's declaration, 2197 at
15 paragraph 22.

16 The facts of *Rambus v. Rea* are instructive here. The Federal Circuit
17 there vacated and remanded the Board's finding of no nexus related to a
18 memory chip using a dual edge data transfer structure. The Board had found
19 no nexus based on the fact that the claims at issue did not recite a specific
20 clock speed and thus embraced slow memory devices.

21 Whereas the evidence of objective indicia that had been presented was
22 for fast memory devices. And the Federal Circuit there held that the
23 evidence of record showed that it was the claimed dual edge data transfer
24 functionality that enabled the praise speed of the embodying chip. And I
25 would submit that the case for nexus is even stronger here, where the

1 evidence of record indicates consistent success across numerous
2 embodiments.

3 Turning now to the --

4 JUDGE COTTA: Can I pause --

5 MS. CURTIS: Yes.

6 JUDGE COTTA: And let me just ask you a question. If we were to
7 find that Schrum discloses basically an mRNA nano protein of a lipid
8 nanoparticle and a vaccine, that seems to me like that's quite a long ways for
9 disclosing the platform that is alleged to be indicative of non-obviousness.
10 How does that impact your argument if we were to make that finding?

11 MS. CURTIS: Yes, Your Honor. So I would point you to, if we
12 could have Slide 109 on the screen. The *Chemours* case is very instructive
13 on this point. And what the federal circuit said there, is that the separate
14 disclosure of individual limitations, and of course, you know, we have
15 arguments about Schrum that Mr. Prussia addressed those.

16 At the very least, Schrum does not disclose the antigen, does not
17 disclose the immune response, neutralizing antibodies. We have a separate
18 disclosure of individual limitations. And the invention itself is a unique
19 combination of, as they say here, three inter-dependent properties, and we
20 have even more inter-dependent properties and elements here. That does not
21 negate a nexus.

22 Otherwise you could never have nexus where the invention is a
23 unique combination of known elements. And I think that is the situation we
24 have here. And that's well-established in the law. *Ranbus* also addresses
25 this as does the *Medtronic* case that we cite in our papers.

1 And I think it really helps to answer this question to think about the
2 unique characteristics of the claimed invention and how, you know, we have
3 all this unpredictability in the art as Mr. Prussia was just discussing.

4 So even if you have known elements, if you combine them in a unique
5 way and have a new way of putting them together, you have to have still
6 some path to nexus there. So if I could have Slide 103 on the screen.

7 The Federal Circuit has explained including in the *Fox Factory* case,
8 you know that a patent owner can also prove nexus by showing that the
9 evidence of the objective indicia is the result of the unique characteristics of
10 the claimed invention. And the evidence of record here is that the unique
11 characteristics of the claimed invention drive its success.

12 First, Dr. Krause opined, and we explained in our response that the
13 efficacy and safety profile of SpikeVax and Comirnaty is due to the unique
14 claimed combination and they haven't rebutted that. So there's the protected
15 feature of the LNP, translation of mRNA into the S protein or subunit, and
16 recruitment of adaptive immune cells to make antibodies. We explain that at
17 63 of our response and he explains it in Paragraph 228 of his declaration.
18 And if I could have Slide 107.

19 The evidence of record here is that SpikeVax and Comirnaty have
20 efficacy within 1 percent of each other, 94.1 percent and 95 percent
21 respectively. Despite all of the many differences they have in structure and
22 formulation, this unrebutted fact alone, we make this argument in the
23 response and in the sur reply, shows that what matters is what the vaccines
24 have in common, not all of these unclaimed features that Petitioners have
25 thrown out in their briefing.

1 Petitioners' briefing points to things like different mRNA sequences.
2 And you heard Mr. Krinsky talk about the 2P modification, there are
3 structural features like bio prime cap. They never actually make any
4 arguments or present evidence that these differences make any difference.

5 And we can see from the evidence on the efficacy that they don't
6 really make a difference. Ultimately, you'd end up in the same place in
7 terms of efficacy. And that shows that what's driving efficacy is the thing
8 that they have --

9 AUTOMATED VOICE: This proceeding is being recorded.

10 MS. CURTIS: That's okay. Which is what is claimed in the patents.
11 Petitioners also state, I'll just say briefly, that there are macroeconomic
12 factors that contributed to success. But again, I would say the reason there
13 was so much focus on development of the COVID-19 vaccine, is because we
14 had a global pandemic and we really wanted to solve that problem, which
15 was an unmet need at the time of the pandemic. And there were 200 entities
16 working on trying to get a vaccine to the market. Despite all that
17 competition, it was Moderna and Petitioners who were able to do so.

18 Now I'd like to address the new claim that Comirnaty and SpikeVax
19 don't practice the vaccine or there's some element that's not met here. If I
20 could have Slide 105. Dr. Krause presented extensive evidence, claim
21 charts, showing that both vaccines do practice the challenged claims. That's
22 Appendices C through F of his declaration. And if I could have Slide 106.

23 Petitioners' expert agreed. So we asked him in his deposition if he
24 prepared any claim charts, he confirmed he didn't. And we also asked him if
25 there were any elements that were not practiced by the vaccines, and he said
26 that, he talks about other elements of the vaccines, mRNA technology, the

1 defect protein translation, and immunogenicity, not claimed in the '127
2 patent. He didn't identify any missing claim limitations. So there's really no
3 dispute about that.

4 And then if I could have Exhibit 2255, this is the deposition of their
5 commercial success expert, Mr. Bakewell. I asked Mr. Bakewell, sitting
6 here today, you're not aware of any paper in these IPRs, where Pfizer and
7 BioNTech dispute that Comirnaty practices the '600 or '127 patents, right.
8 He said, I couldn't cite you anything. I think there's challenges as to validity.
9 And that's at Page 80, Line 17 to 22 of his deposition.

10 What they're pointing to now are just unclaimed features and they
11 certainly have argued that there are unclaimed features. What they haven't
12 argued is that the vaccines don't embody or practice the elements of the
13 claims.

14 So I addressed the argument about elements known in the art in
15 response to your question. So I have about a minute and a half just to kind
16 of do the highlights of the objective indicia evidence that we have put
17 forward and that has gone essentially un rebutted. And if I could have Slide
18 102 back on the screen.

19 I'll just start with commercial success and praise. There's certainly no
20 dispute about this. Just for the time period from 2/4/2020 when the vaccines
21 launched, to the end of 2023, SpikeVax and Comirnaty made a combined
22 \$30 billion just in the U.S. alone.

23 Pfizer is one of the largest pharmaceutical companies in the world.
24 Comirnaty was their top grossing product in 2021 and 2022. This is an
25 extremely significant product. SpikeVax and Comirnaty together make up
26 over 90 percent of the market for COVID-19 vaccines. And we have

1 evidence in the record that this success is due to the claimed combination.
2 We argue that in the response at 70. And that's also in Dr. Krause's
3 declaration, Exhibit 2200 at Paragraphs 224 to 244.

4 Dr. Krause, that goes down not only to efficacy, but also to the speed
5 of development, how fast we were able to get these vaccines out. We have
6 that in the response at 65. And Dr. Krause explains why that's tied back to
7 the claimed inventions at Paragraphs 173 to 175 of his declaration as well.
8 So for the last five seconds, I'll rest on our papers as to the remaining
9 evidence of objective indicia which has gone unrefuted.

10 JUDGE COTTA: Okay. Thank you. So would the parties prefer to
11 take a five-minute break or do you want to go straight through?

12 MR. KRINSKY: Take Your Honor's preference, as far as I'm
13 concerned.

14 MR. PRUSSIA: We're fine either way.

15 JUDGE COTTA: Do you want to keep going? Or get to lunch?

16 MR. MODI: I wouldn't mind a five-minute break, Your Honor.

17 JUDGE COTTA: Okay. We'll take a five-minute break.

18 (Whereupon, the foregoing matter went off the record at 12:11 p.m.
19 and went back on the record at 12:20 p.m.)

20 JUDGE COTTA: Okay, if everybody is ready, I believe you have like
21 one minute over, so you have 19 minutes.

22 MR. KRINSKY: And before we start the clock, may I raise one
23 minor administrative note?

24 JUDGE COTTA: Sure.

25 MR. KRINSKY: I just wanted to be consistent with your comments
26 at the beginning about confidentiality.

1 JUDGE COTTA: Yeah.

2 MR. KRINSKY: I'm going to refer in this next section to a couple of
3 confidential documents but I'm not going to say anything about them that
4 goes beyond what was already in the institution decision, or that I think
5 would even arguably be confidential, but I just didn't want to alarm anyone
6 when they come up and I wanted to explain with a note of apology why I
7 don't intend to bring them up on the screen.

8 JUDGE COTTA: Right, and that's certainly fine with me. I'm
9 assuming it's fine with the Patent Owner's office?

10 MR. PRUSSIA: That is correct, Your Honor.

11 JUDGE COTTA: Okay. You can begin whenever you're ready.

12 PATENT OWNER - ORAL ARGUMENT

13 MR. KRINSKY: All right, thank you, Your Honor. I'd like to hit a
14 number of the points on obviousness in what I hope is a useful order, but I'm
15 going to start with ADE just because we spent a lot of time on it. I want to
16 begin by answering Judge Majors' question about, you know, whether ADE
17 is an immune response, and the answer is, it is. And the record explanation
18 of that is in Dr. Griffin's reply declaration, Exhibit 1159, beginning at
19 paragraph 217. He actually quotes Dr. Fuller so I don't think this is a
20 disputed point, but ADE is caused by eliciting antibodies that link to bad
21 effects, if you will. On ADE, I think --

22 JUDGE COTTA: Are those neutralizing antibodies?

23 MR. KRINSKY: Well typically they're not neutralizing antibodies.
24 A neutralizing antibody is one way that typically people will try to avoid
25 ADE, is by eliciting neutralizing antibodies. The ADE, if I could just point -
26 - this is, I don't think this document is confidential, but I don't need to bring

1 it up on the screen. I just wanted to point Your Honors to it. It's Exhibit
2 2136. This is a white paper about ADE and about the state of the vaccine
3 during the coronavirus pandemic.

4 So to be clear, this is post-priority, but I think it nicely frames the way
5 people in the field look at ADE. And this expert report, this is at 4789, talks
6 about how, you know, the demonstration of some disease enhancement with
7 any candidate vaccine after viral challenge in animal models should not
8 necessarily represent a no-go signal for deciding whether to progress into
9 early trials and clinical development of a COVID-19 vaccine.

10 And it also says suggested data in animal models should not by
11 default prevent clinical development of vaccine candidates. So again, post-
12 priority, but I think that fairly reflects the way people in this field looked at
13 it. They were not actually deterred by the prospect that there might be some
14 ADE, particularly in studies like, and I don't know whether it's Jaume or
15 Jaume, however it's pronounced, that are in vitro.

16 I mean, that was not a test that showed any ADE in terms of enhanced
17 disease in any organism. And it did not, in fact, deter people. You know,
18 we had the point about it is being not an -- ADE being a type of immune
19 response, I think, thoroughly rebuts the notion this has anything to do with a
20 reasonable expectation of success because we're practicing the claim to the
21 extent it's relevant at all, it's the motivation and what people would have
22 wanted to do and the, you know, people were not, in fact, deterred.

23 If we bring up Slide 93, you know this is Du 2009. This is Exhibit
24 1031, this is after the papers by Yang and Nabel that my friend on the other
25 side spent a bunch of time on. And Du 2009, if we go to Slide -- well, first
26 of all, again focusing on the S protein again saying this is an important

1 target, again, working on a coronavirus vaccine using S protein, if we go to
2 Slide 97 Du makes it very clear they're working on full-length S protein.
3 So, you know, they were not deterred from full-length S protein.

4 Your Honor mentioned the Lang reference. I think you characterized
5 it as a failure but it in fact was people right on the cusp of priority date
6 motivated to use full-length S protein. It just wasn't steering, ADE was not
7 steering people away from making COVID vaccine -- coronavirus vaccines,
8 it was not steering people away from full-length S as the antigen for that,
9 and I didn't hear anything that would steer them away from this particular
10 delivery vehicle.

11 In fact, ADE, I think, provides a nice pivot to the question of the
12 delivery vehicle. You know, we heard a lot about interchangeability, but I'll
13 note that the Nabel reference which we heard a lot about today is a DNA
14 vaccine. You know, in the context of ADE, he certainly thought that
15 whether you would see ADE from a full-length spike was relevant. I agree
16 that it's relevant. I don't think it would have deterred anyone or that that
17 reference is all that particularly relevant. But it just goes to show that you
18 know, this notion of interchangeability is the wrong legal standard.

19 The question is, what would the person of ordinary skill in the art
20 have been motivated to do, and I won't repeat them here. We saw, in the
21 opening presentation, reference after reference expressing enthusiasm for
22 mRNA as one possible delivery mechanism.

23 And if we could bring up Slide 15, you know we've looked at it
24 before at Schrum, I didn't really hear any discussion. You know, we heard
25 some on anticipation, some arguments about picking and choosing, I did not
26 hear any real explanation of how Schrum failed to teach as, at least one

1 embodiment, the combination of mRNA encapsulated in an LNP expressing
2 an antigen of interest. That's the whole point, and that is something that we
3 would then be motivated to combine with any of Geall, Altmeyer, or Nash.

4 By the way, Altmeyer -- not only do Yang and Altmeyer both teach
5 full-length S protein, but Altmeyer specifically addresses RNA and found an
6 immune response, so.

7 Let's bring up Geall 2013. This is also important on the, you know,
8 how we look at different possible delivery mechanisms point, because it's
9 obviously Geall again.

10 I'm sorry. You can bring up -- I have a slide on this. It's Slide -- my
11 poor courtroom tech here is waiting for my slide number -- 74.

12 Geall describes his own, you know, Geall's own work as a proof of
13 concept that a vaccines based on RNA whether conventional RNA or self-
14 amplifying replicons are effective at eliciting functional immunity. That, to
15 me, is a pretty strong endorsement of the notion that conventional mRNA
16 and not just self-amplifying mRNA and certainly not just other mechanisms
17 were expected to succeed here.

18 Particularly when combined with, you know, as I said, the closest -- I
19 think I was dinged for having said that there were no failures and then my
20 friend mentioned Brito. I mentioned Brito in the opening, but if we go to the
21 Slide 121.

22 Now Brito, whatever you may think of whether 80 micrograms is a,
23 you know, desirable dose or not, it's certainly suggested by Brito itself that
24 80 micrograms of mRNA would be effective in generating immune
25 responses, and Brito itself attributed the results that Mr. Prussia focused on
26 to the low dose.

1 So I think you have to read Brito in the context of what Brito
2 itself says as, you know, this is another teaching that we would expect
3 mRNA to work, even if perhaps you need to adjust the dose from something
4 that's really low.

5 There was also some discussion of the Petsch reference. Petsch, I
6 mentioned earlier as an example of a successful proof of concept of a non-
7 self-amplifying mRNA vaccine. I just wanted to flag, and this is another
8 document, so I'll just direct it to the Board to, here's Exhibit 2050. You
9 don't need to bring it up because, again, it's confidential, but there, in
10 Exhibit 2050, this is a Moderna -- Bates number is MOD 001416764 to 65.
11 Petsch is cited by Moderna itself to the FDA as evidencing success in animal
12 models.

13 And while I'm on Moderna's FDA submissions, Exhibit 2057 which I
14 believe Your Honors quoted in the institution decision also points to a
15 number of these articles and specifically says the POSA would not be
16 deterred and, in fact, would have been enthused, notwithstanding the
17 possibility of ADE.

18 Shifting gears, you know, there was a suggestion that, you know,
19 expressing a protein doesn't always yield an immune response, and there
20 was a quote from Dr. Griffin. Dr. Griffin, in that quote, wasn't talking about
21 any particular antigen. He wasn't necessarily even talking about an antigen
22 at all. He just said if you express a protein, you need more than that.

23 What I think the record reflects here and that's relevant to reasonable
24 expectation is that in every instance where there was an S protein expressed
25 from a DNA vaccine or where an S protein was administered, not only was
26 there immune response, there were neutralizing antibodies.

1 We'll go to Slide 78. You know, both Wang 2015 and Yang 2004
2 describe neutralization as something that was observed. And I'll submit,
3 there's no reason to think that if you expressed an mRNA vaccine -- excuse
4 me, if you express S protein in an mRNA vaccine, you wouldn't get the
5 same thing. You know, that's a function of the antigen.

6 And maybe, you know, to the secondary indicia point we heard later
7 on, maybe we would need to adjust the formulation in various ways that are
8 not articulated in the claims in order to have something that had a high
9 degree of efficacy or was a big success, but in order to have some
10 neutralizing antibodies, which is all that Claim 3 requires, it doesn't require
11 some threshold limit of neutralization and certainly to have an immune
12 response, you would expect to see that.

13 And we looked earlier at the fact that, you know, Schrum, although
14 Schrum doesn't have vaccine data in the four corners of the Schrum
15 reference itself, it certainly shows that this expression vehicle, mRNA plus
16 LMP, can be used to express things. That's my Slide 108.

17 You know, and this, I think, was also cited in the institution decision
18 on this record. I think Your Honor alluded to it, but Paragraph 998 of
19 Schrum shows data with heightened levels of expression of this particular --
20 I can't remember which protein it is offhand, but it -- you know, you would
21 get expression.

22 And then going to Slide 75, in the specific context of the S protein,
23 Dr. Fuller conceded that once you know that the spike protein is expressing,
24 you would expect that a vaccine candidate would induce an immune
25 response. When she was asked that in deposition, she said, that was your

1 expectation? Answer, yes. Couldn't have been clearer. This is Exhibit
2 1104, Page 50 to 51.

3 That's reasonable expectation of success right there. There's no
4 greater threshold level of efficacy required, and I haven't really heard any
5 explanation for why there wouldn't be a reasonable expectation that when
6 you administer mRNA you'd get at least some expression.

7 The closest that we've seen is an allusion by Mr. Prussia to the size of
8 the molecule. They pointed to no failures based on the size of the molecule,
9 but I did want the Board to note that in Geall 2013, which we talked about a
10 little earlier, the relevant polypeptide was 9,000 base pairs, which is larger
11 than the one here. Now, some of that was the self-amplifying material so
12 that's why there was some question about how big the ultimate protein was.

13 But in terms of being able to get it into the cell and get it translated,
14 plainly that worked. We propose that, likewise, reasonably expect here that
15 Schrum's teaching that you could use this to express any of the various
16 antigens in Geall, including coronavirus spike protein, that would be the
17 reasonable expectation.

18 JUDGE MAJORS: I imagine when you administer these things,
19 you're not just giving, you know, one mRNA molecule. You're doing a lot
20 of it, so, sure, you might have some mistranslation of one strand but if
21 you're getting thousands or maybe millions of strands, some of it's going to
22 --

23 MR. KRINSKY: I think that's exactly right, and, you know, that
24 would be within the, you know, sort of reasonable lack of undue
25 experimentation to get an amount that would yield an immune response.
26 The same, by the way, is true of folding. You know, we have this whole

1 question about the, you know, whether the spike protein needs to form a
2 spike. That's not how I think the claims are properly read.

3 It refers to the S protein, which is a protein that forms a spike, and if
4 you encode that, you practice the claim. The claim doesn't recite expression,
5 let alone folding. But likewise, even if some of it misfolds, perhaps even if
6 all of it misfolds, you know, all that needs to happen is you generate an
7 immune response and you have Dr. Fuller saying you're going to get an
8 immune response, you're likely going to get an immune response.

9 JUDGE COTTA: If it misfolds, are you likely to get a neutralizing
10 antibody?

11 MR. KRINSKY: I mean, very possibly. There is -- I mean, I don't
12 see any reason to think misfolding so there's not a lot of record evidence on
13 what happens when it misfolds, because there's no evidence that it ever did.
14 But I think the reasonable expectation everyone agrees on is, give these
15 mRNAs to people, it's going to express, it's going to have epitopes that the
16 immune system can react to. And then you have an immune response, some
17 of which in every single vaccine study involving this S protein, including
18 those from DNA, includes neutralizing antibodies.

19 JUDGE MAJORS: Just, and Patent Owner can address this too, so on
20 this record, do we have any evidence when there was an attempt to express
21 the S protein full-length that, in the aggregate, there was any misfolding, or
22 lack of expression on the whole?

23 MR. KRINSKY: No, not to my knowledge, standing here right now.
24 And I do want to leave a little bit of time for my colleague, Mr. Modi, but
25 two final real quick points, if I can. Sorry for the speed round.

1 You know, there was a lot of discussion of the OSI case, and how,
2 you know, the level of efficacy that was needed, the unpredictability of the
3 arc. OSI was a method of treatment requiring therapeutic efficacy that's not
4 present here.

5 And the question for unpredictability is not predictability writ large in
6 the field, that's what Allergan makes clear, but predictability in practicing
7 the claimed invention. And I submit on this record, there really is not a lot
8 of unpredictability, there's really not any unpredictability, that you would
9 get some expression, and that you would get some immune response, and
10 you would get some neutralizing antibodies.

11 And I think rather than consume all of Mr. Modi's time, I will sit on
12 the -- our papers and what I said earlier on secondary indicia other than to
13 say that they really haven't come close to showing that the particular
14 features that are in the combination as opposed to the prior art and as
15 opposed to the other aspects of Comirnaty and the Spikevax that I pointed
16 to, are responsible for a nexus, it was a big change from the POR that they're
17 not relying on a presumption.

18 You know, so all they have is this sort of incorporation by reference
19 of their claim chart saying, well, okay, Comirnaty and Spikevax are within
20 the claims they say, that isn't enough to link the product to the patent here as
21 opposed to other patents and the prior art.

22 And in any event, the prima facie case about the nexus is
23 overwhelming on each of the three grounds independently. So, if there are
24 no further questions, I'll yield to Mr. Modi.

25 MR. MODI: Thank you, Your Honors. Just a couple of quick points.
26 One is, if we go to Slide 54, I'm going to address the question on 397 again.

1 I think Your Honors asked the question, well, do we have anything in
2 Schrum that says, what does modified RNA refer to?

3 I think, actually, if you look at paragraph 187 of Schrum, that tells us
4 modified RNA includes, for example, mmRNA. And then we did not hear a
5 response from the other side that their own Patent Owner response admitted
6 that Paragraph 397 actually refers to mRNA, which I pointed to before.

7 And then finally, on that, on this whole point of how do we get to the
8 LNP vaccine. So like I said, 343, 342, 378 that's one way. Second is 397
9 and the third way is what the Board pointed to in the institution decision, and
10 that's at '127 institution decision 85, note 39, and that was with respect to
11 Paragraph 346.

12 I heard my colleague on the other side say, well in the section of the
13 vaccine section, there's no reference to the LNP. Well, there is if you look
14 at Paragraph 346. And I think that was the point that was made in the
15 institution decision.

16 With respect to the construction of mRNA, the only point I'll make is,
17 again, we did not hear a response from the other side on incorporation by
18 reference to Geall 2012. I gave the Board the citation to that. That's in their
19 own patent. And in fact, when they refer to Geall 2012 in their own patent,
20 they say that it is, for example, a mRNA. And that's at Column 40 of the
21 '127 patent, Lines 14 through 15. With respect to --

22 JUDGE MAJORS: Mr. Modi, I'm sorry to interrupt you. And just
23 for my -- was that a point that was actually raised in your papers, that
24 specific citation that you were just pointing to? I guess it's from, was it from
25 Schrum?

26 MR. MODI: The one about the '127 patent, Your Honor?

1 JUDGE MAJORS: Yeah, I'm sorry.

2 MR. MODI: Yes.

3 JUDGE MAJORS: The '127.

4 MR. MODI: No, it was not, Your Honor, and again because they
5 made such a big deal out of the -- in their surreply on the 397, saying it's not
6 related and the whole mRNA, sRNA. It's something that we noticed that
7 their own patent actually incorporates by reference, so this whole idea that
8 their patent doesn't include self-
9 amplifying mRNA just falls apart. I think it's fatal to the
10 argument here.

11 Couple of just quick points, on this point their patents actually don't
12 have any 3D imaging of showing spikes and no neutralizing antibodies. I'll
13 just point you to, again, their own expert's testimony that I pointed to at the
14 opening. It's Exhibit 1104, 6010 through 6018 are self-admitted them, and
15 you have the SARS-CoV S protein, and you're actually going to get
16 neutralizing antibodies.

17 And then the last thing I'll do is on the picking and choosing. We win
18 either way, whether you look at the invention case law or you look at the
19 picking and choosing, here under *Arkley*, the teachings are all related to each
20 other so, and if you look at *Kennametal* and if you look -- again, because the
21 teachings are so interrelated, we believe we win under anticipation.

22 And the very last point I'll make, Your Honors, is the challenged
23 patents. They claim it has data. I think if you actually look at it, you have
24 two working examples that deal with mice and rabbits, that deal with
25 MERS-CoV. There is no MERS COVID vaccine even today, right, no
26 MERS-CoV vaccine today.

1 And then those examples don't tell you the sequence for the protein
2 encoded. They don't tell you what mRNA components are, are they
3 modified, where they're modified. They don't actually give you the
4 formulation, Your Honors. And so it, of course, certainly would not have
5 been able to recreate the examples.

6 So, at the end of the day, from our perspective, what this comes down
7 to is that Schrum and Geall -- Schrum is their own patent. They're trying to
8 run away from it. At the end of the day, Schrum-Geall is simply their own
9 disclosure. You know, Mr. Prussia said something very interesting. He said
10 Schrum's disclosure, quote, is very different, and I gave the Board citations
11 earlier to Paragraphs 378 and 397 of Schrum that essentially appear
12 identically in the 127/600 patents.

13 I encourage the Board to look at Columns -- so if you look at Schrum,
14 Paragraphs 363 to 419, you'll find essentially identical copies of those in the
15 127/600 patents, for example in the '127 you can look at Columns 68 to 92.
16 So at the end of the day, they're trying to run away from Schrum and Geall
17 but the claims are clearly anticipated and are rendered obvious. So we
18 request that the Board find the claims unpatentable. Unless you have any
19 other questions, I apologize that I ran over time.

20 JUDGE COTTA: No problem.

21 MR. MODI: There's another speaker.

22 JUDGE COTTA: No other questions here.

23 MR. MODI: Thank you.

24 MR. PRUSSIA: Can I get an extra time?

25 JUDGE COTTA: Yes, of course. I'll give you --

26 MR. PRUSSIA: Okay.

1 JUDGE COTTA: -- an extra two minutes.

2 MR. PRUSSIA: Thank you, sir. I appreciate it.

3 JUDGE COTTA: Let me get this for you while I set the clock. Okay.

4 PETITIONER - ORAL ARGUMENT

5 MR. PRUSSIA: Okay. Thank you, Your Honors. We appreciate the
6 time and the consideration that the panel is spending on these issues. This
7 is, of course, an important proceeding. Let me first start to answer Dr. --
8 Your Honor, Judge Majors' question with respect to this disease
9 enhancement and immune response, specifically, an immune response.

10 And Dr. Fuller addresses this in her declaration, Exhibit 2199,
11 Paragraphs 580 to 584. And the answer is, it is immune mediated, which Dr.
12 Fuller explains is something that's different from something that neutralizes
13 the virus. So it's immune mediated but it's not the claimed immune
14 response. And --

15 JUDGE MAJORS: Why not?

16 MR. PRUSSIA: I'm sorry?

17 JUDGE MAJORS: Why not?

18 MR. PRUSSIA: Well, it's immune mediated in the sense that it drives
19 what you'll see in the papers being described either as a TH1 or a TH2
20 biased response. The TH1 is associated with no disease enhancement, right,
21 TH2 being -- it is. And that's the cellular response. That's a type of
22 immune response that results from, that is associated with disease
23 enhancement.

24 And with respect to Claim 3, in particular, that requires a neutralizing
25 antibody response. Dr. Fuller explains at the end of her Paragraph 584, that
26 neutralizing -- the type of neutralizing antibody

1 response that neutralizes the virus is different from what you see
2 that's associated with the disease enhancement.

3 JUDGE MAJORS: Right. I suppose what I was trying to get to with
4 my question was I saw some testimony to the effect of, there's neutralizing
5 antibodies and total antibodies --

6 MR. PRUSSIA: Right.

7 JUDGE MAJORS: -- bad antibodies, and it seemed to me, in just
8 reading that, my question was whether the so-called bad antibodies were still
9 somehow interacting in an immune fashion with the spike, but perhaps not
10 neutralizing it.

11 MR. PRUSSIA: I guess with -- yes, and the testimony from Dr. Fuller
12 with respect to how a person with skill in the art would understand Claim 3,
13 is that it's the level of neutralizing antibodies that provides protection, right.
14 And so that's what I mean when I say it's not the type of immune response
15 that's covered by the claims.

16 JUDGE MAJORS: For Claim 3?

17 MR. PRUSSIA: That's right. So, if we could go to Page 137 -- I'm
18 sorry, Slide 78. So the theory with this petition again is this theory of
19 interchangeability. That's the theory that they came forward with for a
20 reasonable expectation of success. And the question that Your Honors are
21 going to have to answer is whether there is any evidence of that. We are not
22 saying that they need to come forward with evidence that, you know, if you
23 get X level of neutralizing antibodies with DNA, that you're going to obtain
24 or observe Y level of antibodies with respect to mRNA. That's not what
25 we're saying is required.

1 There needs to be some reliable indicator of success. And there is
2 none, for a few reasons. One, because there is no experimental evidence in
3 the record at all with respect to any mRNA LNP. There is no -- there is
4 nothing with respect to the platform in the prior art.

5 And then number two, we know from Brito, and we know from Dr.
6 Fuller's testimony that you get different results from these different vaccine
7 technologies. And we know from Dr. Chan that you also get different
8 results when we're talking about delivery vehicles. So where is the reliable
9 indicia of success that a person with skill would have had with an untested
10 platform? It's not there.

11 And so this, if you go to Slide 79, this case, we submit, is very close
12 to the *Eli Lilly* case that was before the Board a few years ago in this way.
13 So that case, the petitioner argued that a person of skill in the art would have
14 had a reasonable expectation of success with, there were antibodies that
15 were claimed in that particular proceeding, and it was based on prior art
16 involving small molecule antagonists.

17 And the theory was, well, both the antibody platform and the small
18 molecules had the same mechanism of action. They had the same shared
19 theory, that they would interact by affecting the interaction between a
20 particular receptor and ligand. So they had a shared mechanism, right, but
21 there was no information in the prior art with respect to the antibody
22 platform.

23 Nonetheless, they argued that you would have an expectation of what
24 you could achieve with the antibody platform based on the small molecule
25 platform simply because they have this shared mechanism. That's very
26 similar to the kind of argument they're making here. And here we have

1 evidence that when you do jump from one platform to another, there is no
2 predictability. In fact, it's unpredictable.

3 So we think that the, if you go to the next slide, that the decision in *Eli*
4 *Lilly* is very informative and on appeal, the Federal Circuit affirmed the
5 Board's finding, emphasizing the burden of proof, and emphasizing also the
6 unpredictability of results equates more with non-obviousness than with
7 obviousness. And they don't have really anything in response to say to that.

8 If we go to Slide 87, it isn't just the *Eli Lilly* case, it's the *OSI* case as
9 well. Now, in that case, the Federal Circuit held that you need some data or
10 a reliable indicator of success, of course, in a field where there's a high
11 failure rate, and that's what we have here.

12 Now even if you credit the teachings in Petsch and Kallen and the
13 like, that doesn't overcome the fact that the majority of the field was in a
14 different direction and the reason for that was because of the challenges that
15 were known to be associated with mRNA.

16 And there was no, again, no efficacy data or any other reliable
17 indicator of success with any mRNA LNP vaccine specifically, and with
18 respect to the things that they point to as providing hope or promise, Petsch
19 and Kallen and Schlake and the like, all of those in particular Petsch
20 exclusively know that the results that were observed there were because of
21 the protamine complexation, which is not an LNP.

22 So if we go, if you pull that down, so on this interchangeability
23 question, again, where is the evidence that one can make, for example, some
24 sort of expectation based on results with DNA or even saRNA. These are
25 different technologies that utilize, that are structurally different. They're

1 functionally different, they utilize different biological pathways. They
2 present to the cellular machinery differently.

3 saRNA uses the cell itself to replicate or amplify production of the
4 antigen, and Dr. Fuller explains that this enhanced delivery, it resulted in a
5 more efficient system and you would only need a small amount of the RNA
6 product to administer. And that's because the cell would do the rest of the
7 work.

8 So it would result in a RNA product that was significantly more stable
9 than mRNA because it's a totally different construct and this is even
10 disclosed in Schrum, Paragraph 344. And so, we know that the head-to-head
11 studies show that results with saRNA did not translate to mRNA even when
12 you hold the protein choice and delivery method constant. We looked at that
13 in Brito.

14 And the reasons for that are explained by Dr. Fuller, Paragraphs 471
15 to 492 and Paragraph 544 to 550 of her declaration. It's because of these
16 differences in structure, and these differences of function. Essentially, what
17 their argument boils down to is the central volume. That simply because
18 mRNA is downstream and it's closer to making the resulting protein, that,
19 you know, if you have success with DNA you're going to have success with
20 mRNA. That's essentially their argument.

21 That just doesn't hold any water at all because number one, it hadn't
22 been done before in terms of an mRNA LMP vaccine, and again these
23 vaccines differ in their stability, they differ in the material that they use for
24 the immunogen. They differ in how they're presented to the body and how
25 the body responds to that presentation.

1 And again, these biological differences, they matter. And the idea that
2 they do not is simply counterfactual. It's counter to what we see in Brito.
3 It's also counter to just your intuition on how science works. I mean, the
4 biological system is highly complex and the idea that you can just simply
5 plug and play based on results you observe with a totally different platform
6 doesn't make sense as a matter of biology, it doesn't make sense as a matter
7 of chemistry when you consider the fact that these delivery platforms are
8 different as well.

9 On disease enhancement, if we go to Slide 60 -- and just to be very
10 clear, our arguments with respect to disease enhancement are with respect to
11 both motivation and a reasonable expectation of success. And picking up
12 where we left off on this point, look, Du teaches that results that were
13 observed in the field were unpredictable. Different vaccine technologies
14 resulted in different levels of disease enhancement or disease enhancement
15 at all.

16 And what Dr. Fuller explains, when you have a situation like this,
17 when you have multiple different vaccine modalities exhibiting different
18 sorts of effects, there's a question about whether the S protein could be an
19 immunogen that could in fact enhance disease when used in the context of
20 that particular vaccine.

21 So the researcher in the field, their considerations with respect to the
22 type of vaccine that they would want to pursue for a Betacoronavirus could
23 be complicated by the fact -- by these observations of disease enhancement.
24 These are vaccines that are given to non-infected people. These are healthy
25 people. You don't want to develop a vaccine that's going to enhance their
26 disease and make it worse for them, to kill them.

1 And Dr. Griffin, if we pull up his deposition transcript, 2114, Page
2 124, Line 21 to 125 and Line 7, we asked him during his deposition whether
3 a person with skill in the art would need to see data to have a reasonable
4 expectation as to whether a vaccine containing, in this particular context, the
5 gene for the N and the M protein, whatever that vaccine caused enhanced
6 disease and early death, and he said yeah, you need to be able to see that
7 data to evaluate it.

8 Now this question, of course, is specific to M and N, but there's no
9 reason why that answer would be different for the S protein when you have
10 reported observations in the field of there being disease enhancement caused
11 by the S protein, and not only that, but that you would get different results
12 based on vaccine technologies. You would need to see the data.

13 So when we're talking about disease enhancement, it's not just
14 motivation, it's a reasonable expectation of success. If you need to see the
15 data to have, to be able to form an expectation -- the question was do you
16 have or would you need to see the data to have a reasonable expectation.
17 When their own expert says, yes, you do, that's pretty strong evidence that
18 they haven't met their burden on reasonable expectation of success.

19 If we go to Slide 62, you know the suggestion that disease
20 enhancement wasn't a big deal, I mean that's also just contrary to the work
21 that petitioners did post-priority. They themselves in post-priority consider
22 disease enhancement to be a dreaded effect and because of that, they were
23 not laser focused on a full-length spike protein.

24 One of the constructs that they were investigating was something
25 called the RBD or Receptor Binding Domain. So to summarize, look,
26 disease enhancement, it is very much a real concern as of the priority date.

1 And a person of skill in the art would not have been laser focused on the S
2 protein, as petitioners suggest. They would have looked at all options,
3 including other surface proteins that did not show, were not associated with
4 disease enhancement, but also showed a neutralizing antibody response.

5 Just on Schrum, just a couple things. Schrum is different than the
6 disclosure in the 127' patent. We walked through that earlier today. There
7 is no disclosure, a single embodiment mRNA LNP vaccine for Schrum as
8 there is in the challenged patents. There is no disclosure in Schrum of any
9 working data associated with any mRNA LNP vaccine as there is in the
10 challenge patents.

11 And the approach that is the focus of Schrum is on therapeutics and
12 the testimony is that the approach for vaccines at the time was thought to be
13 different from therapeutics. Unlike for therapeutics, it was believed that
14 some degree of immune response was useful for an mRNA vaccine because
15 it kick starts the adaptive immune response.

16 And Schrum's disclosure of modified mRNA in a LNP, that was
17 counterintuitive at the time for a vaccine. And you see that discussed in Dr.
18 Fuller's report. Can you go to Slide 77? So, you know, again, this is their
19 burden and where is the evidence that they've shown you to support their
20 theory of extrapolation and interchangeability? They really haven't.

21 And the reason why this is important if we go to Slide 53, is when you
22 take -- they talk about the breadth of our claim. We should talk for a
23 moment about the breadth of their theory, right. One of their combinations
24 is Schrum and Geall. Geall discloses 500 immunogens.

25 Under their theory of the case, any mRNA vaccine, any claim to an
26 mRNA vaccine would be obvious over the combination of Schrum and

1 Geall, over the 500 immunogens that are disclosed in Geall. Keep in mind
2 that Geall included immunogens for rabies and HIV and we know, even as
3 we sit here today, we don't have an mRNA vaccine for those diseases.

4 And in fact, as I read them to you, and Your Honor pointed out, post-
5 priority documents showing that folks failed to develop an mRNA vaccine
6 for those pathogens.

7 So this idea that a person of skill, that it would be obvious and you
8 would have a reasonable expectation of success to use any of Geall's 500
9 immunogens and to stick them in Schrum's mRNA LMP and have a
10 reasonable expectation of success, that is, I would submit, very broad and
11 should not be and cannot be the law.

12 So with that evidence, what do they try to do? You heard them make
13 reference to post-priority documents. They're trying to backfill with post-
14 priority evidence and of course that is improper. And among the post-
15 priority evidence that they try to point to is testimony from Dr. Fuller. That
16 testimony they put up on the screen during rebuttal and earlier today, that's
17 post-priority, that's her experience trying to develop a vaccine for COVID-
18 19 in the 2020 timeframe.

19 And I'll just end with this because it's come up a few times. Slide 24.
20 Expression does not equal immune response. We have that from their own
21 expert and that we think is an important admission that answers many of the
22 questions that came up during the day today. So unless there are any
23 questions, I rest.

24 JUDGE COTTA: Okay. I'd like to thank both parties for your
25 attendance and for the presentations today. Just speaking for myself, I found
26 them helpful in clarifying the issues before us. The matter is now submitted

1 to the Panel for determination and preparation of a final written decision,
2 and we are now adjourned.

3 (Whereupon, the above-entitled matter went off the record at 1:01
4 p.m.)

IPR2023-01358 (Patent 10,702,600 B1)

IPR2023-01359 (Patent 10,933,127 B2)

PETITIONER:

Naveen Modi

Bruce Wexler

Eric Dittmann

Chetan Bansal

Paul Hastings LLP

naveenmodi@paulhastings.com

brucewexler@paulhastings.com,

ericdittmann@paulhastings.com,

chetanbansal@paulhastings.com

David Krinsky

Stanley E. Fisher

Williams & Connolly LLP

dkrinsky@wc.com

sfisher@wc.com

PATENT OWNER:

Emily R. Whelan

Wenli Gu

Anastasia Greenberg

Wilmer Cutler Pickering Hale and Dorr LLP

Whelan@wilmerhale.com

Wenli.Gu@wilmerhale.com

Anastasia.Greenberg@wilmerhale.com