Trials@uspto.gov
571-272-7822

Paper 92
Entered: September 12, 2014

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

AMNEAL PHARMACEUTICALS, LLC,
Petitioner,

v.

SUPERNUS PHARMACEUTICALS, INC.
Patent Owner.

Case Numbers IPR2013-00368, IPR2013-00371 and IPR2013-00372
Patent Numbers 8,206,740, 8,394,405 and 8,394,406

Held: August 12, 2014

Before: LORA M. GREEN, SCOTT E. KAMHOLZ, and GEORGIANNA WITT BRADEN, *Administrative Patent Judges*.

APPEARANCES:

ON BEHALF OF THE PETITIONER:

H. KEETO SABHARWAL, ESQUIRE
PAUL A. AINSWORTH, ESQUIRE
Sterne Kessler Goldstein Fox
1100 New York Avenue, NW
Washington, DC 20005

ON BEHALF OF PATENT OWNER:
GERALD J. FLATTMAN JR., ESQUIRE
GREGORY A. MORRIS, ESQUIRE
Paul Hastings
75 East 55th Street
New York, New York
-and-
STEPHEN B. MAEBIUS, ESQUIRE
ANDREW S. BALUCH, ESQUIRE
Foley & Lardner, LLP
3000 K Street, NW
Washington, DC 20007-5109

The above-entitled matter came on for hearing on Tuesday, August 12, 2014, commencing at 1:00 p.m., at the U.S. Patent and Trademark Office, 600 Dulany Street, Alexandria, Virginia.

P R O C E E D I N G S

- - - - -

JUDGE KAMHOLZ: Can everyone in the room hear Judge Braden? Judge Braden, would you speak again, please?

JUDGE BRADEN: Yes, I can. Can everyone in the room hear me?

JUDGE KAMHOLZ: I think that will suffice.

Good afternoon. We will hear argument now in Case Numbers IPR2013-00368, 00371, 00372, Amneal Pharmaceuticals, LLC, versus Supernus Pharmaceuticals, Incorporated. Counsel for the

parties, would you please introduce yourselves, starting with the Petitioner?

MR. SABHARWAL: Good afternoon, Your Honors. On behalf of Amneal Pharmaceuticals, Keeto Sabharwal of the law firm Sterne, Kessler, Goldstein and Fox.

MR. AINSWORTH: Good afternoon, Your Honor, Paul Ainsworth, also with Sterne, Kessler, Goldstein and Fox.

JUDGE KAMHOLZ: And Patent Owner?

MR. FLATTMANN: Yes, Your Honor. I'm Gerald Flattmann of the law firm of Paul Hastings for the patent holder, Supernus.

MR. MORRIS: I'm Greg Morris, Your Honor, from the law firm of Paul Hastings, also for Supernus.

MR. MAEBIUS: Also Steve Maebius of Foley and Lardner on behalf of Supernus.

JUDGE KAMHOLZ: Welcome, everyone, to the Board.

Per our order dated July 18, 204, each side will have one hour to argue during this hearing. The Petitioner will argue first and present all of its arguments concerning all cases and may reserve rebuttal time. You should begin your presentation by indicating how much time you will reserve, if any. The Patent Owner may not reserve rebuttal time.

I will remind the parties that the Petitioner bears the burden of proving any proposition of unpatentability by a preponderance of the evidence. I will also remind the parties that this hearing is open to

the public and a full transcript of everything that is said will become part of the public record.

Please bear in mind that the third member of this panel, Judge Braden, is attending this hearing by telephone from our office in Dallas. Please remember also to mention by number every slide as you refer to it. This is especially important to ensure that Judge Braden can follow the proceedings.

With that, I would like to invite Petitioner to begin.

MR. SABHARWAL: Thank you, Your Honors. Your Honor, just a couple of preliminary matters. First of all can you hear me? Does this work. Does that work? Hello?

(Discussion off the record.)

MR. SABHARWAL: I can speak loud.

JUDGE KAMHOLZ: Why don't you do that. Someone is coming, and we'll deal with it.

MR. SABHARWAL: Great, thank you. Just a couple preliminary matters, Your Honors. First of all, with respect to the time allocation, with the Board's permission, we would like to allocate 40 minutes for our opening presentation and then 20 minutes for rebuttal.

Also, we have hard copies of our demonstratives, if the Board would like that.

JUDGE KAMHOLZ: Yes, please.

MR. SABHARWAL: Could you hand those out, please. Excuse me.

(Discussion off the record.)

JUDGE KAMHOLZ: Please proceed.

MR. SABHARWAL: Thank you. One other thing, Your Honors, in terms of the allocation, I will be addressing the prima facie and secondary consideration issues in part of our opening, and Mr. Ainsworth will be discussing the alternative arguments, the incorporation by reference, the antedation issue and CREATE Act issue.

JUDGE KAMHOLZ: Thank you. Please make sure that you speak up and into the microphone so Judge Braden can hear.

MR. SABHARWAL: All right. If for any reason you can't hear me, please let me know.

JUDGE BRADEN: Thank you. It would be nice.

MR. SABHARWAL: Sure. Your Honors, on December 17 of 2013, this Board instituted the foregoing IPRs based upon the '932 Ashley reference as well as the Sheth reference.

In the ensuing eight months, Petitioner's case has been strengthened based upon at least three principal reasons: Number 1, the express disclosures of the '932 reference and the Sheth reference. Your Honors, it doesn't matter what Mr. Flattmann or I say. The references say what they say, and we believe that they strongly demonstrate unpatentability of the alleged invention in this case.

Secondly, based upon deposition testimony as well as the pleadings and other exhibits, the Patent Owner, Supernus, has failed to demonstrate that any of the secondary considerations overcome our

case of obviousness, and then finally, and perhaps most uniquely, we are going to be addressing today critical admissions that both Supernus' expert, as well as their real party in interest, Galderma, made with respect to the core issues in this case.

First let me talk about their primary liability expert, Dr. Edward Rudnic. Dr. Edward Rudnic was deposed for seven hours in this proceeding in May of 2013. Dr. Rudnic testified as part of his declaration with Patent Owner's response that it would be inconceivable, inconsequential for a person of ordinary skill in the art to use an IR/DR formulation of doxycycline, in a sworn declaration submitted with the Patent Owner's response.

Nevertheless, what Dr. Rudnic did not inform the Board is that in May of 2004, over ten years ago, Dr. Rudnic himself was the primary inventor on a patent that issued from the Patent Office that claimed an IR/DR formulation of doxycycline, so on the one hand, we have Dr. Rudnic saying to the Board in 2014 or 2013, There's no way that I would ever use -- a person of ordinary skill in the art would ever do an IR/DR formulation of doxycycline.

JUDGE KAMHOLZ: What timeframe was that declaration or that statement directed to?

MR. SABHARWAL: I'm sorry, Your Honor?

JUDGE KAMHOLZ: What timeframe was that statement of his directed to?

MR. SABHARWAL: The declaration, Your Honor?

JUDGE KAMHOLZ: Your reference to his testimony that no one would consider an IR/DR.

MR. SABHARWAL: Do we have the slide? Your Honor, this was going -- this was in the Rudnic declaration that was submitted with Patent Owner's response.

JUDGE KAMHOLZ: This is slide 12?

MR. SABHARWAL: Yes, Your Honor, this is slide 12. And in his declaration, he said "had one of ordinary skill in the art been aware of the narrow absorption window of doxycycline, it would have been counterintuitive to formulate a drug composition as a DR drug product or with a DR component."

But, Your Honor, let's look --

JUDGE KAMHOLZ: What timeframe was that made with reference to?

MR. SABHARWAL: The Patent Owner response? What's the date on that? That was -- that was -- I'm sorry, Your Honor, that was as of the earliest priority date, which is April 7 of 2003. I'm sorry. I thought Your Honor asked for what the date was of Patent Owner response.

JUDGE KAMHOLZ: No.

MR. SABHARWAL: Okay. But, however, this application, Your Honor, published in 2002, before the earliest priority date, and it claims a once a day antibiotic product, which is a tetracycline that has an immediate release and a delayed release, and in Claim 2, Dr. Rudnic claimed the product of Claim 1 wherein said

tetracycline is doxycycline, and I asked Dr. Rudnic during his deposition, Does your invention also encompasses minocycline, and he says, Yes, it does.

Now, we don't -- it's not just Dr. Rudnic's admission. We also have the real party in interest here, Galderma, who is identified in paper number 5 by Supernus as the exclusive licensee and the real party in interest making a statement directly contrary to what Supernus is arguing today.

What do I mean by that? As we put in our reply brief, in December -- on December 22 of 2010, during prosecution of the '240 application, which has a nearly identical spec to the '854 provision, Galderma, relying on the same language that the Board and Petitioner relied upon to argue that the Ashley teaches an IR/DR, on that -- based upon that same sentence, they stated that the claim that they sought to allow cannot include a prolonged release agent. Can we go to that slide?

So, Your Honors, on December 17 of 2013, the Board relying in part upon this language in the Ashley stated --

JUDGE KAMHOLZ: Is that slide 16?

MR. SABHARWAL: Yes, I'm sorry, Your Honor, that's slide 16. The Board stated that the composition can include an IR and DR combination based upon this language. Petitioner relied in part upon this language to argue in its petition that Ashley teaches an IR/DR, and Galderma, the real party in interest, agrees with the Board and the Petitioner.

In December of 2010, Galderma stated that "the only controlled release agents present in the capsules recited in amended Claim 82 are an instantaneous release agent and a delayed release agent. The capsules retied in Claim 82 cannot include a prolonged release agent."

It is impossible to reconcile the contradictions. We have Galderma stating to the Patent Office in December 2010 one thing and Supernus stating to this Board something completely and directly opposite of that.

JUDGE KAMHOLZ: Is there any relationship between the '854 application and the '240 application?

MR. SABHARWAL: Yes, Your Honor. The '240 application has an identical spec to the '854, and it claims priority to the '854 provisional. The '240 was the national phase application of the '106 PCT publication, and again it's the same specification, so here's how this gets even more interesting. Supernus has now tried to convince the Board that under the CREATE Act, they should be treated as essentially a single entity, that Supernus, Shire, Collagenics, which is the predecessor to Galderma, should all be added to the specification of the '740 patent.

Galderma and Supernus have engaged in a ten-year campaign to assert these patents together. They have litigated this against Amneal and Mylan together. Mr. Flattmann represented both entities in the District Court, and now all of a sudden, the only proffered excuse that they have for this critical admission is, Well,

that was Galderma, not Supernus. We said something totally different. That's not the point. The point is that you want the Board to adopt a joint status when it's convenient, and then you want to flee from it when it directly contradicts your position.

Now, aside from these, Your Honor, we also have Supernus, as part of their presentation today, running away from the express language of the actual references, and that's again the most important thing. On the one hand Supernus will argue that a person of ordinary skill in the art would never have relied upon a reference that talks about minocycline to treat rosacea, but the express language, as we pointed out in our petition, teaches the use of minocycline to treat rosacea, 38 milligrams to be precise.

They will also argue today that the Sheth reference teaches what's called a, quote, modified sustained release. That's the teaching of the Sheth reference. There's only one problem with that. The words sustained release don't appear in Sheth. The words modified sustained release don't appear in Sheth, and they want to rewrite the express language of the Sheth reference to change it from delayed release to modified sustained release in order to pigeonhole this into their position.

JUDGE KAMHOLZ: What arguments and evidence are in the record concerning the proper construction of delayed release?

MS. SABHARWAL: Your Honor, neither party proffered a construction of the term delayed release. However, in his petition, Dr. Van Buskirk did proffer an interpretation of delayed release, which is

essentially anything other than an instantaneous release. In other words, there's a lag, and it would not be an immediate release, but everything else would fall into the rubric of delayed release, and the specification actually supports a broad interpretation.

The BRI we would submit or the plain and ordinary meaning is a broad interpretation that would include a lag and then a rapid release, or a release that may start in the stomach. For example, the specification, I believe it is in column 5, talks about an uncoated matrix tablet. Well, an uncoated matrix tablet is essentially a sustained release, and this is what Chang claimed as part of a sustained release.

I asked Dr. Rudnic because Dr. Rudnic said delayed release is only a lag and then rapid release, so I said, Okay, Dr. Rudnic, how do you make it -- according to your interpretation of delayed release, how do you make a formulation that's an uncoated matrix tablet as recited in Chang. His answer, I don't know.

They also talk about a pulsatile delivery system. Pulsatile delivery system is what's talked about in the Sheth reference as a delayed release. Dr. Rudnic told me that his patent, the IR/DR, is a pulsatile delivery system, so the delayed release construction under the BRI should be broad, and it ensnares the prior art.

Your Honor, let me now turn to the secondary considerations experts. Supernus proffered declarations from Dr. Webster, Dr. -- Mr. Grabowski, Dr. Rudnic, based upon the various considerations such as long-felt need, commercial success, copying.

Dr. Webster admitted in deposition that there is no evidence, no evidence that a once a day formulation is more effective than a twice a day 20 milligram formulation, which is in the prior art, so, in other words, what Galderma and Supernus want is to obtain a patent and enforce a patent where the only conceivable thing that could be invented is the fact that you have taken a Periostat formulation, which is 20 milligrams administered twice a week, and you make it once a day. That's it, and once a day teaching of doxycycline is expressly taught in the '932 reference.

Dr. Webster could not point to any specific need for once a day formulation, nor could he show that there was any long-felt need based upon patient compliance. There was no study that he could point to that addressed patient compliance, increased patient compliance as a result of a once a day formulation.

Let me turn to Mr. Grabowski. Mr. Grabowski alleged that this formulation was commercially successful. On deposition, during cross examination, he admitted that the once a day formulation is not the key driver of sales. The fact is that Oracea is the only FDA approved drug, doxycycline drug to treat rosacea. Obviously the sales will be high. There's no generics. There's no other formulation, but at the end of the day, the only thing that they can rely on is a once a day 40 milligram, when the 20 milligram twice a day is taught in the '932, and the 40 milligram doxycycline is taught in the '932.

JUDGE GREEN: But does that mean that any kind of drug -- I don't know, does that mean any kind of drug that has FDA

approval, that you can't have commercial success because of the FDA approval?

MR. SABHARWAL: Certainly not, Your Honor, but at the end of the day, if a party is arguing that commercial success is due to the patented features, they have to point to and demonstrate evidence of what patented feature leads to the commercial success. There may be situations where there are generics on the market, but nevertheless, the branded drug is prevailing, and that may be due to the patented feature, but that's not the case here.

JUDGE GREEN: But the two 20 milligrams twice a day is on the market, even though it's not FDA approved?

MR. SABHARWAL: Correct, it is on the market. That's correct.

JUDGE GREEN: And there's no difference in efficacy between the two?

MR. SABHARWAL: There's no difference in efficacy, and there's also no difference in the adverse event profile, and we asked Dr. Webster about that. He could not say that the 20 milligram twice a day is more toxic.

JUDGE GREEN: And there's no argument that the generic twice a day is much cheaper than the FDA approved once a day?

MR. SABHARWAL: There is no -- there has been no argument about that. Certainly I would suspect that a generic entrant would have a cheaper formulation.

JUDGE GREEN: No. I'm talking about at this point in time, the generic twice a day, which I admit would be an off label use, that would still be cheaper than the once a day formulation that's been FDA approved?

MR. SABHARWAL: Yes, it would be cheaper, I think.

I've covered a number of things here. I just want to briefly talk about the claims. Can we go to slide 3, please?

Your Honors, with the Board's permission, we're going to be talking primarily about the '740 patent, but the limitations of the '405 and the '406 are subsumed within the disclosure of the '740, and it is our position that they all fall together and Supernus has not made any type of distinction either in their papers or vis-a-vis their evidence or declarations of any alleged distinctions between and amongst these limitations.

Next slide, please. On December 17, the Board held with respect to the '740 patent that there's a reasonable likelihood that both the independent and dependent claims are unpatentable in view of Sheth as well as the Ashley '932 disclosure, and it is our position that the Board should not disturb that decision, and instead conclude with a finding of obviousness on patentability based upon these references.

I am now on slide 5. Again these are the two references that the Board relied on in its December 17 decision: The Ashley '932 publication, and the Sheth '748 patent.

Next slide, please, slide 6. Your Honors, we've already submitted detailed claim charts and explanations for all of the various

limitations. Just for the Board's convenience, we have a slide here that is just a snapshot of some of the salient disclosures in Ashley.

Just as a point of note, we have on the very top box -- let me see if I can use this thing here, right here. It says: "In a preferred embodiment, the tetracycline is doxycycline: We cited Ashley '854, but this disclosure is also in the Ashley '932 as set forth in our petition. In fact, all of the disclosures are set forth in the '932. All of the limitations of the patents in this case are set forth in Ashley '932. Ashley '854 we believe is incorporated by reference based upon the prevailing case law, but at the end of the day, it's still in Ashley '932.

Next slide, please. I'm on slide 7. Again this is an independent claim 19, which talks about, in the Ashley disclosure, using doxycycline to treat acne and specifically rosacea.

Next slide, please. Now I'm on slide 8. As I said before, Your Honors, Ashley '932 expressly teaches minocycline, so we have Supernus saying and their expert saying, Well, no one would ever use minocycline. It would be counterintuitive to do that, but we have Ashley talking about a sub-antibacterial dosage of 38 milligrams of minocycline to treat rosacea.

We have the Ashley '932 talking about the fact that that formulation can achieve a steady-state blood plasma level within the claimed range, and let me just pause for a moment and talk about this allegedly narrow claimed range.

Your Honors, by their own documents, they have shown that there are many different types of formulations that can fall and

meet this 0.1 micrograms to 1.0 micrograms per milliliter. We have in silico modeling that they have showing 20 milligrams BID, 20 milligrams twice a day, 40 milligrams, 80 milligrams, IR/DR. They work.

No matter what happens, you're going to get this particular disclosure of .1 micrograms per milliliter to 1.0 micrograms per milliliter. This is like hitting the broadside of a barn. Nevertheless, they want to claim that this is somehow inventive because a once a day formulation on this allegedly critical ratio of 75 to 25 will achieve this. Well, there's lots of formulations that will achieve it based upon their own disclosure. We're going to get to that.

All right. We have Dr. Van Buskirk as part of our petition talking about the fact that minocycline and doxycycline are comparable tetracycline drugs, and then we have the Board saying the close relatedness of the two drugs, meaning minocycline and doxycycline, makes information about one formulation relevant to the other.

Next slide, please. I'm now on slide 9. Not only do we have the Board and Dr. Van Buskirk and Amneal as part of its argument talking about the similarity, this, Your Honors, is evidence that we submitted from their expert, Dr. Guy Webster. Dr. Guy Webster has published before the earliest priority date teachings that talk about how you can use minocycline to treat rosacea. I'm in the top left-hand box. He talks about 50 to 100 milligrams once or twice daily, 50, 75 or 100 milligrams of minocycline. Bottom left box,

"ocular rosacea and more severe inflammatory rosacea respond well to oral doxycycline or minocycline," and then finally, he says in this publication: "Doxycycline and minocycline have the most beneficial effects on acne are and well tolerated and safe."

So Supernus has two experts that are proffering directly contradictory statements. Dr. Rudnic says you wouldn't use minocycline. Dr. Webster says it has the most beneficial effect for the condition that we're talking about here, and this all came out during the course of this proceeding.

Next slide, please. All right. One of the other arguments that we make here today -- thank you. One of the other arguments that we make here today is that the -- somehow there's something magical about this sub-antibacterial dose. Well, it's pretty simple. If you want to use a sub-antibacterial dose, you use a lower dosage. That's it, and they talk about the fact that well Sheth -- the Board should not look at Sheth because Sheth only talks about antibacterial doses. That also is wrong.

Here is the teaching from Sheth that talks about a sub-antibacterial dosage of 25 milligrams. You can go -- Ashley said you can go to 38 milligrams, which is sub-antibacterial so again that's wrong.

Next slide, please.

JUDGE KAMHOLZ: Just so Judge Braden is with us, it's slide 11 now.

MR. SABHARWAL: Yes, I'm sorry, slide 11.

JUDGE BRADEN: I was going to ask that.

MR. SABHARWAL: I'm sorry? Can she hear us all right?

JUDGE GREEN: Judge Braden, can you hear us?

JUDGE BRADEN: Yes. We're on slide 11, correct?

MR. SABHARWAL: Yes, I'm on slide 11, Judge Braden.

JUDGE BRADEN: Thank you.

MR. SABHARWAL: So during Dr. Rudnic's deposition, I also asked him repeatedly, Are you saying that you would never use delayed release, that somehow you as a formulator with all of these years of experience wouldn't use delayed release as opposed to sustained release. Finally, after about ten minutes of going around and around, he finally -- I said: "So you're saying that a person of ordinary skill in the art would consider delayed release as one of the possibilities, but would ultimately decide on using a sustained release or a gastroretentive release."

He finally said: "In general, that's more or less it." That is not teaching away. That is not teaching away. Teaching away is pointing to some sort of disclosure that criticizes or discredits.

Let's go to the next slide. I'm now on slide 12. We already talked about this. We have Dr. Rudnic contradicting himself based on his own patent.

Next slide. I'm now on slide 13. One of the other things that we're going to hear from Mr. Flattmann or Mr. Morris is the alleged criticality of this 75/25. In other words, this is somehow the magical formulation, that if you get this formulation and only this

formulation, you will achieve a steady-state blood level. Well, we only need to look to the '740 reference itself to show that that is not correct.

Your Honor, this is figure 4, which has been cited in our petition and also in our reply. Figure 4 shows what I was talking about earlier. We have a 20 milligram IR, instant release twice a day. We have a 40 milligram IR, 40 milligrams instant release once a day. We have a ratio outside of this critical 75/25, and we have another ratio outside of this allegedly critical 75/25, and look at this.

Their own evidence shows that no matter what dosage formulation you use, you are going to achieve the steady-state limitation of .1 micrograms per milliliter to 1.0 micrograms. They're going to be able to hit that broadside of a barn, and that's not all. They actually went ahead and claimed it too. They actually talked about ratios that are from 99 percent IR, 99 parts IR, one part DR, to 70/30, but they will still tell this Board that the 75/25 was critical. This, by the way, is also in the specification of the '740 patent.

Can you go to the next slide, please?

JUDGE KAMHOLZ: Claim 1 --

JUDGE BRADEN: Moving on to slide 14?

MR. SABHARWAL: Yes, I'm on slide 14.

JUDGE BRADEN: Thank you.

JUDGE KAMHOLZ: Just before we proceed, what range of ratio is Claim 1 limited to in the '740 patent?

MR. SABHARWAL: 75/25, 30 parts -- 30 milligrams IR, 10 milligrams DR.

JUDGE KAMHOLZ: I only ask because I note that the weight -- the massives of doxycycline are specified as comprising, so as I read, an immediate release portion -- an immediate release IR portion comprising 30 milligrams doxycycline. Is that limited to 30 milligrams doxycycline?

MR. SABHARWAL: Well, if it uses the comprising language, perhaps not. There may be something else in there, but they didn't specify anything beyond the 30 milligrams of IR, but, Your Honor, just going back, they -- just to make it clear, can we go back to the claim language again?

Let me just, if I may, just point this out here. If this was so critical, why didn't you claim 99/1 and 70 to 30? Why didn't you claim 80/20 to 70/30? Why didn't you talk about this as your preferred disclosure? Nothing that they say makes sense. Nothing that they say makes sense.

All right. Can we go to the next slide? We also got Dr. Rudnic to finally admit that he misunderstood the legal doctrine of teaching away. I said: "Do you think teaching something different is the same thing as teaching away?"

Essentially he said: "When you are saying that something is your preferred way to go, then, yes."

This dovetails with what he said earlier. He said his preferred methodology would be a sustained release, but he would use

a DR. He would use a delayed release, and then I had asked him, just to be very clear, Okay, tell me in these disclosures anything that criticizes, discredits or is in anyway negative about using an IR/DR? Can we go to the next slide?

He said -- all of a sudden he didn't understand what criticism in a scientific sense made. He didn't know what discredit in a scientific sense meant. All of a sudden he just didn't know what those words meant anymore, so he couldn't point to anything that discredits the use or teaches away from an IR/DR. In fact, he didn't even know what that meant.

Next slide, please, slide 16. We've already gone over this, so unless the Board has any questions, I'm going to speed through that.

And, Your Honors, I have about five minutes left. I would just like to go through the commercial success very quickly, and then I'm going to turn it over to Mr. Ainsworth unless the Board has any questions for me.

Let's go to slide 19. Your Honors, as I said before, our expert, Dr. Gilmore, stated that Supernus did not uphold their burden of long-felt need because they didn't provide any supporting evidence of long-felt need, and if we can go to the next slide, slide 20.

In fact, we asked Dr. Webster, Please tell us if there are any studies that you're aware of between your alleged invention and the 20 milligrams that was in the prior art. He was not aware of any. He said, I'm not aware of any studies that compare the adverse effects,

and he also said that, There's no literature that I'm aware of that discusses nor is there a forum for that literature that talks about the specific need for a once a day formulation, but they're going to stand up here in a few minutes and argue that there was a long-felt need.

My last point is on commercial success.

JUDGE KAMHOLZ: Couldn't it be said that there's a general desire to make any drug that's a multi-administration once-a-day dosage?

MR. SABHARWAL: I would agree with that statement, Your Honor. However, the law requires you to point to a specific need based upon this invention, and they haven't done that. He just said, Generally speaking -- and I don't think that's a disputable statement, that you want to have something you can take once a day instead of twice a day, but that's not enough to demonstrate long-felt need of this particular invention.

Finally on commercial success, how much time do I have left? Three minutes? Let's go to slide 21. Your Honor, these are the features that are all found in the prior art. We put forward a generic Periostat, 20 milligrams, generic doxy 50 and generic doxy 100. All of them are found in the prior art.

In fact, let's go to the last slide, which is going to be 23. Now, we talked to their expert -- I'm sorry if I called him Mr. Grabowski. He's actually Dr. Grabowski. We asked Dr. Grabowski about his allegations regarding commercial success.

"QUESTION: So you didn't consider prior art in forming your conclusions for purposes of your declaration?

"ANSWER: I haven't considered that," even though that is required as part of his duty to demonstrate alleged commercial success.

JUDGE KAMHOLZ: Doesn't the Patent Owner argue the nexus may be presumed here because the product is coextensive with the claim?

MR. SABHARWAL: They do, Your Honor, but this product is the only FDA approved product for the treatment of rosacea.

JUDGE KAMHOLZ: What I'm getting at is: Why does the prior art need to be considered when the nexus is presumed?

MR. SABHARWAL: Because the prior art -- it's my understanding that you need to understand what is the novel feature as distinguished from the prior art that leads to the commercial success. What is the patented feature that links between that and the commercial success, so in order to say, Well, it's this feature, it would be incumbent upon a person of ordinary skill in the art to understand what was in the prior art and differentiate those two things, and they didn't do that.

In fact we also said, What if I told you that once a day dosing exists in the prior art, would that affect your opinions? He said: "No, it's not an area I would consider."

We said: "But isn't it true that if the commercial success is due to some element that's in the prior art, then there's no nexus?"

And he said: "I don't have an opinion on that."

Finally, next slide, which is 24, Dr. Grabowski admitted that the once daily dosing regimen of Oracea is not the key driver of sales.

"QUESTION: If I told you that Oracea's feature as being a once daily regimen is the most important to sales, would you agree with me?"

This is their expert. He said:

"ANSWER: No, I wouldn't agree with that."

He also said: "So to say that once a day is the key driver, I don't think that there's evidence to back that up." This is their expert.

So in conclusion, we have demonstrated through this proceeding that the '932 plus Sheth contain all the limitations of patent features, and there's not a single commercial success element, not a single long-felt need, not a single copying element that overcomes it.

Thank you.

JUDGE KAMHOLZ: Thank you. You have ten minutes.

MR. SABHARWAL: Thank you.

MR. AINSWORTH: Good afternoon, Your Honors. I'll be addressing briefly the four arguments that Supernus raised at the end of the Patent Owner's response, and we are starting here on slide 27 for Judge Braden's benefit. In particular --

JUDGE BRADEN: Thank you.

MR. AINSWORTH: -- I'll be addressing the argument that the '932 publication does not incorporate by reference the '854 application. I'll address the argument that the '854 application was not publicly accessible, and that the argument that the -- their argument that the Chang invention, alleged invention, antedates the publication date of '932, and finally I'll address Supernus' attempt to invoke the CREATE Act here.

If we can turn to slide 28. The '932 publication states with detailed particularity the information that the applicant sought to incorporate. It's plain black and white. It identifies the title of the patent application, controlled delivery of tetracycline and tetracycline derivatives. It gives the filing date, April 5, 2001, and provides even the assignee, Collagenics Pharmaceuticals. There is no ambiguity --

JUDGE KAMHOLZ: Is there evidence that the application was actually assigned to Collagenics?

MR. AINSWORTH: I do not know that there is evidence in the record, Your Honor, that Collagenics Pharmaceuticals was, in fact, assigned that application, but I don't believe that the Patent Owner has disputed that fact.

So there's the information that incorporates the reference. It states clearly the intent of the applicant, "the aforementioned application is incorporated herein by reference in its entirety."

Where is the ambiguity? Patent Owner has not identified another application that has that same name, that same date that might

have led a person skilled in the art to a different conclusion as to what the applicant intended to incorporate.

What the Patent Owner has argued is that this is ambiguous because they didn't provide the file number, the application number for that specific application, but the law has never required, for purposes of incorporating by reference, that you must have the application number to identify a patent application with sufficient particularity, and Patent Owner has not cited a single case to support that argument.

If we look to Mr. Kunin, who is the expert offered by Patent Owner, his own search results showed that when he searched in the ESPACE database, he came to -- at paragraph 74 and 80 of Mr. Kunin's own declaration and Exhibit N to his declaration, he came across the '106 application, which is the PCT that claims priority to the '854, and as he noted, if you look on the face of the '106, it identifies the '854 application.

So a person of ordinary skill in the art doing a search in the database or who went to the Patent Office requesting that document would get that document.

Turning to their second argument, which is that the '854 application wasn't publicly available on the date the '932 application published, which is October 17, 2002, that argument fails as a matter of law. 37 CFR Section 1.14 (c) and (e), as quoted in Mr. Kunin's own declaration at paragraph 42, states quite clearly that once an abandoned application such as the provisional which is the '854 is

referenced in a published application, it becomes available to the public. That's what the law requires. It's available to the public.

Now, Supernus would like to argue, Well, it may take some extra time to get the application from the archives of the PTO, or there may be delays. Their experts say there may be up to 14 days to get an application from the PTO because of delays and challenges and finding the document, but the law doesn't turn on delays at the PTO.

When the law says a document is incorporated by reference and is made available to the public as of that date, that is presumably the date that should apply, and they've offered no real evidence to the contrary, but even if -- even if you credit their argument, even if you credit their argument that on October 17, 2002, you could not have obtained a copy of the '854 from the Patent Office because you didn't have the patent application number for the '854, on October 17, 2002, a week later, the '106 application issued with a substantially similar name -- I'm sorry, the '106 application published, and it has substantially the same name as the '854 application, the same assignee.

And if you, a person skill in the art, searching for an application related to the delivery of doxycycline would come across the '106, and on the face of the '106 would be the '854, it would be a roadmap right to the '854 application at the PTO. So at least as of October 17, 2002, a person of skill in the art would have been able to locate and obtain a copy of the '854.

If we can turn to slide 32, and I want to bring to the Board's attention, there's a couple points here that I'm going to address that the Patent Owner has designated as confidential and subject to the protective order and filed under seal.

And, counsel, I don't know if you have an objection to me discussing this with the public in the room, but I wanted to bring it to the Board's attention.

MR. FLATTMANN: I'm sorry, which specific evidence, slide number?

MR. AINSWORTH: I don't think that's on this slide.

(Pause in the proceedings.)

MR. FLATTMANN: That's fine, Your Honor.

MR. AINSWORTH: In general.

MR. FLATTMANN: In general. Thank you.

MR. AINSWORTH: Now, Supernus has asked the Board -- said to the Board, If we lose on obviousness on the prima facie case, then we want the Board to consider our argument that the Chang inventors can antedate the Ashley reference. The problem with Supernus' argument is they have not shown an actual reduction to practice prior to the publication date of the '932.

What they've argued is they reduced their practice as much as the prior art taught, so what did the prior art teach? What did the prior art teach? The '932 application disclosed delivery of 40 milligrams of doxycycline to treat rosacea and by incorporation of the

'854, the use of sustained release and delayed release formulation to do so.

So in order to antedate the Ashley reference under the case law cited by Supernus, they would have to show that Ashley had to practice that, but as of October 17, 2002, all they had done was a study in earlier that year where they tested immediate release dosage forms and delayed release dosage forms but not IR and DR combinations together.

They had not done any studies to show any formulation that achieved the steady-state blood levels of .1 to 1.0 as taught by the Ashley reference, so they have nothing to point to as an actual reduction of practice prior to October 17, 2002.

If we can turn to slide 33, in addition they also have failed to provide credible evidence of conception and diligence. Absent from the record here is any inventor testimony showing that there was conception prior to the publication of Ashley, nothing.

They came in with a declaration from a non inventor, who put in some documents from the development files of Shire, but nothing showing what the inventors understood or their state of mind, which is critical to conception. Then moreover, they have not shown diligence between conception and alleged reduction to practice. In fact, there's as much as a month's delay that Dr. Bryan could not explain in the course of development of their product.

And lastly, if I can turn to their CREATE Act argument. This is slide 34, Judge Braden. Supernus cannot invoke the CREATE

Act here for the simple reason that they are not entitled to use the CREATE Act to file -- I'm sorry, to file a certificate of correction in this case.

A certificate of correction can only be filed under 255 if it would not require reexamination, but in this case, if they are permitted to invoke the CREATE Act to get behind the Ashley reference, this would raise substantial questions of obvious type double patent, and as a consequence, reexamination would be required, and for that reason, the Board should not permit them to file a certificate of correction to invoke the CREATE Act in this case.

JUDGE KAMHOLZ: Have you identified any specific obviousness types of double patenting that would be implicated?

MR. AINSWORTH: In our reply on page 15, Your Honor, we cited three patents that arose from the Ashley '932 application.

JUDGE KAMHOLZ: But no specific claims?

MR. AINSWORTH: We did not point to any specific claims in our reply, Your Honor.

JUDGE KAMHOLZ: Do you have any questions for Mr. Ainsworth?

JUDGE GREEN: No questions.

JUDGE KAMHOLZ: Thank you.

Mr. Flattmann?

MR. FLATTMANN: Yes, Your Honor. Your Honor, we've also prepared slides, if I could hand the hard copies to the Court.

JUDGE KAMHOLZ: Please.

MR. FLATTMANN: Your Honors, I'll be addressing all of the issues with the exception of object indicia of nonobviousness, and my colleague, Mr. Morris, will address those issues.

JUDGE KAMHOLZ: Okay.

MR. FLATTMANN: Your Honors, this is a Supernus' fourth time down really the same road. As you know, there was litigation against Mylan in the District of Delaware where Mylan asserted essentially the same combination of art of Ashley plus Sheth, and the District Court found that the claims were nonobvious over that combination and in fact found that those references did not disclose an IR/DR formulation or the 3 to 1 ratio that we're talking about here.

The Federal Circuit then affirmed those factual findings on appeal. Amneal's case then proceeded for two years in the District Court where Amneal asserted the same combination of art in the District Court. Amneal, I think of note, abandoned that effort and surrendered its Paragraph IV certification ending the District Court litigation, so here we are for the fourth time confronting these arguments.

I think in -- at bottom Amneal's argument is really about hindsight. I know I do the weekend crossword puzzle, and I think it's an apt analogy here. It's challenging, but it would be a lot easier if I had the answer key in front of me, and often when I look at the answers after I've been stumped, it seems like the answers should have been obvious, but of course they were not.

But what if you didn't have the answer key? What if the puzzle was mis-clued and the clues led you in the wrong direction or down a diversion path? That's really where we are with Ashley and Sheth, and I hope I can demonstrate that to you today.

Also here, when we look at this combination, a crossword is necessarily a combination of across answers and down answers, and they have to match. They have to mesh together, and if they don't, the puzzle is again nearly impossible to solve if I don't have an answer key. That's again what we have I think with Ashley and Sheth. Those references teach divergent paths and shouldn't be combined.

Amneal talks about delayed release formulations, and they talked about it quite a bit in its arguments and in the slides in the abstract, but what I think they did was studiously avoid the two pieces of art that are actually being combined and the only ground that's at issue before the Board, ground 2.

If a person of skill looked at Ashley, he would have learned nothing given its kitchen sink disclosure and its advocacy of a sustained released constant rate of release approach. It really pointed in a different direction, and that person would never have combined Ashley with Sheth because they were aimed at completely different problems. Ashley was trying to strike a balance between delivering enough drug to be effective and not delivering so much as to be antibacterial whereas Sheth was going in completely the opposite direction in advocating an antibacterial approach with much higher levels.

So if a person tried to combine these references, they would have gone in the wrong direction. They would have looked at the sustained release approach of Ashley and/or the immediate plus constant release approach of the secondary loading portion of Sheth as opposed to an immediate release portion and then a delayed release portion as disclosed and claimed in Chang.

JUDGE GREEN: What about Petitioner's arguments as to the '320 patent, which I understand isn't being relied upon, but it is part of the prior art and would have been understood by the ordinary artisan?

MR. FLATTMANN: As to the '240 prosecution history?

JUDGE GREEN: Well, as to why one wouldn't combine Ashley and Sheth in the way suggested by Petitioner.

MR. FLATTMANN: Oh, right. Well, they weren't actually combined by the petitioner in that particular instance.

JUDGE GREEN: No, no. Ashley and Sheth as combined by the Petitioner in their petition as to the obviousness.

MR. FLATTMANN: As to obviousness.

JUDGE GREEN: Right. And they pointed to the '320 patent to discredit your declarant, right?

MR. FLATTMANN: Dr. Rudnic's patent I think we're talking about.

JUDGE GREEN: Dr. Rudnic's patent.

MR. FLATTMANN: Yes, Your Honor, I'm sorry. I misplaced the number.

JUDGE GREEN: That's fine. I'm sorry. I should have said that.

MR. FLATTMANN: Yes, they pointed to Dr. Rudnic's patent, and I was going to address that, and let me do that now. If you look at Dr. Rudnic's patent, it was published in 2002, and it claims a once a day antibacterial product. It claims a use of immediate release plus delayed release for antibacterial activity, and it includes a 50 milligram colonic release, so way down the alimentary canal that he expected to release as a delayed release component but which actually failed, and his testimony is of record on that point from his deposition.

So here he actually did pursue a partial delayed release strategy, in fact a radical delayed release strategy, and it failed, and that's what a person of skill would have encountered or would have expected with a drug like this, if they were aware of its absorption window. That's what he was saying in the testimony that was up in the slide that counsel pointed to, slide 12 of Amneal's presentation.

It's very clear that he was testifying that if someone knew the absorption window, they would have avoided delayed release. Here, no one was certain of the absorption window. What was known indicated that delayed release would not be a good choice because the danger would be to release the drug too far down in the alimentary canal such that it wasn't effective, such that it wasn't absorbed, so that's what he was actually saying.

What I'm trying to argue to you is that you can only get to this invention by picking and choosing elements from each of the

references, including the laundry list of Ashley, the broad, broad genus of Ashley and applying hindsight here, and to the extent that these references disclose anything close to the invention, their antedated by Chang's own work as set forth in our papers, because Chang was the only one who actually knew how to do this.

It's a matter of common sense. Ashley went to Chang and to Supernus to develop this drug because they couldn't do it. Ashley had no idea how to do it, and his disclosure didn't provide any direction to a person of skill as to how to do it. As Mr. Van Buskirk testified, it's very clear from looking at Ashley and in particular his figure 1 that he didn't know what he was doing, and that's how a person of skill would have viewed the reference as a whole.

Again it's very important to look at the reference as a whole, not to pick and choose, not to take an isolated line from Ashley. A person of skill would look at Ashley and have the repeated reference to sustained release and constant release over time and would know that you can't accomplish that with an immediate release, delayed release formulation, and none of those are disclosed in the Ashley --

JUDGE KAMHOLZ: Doesn't Galderma argue exactly that in the '240 application, Claim 82?

MR. FLATTMANN: No, Your Honor. That was a statement by Galderma made ten years after the fact, so it's not a contemporaneous statement, and it's not relevant to what the Ashley reference or Sheth reference actually taught. It's also not a statement

that was made by the inventor, by Chang or by anyone at Supernus for that matter. It was a statement made in a separate line of applications by some other lawyer, not a person of skill in the art, and no such claims issued.

JUDGE KAMHOLZ: Why is that not attributable to Galderma? And why is Galderma's statement not attributable to Supernus?

MR. FLATTMANN: The statement is attributable to Galderma based on the fact that its agent mentioned it. I don't believe it's attributable to Supernus, but I think the relevant point is that it was made ten years later, so even if it's attributable it's not relevant. What Chang actually said I think is relevant, and we pointed this out in our papers. When Chang was confronted with the same Ashley reference in prosecution, Chang very clearly said, No, it does not teach a solely IR/DR formulation at all, and then its claims issued. The Ashley claims in the '240 did not issue.

So, Your Honor, if I could turn to the slides. The critical elements of the change patent --

JUDGE KAMHOLZ: Are you on slide 3?

MR. FLATTMANN: Yes, Your Honor, and I'll try to be careful about mentioning the slide names. The critical elements of this invention are that you have a ratio that's designed to give certain minimum and maximum steady-state blood levels, and what's critical about this ratio is that it maximizes the number of patients that are going to fall within that minimum and maximum. That's critical to the

efficacy and safety of the drug because repeatability across patients is obviously of foremost concern in this industry.

Counsel made reference to blood levels that are shown in the patent for different formulations that can follow within the .1 to 1 range, and he pointed to a figure 4. That figure 4 showed mean drug levels. It didn't show how many patients fell within the range and how many did not. When you go back to the actual clinical data, the 30 to 10 ratio maximizes the number of patients that fall within this critical range of maintaining efficacy but not being antibacterial.

JUDGE KAMHOLZ: Does Claim 1 require -- in the '740 patent, does Claim 1 require a 3 to 1 ratio?

MR. FLATTMANN: Yes, Your Honor. It requires a 3 to 1 ratio of the doxycycline immediate release to the delayed release. You mentioned the comprising language earlier, and I believe that that's to allow for other nonactive antigens, for instance, to be included in the immediate release portion and the delayed release portion.

JUDGE KAMHOLZ: Why doesn't is allow for 40 milligrams of doxycycline in the IR portion?

MR. FLATTMANN: Well, I think because it expressly requires a 30 milligram doxycycline. The comprising language, and I understand what you're saying -- the comprising language here I don't think opens up the term 30 milligrams to something different.

JUDGE KAMHOLZ: Did you brief that?

MR. FLATTMANN: No, we did not. No, we did not. It's not a question that I considered before you asked counsel over here.

JUDGE GREEN: Then how do we read that with claim 3 where you can have an IR to DR ratio of 99.1?

MR. FLATTMANN: Claims 3 and 4 are obviously complete mistakes. They are not even proper dependent claims because they don't fall within these ranges. They're mistakes.

JUDGE GREEN: So Claims 3 and 4 are mistakes?

MR. FLATTMANN: Absolutely.

JUDGE KAMHOLZ: But you haven't moved to cancel them?

MR. FLATTMANN: We haven't.

JUDGE KAMHOLZ: Can you do so now?

MR. FLATTMANN: We would be willing to do so, Your Honor, if the Board requested that.

JUDGE KAMHOLZ: We will not request it.

JUDGE BRADEN: I didn't hear that last statement. Would you repeat it, please?

JUDGE GREEN: Judge Braden, we were talking about Claims 3 and 4 and whether or not --

JUDGE BRADEN: He said he would cancel the claims. I didn't hear his last statements.

JUDGE GREEN: Counsel for Patent Owner said he would be willing to cancel them, and Judge Kamholz said that at this point we're not going to request that.

JUDGE BRADEN: Okay. Thank you.

JUDGE GREEN: You're welcome. Sorry about that.

MR. FLATTMANN: No, thank you, Your Honors. I think it's also important to note that the ground for institution of the IPRs is ground 2, the '932 Ashley patent in combination with the Sheth patent. All of the grounds were denied, and counsel has referred to a number of other pieces of art that it says relate to delayed release, et cetera, but they're not part of the grounds for these IPRs.

When you look at the references carefully, you will see that they fail to disclose key elements of the claims. Sheth doesn't mention doxycycline. The Ashley reference expresses the range of .1 to 1 but only as a wish without providing guidance or any examples of how to get there. Sheth doesn't mention it at all.

The Ashley reference and the Sheth reference do not show a single formulation that consists -- consists meaning solely -- of an IR portion and a DR portion, and they don't show any ratio of 3 to 1 IR to DR, and then Dr. Van Buskirk admitted all of these points during his deposition, and we stated those in our observations.

JUDGE KAMHOLZ: How does the claim language "a once daily dosage will give steady-state blood levels of doxycycline of a minimum of .1 microgram per milliliter and a maximum of 1.0 microgram per milliliter" limit the claim?

MR. FLATTMANN: Does it limit claim, Your Honor?

JUDGE KAMHOLZ: How does it limit the claim?

MR. FLATTMANN: Well, any formulation that fell -- that was administered and fell without that -- outside of that range, let's say it fell at 1.5 micrograms per milliliter, would not be covered.

JUDGE KAMHOLZ: Well, we're talking a claim to a composition.

MR. FLATTMANN: Yes, Your Honor.

JUDGE KAMHOLZ: This blood concentration involves what happens when the drug is inside an organism.

MR. FLATTMANN: Yes, Your Honor.

JUDGE KAMHOLZ: So you're asking us to construe this claim in terms of how an organism processes the drug?

MR. FLATTMANN: In part, Your Honor. I would say that if we constructed the formulation as described here with the 3 to 1 ratio of IR to DR, it's going to fall within that range, and we've proven that through our clinical trials, et cetera.

But, yes, if for some reason there was some 3 to 1 IR to DR drug that did not fall within this range, it would not be covered by the claim.

JUDGE KAMHOLZ: Does this require that all organisms administered this dose will have a blood concentration in this range?

MR. FLATTMANN: The way the case law breaks on that, and I'm trying to think of the correct cite, is that there's infringement when the general population that's involved in the clinical trials is falling primarily within a particular range. There can be some outliers. There always are going to be some outliers in any clinical

administration, but there would be infringement if upon administration per the product insert and per the clinicals that are contained in the product insert and the approvals, the majority of people are within these ranges, and that will be the case if you construct this formulation.

Ashley doesn't teach any immediate release, delayed release formulations at all.

JUDGE KAMHOLZ: Slide 7?

MR. FLATTMANN: Correct, Your Honor, slide 7. As Dr. Van Buskirk admitted, nothing in Ashley discloses any doxycycline formulations that have solely immediate release or delayed release components. What it does talk about over and over again is a requirement of release at a substantially constant rate.

JUDGE KAMHOLZ: Slide 8?

MR. FLATTMANN: On slide 8, Your Honor. And going to slide 9, it defines the term substantially constant rate as referring to maintaining a release rate of that active ingredient over time, and Dr. Van Buskirk testified that the substantially constant rate in Ashley means maintaining a release rate.

It also -- Ashley also tells us on slide 10 that the substantially constant release rate would require a formulation predominated by a sustained release agent to control the release of the drug. You can see that in the quoted material on slide 10.

The sole figure of the Ashley '854 purports to depict a sustained release component that provides a substantially constant rate

of release over approximately 16 hours, and Your Honor can see that in figure 1 here on slide 11. This is not a drawing of delayed release, and Dr. Van Buskirk confirmed that in his testimony.

JUDGE GREEN: Now, does the specification of the '740 patent or any of the patents at issue define "delayed release" in any particular way?

MR. FLATTMANN: The '740 patent refers to delayed release in a number of sections, not an explicit definition as it provides for immediate release, but every time it refers to it, it talks about substantial lag before the delayed release occurs. It says that that delayed release takes place in a non acidic environment outside the stomach.

And that's found, Your Honors, in the '740 patent at column 7, lines 46 through 53, and it talks about that delay release occurring after substantial lag after the immediate release. It also, in the figures, shows you a chart, which I'll put up on the board in a bit -- it shows you a chart of what immediate release and delayed release looks like. Those charts are figure 1 and figure 2. And what you will see is immediate release releasing at a time point 0 in figure 1, and releasing at a very rapid linear fashion over the course of 10 minutes to almost 100 percent release.

Then figure 2 shows what the delayed release is in the context of this invention, the lag of two hours followed by again a very rapid linear release within half hour of 100 percent of the remaining material. That is completely different from what we see in

figure 1 of Ashley regardless of the terms that he uses, and it's no surprise --

JUDGE KAMHOLZ: Does this amount to a definition of delayed release or are these examples?

MR. FLATTMANN: These are all of the examples and embodiments.

JUDGE KAMHOLZ: Why should these examples control the construction?

MR. FLATTMANN: Well, they're also consistent with the common, plain meaning of the term delayed release in the pharmaceutical access.

JUDGE KAMHOLZ: Where is that addressed in the record?

MR. FLATTMANN: That's in the Rudnic declaration, and it was also confirmed by Dr. Van Buskirk on deposition, and I'll be able to point to that in the slides coming up. Here are the slides. On slide 12, Your Honor, here's a chart showing you the immediate release and delayed release embodiments of Ashley -- I'm sorry of Chang, and contrast that to Ashley's substantially constant release over 6 to 24 hours.

So, Your Honors, Ashley viewed as a whole requires a sustained release agent. We know from the case law that it's impermissible within the framework of 103 to just pick and choose isolated lines to the exclusion of all the parts of the reference that are

necessary to understand what the prior artisan was teaching and disclosing to people of skill.

JUDGE KAMHOLZ: Well, Ashley may dwell on sustained release, and the examples it gives may include sustained release, but why does it follow from that that sustained release has to be dragged along with any fact relied upon for Ashley?

MR. FLATTMANN: Well, it follows because in his summary of invention and otherwise, as we pointed out on the board, he says that his whole goal is to produce a composition that maintains substantial, constant release over time, and he says that to do that, you need sustained release. He makes a reference to IR, DR, SR and lots of other things, but if you read that reference as a whole, it requires sustained release and thus is excluded from Chang.

JUDGE KAMHOLZ: So the sentence that they rely on where it lists out immediate release, sustained release, delayed release and combinations thereof.

MR. FLATTMANN: Right.

JUDGE KAMHOLZ: What do you make of that?

MR. FLATTMANN: I think it's just a laundry list. It's the same sort of laundry list that the Federal Circuit has said does not render species claims obvious.

JUDGE KAMHOLZ: It's a pretty short laundry list.

MR. FLATTMANN: As Dr. Van Buskirk testified it involves thousands of permutations. It could have -- if you take that logic, you could have an immediate release alone. You could have a

delayed release alone. You could have an IR/DR. You could have an IR, DR, SR. You could have sustained release alone, and many, many -- an IR coating DR, vice versa. There are thousands of possible combinations.

So which one of those thousands of combinations should the person of skill in the art take? Which path should they take? Well, if they're listening to what Ashley is really saying, they're going to make a sustained release formulation that substantially releases over time.

JUDGE KAMHOLZ: But by that logic, doesn't your claim cover thousands.

MR. FLATTMANN: No, ours covers the one distinct formulation.

JUDGE KAMHOLZ: What are the thousands?

MR. FLATTMANN: Huh?

JUDGE KAMHOLZ: What are the thousands, the choice of the particular coating composition?

MR. FLATTMANN: That's part of it, but let me try to get to the slide numbers. Here. As Dr. Van Buskirk said, almost nothing is excluded from the scope of Ashley, if you read it that way.

JUDGE GREEN: Slide number?

MR. FLATTMANN: On slide 30. You could have all of these types of combinations. You could have three or four different types of delayed release portions, for instance. You could have a gastroretentive entrapped formulation as we see in one part of Ashley.

You could have different types of DR portions, IR combined with sustained release, et cetera. Almost nothing is excluded and therefore it teaches nothing. A person of skill would not know which of these paths to take to make a formulation that could give you the desired blood levels.

JUDGE KAMHOLZ: Perhaps considering Ashley by itself, but that's not the challenge that's before us.

MR. FLATTMANN: Well, no, but if we attempt to combine it with Sheth, we don't have delayed release at all. Sheth teaches an immediate release formulation that is followed by a modified sustained release formulation.

The delayed release -- so-called delayed release portion in Sheth which is actually referred to as a secondary loading portion --

JUDGE KAMHOLZ: Does it use the phrase delayed release formula?

MR. FLATTMANN: It refers a couple times in there, both -- then they actually refer to what it is, they talk about a secondary loading portion, and then they describe that secondary loading portion, and they say that that secondary loading portion starts dissolving immediately in the stomach. It has an immediate release component to it.

And then by virtue of the fact that it has pH soluble and pH non soluble pores in it, it begins releasing a drug over a sustained period of time.

JUDGE KAMHOLZ: So Sheth's --

MR. FLATTMANN: It's not a delayed release disclosure.

JUDGE KAMHOLZ: Sheth's secondary portion includes an immediate release component.

MR. FLATTMANN: Yes, absolutely.

JUDGE KAMHOLZ: Now, does the comprising language in your claim allow for that?

MR. FLATTMANN: No, no, because --

JUDGE KAMHOLZ: So your comprising language doesn't allow for more doxycycline, and it doesn't allow for an immediate release component. What does it allow for?

MR. FLATTMANN: Well, let me try to be clear. My consisting language cuts out the possibility of having an IR/SR. It says consisting of two portions comprising an IR portion and comprising a DR portion. The consisting language excludes the use of a sustained release.

JUDGE KAMHOLZ: Now, you just said Sheth's portion -- Sheth's -- we'll call it the DR portion, just so I can have a label for it, includes an IR portion. Why can't your claim encompass that?

MR. FLATTMANN: Well, because Sheth's secondary loading portion is an IR plus an SR. It's not an IR plus a DR, and I'll show you that. So it repeatedly refers to the secondary loading portion, and this is slide 24, with the term slow release, which a person of skill would identify as a slow sustained release, and that's in Dr. Rudnic's declaration, and it says explicitly -- Sheth says explicitly that "Its modified sustained release approach is improved over the

straight immediate release/delayed release formulations of the prior art," because it can maintain the sustained release over time.

NOW, and there's almost no lag before that secondary loading portion starts dissolving in Sheth, where there is by definition a substantial lag in Chang when the delayed release portion starts releasing. That's the whole point.

JUDGE KAMHOLZ: But all this argument concerning what Sheth discloses depends critically on the construction of delay.

MR. FLATTMANN: Well, I think it depends in part on that.

JUDGE KAMHOLZ: Delayed release.

MR. FLATTMANN: Right.

JUDGE KAMHOLZ: And you have not proffered a construction of that term.

MR. FLATTMANN: The parties have not proffered a construction of that term, but the plain meaning of that term is a release that is delayed as a matter of time, and that is consistent with all the examples --

JUDGE KAMHOLZ: You can give it to me later, but I would like to have a precise list, pinpoint citations of evidence that support your position on the plain meaning of delayed release.

MR. FLATTMANN: Sure.

JUDGE KAMHOLZ: You can give it to me --

MR. FLATTMANN: From the specification, Your Honor?

JUDGE KAMHOLZ: The evidence of record you are relying on for what the meaning of delayed release is.

MR. FLATTMANN: Yes, Your Honor. Understood.

JUDGE KAMHOLZ: Mr. Sabharwal, I'll request the same from you in your rebuttal.

MR. SABHARWAL: Yes, Your Honor. Yes.

MR. FLATTMANN: What does Sheth actually say?

JUDGE GREEN: Slide 27?

MR. FLATTMANN: Slide 27, Your Honors, sorry. It says let's use secondary loading portion to slow release using modified coding composition for the lab, and it's going to be compromise with a small amount of water soluble polymer and the pH-sensitive polymer previously used alone, and it incorporates four creating agents in the polymer coating, and it says that this is the variable that is preferred by Sheth. Okay? And when they are combined, the coating swells so that it slowly releases the minocycline right away.

JUDGE KAMHOLZ: Slide 20.

MR. FLATTMANN: And this is slide 20, Your Honors. It releases right away in the stomach, so this is not a delayed release. This is an immediate release and then there's a slow release over time according to this, so this is not a delayed release acting drug at all, okay?

Dr. Van Buskirk basically validates this in his deposition, and this is slide 23. He said that the section of Chang that he views as defining delayed release states that there is no substantial release in

the acidic stomach environment. There is a lag, and here Dr. Van Buskirk was relying on the column that I took you to, column 7 earlier.

So Ashley and Sheth are teaching away from the use of an immediate release, delayed release formulation. If you followed Ashley or Sheth, you would be lead in a path divergent from the path that was taken in the Chang patents, so you have --

JUDGE KAMHOLZ: Mr. Flattmann, please do try to mention slide numbers so Judge Braden can follow.

MR. FLATTMANN: Yes, Your Honor. I'm sorry, Your Honor. Slide 26, Your Honor.

JUDGE KAMHOLZ: Thank you.

MR. FLATTMANN: Okay. You would be led in a path divergent from the path that was actually taken by the Chang inventors. Ashley again requires a substantially constant rate of release and tell us to formulate the drug such that it does that, and that can't be done with an IR/DR only formulation. Sheth requires the secondary loading portion that immediately begins release in the stomach, whereas the delayed release portion of Chang requires no substantial release, and in fact involves a substantial two-hour lag.

Your Honor, there would also be no motivation to combine the references because they are directed to completely different formulation problems, and this is slide 28. Ashley was looking to maintain the drug level at a certain level that would be efficacious, but below a ceiling. Sheth had no maximum ceiling concentration

because he wanted to kill bacteria, and those are completely different formulation problems when you're looking at a drug with an unknown or only partially known absorption window.

JUDGE KAMHOLZ: Why isn't it simply a matter of scaling up or scaling down?

MR. FLATTMANN: Well, some of the formulations wouldn't work at all, if you simply scaled up or scaled down. Some approaches wouldn't work at all. For instance, a sustained release approach would not work here. It was attempted by Faulding, and it failed. It was attempted for a different drug by Dr. Rudnic, and it failed.

So it's not simply a matter of scaling up and down. It's a matter of trying to hit this very precise window with a specific formulation that's also going to be consistent over a large number of patients to keep their blood levels consistent, and that's a significant formulation problem.

JUDGE KAMHOLZ: Well, as I see the situation Ashley discloses the dose, 40 milligrams doxycycline, and Sheth discloses a ratio for distributing that 40 milligrams between IR and DR. I understand that whether it's DR is a contested issue here, but why wouldn't Sheth's disclosure of that ratio, if you accept for the sake of argument that it's IR/DR only -- why wouldn't that be applicable to any dose?

MR. FLATTMANN: One, it was a different drug. It was minocycline versus doxycycline, and there's no evidence of record that those operate the same in a controlled release formulation.

JUDGE KAMHOLZ: But why -- wouldn't minocycline be a reasonable place to start if you were tasked with developing a once a day formulation of doxycycline and you had no information on how to formulate doxycycline to be once daily? Isn't that a reasonable place for one of ordinary skill to start?

MR. FLATTMANN: I'm not sure, Your Honor. It is a different drug. It has different PK characteristics. The Federal Circuit found in the Abbott case that that isn't a reasonable step for a person of skill to take, to jump from one antibiotic to another one, and I don't think it necessarily would have been here.

JUDGE KAMHOLZ: What about the BMS case a couple months ago, the Baraclude case?

MR. FLATTMANN: The BMS case?

JUDGE KAMHOLZ: Yes.

MR. FLATTMANN: Well, I think in that case you had -- unlike this situation, you had far fewer choices and far fewer divergent paths that a person could take.

JUDGE KAMHOLZ: Minocycline and doxycycline differ at three substituents; is that right?

MR. FLATTMANN: That's right.

JUDGE KAMHOLZ: And in the Baraclude case, they differed at two?

MR. FLATTMANN: It was something like that, yeah. Yes.

JUDGE KAMHOLZ: Again I ask: I mean, is there any better place to start than a closely related member of the same drug class, a second generation tetracycline?

MR. FLATTMANN: It may be one place to start, or a person could have started with Ashley and gone down that wrong path, or -- but if a person started with Sheth, they would have made a drug that didn't work because they would have been releasing the doxycycline in the wrong place with the secondary loading portion. It would have been releasing almost everything in the acidic environment of the stomach.

JUDGE KAMHOLZ: Almost everything?

MR. FLATTMANN: Yes, because the immediate release portion would release there, okay? And let's say they took a 3 to 1 ratio in that case, so you've got 75 percent releasing in the stomach already, and then you would release a substantial portion, half or more of the secondary loading dose of doxycycline in the stomach when that poor infiltrated loading pellet begin to dissolve immediately.

JUDGE KAMHOLZ: Doesn't Sheth say that the minor portion --

MR. FLATTMANN: Well, it shows -- he shows a substantial portion is dissolving in the acidic environment of the stomach. The point is that's not delayed release.

Just getting back to my main point here, Your Honor, so if a person was interested in developing a delayed release drug, they wouldn't even look at Sheth. It's not what it is. They might have tried some of the delayed release attempts, formulations that existed in other art, but that's not what we're talking about.

Just jumping forward, Your Honor. Here is what Dr. Van Buskirk said about Ashley, first of all, on deposition.

JUDGE KAMHOLZ: Slide 31?

MR. FLATTMANN: And this is slide 31, Your Honor. He stated that given that Ashley gives no guidance as to which of the many possibilities was likely to be successful, it would require trial and error experimentation. He said Ashley was silent on which options should be used, and he said that it included formulations which would not work to treat rosacea and would not meet the levels, and he said he personally didn't know which formulations would work without going into the lab.

So how could a person of skill know at that time?

JUDGE GREEN: But isn't that true of most pharmacology? You're not going to know what's going to work until you go into the lab.

MR. FLATTMANN: That's true.

JUDGE GREEN: So I mean, if we're going to use that as our standard, every new drug is going to be patentable because you're not going to know if it works until you go into the lab or ever new formulation is going to be patentable because you're not going to

know if it works until you go into the lab because all we require is a reasonable expectation, not an absolute expectation.

MR. FLATTMANN: No, I accept what you're saying, Your Honor, but here it wasn't -- there wasn't some disclosure in Ashley that said, Use an IR/DR at 3 to 1 and see if it works, okay. There was a disclosure, Use sustained release, and by the way maybe use these other hundreds of thousands of permutations, so there the person of skill has no reasonable expectation because they don't know which path to take.

They don't know which path to try in the first place. They could go down any of those paths, and it's hindsight to say they would have chosen the path that the inventor took. We can only reconstruct that after the fact. The facts are really pertinent here. What did Ashley do when Ashley wanted to make this formulation? Ashley went to Chang and Supernus.

Again Dr. Van Buskirk said a person of skill reading Ashley would think that Ashley doesn't know what he's talking about, so that's how a person of skill would have viewed the reference.

Here there's no merit to Amneal's assertion that there's prima facie obviousness either because there's no overlapping range, and the reason, Your Honor, this at slide 35, is that Sheth doesn't disclose an IR/DR doxycycline range. One it's a minocycline range so it's not an overlapping range, and two, it doesn't have a DR component so it's not an overlapping range or ratio.

Even if the Board disagreed with that, Chang's claims are not prima facie obvious in view of the references because of Ashley's disclosure of an incredibly broad genus, because it showed no preference for IR/DR only, and it taught a wholly different path than IR/DR and a sustained release.

The 30 milligram to 10 milligrams formulation achieves the desired steady state blood levels for nearly the entire patient population. That's why it's critical here, and it maintains bioavailably that's comparable to the immediate release drug that came before, Periostat, which was the goal and the dream of Ashley to begin with.

Other formulations would operate differently, and this is in our papers as listed in the cites on this slide. 40 milligram immediate release would cause a lot of patients to go above that 1.0 level and have an antibacterial effect. If we put in more delayed release to immediate release, it would result in significantly lower bioavailably, and we would get patients below the .1 efficacy level, and that was borne out by the clinical trials, and we have that in our papers here.

JUDGE KAMHOLZ: Now, Claim 1 in the '405 patent --

MR. FLATTMANN: Yes, Your Honor.

JUDGE KAMHOLZ: -- refers to percentage ranges, 70 to 80 percent --

MR. FLATTMANN: Yes, sir.

JUDGE KAMHOLZ: -- IR and 20 to 30 percent DR. Your arguments are a little more narrowly focused than that. They're focused pretty precisely on the 10 milligrams. It says 30 to 10.

MR. FLATTMANN: Yes, Your Honor.

JUDGE: Are these arguments applicable to that claim?

MR. FLATTMANN: They are, Your Honor. I'll explain why. It's because those ranges are just hovering right around the critical range, so are we going to lose a -- 70/30 is the absolute sweet spot. 3 to 1 is the absolute sweet spot.

JUDGE KAMHOLZ: 75 to 25?

MR. FLATTMANN: 75 to 25 rather, 3 to 1. If we move outside of that range slightly, we're going get essentially the same result. If we go too far, we're not, so those claims are there just as protection against copycat infringers who might try to develop a product that's bioequivalent but has a slightly different ratio.

JUDGE KAMHOLZ: In the '406 patent, how is that ratio claimed?

MR. FLATTMANN: In the '406? Yes, Your Honor. In the '406 the ratio in Claim 1 is 75 to 25. Okay?

JUDGE KAMHOLZ: Thank you.

MR. FLATTMANN: Yes, Your Honor.

Your Honor, I'll move on to our alternative arguments which we would ask the Board to consider if the Board disagreed with us on nonobviousness.

Turning to slide 37. First, the '932 Ashley and the Ashley '854 are antedated, and they are not prior art under 102(a), so ground 2 should fail because Amneal has not proven that -- has not met its burden of proving that these are actually prior art.

JUDGE KAMHOLZ: I have to tell you, on this argument, you devoted about two pages of the response, and I couldn't understand it.

MR. FLATTMANN: I'll try to make it may sense.

JUDGE KAMHOLZ: Please do.

MR. FLATTMANN: Yes. Basically, Your Honor, there was a -- the Chang inventors started working on this under a joint inventor agreement with Collagenics in the 2001-2002 timeframe. As shown in Exhibit 2149, which is a clinical study report that details what happened between the period of July 27 and September 4 of 2002, they began work in earnest to develop an IR/DR formulation that would meet these blood levels at that time.

They developed an in silico modeling plan as of October 16 of 2002 as shown in Exhibits 2151 and 52, and they continued operating diligently to reduce that invention to practice all the way through December 9 of 2002, where they achieved an actual reduction of practice, as shown in Exhibit 2039 of an immediate release, delayed release, in silico model formulation that would meet these blood levels, and they suggested at that time the 3 to 1 ratio would be the preferable approach based on their modeling.

JUDGE KAMHOLZ: What is your answer to Petitioner's argument that there was an unaccounted period of a month?

MR. FLATTMANN: Well, they're just incorrect about that, Your Honor. They say that that period is sometime between November and January, and November of 2002 and January of 2003,

and there is a giant study report on the in silico modeling right in the middle of that period on September 9 where the inventors select the 30 to 10 ratio of IR/DR based on their modeling.

So that they relied I believe on a particular timeline that did not include that study and some other material that occurred during that timeframe, but there were multiple instances of diligence during that timeframe. Exhibit 2039 on December 9, 2002, the program expansion on December 17, of 2002 as Exhibit 2157 and others, Your Honor. So that's just incorrect.

There's conception before the '932 is art, and there's diligence all the way through to the filing of the Chang application in April, so the Ashley references aren't art, and if you turn to the exhibits I just outlined, it becomes abundantly clear.

There also -- there was an actual reduction of practice through the in silico modeling, and the case law makes it clear that that is sufficient in many cases, but actual reduction of practice isn't required to antedate under the case law like In re Stryker, In re Spiller, In re Stempel. The inventor needs to only antedate with regards to as much as is shown in the reference.

Here we're talking about Ashley where we don't have any actual formulation. We have a desire for that range. Well, we had a desire for that range in the early Chang conceptions where there might have been arguendo a desire for an immediate release, delayed release. Well, Chang had that as well in these documents that I've pointed out to you, and Chang also had a 3 to 1 ratio.

So effectively whether there was an actual reduction of practice or better or less, the claims were antedated by those activities. So the main references fall out, and there's no ground for obviousness.

Incorporation by reference, just briefly, Your Honor, the '932 does not identify the incorporated document with any detailed particularity. It doesn't give a serial number. It doesn't give a docket number. It gives a title and the name Collagenics, and it refers to an application, the '854, which was filed on the very same day as another application, the Ashley '916, so there was ambiguity in the record, and Amneal hasn't met its burden of proving otherwise under --

JUDGE KAMHOLZ: I'm sorry, the title and the filing date do not unambiguous identify the '854 application?

MR. FLATTMANN: No, not at all because a person of skill could never have found that application at the time.

JUDGE KAMHOLZ: No, no. The question is whether those two pieces of information unambiguously identify one application?

MR. FLATTMANN: One wouldn't know that until one ran a search, Your Honor, and one couldn't run a search to see if there were multiple applications, and if one had run a certainly they would find an application to Collagenics of the same date as '916.

JUDGE KAMHOLZ: You're taking the position that adding the serial number into the '854 disclosure would have constituted new matter?

MR. FLATTMANN: Adding it in? Well, it wouldn't have constituted new matter, but it would have made the -- it would have made the application available to a person of skill because then they could have searched or made a request to the Patent Office for that particular document. Here they could have made no such request, and they wouldn't have even learned the serial number until the '106 patent published many -- a good deal later, and if -- and that's even if they were led to the '106 and somehow stumbled upon it.

JUDGE KAMHOLZ: But isn't there ample case law to the effect that an unambiguous identification on that is the furnishing of sufficient information to pinpoint one application as opposed to all others is effective or sufficient for an effective incorporation by reference? I'm thinking of Harari v. Hollmer, In Re Fouche, and Ex parte Harvey.

MR. FLATTMANN: Well, I don't think in any of those cases there was a missing serial number. I'm not aware --

JUDGE KAMHOLZ: I believe they were all lacking serial numbers.

MR. FLATTMANN: And the docket numbers were in some of them. But here a person could not put their finger -- a person -- they're prospectively relying on the '854 as a 102(a) reference as incorporation by reference. Well, we know under 102(a) that you actually have to -- the public at least has to have access to the reference for it to be known, for it to constitute 102(a) art. Here it didn't exist.

A person of skill might say, Oh, incorporated by reference and want to read it. They couldn't get it. That's really the point, so it's not incorporated sufficiently to constitute 102(a) art as of this time, and it wouldn't have been available as set forth in the Kunin declaration and our papers until after the Chang inventors had already embarked on their case of conception and diligence.

JUDGE KAMHOLZ: This line of argument would not disqualify it as 102(e) art though.

MR. FLATTMANN: The CREATE Act would, Your Honor, yes, and I'll get to that.

So why does the CREATE Act disqualify the reference under 102(e)? This is slide 40, Your Honor. The inventions claimed in the Chang patent were undeniably made by Shire, the parties haven't disputed that, on behalf of Collagenics as a result of some joint research developments which were set forth here.

And these are were joint research agreements within the scope of 103(c)(2), and that has not been challenged by Amneal, so Rule 1.71 (g)(3) permits the names of the parties to that research agreement to be added to Chang, and we submitted a draft certificate of correction to Your Honors as Exhibit 2158, which could be filed at any time.

So Your Honors --

JUDGE KAMHOLZ: Why would such a certificate of correction not prompt the need for further examination?

MR. FLATTMANN: Well, a certificate of -- in the legislative history, it's made clear that a certificate of correction would not prompt the need for further examination. I can refer Your Honor in this to the house report number 108-425 at page 9 on the CREATE Act, and it states that the omission of names of parties to an agreement, to the agreement meaning a joint research agreement, is not an error that would justify commencement of a reissue or reexamination proceeding, so that was made very clear in the legislative history.

JUDGE KAMHOLZ: Is that of record?

MR. FLATTMANN: Your Honor?

JUDGE KAMHOLZ: Is that legislative history of record in this case?

MR. FLATTMANN: No, Your Honor, because it's something that we looked up after we saw their reply papers, and the question had not occurred to us before then. But as a result, Amneal hasn't carried its statutory burden here. The Ashley reference can be removed as a 102(e) reference simply by filing the joint research statement in naming the parties in the specification as we've set forth in Exhibit 2158.

They haven't disputed the facts on this at all. They've merely lodged the procedural argument that perhaps further reexamination would be required. I think the legislative history is clear that it would not be appropriate.

JUDGE KAMHOLZ: Wouldn't the MPEP suggest that an examination for obviousness type of a patent becomes appropriate when a JRA is proffered?

MR. FLATTMANN: I'm not certain of the answer to that, Your Honor, but I can address the substance of the double patenting question very briefly.

JUDGE KAMHOLZ: If you wish. I think you have about ten minutes.

MR. FLATTMANN: You're right, Your Honor, I better hurry up. They haven't raised any claims that would constitute double patenting. In fact, none of the claims of the three Ashley references that they refer to invoke the 3 to 1 IR to DR ratio or anything close to it so they haven't even said that they've proven that there would be an obviousness type of double patenting problem at all. They haven't established that, so there's no reason to say that the CREATE Act can't be invoked based on that argument. Thank you, Your Honor.

MR. MORRIS: Your Honors, Greg Morris for Supernus, and I'm going to talk about the objective indicia of nonobviousness. I would like to start out by talking about Supernus' prima facie case of nexus that it established, and if we could go to slide 43, please. Slide 43 shows that Oracea, the gross sales for Oracea have totaled over $1.4 billion since the drug was launched in 2006.

And Mr. Green, which is -- it's their economics expert, Amneal's economics expert, have admitted that the sales of Oracea

have been substantial since launch so this evidence is relatively unopposed by Amneal.

Also if we can quickly turn to slide 44, this talks about the market share for Oracea. Oracea is the most prescribed drug among those drugs approved by the FDA to treat rosacea. It's also -- even if you consider other oral medications that are prescribed off label to treat rosacea, it's still the most prescribed drug if you include drugs such as Solodyn, Doryx and generic Periostat.

The second prong of Supernus' prima facie case of nexus if we go to slide 45, is that Oracea is covered by the claims of the patents at issue in this proceeding, and this also is unopposed by Amneal, so Supernus has established a prima facie case, and the burden has shifted to Amneal to rebut this strong case of nexus.

JUDGE KAMHOLZ: But is it enough? Is it enough that the claim covered the product?

MR. MORRIS: I think there's additional evidence of nexus that I would like to discuss, Your Honor, if you would permit me.

JUDGE KAMHOLZ: Of course, but I'm having trouble understanding precisely what your position is. Is your position that you have made a prima facie case of nexus that it is for Amneal to rebut, or are you instead arguing that nexus is tied to the claim through a novel feature or is it both?

MR. MORRIS: I think it's both, Your Honor.

JUDGE KAMHOLZ: Okay.

MR. MORRIS: First that the burden has shifted under the Demaco case, which we cited in our briefs, and also I would like to address nexus, if we can go to Exhibit 28, please, and what this is going to show is -- Exhibit 28 shows the total prescriptions for Oracea are neither double that of Periostat, and that's remarkable because Periostat is by the -- their expert, their clinical expert, Dr. Gilmore, admitted that that drug costs ten times less than Oracea does, and if we can turn to Exhibit 2194.

JUDGE KAMHOLZ: Of course, Periostat can't be marketed for this purpose, and any prescription for it is an off label use.

MR. FLATTMANN: That's correct, Your Honor, and there's testimony by Amneal's clinical expert, Dr. Gilmore, that Periostat was -- it was well known that that was a drug -- it is well known that Periostat is a drug that could be used to treat rosacea and that she has in fact known that and other dermatologists know that, and it was well established even before the launch of Oracea in 2006.

So specifically I wanted to look at page 33 where Dr. Gilmore states that the only clinically meaningful difference between Oracea and Periostat is Oracea is prescribed once a day for once a day administration and Periostat for twice a day, so this along with the number of prescriptions for Oracea versus Periostat is powerful evidence that patients care about having once a day medications. They're willing to pay, doctors and patients are willing to pay up to ten times the amount for that feature.

So also as evidence in this case, we heard testimony from Supernus' clinical expert, Dr. Webster, who is a leading physician in the area and has treated hundreds of patients who had rosacea. He said that his patients -- because this rosacea is a chronic disorder, his patients really care about having a medication that's once a day, and that's also effective and has low side effects. They're lower than the traditional antibiotic dose.

What does Amneal give to try to explain away Oracea's strong commercial success? Let's go to slide 47. They say it's 100 percent due to marketing, that Oracea's sales of due to marketing, but Supernus' expert, Dr. Grabowski, did a calculation where he evaluated the number of marketing dollars spent per dollar of Oracea sold and found that that was lo and behold below the pharmaceutical industry average, and Mr. Green did a calculation as well of marketing to sales ratio, but in his calculation he didn't use the full length of time available.

He used a subset of that full length of time available to do his calculation, and when he was asked about that in his deposition, why he didn't use the full amount of data available, he couldn't answer that question. So that attempt to rebut Oracea's commercial success by saying it's 100 percent due to marketing fails, Your Honor.

And I would like to also move -- I know I don't have much time, but I want to move quickly to long-felt need. If we could have slide 48, please. Dr. Webster, who is Supernus' clinical expert, gave testimony in this case that there was a long-felt unmet need for an oral

once daily treatment for rosacea that reduced side effects associated with traditional antibiotic dosages of doxycycline, and Dr. Webster importantly based his testimony on firsthand knowledge treating patients with rosacea.

And Dr. Gilmore on the other hand, Amneal's clinical expert, if we can go to slide 50, her testimony should not be given significant weight, because as we see, her assessment and as she admitted in her deposition -- her assessment of long-felt need was based on published medical literature and not on personal firsthand experience.

In fact, when she was asked in her deposition what her experience was for treating patients with rosacea while during the relevant time period, she answered low, and that makes sense because during the relevant time period for analyzing long-felt need, she had not even graduated medical school.

So I would also, in their presentation -- they said that firsthand practical knowledge wasn't relevant or they seemed to suggest that, the In re Piasecki case at 745 F.2d 1468 certainly discussed that firsthand practical knowledge is very probative of long-felt need.

I would also like to go to Gilmore slide 49 -- or slide 49 in Patent Owner's presentation. Thank you. And Dr. Gilmore also admitted during her deposition in the case that there may have been a market pressure to develop a once daily formulation of Periostat. Let's also take a look at Exhibit 2186, this is -- refers to an expert Dr.

Augsburger, who was an Amneal expert in the litigation involving the '740 patent.

If we look at paragraph 683, hopefully we can see that, and we can highlight that paragraph, you can see that Dr. Augsburger said there existed both a design need and market pressure to develop a once daily formulation of Periostat, so that is long-felt need. I wanted to quickly touch on the failure of others.

Let's go to slide 41, please.

JUDGE KAMHOLZ: Mr. Morris, I'll give you two minutes. There were a couple interruptions during your time.

MR. MORRIS: Thank you very much, Your Honor. I want to go to slide 41. This is a showing by Supernus that there was a real world failure in Collagenics' attempt to make a once daily version of twice daily Periostat. Prior to Shire, Collagenics engaged a firm called Faulding to design a once daily version of Periostat and to design three SR formulations. Those formulations failed. Their bioavailably decreased from 30 to 50 percent.

Dr. Rudnic, who Supernus' world known formulator, testified that such a drop in bioavailably and absorption would be dangerous, and the FDA would be unlikely to approve such a formulation, and if we look at also Exhibit 2049, we can see that Collagenics itself thought that this was a failure. It said: "It's not going to achieve the stated goals," so this is a really world example of a failure and an attempt to design a once daily version of twice daily

Periostat, and those are the secondary considerations that I wanted to touch on.

JUDGE KAMHOLZ: Thank you.

MR. MORRIS: I appreciate it.

MR. SABHARWAL: Your Honor, can we have a moment to set up?

JUDGE KAMHOLZ: Of course. Mr. Flattmann, while they're getting ready, do you have cites concerning delayed release that you can share with me or are you relying on that you presented in your slides.

MR. FLATTMANN: We would like to submit some cites, Your Honor. I haven't pulled them yet, but I was going to do so right now if I could.

MR. SABHARWAL: I have some cites.

JUDGE KAMHOLZ: How about at the end?

MR. FLATTMANN: Certainly, Your Honor.

MR. SABHARWAL: Your Honors, may I have --

JUDGE KAMHOLZ: Please, you have 20 minutes.

MR. SABHARWAL: Thank you. Let me start, Judge Kamholz, by answering your question about where Amneal recited the definition of POSA construction for delayed release. I would like to direct the Board's attention to paragraph 14 of the second declaration of Glen Van Buskirk, our expert, and I'm going to paraphrase. It's paragraphs 19 and 20. He notes that there are limitations in the patent that talk about the PA sensitive layer, which can dissolve after certain

layers pass through the stomach, an example of a repeat action, dosage delivery, pulsatile delivery, and then the uncoated matrix as exemplars, and based upon that, he says that a POSA would have interpreted the term, quote, delayed release, to mean release of a drug at a time, quote, other than immediately following oral administration. That is again on paragraph 20, in the second declaration. That is Exhibit 1066, Your Honor.

In addition, Dr. Rudnic, their expert, in his declaration at paragraph 105 defines DR agent, as, quote an ingredient which prevents the active ingredient, i.e. tetracycline from being made available to the host until sometime after initial administration, and that is Exhibit 1003, so just taking a step back -

JUDGE KAMHOLZ: Exhibit 1003?

MR. SABHARWAL: I'm sorry, that's what I have written here.

JUDGE KAMHOLZ: That's Ashley.

MR. SABHARWAL: I'm sorry, that's Ashley. It's his declaration in paragraph 105, and I'll get you the Exhibit Number.

JUDGE KAMHOLZ: 2016?

MR. SABHARWAL: 2016. Okay.

In addition, Your Honor, and by the way so the two experts have fairly similar propositions for delayed release, and just again to remind the Board in our Petitioner on page 5, we proposed the BRI of certain terms, and then we stated that all other terms of the challenged

claims are presumed to take on the ordinary and customary meaning, and that's on page 5.

Your Honor, Mr. Flattmann and Mr. Morris have told a very nice story, and that's really what it is. It's a story. Many of the things that they said fly in the face of contradictions that are in the record, and the express disclosures, and I think Your Honors asked a number of pointed questions about that, and I'm not here to repeat that, but just to go through some of the misstatements.

Minocycline is a reliable place to start as -- in terms of a formulation for treating rosacea. The '932 application talks about that. Dr. Webster, their own expert, says that minocycline is a particularly useful for the treatment of rosacea.

JUDGE KAMHOLZ: That's not really the issue. The issue is whether information about how to formulate minocycline would be effective to inform the analysis or the design of a doxycycline composition, not whether the two are useful for this particular treatment.

MR. SABHARWAL: Well, actually Ashley talks about a formulation of 38 milligrams of minocycline, which is a sub antibacterial which would be useful to treatment, so they are talking about a specific dosage, and that does overlap. There is overlap between the IR and DR ratios of Sheth and what is claimed in the patents.

We have Dr. Rudnic talking about an IR/DR formulation, and he said under oath at his deposition that my patent that teaches

IR/DR claims includes minocycline. How can they now stand up here and tell this Board that a person of ordinary skill in the art would not have looked to minocycline? It doesn't make any sense. It's flatly contradictory, and the evidence should be given no weight whatsoever.

Now, let me talk about one other thing that Mr. Flattmann said when he first stood up. He seemed to connote that this Board should somehow rubber stamp what the District Court did in terms of its finding of fact. Well, the District Court actually did find that the Ashley '932 incorporates by reference the '854 provision in its findings of fact, but what the District did not know about is the admission that Galderma made during prosecution. In fact, coincidentally on the same day that Mr. Flattmann was standing up telling Judge Stark on July 5 of 2011 that the Ashley requires sustained release, Galderma's patent agent or attorney was paying the issue fee for the '240 application, which included the Claim 82 that said it cannot have a prolonged release. It must have IR/DR.

The real party in interest on the same day is telling the Patent Office one thing and Mr. Flattmann is telling the District Court something else. We think this speaks volumes, and that's why their entire case is smoking mirrors.

By the way, on July 18, 13 days later, for some reason Galderma withdrew the application that claimed the IR/DR only, don't know why, but I think we have a good idea. Amneal did not in any way relinquish its arguments by converting to a Paragraph III. The

decision to convert to a Paragraph III was wholly unrelated to any argument with respect to the prior art, and there's nothing in the record. That was just a gratuitous comment by Mr. Flattmann.

Judge Green, you asked Mr. Flattmann about the '320 patent, the Rudnic patent, and Mr. Flattmann said, Well, Dr. Rudnic stated that it didn't work. Well, the clinical efficacy, the bioavailably are -- none of those things are relevant. None of those things are set forth. Dr. Rudnic did not talk about any type of clinicals or bioavailability. He told the Patent Office that, I believe what is patentable is an IR/DR formulation of doxycycline. That is what he said to the Patent Office. He should not now be permitted to say exactly the opposite, that it would be counterintuitive to reduce something that he himself did, and the Board we respectfully submit should consider that and give his declaration no weight whatsoever.

Now, Mr. Flattmann also talked about Ashley as a wish. I just want to take a step back here. This is their application. Ashley is Collagenics's application, and they are trying to tell this Board that it's essentially worthless. It doesn't teach anything. Even Ashley said it didn't teach anything. Think about the lengths that Supernus is going to try and run away from the company who they claim to be a joint inventor on the '740. Let's just think about that for a second.

First of all under the law, we don't need actual formulations. That's set forth in KSR. The prior art should be read for all that it teaches, and we cited cases in our reply brief In re Mouttet which relies upon KSR. A prior art is relevant for all their teachings. You

don't need working examples. You don't need actual formulations, and the prior art, Collagenics's own application teaches the use of minocycline. It talks about an IR/DR combination. Mr. Flattmann went on and on and on about Dr. Grabowski's alleged admission. Dr. Van Buskirk clarified in his second declaration which he didn't bring that, I agree with the Board that there are essentially a very small laundry list I think was your words of different combinations, and you can vary those a little bit. You can vary some the excipients, but at the end of the day you have essentially seven combinations that are cited from Ashley '854.

And listen, Galderma relied on that same sentence to argue to the Patent Office that we should get a patent on IR/DR, so the fact that they are now arguing that that language is useless and is of no moment again is a direct contradiction of what the real party in interest says to the Patent Office less than four years ago.

Not to belabor this, Sheth let me just say what I said before. The term delayed release is used in Sheth over and over again. What's not used in Sheth is this idea of the modified sustained release. That just is pulled out of pure thin air like much of their arguments and allegations in this case. In fact, I would just like to point the Court out to something. Can we go to the Sheth -- yes. Your Honor, this is from their slides.

JUDGE KAMHOLZ: Slide 21?

MR. SABHARWAL: Yes, slide 21 of Supernus'. Your Honor, you see this coating on the outside? That's an enteric coating.

These are the pores that allow for this alleged slow release. This is from the hydrophilic polymer. What Sheth actually teaches is that you can close these up so that you have very little release in the stomach, just like what they're talking about, so you can make this entire thing even under their definition a delayed release.

In fact, Sheth actually says that only 5 to 20 percent of the delayed release portion should be released in the stomach, a very small portion. It's co-extensive, if you will, with which they're saying about what delayed release is.

I would also like to correct the record on some of the Sheth -- excuse me, the Ashley references. Can we go to their alleged substantially concentrated release? Yes. Your Honor --

JUDGE KAMHOLZ: Slide 8?

MR. SABHARWAL: Yes, I'm sorry, slide 8. I believe that Mr. Flattmann may have misspoken, and I'm not impugning any ill will here, but these passages, these passages are not talking about a substantially concentrated release of the drug. These passages are talking about a substantially constant rate of blood serum, blood plasma. In fact, it says here the composition, the unhighlighted portion, it says the composition of the invention provides its therapeutic effect by providing a dose of tetracycline below that which is required to produce an antimicrobial effect in the host at a substantially concentrated rate.

It then goes on to say the controlled release agent is designed to maintain, and here's the important part, the specific serum

concentration levels over an extended period of time, for example, 6, 8, 12 or 24 hours at a substantial concentrated rate, so this idea that Ashley requires substantially concentrated rate meaning the date of release is dead wrong. This is talking about the rate of the blood plasma.

In fact, as our Dr. Van Buskirk said in his declaration, Ashley actually teaches that the amount of drug and the amount of release can vary but what you need is this broadside of the barn. You need that .1 to 1.0.

Okay. I believe, Judge Green, you asked a question about their theory of obviousness. Excuse me, our theory of obviousness. Our theory is simple. Number 1, a person of ordinary skill in the art would have arrived at this allegedly critical range of 75/25 through routine experimentation, and we cited case law that talk about that, for example, the In re Peterson case. Routine experimentation. This is a mature product. We're not talking about a cutting edge product. We're talking about a sustained release drug which has been made for many, many, many, many decades.

We're talking about instantaneous release, delayed release of oral solid dosage. This is nothing more than using routine procedures with known results to obtain predictable -- excuse me, routine procedures, retain methodologies, predictable results. Seven minutes? Thank you.

Okay. I would now like to correct a few things on the '740 patent. Your Honor, Mr. Flattmann just made a rather critical

admission that Claims 3 and 4 I believe of the '740 patent are mistakes. Well, I'm surprised by that because they've been litigating this patent for a long time against Amneal, and this is the first time I ever heard them concede these were mistakes. In fact, I deposed Dr. Rudnic about these claims, and he never said they were mistakes, and we would object to the extent they're relying upon the limitations of these claims to in any way impermissibly narrow the scope of the disclosure of Claim 1.

I think, Judge Kamholz, you were spot on that there's comprising language. It's not limited to 30 milligrams. It could be more, and they shouldn't rely on Claims 3 and 4, which they've said now are a mistake, to in any way narrow the limitation.

I think -- I believe that was all of the things I had on the prima facie case. Two minutes left? This won't take more than a minute.

Judge Kamholz, I wanted to correct one answer that I may have mistakenly given you at the beginning. We do not concede that the commercial success is coextensive with the patent. There are many limitations. All of the limitations that are recited are in the prior art, and there's no evidence to show that the patented features drive the sales.

Mr. Morris was talking about the big commercial sales. Well, what Mr. Green said is that's a function of not just marketing but also the fact that it is the only approved drug to treat this condition and that is current.

JUDGE KAMHOLZ: The only approved doxycycline.

MR. SABHARWAL: I'm sorry, the only approved doxycycline, thank you. Thank you. And we have Dr. Grabowski saying that the once a day formulation is not a key driver. We have admission after admission about this.

My last point, last two points: They also made a lot about this Faulding study, that the Faulding study demonstrated failures of others. That's incorrect. The Faulding study did show that patients achieved a blood plasma level of .1 to 1, at least some of the patients did. This is not a situation where the claims talk about bioavailably or that a majority of the patient need to receive it. All they need to show is that at least a patient using the Faulding formulation fell within that, and they did, and the evidence is very clear about that.

This is not about bioavailability. There's no limitation about bioavailability. That's just a red herring.

Lastly, the one thing, the one commercial success item that they did not mention is copying. Can you go to their alleged evidence of copying, and I think --

JUDGE KAMHOLZ: I think if they didn't discuss it --

MR. SABHARWAL: I'm sorry. They were talking about the secondary consideration evidence. It's in their slide.

MR. FLATTMANN: Yeah. We didn't discuss copying.

MR. SABHARWAL: It was just in their slides.

JUDGE KAMHOLZ: I believe they didn't address it during their arguments.

MR. SABHARWAL: In that case, do Your Honors have any questions about the antedation issue or the incorporation by reference? Mr. Ainsworth can address those.

JUDGE KAMHOLZ: Judge Braden?

JUDGE BRADEN: I do not have any questions at this time.

MR. SABHARWAL: With that, we have nothing further.

JUDGE KAMHOLZ: Mr. Flattmann.

MR. FLATTMANN: I simply have the list of citations --

JUDGE KAMHOLZ: Please.

MR. FLATTMANN: -- that Your Honor requested relating to the term delayed release and how that would be understood by a person of ordinary skill in the art at the time of the invention.

I would like to refer Your Honors to Dr. Rudnic's declaration, Exhibit 2016, at paragraph 176 where he discusses the meaning of delayed release in the context of the invention with reference to both the art and the figures I showed Your Honors earlier.

I would also like to direct Your Honors to the Van Buskirk declaration, Exhibit 1066, page 14, paragraph 20, where he discusses the fact that delayed release involves a delay subsequent to administration.

JUDGE KAMHOLZ: Mr. Sabharwal, is that the same paragraph you cited?

MR. SABHARWAL: I believe so. I know it is for Van Buskirk. I'm just checking my notes.

JUDGE KAMHOLZ: It's not the same for Rudnic.

MR. SABHARWAL: It's not the same for Rudnic? Maybe there's two places, Your Honor, where he says it.

MR. FLATTMANN: I would also like to direct Your Honors to the Van Buskirk deposition transcript, Exhibit 2193, at pages 11, line 7 through 13, and line 6.

JUDGE KAMHOLZ: I'm sorry, would you say that more slowly?

MR. FLATTMANN: Yes, Your Honor. Exhibit 2193, at page 11, line 7 through page 13, line 6, and page 16, line 14 through 17, line 2, where Dr. Van Buskirk discusses delayed release and how he views it as being defined in the Chang patent.

Also, Your Honor, I would direct you to two pieces of guidance for industry that are submitted in our papers, Exhibit 2058 at pages 30 and 32, and Exhibit 2047, at page 7, Your Honor.

JUDGE KAMHOLZ: Exhibit 2047 at page 7?

MR. FLATTMANN: At page 7, Your Honor. And again the intrinsic evidence, Exhibit 1001 at column 7, lines 47 to 53 and figures 2 and 3.

Thank you, Your Honor.

JUDGE KAMHOLZ: Thank you. That concludes the hearing for these proceedings. We are adjourned. Thank you.

(Whereupon, at 3:13 p.m. the oral hearing was concluded.)