

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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FORTE BIOSCIENCES, INC.,  
Petitioner,

v.

UNIVERSITY OF MASSACHUSETTS,  
Patent Owner.

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PGR2023-00014  
Patent 11,278,505 B2

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Record of Oral Hearing  
Held: March 20, 2024

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Before GEORGIANNA W. BRADEN, ROBERT A. POLLOCK, and  
MICHAEL A. VALEK, *Administrative Patent Judges*.

APPEARANCES:

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The above-entitled matter came on for hearing on Wednesday, March 20, 2024, commencing at 2:00 p.m., via video teleconference.

P R O C E E D I N G S

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JUDGE BRADEN: All right. Good afternoon, everyone. We are convened here for oral argument in PGR2023-00014, which challenges U.S. patent number 11,278,505. I'm Judge Braden, also appearing are my colleagues Judge Pollock and Judge Valek. Before we begin, I want to thank you for your flexibility in conducting this hearing via video today. Given that it is a virtual hearing, we're going to start by clarifying a few items. First, our primary concern is your right to be heard. If at any time during the proceeding you encounter technical difficulties that undermine your ability to adequately argue your case, please disconnect from the Webex, then try to reconnect to Webex, and let the panel know when you dropped off. If you cannot reconnect, please dial in using the phone number provided by our hearing and IT personnel.

Second, for the benefit of the Judges, opposing counsel, and especially our court reporter, please identify yourself when you begin your argument and speak clearly into your microphone. Please do not speak when others are speaking. Also, please, identify the specific slide numbers when referring to demonstratives.

Third, please mute yourself when you are not speaking. Finally, we have not received a notice from either party that business confidential information will be discussed or disclosed during the course of this hearing. That being said, please be aware that third parties may virtually attend this hearing. Therefore, if you plan to divulge any business confidential information, you need to inform the panel so we can wall off the third parties for that portion of the hearing.

1                   Petitioner's counsel, do you understand?

2                   MR. MILLS: Yes.

3                   JUDGE BRADEN: Patent Owner's counsel, do you  
4 understand?

5                   MR. FELDSTEIN: Yes, Your Honor. Thank you.

6                   JUDGE BRADEN: Very good. Per the Hearing Order, which  
7 is paper 31 in this proceeding, each party has 60 minutes total time to argue  
8 their case. We note, however, in paper 40, that Patent Owner has a counsel,  
9 Ms. Collette Corser, who has requested and received recognition under  
10 PTAB's Legal Experience and Advancement, or LEAP, program.  
11 Accordingly, Patent Owner is granted up to 15 minutes of additional  
12 argument time, as long as the LEAP counsel uses a portion of that time.  
13 Patent Owner is not required to use the entire 15 minutes.

14                  Petitioner, Forte Biosciences, Inc., has the ultimate burden of  
15 establishing unpatentability. Therefore, Petitioner will open the hearing by  
16 presenting its case as provided in its Petition regarding the alleged  
17 unpatentability of the challenged claims. Petitioner may reserve rebuttal  
18 time, but no more than half of its total argument time.

19                  Thereafter, Patent Owner, the University of Massachusetts, will  
20 respond to Petitioner's arguments. Patent Owner may preserve surrebuttal  
21 time of no more than half its total argument time to respond to Petitioner's  
22 rebuttal. Otherwise, the parties may use its allotted time to discuss the case  
23 however you choose. We ask, however, that you make it clear which  
24 challenges and claims you are addressing. In order to ensure clarity of the  
25 record following the hearing, please ensure that the court reporter has a list  
26 of spelling words to make sure that there is no miscommunication so unless

1 you have already done so.

2 Lastly, we ask that the parties please hold any objection  
3 regarding opposing parties argument until it is your turn to talk. To be clear,  
4 we will not take any objections during a party's arguments. You must wait  
5 until it's your time to talk to note any objections. I will maintain a clock and  
6 inform the parties when they have five minutes left. That being said, I think  
7 it prudent if you also keep track of your own time. So, let's get started with  
8 appearances from both sides. We will start with Petitioner.

9 MR. MILLS: Hi. My name is Jad Mills, counsel for Forte  
10 Biosciences, Inc., and with me is Mike Rosati, lead counsel for the  
11 Petitioner.

12 JUDGE BRADEN: Very good. Thank you. And Patent  
13 Owner.

14 MR. FELDSTEIN: Your Honor, Mark Feldstein from  
15 Finnegan Henderson on behalf of Patent Owner, University of  
16 Massachusetts. I'm joined by my colleague, Collette Corser, who will also  
17 be speaking today.

18 JUDGE BRADEN: Very good. Thank you. Petitioner, do you  
19 wish to reserve any rebuttal time?

20 MR. MILLS: Yes, Your Honor. We would like to reserve 20  
21 minutes, please.

22 JUDGE BRADEN: Twenty minutes. Very Good. Are there  
23 any questions or issues the parties would like raise before we begin, starting  
24 with Petitioner?

25 MR. MILLS: No, Your Honor. Thank you.

26 JUDGE BRADEN: Patent Owner?

1 MR. FELDSTEIN: No, Your Honor. Thank You.

2 JUDGE BRADEN: Very good. Petitioner, you may begin  
3 your arguments when ready.

4 MR. MILLS: Thank you, Your Honor. Good afternoon. I'd  
5 like to begin on slide 2, please. So this is just a slide showing the grounds of  
6 challenge and the challenge claims. I'm going to start with the 112 ground,  
7 and then we can talk about the prior art ground. There are two 112 grounds.  
8 I'll talk first about written description. One of the key problems with the  
9 '505 patent is that its claims are incredibly broad, and the disclosure in the  
10 specification is incredibly limited. We see this as a preview looking at  
11 Claim 1. The claims are broadly directed to administering any inhibitor of  
12 IL-15 or the IL-15 receptor. What we'll talk about today is the incredible  
13 breadth of these claims.

14 Anything that inhibits IL-15, anything that inhibits the IL-15  
15 receptor, or any of its subunits to any degree, and it could be anything that  
16 inhibits it. Any antibody, small molecule, peptide, nucleic acid, and still  
17 others. The claims are so broad that they're not limited to molecules that  
18 interact with IL-15 or the IL-15 receptor themselves. Patent Owner's expert,  
19 Dr. Damsky, clarified that the claims include any inhibitors of any of the  
20 subunit or anything upstream or downstream of IL-15 that affects the  
21 signaling pathway.

22 So the scope of these claims is truly immense. With that in  
23 mind, I'd like to turn briefly to the legal requirements for written description.  
24 Please turn to slide 6. Obviously, the Board is well aware of the legal  
25 standards for Written Description. In fact, the Institution Decision provides  
26 a concise analysis of that. Sufficient description of the genus requires

1 disclosure sufficient so that a skilled artisan can visualize or recognize the  
2 members of the genus.

3           This might be accomplished in several ways. It might be  
4 accomplished by disclosing species representative of the genus, by  
5 disclosing structural features common to the members in the genus, and  
6 when the claims are defined functionally, it might be satisfied if the art has  
7 established correlation between identified structure and function. As we will  
8 discuss, none of these requirements is satisfied here. Please turn to slide 7.

9           While the law identifies what must be present, the guidance in  
10 the case law also informs us about what is not sufficient. What we know is  
11 non-sufficient, broad aspirational discussions in a specification. A wish, a  
12 plan is not good enough. The cases explain that a patent is a hunting license.  
13 The question is what have the inventors themselves invented? And we know  
14 that a research hypothesis doesn't satisfy the requirements, but a hunting  
15 license and wishful thinking is all that the '505 patent gives us for written  
16 description support for the broad, broad genus that is claimed. Please turn to  
17 slide 8.

18           So one final point on these written descriptions' legal standards,  
19 and this also, of course, was recognized in the Board's Institution Decision.  
20 The Patent Owner incorrectly argues that there's some critical distinction for  
21 written description between composition of matter and method claims. But  
22 the key point of the analysis is that an inventor cannot lay claim the subject  
23 matter where he or she has not provided a description that is sufficient to  
24 distinguish what infringes from what does not. That is true whether it is a  
25 method claim or a composition and matter claim. For this case, they claim a  
26 massive genus, and their argument that the claims are method claims is a

1 semantic distinction without a difference. Please turn to slide 9.

2 JUDGE BRADEN: Counsel, so what do you say about Patent  
3 Owner's arguments that their invention really is about use of a group of  
4 compounds that are well known in the art, and it's just this novel use of those  
5 compounds to treat vitiligo, and they cite to the Uropep case. Why is that  
6 not distinguishable from the Rochester case?

7 MR. MILLS: So they want to say that it's a use and therefore  
8 they don't need to provide written description of the genus, and that's simply  
9 not correct. The invention, whether it is a method or whether it's a  
10 composition, they must provide written description to be able to distinguish  
11 infringing methods from non-infringing methods. And the focus of that  
12 analysis is all about the scope of the claims which are incredibly, incredibly  
13 broad and comparing that to what is disclosed.

14 We're going to talk about that in some depth today, but what the  
15 only working example that is disclosed is so narrow that it simply does not  
16 support the massive breadth of that genus. And that's true whether one looks  
17 at exactly what's disclosed in the patent. It's true, whether you look at the 20  
18 individual inhibitors that were molecules that the patent recites, and it's true  
19 regardless of all of the additional documents that they've pointed to in their  
20 patent response.

21 JUDGE BRADEN: What --

22 JUDGE VALEK: Counsel?

23 JUDGE BRADEN: Oh, go ahead, Judge Valek.

24 JUDGE VALEK: Counsel, this is Judge Valek. I have a  
25 question about the scope of that genus. Does Claim 1 encompass the use of  
26 any IL-15 or IL-15 receptor inhibitor, or does it also impose a functional

1 requirement on those inhibitors? That is, that they are capable of being  
2 administered in an amount that is therapeutically effective to treat vitiligo.

3 MR. MILLS: So there does seem to be both a requirement that  
4 there be an inhibitor of IL-15 for the receptor, which is incredibly broad in  
5 itself, as well as a functional requirement. Yes, regarding the purpose of the  
6 administration.

7 JUDGE VALEK: In Petitioner's view, what is that functional  
8 requirement?

9 MR. MILLS: So, the requirement is that it's the inhibitor that is  
10 useful for treating the vitiligo, right? This is one of the critical problems  
11 with their specification, right? They have this extremely limited, very  
12 narrow disclosure of a single working example with a single antibody. That  
13 disclosure doesn't actually tell us what it is they've used. It's a black box,  
14 essentially. There's no disclosure. This one is the things that we want to  
15 talk about today.

16 There's no disclosure of the sequence, no disclosure of a  
17 structure, and critically no disclosure of the epitope that is being bound and  
18 the portion of the function that is been performed. So the extremely narrow,  
19 narrow disclosure in the specification contrasts starkly with the breadth of  
20 the claims, which really extend to anything in the pathway upstream or  
21 downstream. The breadth is really simply breathtaking.

22 If we could turn briefly to slide 11. So slide 11 provides a  
23 summary of exactly that comparison. So this is a checklist of the  
24 information that the Board, the salient facts that Board identified in the  
25 Institution Decision, talking about the breadth of the claims and the  
26 narrowness of the description. And making that comparison, comparing

1 those two things, and seeing that there is simply no match or no comparison  
2 between them. We have a single working example, one antibody tested only  
3 in one mouse model. The working example vanishingly small.

4 When they point to the list of 20 compounds, whether you look  
5 at that one working example of the 20 compounds, or even other compounds  
6 that they canvas the prior art to go to discuss, it does not matter because the  
7 incredible breadth of the claims is not supported.

8 So these are key facts that were established in the Petition.  
9 They were recognized in Institution Decision. And during trial, really  
10 nothing has changed. So please turn to slide -- yes, I was on slide 11.

11 JUDGE BRADEN: Actually, before you turn to enablement, I  
12 want to make sure that I'm understanding this and making sure I am seeing a  
13 difference between this and the Uropep case, because it seems to me that  
14 Patent Owner has submitted a number of, you know, prior art references,  
15 they're making the argument that these types of compounds, these inhibitors,  
16 are very well known in the art. They've submitted a ton of the art, and they  
17 are saying this is very similar to Uropep. So why is that not the case? Why  
18 is it when they say, look, you've got inhibitors and we're using them to treat  
19 vitiligo? This is a new way of using these known, you know, compounds or  
20 components, why is that not the case?

21 MR. MILLS: So one reason is that they have not established  
22 the premise of their argument. There is no art recognized genus for what  
23 they're claiming. They have a hodgepodge of things that they put together;  
24 they've drawn a fence around it. It's not a recognized class. This case is  
25 nothing like Uropep, where they were dealing with PDE-5 inhibitors. The  
26 Juno case discusses this, the Juno case from the Federal Circuit discusses

1 this in detail. They distinguish the Uropep case.

2           They explain that in that case, the patent itself identified the  
3 compounds by chemical name and structure, structural drawings, and that  
4 the compounds there shared a common physical structure to fit the active  
5 site of the PDE5 enzyme to inhibit its activity. So there was a single binding  
6 site. There was a known identified common physical structure that was  
7 provided by the prior art. And here in contrast, in the Juno case, which is  
8 also similar to here in contrast, the patent does not disclose any sequence or  
9 structure for their working example. They don't tell us what is needed to  
10 find the -- they don't actually even tell us which portions of the targets  
11 matter to what they're doing. It's really a black box. So this case really is  
12 nothing like Uropep. It's more on the force with the Juno decision.

13           And even more particularly, I think very persuasive, looking at  
14 the Amgen decision, and I know the Amgen is an enablement case, but it  
15 is -- it's useful to look at it to understand for a 112 analysis.

16           So in the Amgen case, the genus that's claimed is much, much  
17 narrower than what we're dealing with here. The genus is limited to  
18 antibodies. It's not opened up to every single -- every potential compound  
19 out there. It is narrowed just to the antibodies, and also importantly, it's  
20 narrowed to a very specific epitope. So they had 26 antibodies there for that,  
21 just that one epitope. And the Supreme Court and the Federal Circuit has  
22 told us that that is not enough.

23           So 26 antibodies for one epitope where they have identified the  
24 key epitope is not enough for a 112 support for genus just to the antibodies.  
25 And here, the claims are much, much broader. The genus is much much  
26 broader. It's not limited to any particular epitopes, even of a single target.

1 It extends to at least the four targets, the three subunits of the receptor, the  
2 various iterations of receptor, the cytokine itself, and then it also extends  
3 downstream and upstream. So the case really is nothing like the Uropep  
4 case.

5 To illustrate this principle, the breadth of claims, I'd like to turn  
6 to slide 23 if I can. So this is slide 23. Yes, I'm showing you exactly what I  
7 am talking about. So there are three subunits, those three subunits are  
8 implicated in multiple different pathways and the effects of those different  
9 pathways and also depending on how one interacts with those pathways, the  
10 affects are different. So you have many different permutations that are  
11 implicated by their claims, most of which they don't even address  
12 whatsoever in their working example in any manner. For the one that they  
13 do address, it's not representative of even that example.

14 And then here, this key point, it does not even require that the  
15 inhibitor physically interact with any of those targets. It can be upstream or  
16 downstream. There's really nothing that's limiting it. And this was  
17 confirmed during trial. Please turn to slide 31. We asked Dr. Damsky about  
18 this. Here in slide 31 he's simply confirming that yes, any inhibitor of the  
19 alpha subunit, any inhibitor of beta subunit. We look at slide 32. Here he is  
20 confirming yes, any inhibitor of the gamma subunit. Now, this is the six  
21 different pathways with completely differential effects. These things that are  
22 all implicated by the broad, broad genus that they've claimed. So, and it gets  
23 even worse than that. So we're looking at slide 48, please. So here on slide  
24 48, you can see the problem.

25 Dr. Damsky testified, the claims are so broad that they  
26 encompass anything that inhibits what he called a biological effect of IL-15

1 or its receptor. So the patent claim also is encompassing anything that  
2 inhibits an IL-15 induced cellular response. So, the genus has expanded  
3 even further beyond IL-15 and the IL-15 receptor so that it's incredibly,  
4 incredibly broad. We have a summary of this on slide 35. I'll pause there  
5 for just a moment. So as we step back and consider the language of the  
6 claims and weigh this issue of claim breadth, what we see here are the  
7 claims are incredibly broad. They're not limited to any particular target.  
8 Whatever the compound is, it can interact with any portion of any one of IL-  
9 15 or any of the three subunits, any of these different six pathways. It can  
10 inhibit any point of various mechanisms of action. Those are discussed on  
11 slide 25.

12                   And making matters worse, it could inhibit at any time  
13 upstream or downstream in the pathway. That's something we discovered  
14 during trial from Dr. Damsky, as long as it inhibits it to any extent. He said,  
15 if there's one percent inhibition, even that's going to count. Even if we think  
16 just about the different antibodies that the claims implicate, it's difficult even  
17 to wrap one's head around the number of antibodies different that are  
18 implicated. I talked about Amgen earlier, and that illustrates exactly the  
19 problem.

20                   Here, there is no limitation to epitope, four different targets, as  
21 well as upstream and downstream targets because the number of antibodies  
22 that can bind to one epitope is already too large even when you have a  
23 disclosure of 26 antibodies as Amgen tells us.

24                   The number of antibody is implicated by the challenge claims  
25 which is simply incalculable we're told by experts and that's undisputed. We  
26 haven't even begun to discuss the small molecules, the peptides, the nucleic

1 acids, organic like molecules, other types of molecules encompassed by the  
2 claim.

3 JUDGE VALEK: Counsel, this is Judge Valek again. I have a  
4 question. I get that the genus of inhibitors is quite broad, but what about that  
5 functional requirement that it actually be effective for the treatment of  
6 vitiligo? How does one of skill in the art understand or figure out whether or  
7 not any individual one of these inhibitors actually meets that functional  
8 requirement? Is that described in the specification?

9 MR. MILLS: Right. So this is exactly the problem. Because  
10 of the limited nature of the disclosure, I'm turning to slide 28. Because it's a  
11 black box, because it doesn't tell us how it works or how they got the results  
12 that they want, and it gives us no reason to expect that the results they've got  
13 are going to work in a natural vitiligo as opposed to in and they can try the  
14 mouse model that they're using. There's no way that anyone has to be able  
15 to know which of the potential compounds, the compounds they said that  
16 might be used to know which of those might work and which ones won't  
17 work. We asked Dr. Damsky about this. Let me see if I can find that.

18 So I'm going to turn to slide 52, right? So first we asked him,  
19 can you tell by looking at them? Which really is, you know, for written  
20 description, you need to be able to tell. You need to have a common  
21 structure, you need you have structures that are representative. They put  
22 him forward as a person of ordinary skill in the art. He's putting himself  
23 forward as that, you know, there is a bit of a dispute as to the timing of that  
24 between the parties, but certainly at his deposition he is being put forward.  
25 As a person of ordinary skill in the art he says, if I'm given a structure I have  
26 no idea. I can't tell, the Patent Owner has no idea.

1           When the Patent Owner has no idea what compounds are within  
2 the scope of the claims in which you're not. That's a problem for 112. And  
3 then we asked him, what about assays? He said, well, you can do in vitro  
4 assays. You can do binding assays, and that gives you some indication.  
5 You could do in vitro proliferation assays, and that may give you some  
6 indication. But that doesn't tell you conclusively what the answer is. So we  
7 asked him what -- how can you tell? What else can you do? And he said, I  
8 wouldn't say there is an absolute standard. There's no absolute standard to  
9 be able to know what falls within these claims and what doesn't.

10           JUDGE VALEK: Counsel.

11           JUDGE BRADEN: Counsel.

12           JUDGE VALEK: Oh, go ahead, Judge Braden.

13           JUDGE BRADEN: Go ahead.

14           JUDGE VALEK: I was just going to say, it looks -- you go  
15 head, sorry.

16           JUDGE BRADEN: I just want to know if it is a one-to-one,  
17 meaning if it inhibits the IL-15 receptor, then it treats vitiligo?

18           MR. MILLS: There's certainly no evidence that that's the case.  
19 No, that's not true. So if we look at, I think, slide --

20           JUDGE BRADEN: I'm sorry. I believe that Judge Valek has a  
21 question for you.

22           JUDGE VALEK: Yeah. I want to follow up. Is there evidence  
23 that says it's not the case? In other words, is there evidence of molecules  
24 that are inhibitors of an IL-15 pathway, but they aren't effective for use in  
25 the recited method?

26           MR. MILLS: Yes, yes. So, I'm going now to slide 26. So here

1 on slide, 26, we talked about some of the diverse areas of the different  
2 pathways, the different things that happen. One of the things we discovered  
3 when they came in with their Patent Owner Response, and they were trying  
4 to argue that there was this class wide efficacy. Now, I can step back just  
5 for a moment to kind of describe their argument. Their argument was  
6 premised on this 2006 article from Dr. Waldman. So we're going to try  
7 some of these compounds in some different diseases.

8           They said, well look, that proves that there's class wide  
9 efficacy. And there was a later Waldman publication that says, well those  
10 ones, they didn't work out so well but we're going to try some others. You  
11 know, so decades go by, they're doing different diseases, they are not seeing  
12 class wide efficacy. Instead what they're saying is, sometimes I'll do an  
13 experiment and I see that it blocks binding. I'll do another in vitro  
14 experiment, I'll see that it blocks T-cell proliferation when I'm doing the in  
15 vitro assay.

16           But when actually put it in the body, I don't get the effect that I  
17 was getting when was doing things in-vitro. So, especially for these IL-15  
18 antibodies, which remember, because of the scope of the genus, they're  
19 claiming all of those IL-15 antibodies. And what they discovered is they are  
20 using some of these in IL-15 antibodies that they thought would be  
21 efficacious, and instead of it killing the CDA-positive T-cells, it's having the  
22 opposite effect, it's enhancing it.

23           So it is a very unpredictable field. There are several examples  
24 of IL-15 antibodies where they saw that. And so it simply is not the case  
25 that there is class-wide efficacy for a known genus. That's just not the case  
26 we're looking at here. One of the ways we know that --

1 JUDGE VALEK: Counsel, before you move on while we're  
2 still on slide 26.

3 MR. MILLS: Yes.

4 JUDGE VALEK: The citations at the bottom of the slide here,  
5 is that your best evidence in support of the fact that there's no class-wide  
6 efficacy?

7 MR. MILLS: So, I would say that the slide here is simply -- it's  
8 simply exemplary. Our papers contain the evidence that we've cited on that.  
9 You know, I --

10 JUDGE VALEK: Other than what you've cited here, is there  
11 anything else that you could point us to? Because it would be helpful if you  
12 could help identify that. There's a lot of voluminous papers here.

13 MR. MILLS: Right. Let me come back to that if I can with  
14 additional slides. Okay.

15 JUDGE VALEK: Thank you.

16 MR. MILLS: So what I wanted to point out is that even the  
17 patent and even their expert, even for the 20 compounds that they pointed to,  
18 they can't tell the difference between what they've claimed and that they  
19 haven't claimed. So here on slide 49, this is Dr. Plott and he's summarizing  
20 both the exhibits that the patent pointed to that Dr. Damsky relied on, that  
21 list of 20.

22 And he is also pointing to Dr. Damsky's deposition testimony  
23 here. So you recall that the pattern points to this compound in the middle,  
24 Cefazolin, and it's cited in the patent as being one of what they call an IL-15  
25 inhibitor. It points at some of these others, the row 26, 45, 50, et cetera, et  
26 cetera. They're pointing to things that are identified as IL-2 inhibitors, not

1 IL-15 inhibitors. And when you actually look at the reference to see what  
2 it's telling you, for example, that row, 26, 45, 50, it's inhibiting IL-2 to its IL-  
3 2 specific alpha subunit.

4 It has nothing to do with IL-15, right? So their list of 20 that  
5 they're pointing to, they can't tell the difference between the compounds.  
6 They have no idea what they're pointing at. When we asked Dr. Damsky  
7 about the Cefazolin, I'm turning to slide 50, we said -- we asked him, well, is  
8 it an inhibitor? He said, yes, it's on the list, so it's got to be an inhibitor.  
9 Does it satisfy the steps of the claim? He says, I don't know. I'm not sure. I  
10 can't tell. This is years after the critical date. With all the benefit of the  
11 specification, he can't tell. And there's another example of this as well.

12 Now this is cite 51. This is Tofacitinib. So it's inhibiting the  
13 exact same thing that half of these are the results of the signaling, the  
14 delta/gamma receptors that they're trying to target with the inhibition of IL-  
15 15. So, it is inhibiting the exact same thing. It's the downstream effect. It's  
16 a downstream effect of IL-15 he admits. And we asked him, is that an  
17 inhibitor of IL-15 within the meaning of the claim? He says, it is really  
18 complicated. It's really complicated.

19 He says at one point, well people wouldn't have thought that it  
20 was, they wouldn't have thought that was, but it's something that would have  
21 to be evaluated. And that's a problem. It's a problem when you cannot tell  
22 from their specification because there isn't a representative structure, there  
23 isn't a common structure to the genus. You can't tell what is within the claim  
24 and what it's not. So that is problematic.

25 And then we already talked about slide 52, where he says, we  
26 can tell from the structures. And not only can we not tell this from the

1 structures, but there's no absolute standard to determine between them. So,  
2 looking at slide 40, actually I want to go to 43. Okay. So this is not a  
3 random problem. It's a problem that arises because of the limited nature of  
4 the disclosure in this specification. Because it's the black box disclosure that  
5 doesn't tell you how they're getting, what they're getting. It doesn't give you  
6 any structural requirements for the claimed inhibitors. It doesn't give you  
7 the sequence or the structure corresponding with the working example, the  
8 binding site. It doesn't tell you how it binds or how blocks or how that's  
9 representative of that massive, massive genus. And it doesn't even tell how  
10 or whether it is targeting specifically IL-15 signaling.

11               So because of the critical deficiencies in the specification, what  
12 you're left with is just an iterative trial and error process. They have a  
13 massive pile of compounds that are implicated that they say might work.  
14 And they're saying, go up there and try it, but there's absolutely no guidance  
15 as to which will work and which are encompassed by the claims. I'd like to  
16 follow up with slide 46.

17               So though the Patent Owner argues that the '505 patent  
18 provided the proof of concept that every inhibitor of IL-15 or an IL-15  
19 receptor would work to treat vitiligo, Dr. Damsky's own statements made  
20 outside the context of litigation confirmed that still years after the critical  
21 date, one could still only engage in an iterative trial and error process,  
22 hoping that IL blockade is going to work in patients with vitiligo. He stated  
23 this in December 2021. This is years after the critical date. He said that  
24 only then a proof-of-concept study for IL-15 blockade in patients with  
25 vitiligo was underway.

26               And he said, we've all got our fingers crossed that it is going to

1 work. So at that time, years after critical day, one could still only conceive  
2 of a conditional response. If you were able to turn off that memory  
3 response, maybe you're looking at long lasting treatment. So after years of  
4 post-critical date trial and error, one still could only hope that proof of  
5 concept would someday be established.

6 The '505 patent is a paradigmatic example of an improper  
7 attempt to preempt the future in violation of Section 112.

8 JUDGE BRADEN: Counsel, with the time that you have  
9 remaining maybe we could redirect you back to enablement since we got  
10 you off target to talk a little bit more on written description with us.

11 MR. MILLS: Yes. Thank you. So looking at slide 20, we've  
12 talked about many of these same facts in the context of written description.  
13 But the same limited disclosure is a problem for enablement. I won't march  
14 through all of the underlying evidence again, but all of the salient facts  
15 showing that there's no enablement have been confirmed now at the end of  
16 trial. The claims are still just as broad and functionally defined. There is  
17 still a large variety and number of species that might be used, but essentially  
18 no guidance for which will operate similarly to the sole working example.

19 Why is there no guidance? It's because of that black box  
20 specification. It doesn't provide any structural requirement, explain how the  
21 inhibitors are structurally related, provide sequence or structure for the  
22 working example antibody. It doesn't provide the binding site. It doesn't  
23 explain how the antibody is binding and blocking, how that's representative  
24 of the entire genus, and it doesn't even demonstrate that the antibodies is  
25 only targeting IL-15 signaling.

26 So, with these facts, there's no question that the claims lack

1 enablement, and I'd like to turn to slide 16 to discuss that further. The  
2 claims are clearly not enabled under the controlling Amgen decision. We  
3 talked a little bit about this earlier, but the Supreme Court affirmed there that  
4 there is no enablement of a claim to an entire antibody genus, even when  
5 that genus is narrowed to the function of binding a specifically identified and  
6 individually tested epitope.

7           Just a single epitope, there was not enablement support even  
8 though they had 26 antibodies. Here, the broader claims of the '505 patent  
9 need much, much more support. That's another thing Amgen tells us. When  
10 more is claimed, more support must be provided. So in Amgen, even with a  
11 claim that was narrowed to a specific epitope and they had 26 antibody  
12 sequences specifically for that epitope, that was insufficient. It only  
13 supported claims to the specifically disclosed antibodies, but the challenged  
14 claims here are much, much broader than an Amgen, and the specification  
15 provides much less support. It fails to disclose the epitope. It doesn't --

16           JUDGE BRADEN: Counsel, why is that the case when these  
17 claims are directed to the method of use of something and not to the  
18 inhibitors themselves?

19           MR. MILLS: The claimed invention encompasses a broad  
20 variety of diverse methods. The method itself that's claimed is broad, both  
21 in the scope of the compounds that are implicated, but also the different  
22 means of approaching that. We talked about the three separate subunits,  
23 those three separate subunits. They appear in different iterations of the  
24 receptor. Depending on how you interact with those, you are implicating  
25 different effects.

26           And the specification doesn't tell us which effects are the ones

1 that are the one that they got and which are the once that you wanted. So  
2 they leave you completely at sea as to know, you know, when you're  
3 prospecting this field, which is all they've identified. Here's a field that we  
4 can look at. When you're prospecting that field, there's absolutely no  
5 guidance in the specification telling us which approach we need to be taking.  
6 The only thing that it really tells us is that if we want this effect, we should  
7 use mice for which we eliminate their entire immune system and replace it  
8 with CDA positive T-cells.

9           With regard to what we need be doing, what molecules we  
10 should be using, or the approach we should be taking, it simply doesn't tell  
11 us anything about it. And it requires undue experimentation because of that  
12 lack of guidance. There's really no direction that's provided. We have a  
13 summary of this on slide 62. So here are the Wands factors. And of course,  
14 the Board is very familiar with the Wands factors, whether we look at this  
15 simply based on Amgen, whether look the Wands factors, the result is the  
16 same. And I'll go through the factors briefly.

17           The factors four and five deal with the type of the claims. Here  
18 the claims are complex and they're functionally defined. The state of the art  
19 for using cytokines for treating autoimmune disease, and specifically vitiligo  
20 we're still at early stages. There were trials and attempts that had not been  
21 successful. So Factors 4 and 5 weigh against finding enablement. For  
22 Factor 8, we've talked at length about the extreme breadth of the claims.  
23 Factor 8 clearly weighs against enablement. For Factors 2 and 3, we've  
24 talked about that guidance and the working examples. They're extremely  
25 limited, they're extremely narrow. They clearly weigh against finding  
26 enablement. And the effects of --

1 JUDGE BRADEN: Counsel, I hate to interrupt you while  
2 you're going through your factors, but what are your comments about Patent  
3 Owner's arguments that this was not a nascent state of art, that there was a  
4 great deal of prior art written about it. There was great a deal known about  
5 the inhibitors. And so they didn't need to give that much guidance or  
6 working examples because it so well-known in the art. I think those, not to  
7 put words in the mouth of Patent Owners, but I believe that to be their  
8 arguments for those factors. What do you say?

9 MR. MILLS: Yeah. So that it's simply not true. There is no  
10 evidence that people were using cytokines for treating vitiligo. There is  
11 no -- this isn't a situation where there are existing classes of -- existing  
12 examples where they're working in the system. They're pointing to things  
13 where somebody is going out and they have a speculative disclosure of some  
14 compounds. And to give you an example, in one of their references, there's  
15 in vitro studies for six compounds, okay?

16 And then based on that, they go and their expert got confused  
17 about what's an IL-15 inhibitor and what isn't. And so he pointed to  
18 reagents, he point to intermediates in the synthesis process, and he said,  
19 okay, well, it's not just six, you know, he thought that it was something like  
20 50. And he says, well look, its well established now that there are all of  
21 these inhibitors out there, because he's counting reagents, he's counting  
22 things that aren't IL-15 inhibitors at all. But when you actually look at those  
23 references, what this is, they're doing in vitro studies.

24 All they are doing is looking at in vitro proliferation, which  
25 doesn't tell you what happens when you actually put this in the complicated  
26 system in the body. The complicated system in the body where there's

1 different iterations of the receptor with different effects with six different  
2 pathways that are involved. It's much, much more complicated. It is a  
3 completely different thing.

4               So there is no class wide efficacy. There's certainly no class  
5 wide efficacy for autoimmune diseases generally, and it's really a false  
6 picture that they're trying to paint of the state of the art. And one of ways  
7 that we know that is because of the unpredictability in the art. You know,  
8 that's Factors 1 and 2, talking about the experimentation and the  
9 unpredictability in art, as we mentioned earlier, they have situations where  
10 they're pointing at something, they're calling it an IL-15 inhibitor. But when  
11 you use --

12               JUDGE BRADEN: Counsel, you have five minutes before you  
13 start going into your rebuttal time.

14               MR. MILLS: Thank you. I would like to address, even if  
15 briefly, the obviousness case. So if we could turn to slide 64, please. So  
16 turning to Ground 3, I want to make sure that we discuss this, that broad and  
17 supported claims like those at issue here they certainly can lack 112 support  
18 also encompassing obvious subject matter. So a claim as obvious, as the  
19 Board well knows, when it encompasses an obvious embodiment, and that is  
20 the case here. We're not required to prove that every embodiment within the  
21 scope of the claim would have been obvious.

22               And it turns out that there is a commensurate nature between  
23 what they've disclosed and what is obvious because the claims here certainly  
24 include -- encompass their working example. And that is what is obvious in  
25 the circumstances, these Harris mice. I mentioned earlier, the Harris mice  
26 are a very narrow, narrow example where they've taken the mice, they've

1 have irradiated them to eliminate the immune system. They don't have, for  
2 instance, CD4 positive T regulatory cells. Many of the different  
3 complications that exist in reality are eliminated by irradiating the mice and  
4 then amping them full of CD8 positive T-cells.

5 So that's the only thing in there that is causing the lesions. Dr.  
6 Abbas talks about this. We've discussed it at page 16 of our reply, for  
7 example. He's talked about how this is very, very different from an  
8 immunological perspective. And I do just want to say a word about Dr.  
9 Abbas who really is evident in the field of immunology, decades of  
10 experience specifically studying these beta-gamma receptors, and, you  
11 know, really a father of the field in this circumstance. So he's talking about  
12 that this model that they use is a very limited, very narrow example.

13 And it happens to be an example in which it was obvious that  
14 using the TM beta one antibody, for instance, is depleting the CDA positive  
15 T-cells. So the one thing that we know in that mouse model, the only thing  
16 that's there, the only thing that can be causing those lesions is the one thing  
17 the Tm beta 1 antibody eliminates. And that what the Xing reference tells  
18 us. It tells us that they eliminate them from the skin. And that's the  
19 important part. The Patent Owner wants to point out and say, well, in the  
20 Xing reference, it wasn't able to get deep down into the hair follicle. It's not  
21 what we're talking about with vitiligo. The question is the skin. That's  
22 where the condition in the Harris mice, that's what that condition is  
23 happening. And the Xing reference tells us that the accumulation of the CD8  
24 positive T cells in a skin is what's precluded by the TM beta-1 antibody, and  
25 that why it's obvious.

26 So if I could just briefly touch on the secondary considerations.

1 The Patent Owner is arguing that there is unexpected results, but again, their  
2 results are just in that contrived mouse model that we're talking about. They  
3 say that the jack inhibitors, you know, they're not getting the same results.  
4 But the jack inhibitors, that's in the natural, the spontaneous vitiligo. They're  
5 not making an apples-to-apples comparison. So, in the context of these  
6 mice, it's entirely expected that administering the TM beta 1 antibody, but  
7 that's going to get the effect of its reversing the CDA positive T cells, which  
8 are the known cause of those lesions.

9 And then the second problem with their secondary  
10 considerations is they're simply not commensurate in scope with their  
11 claims. As we discussed, the claims are incredibly broad, they encompass  
12 many different classes of compounds starting at many points in the pathway,  
13 and they're pointing to this experiment that is much, much more limited in  
14 scope. Their evidence is testing one antibody and one mouse model. So,  
15 secondary considerations are addressed in greater detail on the briefing, but I  
16 will stop there unless there are any further questions.

17 JUDGE BRADEN: I do not believe we have any questions at  
18 this time. And we will note that you have 20 minutes of rebuttal time.  
19 Patent Owner, will you please confirm the amount of time you wish to  
20 reserve for rebuttal?

21 MR. FELDSTEIN: We're going to save 15 minutes for a  
22 rebuttal, Your Honor.

23 JUDGE BRADEN: Fifteen minutes. Very good. I'll try and  
24 give you a five-minute warning.

25 MR. FELDSTEIN: And just to let you know, Your Honor, I'm  
26 going to first address the Petition and the Petition arguments, and then Ms.

1 Corser is going to address the motion to exclude that is filed.

2 JUDGE BRADEN: Very good. You may begin your argument  
3 when ready.

4 MR. FELDSTEIN: Thank you. Could we have the slides,  
5 please? So I am going start us on slide 3 of the deck again. It's Mark  
6 Feldstein on behalf of Patent Owner. At a high level, there's no way to  
7 meaningfully address whether a patent has 112 support without considering  
8 the art. That's something that Petitioner and its declarants failed to do. They  
9 ignored the state-of-the-art, they ignored most of the 300 references that are  
10 incorporated into the specification.

11 And with that failure, their opinions are just not competent to  
12 say that there's a lack of written description or a lack enablement. It is very  
13 easy if you close your eyes to what's actually known to be able to say, this  
14 doesn't teach me enough to do it. If you gave me a computer invention and  
15 said, hey, is this described or enabled? To me, it probably wouldn't be,  
16 because I don't know the art, and I haven't investigated the arts. And that  
17 failure applies here very much so. What we have instead is we had  
18 admissions that, contrary to the premise of Petitioner's argument, there was a  
19 class-wide efficacy expected.

20 We have a quote from Dr. Abbas, or Dr. Abbas agreeing that  
21 you would expect something that antagonizes IL-15 singling would be  
22 useful in an autoimmune disease identified as having an IL-15 mechanism.  
23 That's what our inventors discovered. They discovered uniquely that vitiligo  
24 has a IL-15 mediate mechanism that is necessary and sufficient for vitiligo.  
25 And once you have that discovery, as Dr. Abbas, what they called an  
26 eminent expert in the field with decades of research, he agrees that you

1 would have expected something that antagonizes the signaling to be  
2 effective there. So that's an important common property that is expected in  
3 the art admitted by their expert, who they call a preeminent expert in the  
4 field.

5 In terms of the content of the art, we have in middle of slide 3,  
6 we have essentially unrefuted evidence that there were hundreds of known  
7 inhibitors. They do pick out a few of them, somewhere around 15, but more  
8 of a 300 known IL-15 or IL-15 receptor inhibitors disclosed in the art from  
9 1994 up to 2016, 2017. And that is something that their experts just didn't  
10 investigate, didn't know, and didn't consider at the time they offered their  
11 opinions. That, I think, renders their opinions rather meaningless.

12 A third --

13 JUDGE BRADEN: Counsel, do all of those inhibitors work in  
14 the same way? Do they bind at the spot? Do they all target the same  
15 mechanism?

16 MR. FELDSTEIN: They all inhibit the pathway. They are  
17 different types. Some are inhibitors of IL-15. Some of them are the  
18 inhibitors of the IL-15 receptor, and some are antibodies, some are  
19 molecules, some are peptides. And so there's been no question -- it has not  
20 been addressed, Your Honor, on the record because, again, Petitioner didn't  
21 investigate the art, didn't go through this, exactly how each one does it. I  
22 submit to you, Your Honor, that it doesn't matter how they do it, it matters  
23 that they do because this is the function, this what the art recognized was  
24 useful for treating IL-15 mediated autoimmune disease. And there was an  
25 expectation that if you could block the signaling, you would treat a disease  
26 that is mediated through that single pathway.

1 JUDGE BRADEN: And how much inhibition is necessary for  
2 the treatment of vitiligo?

3 MR. FELDSTEIN: You know, they raised the point about will  
4 a one percent inhibitor be effective? And, you know, clearly the claims do  
5 have an effective amount limitation, but there's agreement from Petitioner  
6 that you can just adjust dose, that dose adjustment is routine, and there's no  
7 requirement in the claim for a certain threshold of vitiligo reduction. There's  
8 a threshold for an effective amount to treat vitiligo, which would presumably  
9 be at least some reversal of the disease.

10 JUDGE VALEK: Counsel, this is Judge Valek. I have a  
11 question and follow up to that. Do you agree that the claims require the use  
12 of an inhibitor that is actually effective to treat vitiligo?

13 MR. FELDSTEIN: The claims recite administering an  
14 effective amount of an IL-15 inhibitor for the treatment of vitiligo. There's  
15 been no dispute from Petitioner that effective amount is somehow not  
16 described or enabled. But Petitioner has said instead is that adjusting dosing  
17 is routine. The methods of administration are routine, this was all part of  
18 their obviousness argument. They've conceded that these are all routine to  
19 be able to come up with an amount and deliver an amount. If we could -- I'll  
20 go to slide 63 for a second.

21 JUDGE VALEK: Counsel, before you move on, I'm not asking  
22 for Petitioner's position right now, I'm asking for Patent Owner's. Do you  
23 agree that the claim requires the use of an inhibitor that is actually effective  
24 to treat vitiligo?

25 MR. FELDSTEIN: The claim requires administering an  
26 effective amount, I agree with that.

1 JUDGE VALEK: Please go ahead.

2 MR. FELDSTEIN: And I was just going to answer your  
3 question. I was turning slide 63 to point to the fact that Petitioner itself is  
4 arguing that dosing can be determined by standard pharmaceutical  
5 procedures, and skilled artisans will appreciate the factors that may influence  
6 dosing. So dosing and an effective amount shouldn't be an issue with  
7 respect to the claim written description or enablement because Petitioner  
8 itself, A, hasn't argued that, and B, has conceded the opposite.

9 JUDGE VALEK: Counsel, this is Judge Valek again. But  
10 doesn't that assume that you know which of the inhibitors actually could be  
11 effective at any dose? In other words, after you figure out that an inhibitor  
12 actually could be used, a specific inhibitor could be used in the claimed  
13 method, then you could figure out the dose. But don't you have to figure out  
14 the predicate first—whether or not that inhibitor actually is effective in some  
15 amount to treat the disorder?

16 MR. FELDSTEIN: We can state on slide 3 where we are, Your  
17 Honor, on the screen. This is the agreement from their expert Dr. Abass on  
18 the left, that if you can antagonize IL-15 signaling, that is going to be useful  
19 in autoimmune disease that is mediated by IL-15. So it is the fact, though  
20 true, that if you're an IL-15 inhibitor and you inhibit the IL-15 signaling,  
21 you're going to treat a disease that, an autoimmune disease, that has an IL-15  
22 mechanism.

23 JUDGE VALEK: Counsel, I'm looking at the testimony you  
24 have quoted here. He says that one of skill in the art would expect that the  
25 species would be useful in these diseases if it antagonizes IL-15 signaling.  
26 Isn't the fact that something -- let me ask this a little bit differently -- The

1 fact that something might be expected to be useful is not the same as  
2 actually being effective to treat a particular condition, right?

3 MR. FELSTEIN: So, you know, without actually having tested  
4 these 300 plus inhibitors and finding one that doesn't work in vitiligo, all you  
5 can go with is how would a person of ordinary skill understood the  
6 specification? They're going to understand the specification that says an IL-  
7 15 inhibitor will treat vitiligo. That's going to be consistent with what they  
8 would have expected from the art, as admitted by Dr. Abbas.

9 JUDGE VALEK: Is it Patent Owner's position that all of those  
10 300 or so inhibitors would be therapeutically effective to treat vitiligo?

11 MR. FELDSTEIN: The position is, Your Honor, that a person  
12 of ordinary skill would've expected them to work for it. Again, there's been  
13 no evidence that any of them wouldn't work. Petitioner has primarily  
14 ignored these, and the expectation is that if you're an IL-15 inhibitor and you  
15 inhibit IL-15 at an effective dose or a correctly administered dose, you will  
16 be effective to treat vitiligo, yes.

17 Let me turn a little bit to slide 8 on the common autoimmune  
18 therapy, common autoimmune -- the expectation of common efficacy. By  
19 2015, cytokine targeting was recognized as an established field for treating  
20 diseases, including a number of autoimmune diseases. And 2014, even  
21 earlier, it was recognized that the strategy has been proven that IL-15 is  
22 going to work in autoimmune diseases. We haven't -- we couldn't fit it on  
23 the page, but the excised text from Exhibit 2014 is a list of about a dozen  
24 references in all sorts of different autoimmune diseases where the conclusion  
25 is that it always resulted in alleviating disease symptoms.

26 And so this is the foundation, the foundation that Petitioner's

1 experts ignored when reading the specification. With this foundation in  
2 place, a person of ordinary skill in the art reading this specification would  
3 understand that they've described and enabled the treatment of vitiligo by  
4 identifying it as having an IL-15 mediated mechanism.

5 I want to turn to talk about the mouse model for a minute. On  
6 slide 15, they have -- Petitioner raises issues and they have from the start  
7 that the mouse model that's used somehow doesn't -- it's not a meaningful  
8 model of vitiligo. They really don't have basis to say this. They're expert.  
9 We're not familiar with these factors. These are nine undisputed hallmarks  
10 of human disease that the Harris model reticulates. These are all undisputed.  
11 The Harris paper that's come out of Exhibit 1006 that has been, again, used  
12 in Example 5 in the specification is incredibly detailed, and it's incredibly  
13 detailed in how you initiate the disease, and then it takes weeks before the  
14 diseases fully develops. And then it has, for example, the signals, the  
15 common cytokines like IFN gamma that correlate with depigmentation in  
16 both human and in the mouse model.

17 I'm going to skip ahead just to slide 18. Slide 18 is a -- I'll go  
18 back to slide 17 if it's okay. Slide 17 is the claims. You're familiar with  
19 them. They are, as has been noted in the questioning, they're treated to their  
20 method claims using a class in a novel method. The novelty is not to the  
21 inhibitors that this is a fact that distinguishes all of the written description  
22 and enablement cases that Petitioner relies on. It distinguishes the facts of  
23 Amgen. It distinguishes the fact of Rochester, that the novelty here is not in  
24 the inhibitor of IL-15 or the IL-15 receptor. Hundreds of those were known.  
25 It's not purported to be put in novelty and the put in novelty is novel.

26 JUDGE BRADEN: Counselor, help me understand this. That

1 just because it's a method, it is therefore per se different. Do you not -- does  
2 Patent Owner not still have to show that what is a therapeutic effective  
3 amount of an inhibitor of IL-15 or IL-15 receptor? Even though it's, the  
4 argument is that you're using these known compounds in a novel way, are  
5 these really known compounds?

6 My understanding of Uropep is that it was a very specific  
7 known pathway, very well-known receptors that had been structurally  
8 identified. Here we have no structures, we have multiple different pathways,  
9 we have multiple different binding sites, we have multiple different levels of  
10 inhibition. How is it somebody is supposed to know what this inhibitor of  
11 IL-15 or IL-15 receptor is that's being used in this method?

12 MR. FELDSTEIN: Okay. So thank you, Your Honor. With  
13 respect to Uropep, the Uropep claim is as broad or broader if you want to  
14 make the equivalence between them, is it's just an inhibitor of PDE5 period,  
15 a method of administering a PDE5 inhibitor period. It's not limited to small  
16 molecules, it is not limited to antibodies, is it an element of proteins. It  
17 doesn't matter, it just PDE5 inhibitor period. There were a handful disclosed  
18 in the specification there, fewer than we have here and the art was even less  
19 well developed than what we have here.

20 The use in Uropep of using it for BPH was a new use.  
21 Different -- what we have we here that makes our case stronger than Uropep  
22 is we're using IL-15 and IL-15 receptor inhibitors in the same way that they  
23 were being used and recognized as being useful for other autoimmune  
24 diseases. And so the foundation is even better than Uropep. And in terms of  
25 your question, in the target and the epitope, the patent is incorporated by  
26 reference in this specification, Exhibit 2013 and 2014, and in 2014 I believe

1 all three of those are incorporated. And they describe IL-15 inhibitors and  
2 they described in silico methods. They know the structure. The structure of  
3 IL-15 was completely known.

4 It was a (INDISCERNIBLE) determined structure back in  
5 1994, and these are our patent publications and the patent publications  
6 identify different inhibitors like entirely computer methods because they can  
7 look at -- they know the structure and they what's going to fit in the  
8 structure. And so the facts here are even better than in Uropep because we  
9 know people have done exactly -- be able to look at the structure of IL-15  
10 and identify inhibitors from already existing molecules. So the facts are, or I  
11 would say, better than Uropep in terms of what the prior art already taught.

12 JUDGE VALEK: But again, counsel, this is Judge Valek.  
13 You're saying that one of skill in the art could identify the inhibitors, but  
14 how does one of skill in art know whether a particular inhibitor is actually  
15 going to be effective to treat the disorder without testing it?

16 MR. FELDSTEIN: So, what Dr. Abbas agreed is that if you are  
17 an IL-15 inhibitor, you're going to be useful for the disease, and then it's just  
18 a matter of adjusting the dose.

19 JUDGE VALEK: Counsel, is that the testimony you referred  
20 us to before where he says one would expect that?

21 MR. FELDSTEIN: Yes, Your Honor.

22 JUDGE VALEK: Does anyone actually know that?

23 MR. FELDSTEIN: You know, yes, Your Honor, it's that same  
24 testimony. And again, without requiring testing of everything in the  
25 specification, I don't think one can require the applicant to have gone  
26 through and tested the universe to see what universe is going to work at a

1 sufficient level. You know, in the --

2 JUDGE BRADEN: Given the breadth of the claim, should  
3 Patent Owner have to test more than one thing in order to get that entire  
4 scope?

5 MR. FELDSTEIN: Given what was known in the art, Your  
6 Honor, that IL-15 inhibition was recognized to have utility for IL-15 -  
7 mediated autoimmune diseases, showing that vitiligo is an IL-15 mediated  
8 autoimmune disease is enough to establish that. I would submit we don't  
9 even need the working example in the specification. The earlier examples  
10 established the IL-15 mechanisms, examples one, two, three, and four  
11 established the IL-15 mechanism of vitiligo, and then that is confirmed that  
12 blocking that pathway works.

13 And so the question is, if you block the pathway, does that treat  
14 vitiligo? The patent answers it yes. Therefore, blocking the pathway works,  
15 and if you have an inhibitor of the pathway, you will likewise be expected to  
16 work. And that's what a person of ordinary skill in the art, reading the  
17 specification, would understand. They've proven it with one. My  
18 expectation is, and my understanding is that this applies generally. We've  
19 talked, we cite in our Petition, I mean, excuse me, in our papers, our Patent  
20 Owner response, we cite, for example, Forte, the Petitioner here, I'm on slide  
21 26. Forte relies on the very same data in the patent to be able to extrapolate  
22 and expect that their antibody is going to work in vitiligo.

23 They had an interrogatory they were compelled to respond to.  
24 If you go back to slide 25, they had publicly presented to their investors and  
25 press release that published preclinical proof-of-concept data supports the  
26 therapeutic potential of anti-CD-122 in multiple autoimmune diseases,

1 including vitiligo. And what do they rely on? They rely, from slide 26 in  
2 their response to the interrogatory, they rely on the patent's same data.

3 So the same data that they say in the patent, nobody could work  
4 with. It's a black box. You would need to know more, more, more. They're  
5 able to expect efficacy and see potential for a billion-dollar market based on  
6 the same data. It undermines the entire premise of their argument, and it is  
7 consistent with what Dr. Abass said, that if you're an IL-15 inhibitor, you  
8 expect to do an IL-15 inhibitor has been shown to do.

9 JUDGE BRADEN: So, counsel, explain to us what is a person  
10 of ordinary skill in the art expected to understand when they see that some of  
11 these inhibitors will act differently depending on the form of the IL-15 or the  
12 IL-15 pathway. And that in some of these references, it seems as though  
13 some these inhibitors are actually capable of enhancing IL-15 signaling, and  
14 doing the opposite of what is stated in the '505 patent. What does that do  
15 then to the expectation?

16 MR. FELDSTEIN: Okay. Thank you, Your Honor. So there  
17 are again, additional challenges, a small fraction of the over 300 IL-15  
18 inhibitors, and they do point to some, they say that they do the opposite of  
19 what would have been expected. And they increase the production of pro-  
20 inflammatory cytokines, for example, unexpectedly. And so I'd submit that  
21 things that a small fraction do unexpectedly don't violate the rule that you  
22 would expect and the reader would expect that generally or predominantly  
23 IL-15 inhibitors are going to work as taught.

24 And moreover, the differential effects that you're talking about,  
25 Your Honor, and the Petitioner talks about are off target effects. These  
26 differences, increasing pro-inflammatory cytokines are off target effects.

1 They don't change the idea that they're going to block IL-15 itself and do  
2 what an inhibitor does. They do point to one example of reverse signaling  
3 that Your Honor may be referring to, and they refer to that in their briefing.  
4 The reverse signaling, they referred to a compound, an antibody, Amgen  
5 714, also known as Humax. This is the compound they say does reverse  
6 singling, and therefore wouldn't work.

7 We have their data, Exhibit 1052, we address this in the sur-  
8 reply at pages 8 to 9. Exhibit 1052 shows that Amgen 714, the compound  
9 they say does this reverse signaling problem, is statistically effective in  
10 treating clinical symptoms of celiac disease, another autoimmune disease.

11 And so even where they say that there are these off target  
12 effects, even where they say that it can actually increase cytokines, the fact  
13 is it's still effective in treating autoimmune disease. Is that maybe the best  
14 molecule ever to use if you're going to treat a patient when you choose  
15 something that might not have that reverse signaling question? That may be  
16 a question of optimization. It may a be question what is the commercial  
17 embodiment, but it still works. It still works that if you block IL-15, you  
18 block IL-15 and you're able to treat IL-15 mediated diseases.

19 JUDGE VALEK: Counsel, that's for celiac disease. So let me  
20 ask you a question specific to the claim here, which is a method for treating  
21 patients with vitiligo. How many inhibitors is there data -- or how many  
22 inhibitors, is their data in the record that shows that those compounds  
23 actually are therapeutically effective for treating the claimed condition?

24 MR. FELDSTEIN: There's one working example showing  
25 efficacy in the specification. That's true. And then the evidence is, and  
26 we've talked about it before, Your Honor, that the expectation is that other

1 ones would work as well.

2 JUDGE VALEK: Okay. But there's only data for one.

3 MR. FELDSTEIN: That is correct, Your Honor. And I submit  
4 that you don't even need -- a working example is not required. And the  
5 working example can only inhere to the benefit of the patent here.

6 JUDGE BRADEN: And confirming, that working examples is  
7 the one that's in the mouse model, correct?

8 MR. FELDSTEIN: Correct, Your Honor.

9 JUDGE BRADEN: Right. And can you address Petitioner's  
10 citations that there are IL-15 inhibitors that have been shown to work in in  
11 vitro mouse models, that have now been shown not to be effective in in vivo  
12 human?

13 MR. FELDSTEIN: Well, I think that's the Exhibit 1052 of  
14 Amgen 714 that I was referring to. They say that it didn't work and that it  
15 was abandoned. And that is not true. The evidence -- it did not meet the  
16 primary endpoints. It met some endpoints. And so the idea to say that it  
17 didn't have any effect is wrong. Maybe it didn't have enough effect to  
18 develop commercially or get FDA approval with balance of safety and  
19 efficacy, that's an entirely different question.

20 But Exhibit 1052, something overlooked by Dr. Plott, their  
21 expert, showed that CIOQ is an IL-15 mediated disease, an IL-15 inhibitor,  
22 Amgen 714 had a positive effect there. They also point to a Waldman  
23 reference, Exhibit 1012, and say it didn't work in Exhibit 1012. Exhibit  
24 1012 is a leukemia model. And what is discussed in Exhibit 1012 is that the  
25 leukemia cells, not an autoimmune disease, but the cancer cells are defective  
26 in some way that they're -- the IL-15 mechanism is perverse there. And

1 that's why it doesn't work there. So the point two example where they say it  
2 didn't work in celiac disease, it did. Maybe not as much as you would want  
3 for a commercial product, but it did. They point to an example where it  
4 didn't work in leukemia irrelevant.

5 JUDGE BRADEN: And you don't believe that those inform a  
6 person of skill in the art's expectation about whether inhibitors will work for  
7 vitiligo?

8 MR. FELDSTEIN: I think that Exhibit 1052, the use of Amgen  
9 714 and celiac diseases has a positive implication for the use of IL-15  
10 inhibitors in other autoimmune diseases that are IL-15 mediated. I think that  
11 the absence of efficacy with leukemia has no bearing, and Exhibit 1012  
12 where they found an absence of utility in leukemia they said, we should still  
13 use this for autoimmune diseases. And so the reference as a whole still is  
14 consistent with the idea that if you're an IL-15 inhibitor you should use it  
15 where IL-15 is part of the mechanism. It wasn't in those leukemia cells.

16 JUDGE BRADEN: So the fact that you've got these 15 or so  
17 outliers that we see in slide 64, you're saying that because those are  
18 unexpected that they don't undermine a person of skill in the art's  
19 expectation for this invention to work?

20 MR. FELDSTEIN: Well, it's not even, essentially yes, but I  
21 would like to clarify the numbers. They challenge about 15 out of the 300.  
22 They don't show that there are unexpected or differential effects in 15. I  
23 think there are only two or three where they point to and they say there's  
24 something different going on. And those two are three include the Amgen  
25 714, which did work, even though what they call there was some recognition  
26 that was a reverse signaling that may limit its therapeutic potential long

1 term, its balance of safety and efficacy.

2 But they don't show that 15 have some unexpected effects.

3 They show a few that they claim have unexpected effects for, I think, three.

4 And one of them, in fact, the Amgen 714, in fact works, they just overlooked  
5 that. And so, yes, if you have -- this is Atlas powder in many other cases,  
6 even if have a few inoperative embodiments, that doesn't make the claim any  
7 less enabled.

8 I'm going to jump ahead to slide 35. They had their chart of all  
9 the things that are relevant to 112. We have our chart of what's relevant to  
10 112, and these are facts that were largely or wholly unrebutted. Uropep,  
11 until today, we didn't hear one word about Uropep and its applicability. I  
12 think that Uropep is applicable and for the reasons we've argued and in  
13 response to questions, our facts are better than Uropep because, again, IL-15  
14 inhibitors were recognized in the art as utility for IL-15 mediated diseases.  
15 And that's a fact that the Uropep case did not have.

16 In terms of the law, slide 36 from Uropep. Uropep did analysis,  
17 Uropep did analysis distinguishing, for example, Rochester. Show why  
18 Rochester, even though, yes, Rochester is a method claim, why it's not  
19 relevant, and why when the genus is well understood in the art and not itself  
20 the invention, background knowledge may provide the necessary support for  
21 the claim.

22 We put on evidence that there was a well-understood genus in  
23 terms of the function of inhibiting IL-15. That's something that the  
24 Petitioner and Petitioner's declarants just ignored in their Petition. And so  
25 they can't really come forward and say it was not a recognized genus when  
26 they didn't look for the genus. They didn't investigate the genus; they didn't

1 investigate what was known in terms of the art.

2 Uropep doesn't stand alone. The --

3 JUDGE BRADEN: Counsel, define for me the genus. Is it any  
4 and everything that blocks or inhibits IL-15 or IL-15 receptor? Is that the  
5 genus?

6 MR. FELDSTEIN: The genus is -- the inhibitors are  
7 compounds that inhibit IL-15. They were recognized as IL-15 inhibitors in  
8 the art. It's not a structural genus. It is different from all the structural genus  
9 cases like *Ariad*, where the structure was novel; is different from the *Idenix*  
10 case, where structure is novel; is different from *Rochester*, where there are  
11 no compounds disclosed that could practice the method. *Amgen* on slide 40,  
12 I think, supports what it's --

13 JUDGE VALEK: It's Judge Valek.

14 MR. FELDSTEIN: Yes.

15 JUDGE VALEK: I want to make sure we get an answer to this  
16 question, because I think it is very important. It's not a structurally defined  
17 genus. It's a functionally defined genus, and as I understand it, there are two  
18 functional requirements. One, it either -- the compound has to inhibit IL-15  
19 or an IL-15 receptor, and two, it has to be capable of treating vitiligo. Do  
20 you agree with that characterization of the claim, the recited genus?

21 MR. FELDSTEIN: The claim requires administering an IL-15  
22 inhibitor. An IL-15 inhibitor is something that inhibits IL-15 or IL-15  
23 receptor. The claim requires administering that in an effective amount.  
24 And as I responded to some of your earlier questions, there's no dispute on  
25 the written description or enablement for the effective amount. That's not  
26 something that's been challenged by Petitioner. That's something they've in

1 fact conceded the opposite of in terms of their obviousness arguments for  
2 being able to administer and administer by adjusting doses.

3 JUDGE VALEK: I'm just understanding -- I want to  
4 understand your position. You're saying that you're agreeing that it has  
5 those two functional requirements. It must inhibit IL-15 and IL-15 receptor,  
6 one of those two. And two, that it must be effective for use in the claim  
7 method?

8 MR. FELDSTEIN: I'm not -- I wouldn't have characterized it  
9 the way Your Honor is. There's a functional requirement. There is a  
10 requirement that you administer something that has the function of inhibiting  
11 IL-15, and there is an affirmative step in the claim of administering an  
12 effective amount of that drug. The effective amount I wouldn't characterize  
13 as a functional limitation on the IL-15. That's not been raised, and I don't  
14 think that that actually is appropriate, an accurate characterization of the  
15 claim. You're administering something that has a property that has function,  
16 and then you're administering an effective amount of that thing.

17 JUDGE BRADEN: And it's an affective amount to -- the  
18 amount must be affected to treat vitiligo, correct?

19 MR. FELDSTEIN: Correct, Your Honor. In terms of the law  
20 supporting the idea of, you know, whether it's a functionally defined genus  
21 or a structurally defined genus, again, all their arguments rest on the idea  
22 that you have to have common structure, common structure, common  
23 structure. That's not what Amgen says. In the facts of Amgen, the issue  
24 was, is there common structure? Have you defined enough for when you're  
25 claiming a novel antibody to the target, to the epitope? Amgen makes clear  
26 that you can give an example or a few examples if the specification also

1 discloses some general quality running through the class that gives it a  
2 peculiar fitness for the particular purpose.

3           In some cases, disclosing the general quality may reliably  
4 enable a person of skill in the art to make and use what is claimed, not  
5 merely a subset. And if we move on to slide 41, that is what is going on  
6 here. General quality is inhibiting IL-15. That gives it a pure fitness for  
7 treating autoimmune diseases that was recognized in the art. And then the  
8 inventors further discovered that in fact is critical to vitiligo that general  
9 quality of inhibiting IL-15 here, we submit, enables a person of ordinary  
10 skill in the art to make and use all of what is claimed and not milieu's subset  
11 because we know the general quality. We know what an IL-15 inhibitor  
12 does, it inhibits IL-15, and we know that inhibiting IL-15 has a peculiar  
13 fitness for inhibiting IL-15 or treating IL-15 mediate diseases. The inventors  
14 further showing that it is effective for treating vitiligo.

15           I'm turning to slide 44 just to continue on the case law point.  
16 Again, as I mentioned --

17           JUDGE BRADEN: Counsel, I realize that you're saying there's  
18 no structural requirement here. But what do we do with compounds that  
19 target or physically interact with different subunits of the IL-15 receptor, and  
20 those subunits affect different signaling pathways? Or if you've got a  
21 subunit that effects multiple pathways and the fact that you got compounds  
22 that can interact with both IL-2 and IL-15, and what do we do with that?  
23 How is what's in the claim or what is in this specification sufficient to give a  
24 person of ordinary skill in the art information to be able to delineate what's  
25 within the scope of your claim and what's not?

26           MR. FELDSTEIN: Thank you, Your Honor. So I do also

1 submit that a lot of the arguments that were being presented and it's reflected  
2 a little bit in the question too, are two -- effectively 112, part 2 on the claim  
3 scope, and what the bounds of it are. That's not something that's before --  
4 that wasn't something raised in the Petition, not something before it. And I  
5 also don't think it's an issue because we have extensive evidence that you  
6 can assay a compound to identify whether it is an IL-15 inhibitor. There  
7 were techniques used in all the references that identified IL-15 inhibitors.  
8 They established they are IL-15 inhibitors with assays. In terms of, you  
9 know, the different --

10 JUDGE BRADEN: Is that assay in the specification?

11 MR. FELDSTEIN: It may be incorporated by reference, for  
12 example, in some of the other references, including 2013, 2014, and 2015.  
13 Again, there are 300-ish references that are incorporated by reference in this  
14 specification that Petitioner just hasn't addressed.

15 JUDGE BRADEN: But an assay that would specifically  
16 identify an IL-15 or IL-15 receptor inhibitor exists, but it is not, or you've  
17 got multiple assays, exist but they're not in the specification and we don't  
18 know which reference may have one. Is that correct?

19 MR. FELDSTEIN: No. I'm saying, Your Honor, that that we  
20 have on slide 60, we have a list of references addressing routine assays. So,  
21 Dr. Damsky did testify that if you're given a proper assay, you can  
22 conclusively determine whether a compound is an inhibitor of IL-15 or IL-  
23 15 receptor. And then Exhibits 2013, 2014, and 2015, at least those three  
24 that describe assays, those are all incorporated in the specification, so those  
25 assays are in this specification. I have to check if 2024, 21, 18 -- if 2024 is  
26 also included in specification. So, there are assays known, they're assays in

1 the specification.

2           Returning to slide 6 to, I think, part of what your question was,  
3 Your Honor, in terms of how do you know what's going to happen? What  
4 we have is, for IL-15, we have a relatively unique situation of this, what is  
5 called trans-presentation, where signaling through IL-15, this is the  
6 predominant mechanism of IL-15 signaling, where it requires concerted  
7 action of the receptor component alpha, the receptor from beta, the receptor  
8 from the gamma, and IL-15. These four elements all have to come together  
9 for there to be signaling through IL-15, of IL-15.

10           What Dr. Abbas agrees that if you inhibit anything, at least  
11 theoretically, he says, you should be able to inhibit the signaling through that  
12 pathway. And so it doesn't matter whether you are binding to an epitope of  
13 IL-15R alpha as long as you block IL-15 signaling. It doesn't matter if  
14 you're blocking to IL-15 beta as long you're blocking IL-15 signaling. If you  
15 have other effects on IL-2 or IL somewhere else, those are what I was  
16 characterizing earlier as off target effects in effect. You're still inhibiting IL-  
17 15. If you're an IL-15 cytokine or receptor inhibitor, you have inhibited that  
18 pathway and the patent teaches, consistent with the art on IL-15 for  
19 autoimmune diseases, is generally a patent teaches that this will treat  
20 vitiligo. Whether other things happen is off target side of the point, I think.

21           Slide 44, again, we were talking about distinguishing  
22 Petitioner's -- in the description case law, the issues there, even where there  
23 were methods that, for example, in Rochester, Rochester lacks written  
24 description because it didn't disclose any compounds, and that was why it  
25 was a distinction without a difference there, because it didn't disclose any  
26 compounds. You could not practice the method based on Rochester,

1 because you didn't have any compounds, and there was no evidence that any  
2 compound was known in the art. Our facts are exactly the opposite. We  
3 disclose 20 compounds from nine classes and hundreds were known in art,  
4 facts that were ignored in the Petition.

5 Slide 45, similarly on the enablement cases, the enablement  
6 cases the novelty turned on --

7 JUDGE BRADEN: And counselor, I wanted to let you know  
8 that you've got five minutes until you would start going into your LEAP  
9 time and then before you start going to your rebuttal time.

10 MR. FELDSTEIN: Thanks, Your Honor. So to finish it up  
11 then. So, the enablement cases are similar in that there are issues of novel  
12 structures that are matter. For completeness on the section, we have  
13 dependent claims that do narrow down Claim 2. They're not really  
14 addressed in Petitioner's reply. I will address very quickly obviousness as  
15 well, that's on to slide 66. In fact, slide 69, 69 pointed out substantial  
16 differences between what Xing's model is and why you wouldn't expect  
17 something to happen in Xing models with their very different NK -- with the  
18 phenotypically different cells.

19 They have phenotypically different cells in Xing that they're  
20 CD8 NKG2D cells in in the Xing model, why there's no basis to extrapolate  
21 that to female -specific, melanocyte-specific cells that are present in the  
22 Theros model. And why IL-15 would be the last thing that you would pick  
23 from Xing, because it didn't even reverse it there.

24 In terms of unexpected results, Petitioner continuously ignores  
25 that is not just re-pigmentation that is an unexpected result because you  
26 couldn't have known that IL-15 would have done this, but that it is durable.

1 And so we show slide 8D, for example, on slide 71, that you stop the  
2 treatment and the dark circles continue to rise in terms of pigmentation. And  
3 that is something that's unprecedented in the literature. It's the opposite of  
4 what is known for other attempted treatments of vitiligo. It is the of opposite  
5 what Xing showed for treating alopecia areata. So let me stop there, Your  
6 Honor. Unless there are questions, we'll move on to Ms. Corser for  
7 responding to Petitioner's motion to exclude.

8 JUDGE BRADEN: Very good. Thank you, counselor.

9 MS. CORSER: Good afternoon. My name is Collette Corser.  
10 I'm here on behalf of Patent Owner, University of Massachusetts, responding  
11 to Petitioner's motion to exclude Exhibit 2005, which is the Declaration of  
12 Patent Owner's expert, Professor William Damsky, MD PhD.

13 We turn to slide 77. As an initial matter, Petitioner's motion is  
14 improper. Petitioner's objections to evidence did not allege any of the basis  
15 for exclusion that its motion now seeks. It did not allege that Dr. Damsky  
16 was not a person of ordinary skill in the art at the time of invention, and it  
17 did not allege he is not an independent expert. Petitioner's motion fails as  
18 being untimely and in contravention of this Board's rules. Regardless,  
19 Petitioner's challenges to Damsky fail on the merits.

20 As shown on slide 78, Dr. Damsky is and was a person of  
21 ordinary skill in the art as of the April 2017 critical date. As shown on slide  
22 78, he holds a Ph.D. in cell and molecular biology which he obtained in  
23 2011, six years before the critical date. He also holds a medical degree,  
24 which he obtained in 2013, four years before that critical date. And between  
25 2014 through 2017, just the three years before a critical date, Dr. Damsky  
26 was a dermatology resident and chief resident doctor.

1           Turning to slide 79, in addition to Dr. Damsky's academic  
2 credentials before April 2017, he also had the requisite experience to exceed  
3 the definition of a person of ordinary skill in the art. In fact, he is doubly  
4 qualified under the parties' definition.

5           Regarding Dr. Damsky's research experience, while he was  
6 obtaining his Ph.D., you can see on the slide here, he intensively studied  
7 intracellular signaling pathways, the effects of alerting signaling to those  
8 pathways such as the cytokines at issue here. In addition to his pre-Ph.D.  
9 research between 2011 and 2017, he also testified that his research group  
10 continued to conduct relevant research, testified that his group was, quote,  
11 active in researching cytokines in dermatology and beyond dermatology in a  
12 number of different settings using translational approaches, invasive  
13 approaches in clinical trials.

14           In addition to these years of pre-critical date relevant research,  
15 Dr. Damsky also had relevant medical treatment experience. As I've already  
16 said, and as is set forth in our opposition to the motion to exclude, Dr.  
17 Damsky obtained his medical degree four years before the critical date in  
18 2013, and he was a dermatology resident doctor or chief resident for the  
19 three years before the critical date between 2014 through 2017. But Dr.  
20 Damsky testified his treatment of patients specifically with vitiligo began  
21 even before that as a medical school student before 2013.

22           JUDGE BRADEN: Counsel, is your argument then that his  
23 testimony shouldn't be excluded but rather should go to the weight of his  
24 testimony?

25           MS. CORSER: Our position, Your Honor, is that his testimony  
26 should not be excluded, and because he is - he exceeds the credentials of a

1 person of ordinary skill in the art, his testimony should carry great weight  
2 because he had both the treatment and research experience as of the critical  
3 date through today.

4 JUDGE VALEK: Counsel, this is Judge Valek. I have a  
5 question for you. What about the Petitioner's argument that he has some sort  
6 of conflict of interest that prevents him from acting as an independent  
7 expert? Why doesn't that support their motion?

8 MS. CORSER: Sure. Thank you for your question. We can  
9 skip ahead to that. I'll direct you to slide 82. Our response to Petitioner's  
10 argument that Dr. Damsky is somehow biased is that that's incorrect. First,  
11 just as an initial matter, Dr. Damsky, is not biased. One of Petitioners'  
12 arguments is, that, Dr. Damsky somehow concealed his relationship with the  
13 inventors or the real parties in interest. And that's not the case at all. As you  
14 can see on slide 82, Exhibit 2006 is an excerpt from Dr. Damsky's CV,  
15 which was served with his expert report in this case. And you can see that  
16 Insight is identified in Dr. Damsky's CV as being a group with which Dr.  
17 Damsky had a pending clinical work with. That was never concealed from  
18 Petitioner, and Dr. Damsky testified under oath that this work with Insight  
19 was very limited and did not raise any conflicts with the instant case.

20 Petitioner also alleges that in other forums, Dr. Damsky was  
21 perhaps more forthcoming with his relationship with the inventors or the  
22 patent at issue. And I would just like to point out that the cases in which  
23 Petitioner is citing are publications that Dr. Damsky co-authored with the  
24 inventors. And as you can see on slide 82, those conflicts of interest  
25 statements actually confirm that Dr. Damsky has never had a conflict with  
26 the patent at issue in this case.

1           In both of those conflict-of-interest statements, only the named  
2     inventors list any sort of conflict with the patent issue. I would also submit  
3     that as set forth in our opposition, Dr. Damsky testified unambiguously  
4     under oath as shown on slide 83 that he has never discussed this case or  
5     anything having to do with the case with either of the inventors. He's never  
6     spoken with anyone other than attorneys when preparing this declaration,  
7     and he also signed his declaration attesting that he was an independent  
8     expert in this case. Petitioner doesn't refute any of Dr. Damsky's testimonial  
9     evidence or his signed declaration, let alone specify how Dr. Damsky's  
10    testimony has been -- was improperly biased.

11           I would also like to submit that regarding Dr. Damsky's  
12    qualifications, all of the evidence that I described regarding Dr. Damsky's  
13    pre-2017 qualifications, his research, and his treatment experience,  
14    Petitioner did not address or refute that in their motion to exclude reply. In  
15    fact, if you go to slide 81, Petitioner itself has relied on Dr. Damsky. What  
16    you can see on slide 81 is an excerpt from the Petition, and this is in the  
17    background state-of-the-art section. The Petitioner cited to Exhibit 1021,  
18    which is an article that Dr. Damsky is a first author on, and they are citing to  
19    Dr. Damsky for evidence on the state of the art, specifically the pathogenesis  
20    of alopecia areata, and related cellular signaling.

21           So Petitioner -- Petitioner's own pleadings in this case, confirm  
22    that Dr. Damsky is in fact a person of ordinary skill, and was as of 2017.

23           If you have no further questions, it's our position that  
24    Petitioner's motion to exclude should be denied. And if you have no  
25    questions, I'll yield the rest of my time to our sur-rebuttal.

26           JUDGE BRADEN: Thank you very much. And we will

1 include eight minutes to your sur-rebuttal time. And now we'll go back to  
2 counsel for Petitioner. You may begin your rebuttal time when you are  
3 ready.

4 MR. MILLS: Thank You. So I'd like to begin with just  
5 stepping back to what we were talking about before. So after everything that  
6 the Patent Owner said during their argument, none of it changes the two key  
7 fundamental aspects of the case. You notice they didn't make any argument  
8 that the claims are anything other than immense, incredibly broad,  
9 essentially claiming an entire universe. And you also heard the admission to  
10 Judge Valek's question that the claims require not only that it be -- that the  
11 compounds inhibit IL-15 but that the therapeutically effective amount of the  
12 claim refers to the treating of vitiligo.

13 So those dual functions are required and the entire universe is  
14 staked out. You'll also notice that there was nothing that they did or could  
15 do to rehabilitate the narrowness of the working example. And indeed, they  
16 went even so far to say, well, we didn't even need a working example, you  
17 could ignore the working examples. And that's because it simply provides  
18 no value, because the working example doesn't tell you what common  
19 structural features. It doesn't tell you a correlation between structure and  
20 function. It gives you no information to know either of those two questions.  
21 Is this an inhibitor of IL-15?

22 And is it something that is going to be treating vitiligo? Now, I  
23 would caution the Board, and of course the Board knows very well, it's so  
24 important to check the record. The quotes that the Patent Owner is relying  
25 on from the deposition quite frequently don't support the position that they're  
26 making. They talk about Dr. Abbas repeatedly saying, well if you had

1 isolated an IL-15 mechanism for a particular disease, you know, then that  
2 would tell you something. He testified repeatedly that that's not the case  
3 here. He talks about that. We've cited those -- that testimony in the reply at  
4 16, for instance, his deposition transcript on pages 90 and 91. He talks about  
5 it in his opening declaration, paragraphs 35 through 36.

6 And here on slide 42, which is what I have up here, remember  
7 that immensely broad genus, right. It includes the nucleotides, for instance,  
8 he was asked about this. He was asking about this by opposing counsel. He  
9 says, they work in completely different ways. The interfering RNA blocks  
10 the expression of the receptor. We have no idea whether they'll have the  
11 same effect or not.

12 I want to point to also, so this is cite 48. I want to point out, I  
13 was asked a question by Judge Valek about the uncertainty in the art, the  
14 unpredictability in art because of the variation. So in paragraph 18 of Dr.  
15 Plott's declaration, he discusses a couple of examples of this with regard to  
16 especially Exhibit 1040 on page 2, and Exhibit 1048 on page 3. These are  
17 examples where post critical date, the inventor Dr. Harris himself is saying,  
18 well, look, you know, we've tried. We did some experimentation. And this  
19 entire category of the IL-15 antibody, it's not working. There are problems  
20 with it. So we know the IL-15 isn't working. If we can go to slide 46.

21 JUDGE BRADEN: And counsel, just to confirm, this was Dr.  
22 Plott's reply declaration, paragraph 18?

23 MR. MILLS: Yes. Exhibit 1047.

24 JUDGE BRADEN: Okay. Thank you.

25 MR. MILLS: Right. So they dabbled with IL-15 specific  
26 inhibition. They couldn't get that to work because there were problems with

1 that. And now here in 2021, years after the critical date, now they're trying  
2 an inhibitor of the receptor and they still don't know if it's going to work.

3 Judge, you asked a question about the reply declaration. It's  
4 important that the reply declaration is talking about the evidence that that  
5 Patent Owner pointed to. So during the argument, counsel said, well, they  
6 pointed to celiac disease, they've pointed to leukemia and this and that.  
7 We're responding to what they pointed to, right? That they pointed to the  
8 leukemia reference, the review that was discussing it. They pointed to these  
9 references talking about rheumatoid arthritis, et cetera. They're pretending  
10 like this is something that's well established that has a class wide efficacy,  
11 and that's simply not the case.

12 So what we're left with is an incredibly broad genus. It's  
13 functionally defined. It has essentially no limits. We're left with a black box  
14 specification that provides us no guidance, absolutely no guidance as to what  
15 structures and how, which of these candidate compounds that they've  
16 identified are going to serve the functions. Which of them are going to  
17 inhibit IL-15? Which are them going to treat the vitiligo? No one knows.  
18 They don't know. We don't know, that's not an invention. It's not written  
19 description. They haven't shown possession. It is not enablement because  
20 they haven't enabled the person of ordinary skill in the art to practice the  
21 immensely broad genus that they play in.

22 JUDGE VALEK: Mr. Mills, I have a question for you. This is  
23 Judge Valek. What about counsel's argument that their facts are actually  
24 better than the facts in Uropep, which I guess in that case, the jury found that  
25 the written description defense hadn't been sufficiently made out, and the  
26 claims were upheld?

1           MR. MILLS: Yeah, we very much disagree with that. We've  
2 discussed that somewhat today. That's not the case at all. It's a completely  
3 different situation. There is one single target and there is a one particular  
4 place on that target where these known group of compounds are acting.  
5 They've been developed, they've been in use, it's completely a different  
6 situation. The Juno case distinguished that.

7           They talked about it, they said in Uropep, they shared a  
8 common physical structure to fit this active site, but in Juno they said the  
9 contrast here is that the patent that's challenged does not disclose any amino  
10 acid sequence or structures to distinguish the SCFVs that bind to the selected  
11 targets from those that do not, and the modification of the sequence can  
12 change the binding ability. That is exactly what's the case here. They are,  
13 the claims are aspirational. They're saying this is the goal we would like to  
14 have; we'd like to treat vitiligo. We'd like to do it by interacting someplace  
15 in the IL-15 pathway, but they don't tell us what we need to know to be able  
16 to do that.

17           Unless there are further questions, I will yield the balance of my  
18 time.

19           JUDGE BRADEN: I do not believe we have any additional  
20 questions for you, counselor. Thank you. And we will change over to  
21 Patent Owner's counsel. You may begin your -- and you have 23 minutes of  
22 rebuttal time because Ms. Corser yielded up eight minutes.

23           MR. FELDSTEIN: Thank you, Your Honor. Again, Mark  
24 Feldstein for Patent Owner. I do appreciate the comment from Petitioner's  
25 counsel that you should obviously look at the record. They had their slide  
26 49 on the screen for a long time just now to suggest that even post-critical

1 date, things didn't work out as expected. They have stars in their -- in their  
2 slide where they excerpted the key responses from Dr. Damsky. So, on  
3 Petitioner's slide 49 they're citing to Exhibit 1046, which is Dr. Damsky's  
4 deposition testimony.

5           They omit his testimony at page 235, lines 3 through 12, where  
6 he explains that the question is about a balance of safety and efficacy. And  
7 so a balance of safety and efficacy, sure, that is something that ultimately is  
8 a -- you can only establish in human clinical trials. Clearly, there's no law  
9 requiring that you do human clinical trials to establish written description or  
10 enablement. United Therapeutics, for example, very recently just reaffirmed  
11 the idea that that's the question for the FDA, that's a question for something  
12 else, it's not a question of patentability on whether it is going to be FDA  
13 approvable balance of safety and efficacy.

14           So I think that the Board will obviously look, but I think that  
15 since they had slide 49 up for so long, I wanted to point that out and point  
16 that out that every time they are talking about humans, they're suggesting  
17 that there's a requirement for human testing and that is not the law, that's  
18 contrary to the law, that would be an error to establish that.

19           In terms of what's common and knowing that things are going  
20 to work, turn to slide 54, we had this slide up or this same image up before  
21 about the trans-signaling that is present as part of the IL-15 mediated  
22 pathway. There is no dispute that that's the relevant and predominant  
23 mechanism. And this was all characterized. This is how the in-silico  
24 methods were established by being able to look at the structure of this. And  
25 all of these was known, the structures were known. The relevant binding  
26 sites were known.

1           That's why we're able to do -- why the multiple references  
2 incorporated in the specification on slide 60, 2013, 2014, 2015, and maybe  
3 2024, I apologize I didn't check, where they were using in silico methods to  
4 be able to identify inhibitors of the IL-15 or IL-15 pathway. It was known,  
5 it's incorporated in the specification, is part of specification that their experts  
6 just didn't consider in rendering their opinions.

7           In rebuttal, you heard more about Dr. Abbas. You heard about  
8 more Dr. Plott. If we turn to slide 49 for Dr. Abbas, their Petition, and the  
9 arguments you just heard were supported by Dr. Abbas. Dr. Abbas's  
10 testimony doesn't really go anywhere because he didn't consider the majority  
11 of the references that are incorporated in the specification. He didn't  
12 consider the Art. He didn't investigate it. We cite to CSL, IPR decision, and  
13 Gilead IPR decisions on why testimony from someone who hasn't  
14 considered the entire specification or considered the entire art is not  
15 competent testimony. We cite to Kyocera that the testimony has to be from  
16 the perspective of a person of ordinary skill in the art. Having not been  
17 aware of, having not considered the extent of the IL-15 art, Dr. Abbas did  
18 not provide testimony from that perspective. His testimony that there's no  
19 written description and no enablement is not competent.

20           We heard about Dr. Plott again in rebuttal just now, and Dr.  
21 Plott has similar problems, and perhaps even more. He has little to no  
22 experience with IL-15 signaling. He didn't consider the references cited in  
23 the specification. He didn't consider art as a whole. He would need to  
24 consult other experts for cytokine signaling. And he really hasn't done  
25 anything in vitiligo since like, 1989 and 1990.

26           And so Dr. Plott, just like Dr. Abbas, their testimony is not

1 competent to challenge the written description here. His head-in-the-sand  
2 approach where if you give someone a specification you say it's a black box,  
3 it is too complicated to understand, there is too much variability, but you're  
4 testifying without the basic foundation of knowing what is actually taught in  
5 the art for IL-15 signaling, the utility of IL-15 signaling that was recognized  
6 in the art.

7               For example, on slide 8 the expectation of common  
8 autoimmune therapeutic efficacy, what people did in the art is they said, we  
9 found a new IL-15 inhibitor, I developed a new IL-15 inhibitor. What is it  
10 going to be good for? It's going to be for the things that IL-15 inhibitors are  
11 good for. They're good for treating IL-15 mediated autoimmune diseases.  
12 You don't need to have tested other ones to know that. We have --

13               JUDGE VALEK: Counsel, let me ask you a question about  
14 that because it seems like, sure, they have that expectation. I found a new  
15 IL-15 inhibitor. It's expected to be useful for treating autoimmune disease,  
16 and so now I'm going to test it to see if it actually is. And I'm going to test it  
17 across all these different assays and models for all of these various  
18 conditions, and maybe it will, maybe, it won't be. But why isn't that just a  
19 hunting license to go and search for these things?

20               MR. FELDSTEIN: It's not a hunting license because the proof  
21 of concept that inhibiting -- it's known, there were known compounds that  
22 inhibit signaling of IL-15. That was known. There's no dispute about that.  
23 There were no models for rheumatoid arthritis, psoriasis, and Crohn's  
24 disease that said these are IL-15 mediated diseases. If you inhibit IL-15, you  
25 will be treating that disease. That's not a hunting license that was  
26 established in proof-of-concept studies using the classic research paradigm

1 that Dr. Abbas endorsed, that we refer to in the specification.

2           It's what Xing did. It is what the patent did. And it's a not  
3 hunting license because building on this background of what was known for  
4 cytokine targeting, the patent here established that vitiligo has an IL-15  
5 mediated mechanism, and then if you inhibit that pathway, you treat the  
6 disease. And so it's not a hunting license. It's established proof of concept.  
7 It is established from proof-of-concept model that this pathway is now  
8 relevant to vitiligo and inhibiting it will inhibit vitiligo is what the  
9 expectation was here. You don't have to test it. The question is, when a  
10 person picks up and reads the specification, are they going to understand that  
11 what's described is described? Yes, it is.

12           Are they even going understand it's enabled for what is  
13 claimed? They're going to understand its enabled for what's claimed  
14 because the expectation built on the art is that they will work. The  
15 expectation for other autoimmune diseases was it would work, we read the  
16 specification, we (INDISCERNIBLE) on a foundation, you would likewise  
17 expect it to work for vitiligo because they show that inhibiting the pathway  
18 is effective for treating vitiligo.

19           Again, on slide 26, 25, and 26. This is what Forte did with our  
20 data. Forte it relied on our day to say, hey, I've never tested my compound,  
21 vitiligo, but I'm recognizing that it's worth -- that it has value in this billion-  
22 dollar market. And they're relying on the exact same data to make the  
23 expectation that it's going to work. That expectation is, again, equivalent to  
24 enablement. You read the patent. Do I think this is -- does this enable me to  
25 do it? Yes, it does, because like Forte, I expect it to work based on what was  
26 known in the art for IL-15.

1 JUDGE BRADEN: Counsel, both the specification and what  
2 you're pointing to for Forte is about a specific antibody that you've shown to  
3 potentially work in a mouse model. And first of all, I mean they're not  
4 trying to claim everything besides use of this one antibody. I'm trying to  
5 understand that in your claim, you've got a huge, broad swath of molecules  
6 falling within the scope of that. You've shown one example of something  
7 that may work. It does work in a mouse, may work in a human, but now  
8 we've got challenges. Your claim covers over 350 molecules, got  
9 challenged with at least 15 of those without being able to show that a nucleic  
10 acid, a peptide, and some other biologics work besides this one antibody.  
11 How are we supposed to show that that is both enabled or has sufficient  
12 written description?

13 MR. FELDSTEIN: So we also, first, thank you, Your Honor.  
14 To clarify, they don't challenge that 15 won't work, they challenge that  
15 maybe some were misclassified, and so it's not that there are 15 that work. I  
16 think there were three that they said would work. One of them actually  
17 worked to treat celiac disease. So I just want to clarify that for the record.

18 In terms of the expectation will work, there is no dispute that  
19 the nucleic acid inhibitor can inhibit IL-15 singling. There is not dispute  
20 that there are small molecules that can inhibit the IL-15 signaling, that  
21 they're antibodies that can be inhibited, that their peptides that are inhibit it.  
22 That there're mutations that have been inhibited. And the very fact that you  
23 can inhibit the signaling is going to treat a disease that depends on that  
24 signaling. And so there's no dispute that can have all these classes of  
25 inhibitors. There's not dispute all of these class of the inhibitors were  
26 known. There is no disputes that people weren't developing them with in

1    silico methods or rationally designing them. And that is what you need to  
2    know. You need know, can I inhibit it? Now that I know I can inhibit it by  
3    any of these inhibitors, can I apply it to places where IL-15 is relevant? The  
4    Patent shows that IL-15 is necessary for vitiligo, ergo it treats vitiligo.

5               I hope that answered your question, Your Honor.

6               JUDGE BRADEN: I think I understand your position. Thank  
7    you, counselor.

8               MR. FELDSTEIN: Okay. Thank you. There's nothing for --

9               JUDGE VALEK: Counsel, counsel, I have a question. This is  
10   Judge Valek.

11              MR. FELDSTEIN: Please.

12              JUDGE VALEK: Just so that I understand, and I'm looking at  
13   the slide that you have up right now, slide 3 of your deck, and that bar graph  
14   that shows the cumulatively disclosed inhibitors, and I think the number is  
15   somewhere between 350 and 400. Is that the right number?

16              MR. FELDSTEIN: Yes. I think the number is 375.

17              JUDGE VALEK: Okay. Is that 375, is that the total amount of  
18   IL-15 and IL-15 receptor inhibitors, or is there a larger class of molecules  
19   here?

20              MR. FELDSTEIN: That's the total that Dr. Damsky identified.  
21   Whether there are other ones that's not on the record, this is a total number  
22   that Dr. Damsky identified. Again, Petitioner didn't make a showing one  
23   way or another on what the content of the art was. We didn't have a -- I  
24   don't think we had a burden to put this on the record, but we did put this  
25   evidence on record. It's roughly over 300 total by 2017.

26              JUDGE VALEK: And that's all of it. There's no other ones out

1 there?

2 MR. FELDSTEIN: These are the ones that Dr. Damsky  
3 identified. There's not evidence one way or another whether it's an  
4 absolutely closed universe or not.

5 JUDGE VALEK: Okay.

6 MR. FELDSTEIN: But these -- there were certainly at least  
7 300, over 300 that were known by 2017. And known and recognized in the  
8 art as being IL-15 inhibitors that again, we didn't have a burden, I don't  
9 think, to show this, but we have. And this is information that Petitioner and  
10 its declarants just ignored in making their declaration, make the Petition.

11 If there are no other questions, Your Honor, I'll rest.

12 JUDGE BRADEN: I do not believe that we have any other  
13 questions. They're very good. So I want to thank everyone for your time  
14 today. We appreciate your flexibility in presenting your case virtually.  
15 Your answers have helped the panel tremendously. As a reminder, we ask  
16 that you please stay on the line a little bit longer to answer any questions that  
17 the court reporter may have regarding spelling. And with that, we wish you  
18 a good day. Thank you very much. And this hearing is now adjourned.

19 (Whereupon, the above-entitled matter went off the record at  
20 3:59 p.m.)

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