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Paper No. 67

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

INCYTE CORPORATION,
Petitioner,

v.

CONCERT PHARMACEUTICALS, INC.,
Patent Owner.

PGR2021-00006
Patent 10,561,659 B2

Record of Oral Hearing
Held: February 10, 2022

Before CHRISTOPHER G. PAULRAJ, ROBERT A. POLLOCK, and DEVON ZASTROW NEWMAN, *Administrative Patent Judges*.

APPEARANCES:

ON BEHALF OF THE PETITIONER:

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The above-entitled matter came on for hearing on Thursday, February 10, 2022, commencing at 1:00 p.m., EDT, at the U.S. Patent and Trademark Office, by video/by telephone.

P R O C E E D I N G S

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JUDGE NEWMAN: Hello everyone. Welcome. We are here in the matter of Incyte Corporation v. Concert Pharmaceuticals, Inc., in PRG 2021-00006 regarding patent No. 10,561,659. Can you please for Petitioner's side identify who is here with us today? I'm sorry, I can't hear you speaking. You need to unmute yourself on the microphone.

MR. FELDSTEIN: Sorry, Your Honor. This is Mark Feldstein from Finnegan, Henderson on behalf of Petitioner Incyte Corporation. I'll be joined today in the argument by my colleague, Drew Christie, also of Finnegan, Henderson.

JUDGE NEWMAN: Thank you. And for Patent Owner?

MS. DELSIGNORE: Good afternoon. Marta Delsignore of Goodwin Proctor. I am here today with Gerard Cedrone, Emily Rapalino and Daryl Wiesen who will be speaking on behalf of Patent Owner.

JUDGE NEWMAN: All right. I have to admit I'm having some trouble hearing you. We need to find a way to get your volume much higher if possible.

MS. DELSIGNORE: Can you hear me now, Your Honor?

JUDGE NEWMAN: Still very light. Panel members, are you also having trouble hearing? Yes. We're going to need your volume much higher or if you could be closer to the microphone

somehow that would be helpful.

MS. DELSIGNORE: Your Honor, can you hear me now?

JUDGE NEWMAN: That is slightly better but it's still going to be a bit difficult.

(Pause.)

JUDGE NEWMAN: Okay. Why don't we take five minutes and see if we can't get our technology team to get better access on this.

(Pause, due to technical difficulties.)

MS. DELSIGNORE: Is this better, Your Honor?

JUDGE NEWMAN: I can hear that a little bit more clearly. Other panel members as well? Okay. I think we can proceed with that. Thank you. All right. So would you please, Ms. Delsignore, please identify again who is representing Patent Owner, yourself and who else.

MS. DELSIGNORE: Representing Patent Owner today are Gerard Cedrone, Emily Rapalino and Daryl Wiesen. I apologize for the delay, Your Honor.

JUDGE NEWMAN: That's quite all right. And court reporter, do you need spelling on any of those names?

THE REPORTER: No.

JUDGE NEWMAN: Great. Okay. We'll proceed, and each side has 60 minutes but because there also has been an application for a LEAP practitioner speaking on each side we have an additional 15 minutes bringing the total to 75 minutes

per side. Petitioner will proceed first and Petitioner, would you like to reserve any time for rebuttal?

MR. FELDSTEIN: Yes, Your Honor. I'd like to reserve 15 minutes for rebuttal.

JUDGE NEWMAN: All right. And for Patent Owner?

MS. DELSIGNORE: We would like to reserve 15 minutes for rebuttal.

JUDGE NEWMAN: And we'll give you a one minute warning unless you wanted some different period of time.

MR. FELDSTEIN: That's fine for us, Your Honor.

MS. DELSIGNORE: That's fine.

JUDGE NEWMAN: Okay. Great. And we can jump right in but does anyone want to address the Motions for Exclusions of Testimony first? You don't have to but you're welcome to.

MR. FELDSTEIN: Your Honor, on Petitioner's side we were going to address the motions. We had intended to do them second but we'll do them first if you prefer.

JUDGE NEWMAN: You may choose the order, that's fine with us.

MR. FELDSTEIN: We'll do it second then.

JUDGE NEWMAN: All right. Are we ready to go? We can start the testimony clock. Okay. Let's go. Please begin.

MR. FELDSTEIN: Thank you, Your Honor. Again, Mark Feldstein on behalf of Petitioner Incyte Corporation in this PGR. I'd like to direct the Court's attention, I understand we're not

going to be showing slides, but direct the Court's attention to slide 3 in our slide deck in our demonstratives just to lay the foundation for what the grounds are. The petition initially had three grounds, grounds 1 and 2 covering obviousness of claims 1 through 21 under 103 based on two different sets of references and then a third ground, ground 3 anticipation of claim 8. Patent Owner disclaimed claim 8 prior to Institution mooting ground 3 and reducing grounds 1 and 2 to all claims except for ground 3.

Looking at slide 4 of our slide deck. The obviousness argument which is substantially the same in terms of the issues that have come up in the case, substantially the same between ground 1 and ground 2. On slide 4 there are three basic elements of the obviousness case and that (indiscernible) fundamentally simple. The Ruxolitinib was known to treat Alopecia Areata, that's a hair loss disorder. There are express teachings in the art to use Compound (1) in place of Ruxolitinib and the claimed dose ranges are within known ranges and are obvious to optimize.

At a high level Concert's responses are that they're asserting a prior art exception of the 102(b) for parts of the Silverman reference but even if they could establish the 102(b) exception for parts of Silverman, it does not remove other relevant subject matter of Silverman that's more than sufficient to establish unpatentability. Concert also relies fairly extensively on trying to assert that the field is actually very

complex and that alternatives to -- there were alternatives that taught away from oral Ruxolitinib for Alopecia Areata. None of those, as we'll get into, hold water given that Ruxolitinib and other JAKs were already being used to treat Alopecia Areata and in fact were used by all clinicians in this case. So this is not a case where we have to hypothesize what wouldn't a person of ordinary skill in the art have done. We know they were already using oral JAK inhibitors including Ruxolitinib to treat Alopecia Areata and of course as we'll get into it Concert's allegation that alternatives teach away is mistaken legally and factually. More than one possibility can be obvious at the same time and the mere fact that you have alternatives doesn't teach away from another alternative, even if one of them is preferred over the other.

Concert's third main response is to rely on objective indicia and as we'll see there too none of the information they rely on is unexpected. None of the events they rely on has nexus with the claim and none is commensurate in scope and I'll note here, in case I forget to do it later, Concert doesn't appear to argue any of its objective indicia separately for any claim so we think for objective indicia focus on claim 1.

We direct your attention now to slide 5 to the first point in the three elements of the obviousness case, the Ruxolitinib JAK inhibitor was known to treat Alopecia Areata. This is disclosed in the Christiano reference where it's taught and provided

rationale for why Ruxolitinib would be effective in treating Alopecia Areata and that it specifically claimed in the Christiano patent as a drug for the treatment of hair loss disorders.

Xing goes one step farther, they're actually related groups Xing and Christiano, Xing goes one step farther and includes both a mechanistic basis of why JAK inhibitors treat Alopecia Areata, includes pre-clinical data in a mouse model of hair loss disorders and shows efficacy and in fact it shows clinical efficacy in pre-patients. One of them is shown in this figure that's been described in the art as providing striking efficacy in the treatment of Alopecia Areata and I noted and let me just reiterate that it was this pre-clinical efficacy that's important. We hear from Concert one of their arguments is that well, you can't trust your eyes basically in what you see in this figure and what the clinicians saw in terms of hair regrowth because there could have been spontaneous remission. Now there's no evidence and no suggestion that any of these patients actually underwent spontaneous remission so it's pure speculation on their part that it's something that could have happened but moreover, where Xing studied in a pre-clinical model they included a mouse that was -- mice that had no hair on their abdomen and they treated one half with a JAK inhibitor, one half was left untreated and they saw efficacy on the treated half and the untested area remained alopecic and that's in Xing, Exhibit 1003 at page 10 and so you know from the mechanism, you know

from the pre-clinical data that there's proven efficacy than a treatment effect from the drug.

It's not just Christiano and Xing. The results of Xing and the treatment of Alopecia Areata with a JAK inhibitor including Ruxolitinib are reinforced by larger studies for both Ruxolitinib and another JAK inhibitor called Tofacitinib. Both were presented in 2015 at the Alopecia conference and what the right hand side of our slide 5 the Mackay-Wiggan publication is an abstract Exhibit 1143. It had nine of twelve patients demonstrated a remarkable response to treatment with Ruxolitinib. The next citation on slide 5 is a reference to a treatment with Tofacitinib that actually included in the working group Concert's expert Dr. Ko and it was presented in 2015 and it would show that over three months this other JAK inhibitor produced significant hair growth in 75 percent of the patients.

Concert argues that somehow notwithstanding all this evidence that somehow our focus on JAK inhibitors for Alopecia Areata is hindsight. That's not so. If we turn to slide 19 we have part of their argument on the left hand side of slide 19. Concert argues that the prior art as a whole did not single out JAK inhibitors as a particular subject of interest and in fact that is not true. We can again look at what was going on in 2015 at a national Alopecia Areata Foundation summit. They listed a number of future research priorities. Three of these were directly related to the treatment of Alopecia Areata with JAK

inhibitors. It got down to the level of advocating for insurance coverage of systemic or topical JAK inhibitors, so it clearly was a research priority. The reference Exhibit 2063 similarly recognizes that studies are focusing attention on the JAK pathway. The Schwartz reference, Exhibit 1015, recognizes that JAK inhibitors are "a new chapter in the treatment of new disorders" in which the paradigm has been fundamentally shifted yet again. Earlier in Schwartz, Exhibit 1015 at page 12, Schwartz recognizes that Ruxolitinib among others had been used successfully to treat Alopecia Areata and Alopecia Universalis-related disease.

We also know it's not hindsight, if we can turn to slide 17, we know it's not hindsight to focus on JAK inhibitors for the treatment of Alopecia Areata because all the clinicians in this case are using JAK inhibitors for the treatment of Alopecia Areata by May, 2016. Dr. Ko, then Concert's expert, was using JAK inhibitors for Alopecia Areata. Dr. Shapiro and Dr. Damsky, our experts, were likewise using JAK inhibitors for the treatment of Alopecia Areata.

In addition to Dr. Ko, Concert's expert, admitting that he used it he also, outside of litigation context, has published that Xing, our primary reference in ground 1, recognized that Xing taught that Ruxolitinib "induced inflammatory remission hair regrowth." This is in a paper written where Dr. Ko is the second author. It's Crispin paper Exhibit 1152 at page 2 and what the

authors write in Exhibit 1152 at page 2 on the right hand side is,

"An important therapeutic insight was a discovery that blockade of common signaling pathways downstream of cytokine receptors, in particular JAK/STAT could reverse AA in mice," citing reference 5 which is Xing. "Subsequently, treatment of 3 patients with the JAK1/2 inhibitor Ruxolitinib," citing reference 5 which is Xing, "induced inflammatory remission and hair regrowth."

So there's no basis for Concert to assert that there's any hindsight in the focus of JAK inhibitors. JAK inhibitors were in fact in use. JAK inhibitors were a focus. JAK inhibitors were a priority for the treatment of AA.

Concert's next argument is that preferences -- there were preferences for Tofacitinib, there were Ruxolitinib and preferences for oral -- excuse me, topical over oral -- that also was not the case and if we can go to our slide 2 even if it was the case the law is actually clear. In re Moutet is a well known case and it makes the point very well.

"Just because better alternatives exist in the prior art does not mean that an inferior combination is inapt for obviousness purposes."

In other words, even if there was a preference for Tofacitinib, even if there was a preference for topical JAK inhibitors, that does not make the use of Ruxolitinib orally any less obvious.

But in fact if we move on to slide 24, the alternative Tofacitinib did not teach away from Ruxolitinib. There is nothing shown in the evidence that Tofacitinib was better. If we look back at the Xing reference on the left hand side of slide 23, the graph -- you may have to zoom in on your screen if you're looking electronically -- but the two lines that go up on the graph are essentially overlapping curves, one for Ruxolitinib JAK1/2 and one for Tofacitinib, the JAK3, their efficacy was as one can see equivalent and so there was nothing to show that Tofacitinib was better and --

JUDGE NEWMAN: Counsel, just to interrupt you for one second. One of those if Tofacitinib and one of those is Ruxolitinib?

MR. FELDSTEIN: Correct, Your Honor.

JUDGE NEWMAN: Okay.

MR. FELDSTEIN: The JAK1/2 is Ruxolitinib and the JAK3 -- so the orange curve is Ruxolitinib and the blue triangles is Tofacitinib.

JUDGE NEWMAN: Thank you.

MR. FELDSTEIN: You'll hear, and I think Concert tries to make too much of this unfortunately, that Dr. Shapiro was prescribing at the time Tofacitinib for Alopecia Areata and that's true. He testified to that. But the reason that he explained multiple times was because as a practical matter Ruxolitinib was more expensive and thus unavailable to the patients and what he

explained in Exhibit 2054 which was his deposition on cross-examination, lines 33 to 19, he was asked,

"Q But you never used Ruxolitinib prior to May, 2016 to treat AA?"

"A I wanted to, okay, but it was difficult for us to obtain for patients because of the high cost so we went with more for the Tofacitinib route."

And there are other quotes and you may see in Concert's slides depending on if they use them, other times where they point to Dr. Shapiro's use of Tofacitinib prior to May, 2016 and if Your Honors read the context of the transcripts around those questions in each case he explains that it was a cost issue, a cost issue alone and as we cite in the Butamax Advanced Biofuels v. Gevo, Inc., IPR on slide 23 commercial viability does not control the obviousness situation. It was entirely obvious to use Ruxolitinib. It was already in use and the fact that doctors chose the less expensive Tofacitinib doesn't make Ruxolitinib any less obvious.

If we go on to slide 24, in terms of topical the situation is similar but as Dr. Damsky explained, and I think there's no dispute on this in the evidence or the testimony from their experts either, in practice most often the use the JAK inhibitors for AA was oral, most of it was oral and they're going to rely heavily -- Concert's going to rely heavily on generic preferences for topical over oral and what they leave out every time they

point to this is Dr. Shapiro's explanation here on slide 24 that you would favor topical over oral if they have the same efficacy. So the problem with Concert's argument is there is no evidence that they had the same efficacy. They were using oral because oral had been shown efficacious in humans. It hadn't been -- topical hadn't been shown to be equally efficacious with oral and so it's just wrong that topical was preferred in this case because there was in fact no equal efficacy of the topical.

I can go on to the second point of our argument, go back to slide 6, the obviousness of substituting known equivalents. This is a legal principle I don't think is disputed by Concert. In re Fout, Coalition for Affordable Drugs IX LLC v. Bristol-Myers Squibb Co. IPR and In re Ruff basically explain that where that it's prima facie obvious to substitute one known equivalent for another and that is exactly our facts here.

If we go on to slide 7 which is on the left hand the Silverman patent. The Silverman patent expressly teaches the substitution and the equivalents and the interchangeability of Compound (1) for Ruxolitinib. It tells you in column 20, lines 57 to 62 of Exhibit 1002, it tells you,

"According to another embodiment the invention provides a method of treating a disease that is beneficially treated by Ruxolitinib and the subject in need thereof comprising the steps of administering to the subject an effective amount of a compound or a composition of this invention."

So Silverman tells you explicitly that to substitute its compounds which would include Compound (1), its compositions which would include compositions of Compound (1) in where Ruxolitinib is being used. Concert's counter to this, as I understand it, is that there's no motivation to select Compound (1) specifically from Silverman relying on -- I think they rely on at least the lead compound analysis, for example UCB, Inc. v. Accord Healthcare, Inc., and if we can go to slide 26 in our deck the lead compound analysis just doesn't apply in the context of the method claim with the one they're claiming. The Novartis case, Novartis Pharms. Corp. v. W-Ward Pharms. Int'l. Ltd., from the Federal Circuit 2019 rejected the idea that there had to be a reason for the compound to have stood out in the lead context analysis and what it held was that all you need is motivation of one of several potential alternatives and so it matters not that there are 63 or something like that species in Silverman of Silverman formula A. They're all taught to be used in place of Ruxolitinib and you don't need a lead compound analysis pointing to Compound (1) specifically to make the use of Compound (1) obvious where Silverman tells you use my compounds in place of Ruxolitinib.

But in fact there's additional motivation that does point directly to Compound (1) in particular and we go to our slide --

JUDGE NEWMAN: Counsel, if I could interrupt one moment to ask a question. There is some evidence on the record

that some of these compounds could be toxic and so is there any reason to believe that any one of the disclosed compounds in Silverman would not be toxic?

MR. FELDSTEIN: There's no --

JUDGE NEWMAN: (Indiscernible).

MR. FELDSTEIN: -- there's no reason and I don't believe there's any evidence that the deuterated versions of Ruxolitinib could be toxic. I think the toxicity is a hypothetical issue where deuteration can affect other processes like side reactions and such, metabolic side reactions, and what we know is that -- and if I can direct us to slide 31 -- Silverman tells you where the metabolic hotspots are on formula A. It tells you that they're the 2 and 3 positions and what the art taught and what actually -- if I can actually go back to slide 30 for a second, what the art taught and it was basically the premise of the prior IPR between the parties -- a finding was that you would know to deuterate Ruxolitinib's metabolic hotspots to achieve improved safety, tolerability, efficacy and that's confirmed here by Dr. Montellano in this case as well as Dr. Guengerich and Dr. Patterson and so to answer your question if I can more directly, there is evidence that in other systems where the metabolism is different that you could maybe create a toxic metabolite. Here we know what the metabolites are. We know the metabolites have in the 2 and 3 positions and there's no evidence that the metabolites of Ruxolitinib are toxic.

JUDGE NEWMAN: All right.

MR. FELDSTEIN: There's no reason why Ruxolitinib at these hotspots would shift to some other toxic metabolite. So in essence I see it as a hypothetical concern, sort of an abstract metaphysical possibility that sometimes you have a problem of toxicity but it's just not applicable to the facts that we have Ruxolitinib that has a very well established metabolism and a teaching where its hotspots are.

JUDGE NEWMAN: All right. Let me ask this question then. Of the compounds disclosed in Silverman how many of them are deuterated at that 2 and 3 position?

MR. FELDSTEIN: I think Compound 111 using the Silverman nomenclature is the only that's deuterated at all eight of those positions because there are four 2-positions and there are four 3-positions (indiscernible) and so there's only one compound that has those eight. There's another one, Compound 127 that has all nine, looking at our slide 31, there's a Y1-position that's not circled. Compound 127 has that ninth turning to deuterium and there are multiple versions where the Y2s are deuterated or the Y3s are deuterated but not both. Compound 111 is the only one where it's eight and just eight.

JUDGE NEWMAN: So if I'm understanding your argument, you're saying that one of skill in the art would naturally be looking at those deuterated 2 and 3-positions and selecting which compounds to proceed with?

MR. FELDSTEIN: Correct. It you deuterate at the 2 and 3-positions as suggested by the statement in Silverman there's one unique compound that you get out of that and that is in Silverman nomenclature Compound 111, in the '659 nomenclature it's Compound (1). It brings you to a single compound.

JUDGE NEWMAN: Okay. Thank you.

MR. FELDSTEIN: So again, to back up half a step. It's not necessary that the art pointed to Compound (1) but the art did point to Compound (1) based on the deuteration of its metabolic hotspots.

If I go now to the third element of our obviousness position on, if we turn to slide 35 regarding the dosage amounts and there's lots of clear law such as E.I. DuPont de Nemours & Co. v. Synvina C.V., such as Galderma Lab'ys, L.P. v. Tolmar, Inc., that makes it clear that when the claimed invention falls within a prior art range there's a presumption of obviousness and a burden of production falls on the patentee to come forward with contrary evidence. That here those apply here because if we go on to slide 36 Silverman provides repeated sub-ranges within the range of 5 to 50 milligrams, all of which would be obvious to optimize within. Silverman points to the Ruxolitinib prescribing information,

"For example, guidance for selecting an effective dose can be determined by reference to the prescribing information for

Ruxolitinib."

So Silverman points you to the prescribing information. The Ruxolitinib prescribing information provides a dose range of 5 to 50 milligrams per day and so there is an effective dose range for Ruxolitinib. There's an effective dose range for Compound (1) and it's a range that includes 5 to 50 within which it would have been obvious to optimize.

What Concert argues, as I understand it, is that they ignore all the green ranges that we have marked on slide 36 or at least try to point away from those in favor of the very first range 1 to 500 milligrams with the argument relying on DuPont that broad ranges are not necessarily obvious to optimize. There's actually no reason to think that in the evidence we have that a 1 to 500 milligram range is not obvious to optimize. What DuPont pointed to, for example, on an example of the range that would be too big would be a prior case where there were 68,000 permutations of a protein and that was too big for obvious optimization but Galderma, for example, went in a range I believe of from a hundredfold range of .005 to 5 -- excuse me, from .01 to 1 percent and so Galderma relied on a hundredfold range from 1 milligram to 500 is a five hundredfold range but there's nothing particular to say that you couldn't even optimize the 1 to 500 milligram range and don't think that Concert points to anything to say otherwise.

Concert also argues that none of these ranges are specific

to Compound (1) for Alopecia Areata, in fact Silverman ranges are very specific to Compound (1). Those are the doses for the compounds of their invention which include Compound (1) and moreover, what Silverman teaches is it's teaching methods of treating diseases that are beneficially treated by JAK1/2 inhibition and so these are the doses for treating diseases by inhibiting the JAK1/2 pathway which is the mechanism for treating Alopecia Areata. So we would beg to differ with Concert that these are not doses for Alopecia Areata, they may be doses for other JAK mediating conditions as well but based on Silverman, Silverman is teaching doses for Compound (1), for immune diseases and for diseases where Ruxolitinib is beneficial and that would include Alopecia Areata.

Even if we didn't have these ranges, if we go on to slide 37 there's additional bases for --

JUDGE NEWMAN: Counsel, let me ask one quick question here. For prescribing information for Ruxolitinib what other applications did Ruxolitinib have that were different from Alopecia Areata?

MR. FELDSTEIN: So to be clear the Ruxolitinib package insert was not approved for Alopecia Areata so the use of Ruxolitinib for Alopecia Areata was according to Xing and these other references. Ruxolitinib was approved in its package insert covered treatment of two different JAK mediated cancers, myelofibrosis being one of them.

JUDGE NEWMAN: And Xing, was there information about dosing or Christiano?

MR. FELDSTEIN: Correct. And that's actually on our slide 37 we include that and in the chart at the bottom we can see that there is on the bottom right there's a 40 milligram dose of Xing. They just use one daily dose, 40 milligram dose of Ruxolitinib and what we're illustrating here on this slide and the testimony supports this, when people used Ruxolitinib off-label for other than its cancer indications, when they used it off-label for immune diseases they worked within the approved dose range, Ruxolitinib approved dose range, of 5 to 50 milligrams and so I think all or essentially of the evidence in the record showing the off-label use of Ruxolitinib it falls within this 5 to 50 milligram range and so Silverman pointed you to the Ruxolitinib label. It's consistent with the way persons skilled in the part used Ruxolitinib and other similar drugs off label to work within the prescribed range and it makes sense that they did that because this is something explained by Dr. Shapiro in his declaration which is Exhibit 1009, paragraph 50. What Dr. Shapiro explained is that, he said,

"Given that Ruxolitinib provided systemically effective JAK inhibition of these doses, the 5 to 50 milligram doses, a POSA would have expected that doses in this range also would treat hair loss disorder via JAK inhibition as described in Christiano, Xing and others."

In other words, you're administering Ruxolitinib in its approved range and you're getting systemically effective JAK inhibition. You would expect to have systemically effective JAK inhibition for other diseases within that dose range too because you've established that for its approved condition you're getting systemic efficacy and JAK inhibition. Dr. Patterson, Exhibit 1007, one of our other experts at paragraph 119 makes a similar point that these dose ranges of the 5 to 50 milligram per day dose ranges on the Ruxolitinib label are the known effective doses for systemic JAK1/2 inhibition by Ruxolitinib and so it's consistent that Silverman points to the Ruxolitinib prescribing information because that's where a person of ordinary skill would have looked anyhow and we know they would have looked there, or at least their prescribing habits are consistent within that range and so you've got a range of 5 to 50 in the approved dose range that guides treatment.

Just briefly, if we can go to slide 39 there's a strong response of Ruxolitinib in 30 and 40 milligrams per day plus it's linear form of kinetics provided motivation for lowering the dose to be able to still get efficacy as a further reason to lower the dose and then just briefly also on slide 40 there's a whole ton of art to this effect but the point of deuterium modification or a point of deuterium modification is optimization and of dosing including achieving a smaller dose. The main purpose of deuteration is that you reduce the drug's metabolism, you slow

the drug's metabolism so that the exposure per a same dose builds up and if exposure goes up you can cut the dose down and so it's entirely expected that especially for a drug that has the properties of Ruxolitinib and it's known metabolism, that if you deuterate its hotspots you're going to be able to achieve the same exposure with a lower dose and I had mentioned this earlier in response, on slide 41 I had referred to this earlier in response to an earlier question from Your Honor regarding toxicity. The issues of -- that consequence here that confound and allegedly make deuteration unpredictable, things like metabolic switching, ultimate routes of clearance, rates of blood flow, the evidence is clear that none of them apply to Ruxolitinib and so what Dr. Guengerich, one of our other experts explained, is that the specific metabolic reactions by which Ruxolitinib is metabolized at its metabolic hotspots that there was even higher expectation that Compound (1) would be more stable than Ruxolitinib and so you can't take all their abstract arguments about metabolic switching leading to toxicity and things like that as applicable here because Ruxolitinib that art was known and we knew where were.

We can go on, the last point on this section on slide 43. In terms of reasonable expectation of success, we read Concert's arguments as essentially arguing that you would want to -- we don't establish that a lower dose would be the optimal dose. We don't need to establish that a lower dose would be the optimum

dose, again there's a shifted burden here. There's a presumption of obviousness in the range and a reasonable expectation of success doesn't mean achieving optimal results. Moreover, we have an undisputed construction of the claim term treating a hair loss disorder that includes, based on definition in the patent, regrowth of hair, preventing a further hair loss, or merely diminishing the rate of hair loss and all the evidence including from Dr. Silverman, Dr. Patterson, Dr. Damsky points to the expectation that within the Ruxolitinib approved dose range and even more so for the deuterated analog you would expect efficacy for Alopecia Areata of regrowing, preventing or diminishing the rate of loss.

If we go back to slide 10 on their unexpected results, the alleged unexpected results, they rely on clinical data. They don't compare the clinical data to the closest prior art. They don't provide clinical data that's commensurate in scope. They use oral doses in humans for Alopecia Areata and none of the claims are so limited. They don't establish a nexus with the deuterium limitation. What they show is that there is a responder rate compared to -- numerically higher responder rate compared to Baricitinib but in fact it's not physically significant and at best it's not a difference in kind, it's just a difference in magnitude. It's not even significant and they provide no safety advantage.

On slide 11 we have their drug-drug interaction data. Again, they didn't compare it to the closest prior art and the

closest prior art is from the Ruxolitinib package insert where Ruxolitinib was administered in combination with 200 milligrams of ketoconazole. Concert is using a study that uses CTP543 with a different metabolic inhibitor. Itraconazole the evidence shows is a weaker inhibitor in vivo but even beyond that they don't establish nexus with the deuterium limitation. They use a 12 milligram dose that's not in any claim and they were treating healthy patients rather than Alopecia Areata patients such that any effect that they're seeing on drug-drug interaction is a property of the compound that's claimed in Silverman and has nothing to do whatsoever with the claimed method. There's no nexus with the claimed method.

JUDGE POLLOCK: Counsel, this is Judge Pollock. You're certainly welcome to use your time as you wish but I think the panel would be quite interested in what you have to say about Silverman's prior art status and the exceptions.

MR. FELDSTEIN: Thank you, Your Honor. If we could go to slide 13. Concert has not met its burden of production for establishing a 102(b) exception. 102(b) applies only if the disclosure, the intervening disclosure was less than a year before the effective filing date and it's only excluded by something an inventor directly or indirectly contributed to the claimed invention. Concert has not established either of those points.

If we go to slide 63. Concert's best effort at asserting that they're supporting the provisional which they need to do to

establish an earlier effective filing date is a compare cite either in the POPR which they were not properly able to rely on or here in their surreply which comes too late. But in any event it's a compare cite that doesn't show 112 support in the provisional application. Without that they can't establish an effective filing date early enough to establish that Silverman was within a one year window and so they're unable to establish a foundational element of 102(b) exception. Similarly, if we go to slide --

JUDGE NEWMAN: Counsel, could I interrupt you for a second there?

MR. FELDSTEIN: Please.

JUDGE NEWMAN: Can you show us in the record where Petitioner asserted that the Patent Owner was not entitled to the benefit of that provisional?

MR. FELDSTEIN: So we -- in our reply we pointed out they failed to establish in their response. In our petition we never conceded they were entitled to that. We took the worst case scenario and established that compared to, even if it is entitled to its earliest priority date, that Silverman as prior art stays relative to that. This is similar to, if we look at slide 59, to what actually happened in Dynamic Drinkware, LLC v. National Geographics, Inc., where the first thing that happened in Dynamic Drinkware is that Petitioner met its burden of showing that the reference is 102(e) art on its face. That's what shifted the burden to the Patent Owner to establish that the reference

was not prior art. They did it by then pointing to earlier conception date but we didn't need to -- we established in our petition that Silverman was prior art on its face as the Board recognized in the Institution decision. We didn't need to at that time anticipate all possible affirmative defenses that Concert might make including a 102(b) affirmative defense and so there was no requirement that we (audio interference) in the petition an explicit challenge to the priority date. We established that Silverman was art on its face. That shifts the burden to Patent Owner to establish that it's not by whatever affirmative defense they want to rely on.

JUDGE NEWMAN: Counsel, would you agree that in Dynamic Drinkware the situation was somewhat different because the issue was prior art from the beginning and here this is a secondary situation where the prior art issue came up as a by-product of the defense of what prior art exceptions were raised by Patent Owner?

MR. FELDSTEIN: So I think, I mean Dynamic Drinkware is obviously the -- I think obviously the relevant precedent on burden shifting that once the Petitioner establishes art on its face basically a prima facie case, the burden then shifts. The burden of production then shifts and that's what happened here. The way Concert has tried to establish their burden is with a 102(b) exception and they are required to establish the elements of their affirmative defense and it is actually I think much like the first

steps of Dynamic Drinkware where the reference was 102 art on its face and then the Patent Owner came back with evidence of prior conception and here Concert came back asserting a 102(b) exception. They have to meet their burden to establish 102(b) exception that includes establishing an effective filing date early enough and it includes needing to establish that Dr. Uttamsingh was an inventor of each challenged claim. They've done neither. There's no claim-by-claim analysis for either and so there's no basis to say that for any of the challenged claims, much less claim 1, that it has an earlier effective filing date. There's no basis to say that Dr. Uttamsingh is the inventor, in fact there's basis to say that she's not the inventor.

JUDGE POLLOCK: Counsel, am I correct that in the pleadings of record Petitioner has not identified what features or claims are not supported in the provisional, just made a blanket statement that the patent is not entitled to the benefit of priority of it?

MR. FELDSTEIN: We made the claim that Patent Owner has not established the benefit of priority, that's true. They only put it in -- they didn't have anything in their Patent Owner response that we could respond to to show they're wrong, they're wrong on several points. So they didn't put forward any assertion on the basis of entitlement to priority for us to rebut. The only time they did it, they did it in the POPR which showed they recognized that the issue was on their plate but then they

dropped it for the POPR, excuse me the POR, and didn't raise it again until the surreply to which we had no clear opportunity to respond. But you can see on slide 63 what they did is just this compare cite that doesn't show anything about recognition by a person of ordinary skill that the disclosure would provide written description support. They don't even purport to address enablement either.

JUDGE NEWMAN: Can you clarify for us at what point you are alleging the burden shifted to them to show entitlement to that priority date?

MR. FELDSTEIN: When Concert chose to rely on a 102(b) affirmative defense, the burden shifted to Concert to show that Silverman was not prior art by whatever means they wanted to do. They chose -- and so that happened on Institution. It happened based on our prima facia showing in our petition that Silverman was prior art that shifted the burden to them to show that it was not prior art. They chose to use a 102(b) exception to assert a 102(b) exception and in so doing they took on the burden of establishing the elements of that 102(b) exception. They were forced to go the 102(b) route when they chose the 102(b) route. They took on all the intended burdens of production with respect to 102(b).

JUDGE NEWMAN: And that would include in your argument establishing that Dr. Uttamsingh was the inventor of at least one claim or --

MR. FELDSTEIN: Any claim for which they want to assert the 102(b) exception.

JUDGE NEWMAN: So your argument is that she has to be an inventor of every claim for the information that was disclosed?

MR. FELDSTEIN: Yes. It wouldn't make any sense if Dr. Uttamsingh invented claim No. 8, the formulation claim, for her intervening disclosure to exclude prior art to claim 1. It wouldn't make any sense for that and the wording of the statute refers to an inventor and the analysis for anticipation is proper on the claim-by-claim basis for both priority and exceptions.

JUDGE NEWMAN: Please continue.

MR. FELDSTEIN: Okay, thank you. So I'll jump ahead to slide 56. Even if they had established a 102(b) exception the 102(b) exception is narrow. It's narrow under the first inventor to file guidelines. It's narrow to the identical subject matter and for example, if there's a genus disclosed, for example Compound (1), that doesn't (audio interference) a species like Compound (1) 95 percent deuterated. Like Compound (1) phosphate salt. Like Compound (1) in the treatment of a disease. Like Compound (1) in a formulation and so even if they could establish a 102(b) exception for either of the disclosures they attribute to Dr. Uttamsingh, on slide 57 they don't challenge these other disclosures from Silverman which by themselves are more than sufficient to establish unpatentability. They don’t have a basis

under 102(b) to exclude using Silverman's teaching of using Compound (1) to treat a disease treated by Ruxolitinib.

This is a little different than what they argued in the POPR. In the POPR they argued that the Uttamsingh disclosure could knock out the entirety of Silverman. They backed that down to just the structure in example 4 and so there's no basis under 102(b) even if they could establish it to knock out these disclosures including the use of Compound (1) to treat disease with Ruxolitinib.

And just very quickly on slide 68 one of their bases for a 102(b) exception is this internal presentation from a quarterly update meeting and that they were -- apparently the example 4 data in Silverman was disclosed. But what the evidence shows is that Dr. Uttamsingh did nothing more than review, analyze and approve for quality control that data. She didn't conduct the testing. She didn't analyze the data. She didn't prepare the slides. She didn't present the slides and there's no basis to say that reviewing, analyzing for quality control gives her mental possession of the disclosure that Mr. Gallegos made such that it falls in the 102(b) exception that his work is somehow now her work for the purposes of 102(b). They've got no support for that at all and lastly, slide 69 the Uttamsingh 2015 declaration is not necessary to find the claims unpatentable.

We talked about this earlier that the art taught, as recognized in the prior IPR, the art taught to metabolize

Ruxolitinib at its hotspots. That leads uniquely to Compound (1) and so there's reason to get to Compound (1) entirely independently of Uttamsingh, that being the deuteration of Ruxolitinib's known metabolic hotspots.

That's what I have, Your Honor, and I'll just answer question. Otherwise I would turn over to my colleague to address the Motion to Exclude.

JUDGE NEWMAN: All right. Please go ahead.

(Pause.)

JUDGE POLLOCK: Do we have a technical issue?

MR. CHRISTIE: Can you hear us all right?

JUDGE NEWMAN: Yes, we can hear you. Cannot see you.

MR. CHRISTIE: Yes, can you --

JUDGE NEWMAN: Yes, okay. I can. Please go ahead.

MR. CHRISTIE: Great. Sorry about that. So if we can turn to slide 70, please. Incyte has moved to exclude Exhibits 2083, 2084 and certain paragraphs from Concert's expert declarations that rely upon those exhibits as unauthenticated hearsay and double hearsay. Today I'd just like to focus on hearsay and double hearsay.

Concert does not dispute that both Exhibit 2083 and 2084 are double hearsay under FRE 805 and fails to offer any exception to double hearsay for either exhibit. This failure alone is enough to exclude the exhibits, and if we could please turn to

slide 73 I'd like to address each of these in turn.

Exhibit 2083 is characterized as a patient tracker purportedly containing clinical data for CTP 543. Concert offers Exhibit 2083 as evidence of the alleged unexpected superior efficacy of CTP 543 as measured by SALT scores. It is the only efficacy data for CTP 543 that Concert relies on. The document itself is a mashup of an Excel spreadsheet reporting patient's SALT scores and a PowerPoint on page 7 of the document that appears to be from another document. Exhibit 2083 itself does not identify who, how or by whom this patient data was collected, compiled or maintained. Concert supports Exhibit 2083 with a declaration from its employee, Dr. Cassella. Dr. Cassella does not contend that he prepared the document and provides no information regarding who conducted the clinical trial, who recorded the patient data or who compiled the data in the exhibit itself. Rather, Dr. Cassella only asserts the data was collected during a Concert-sponsored study and that the data was maintained by Concert in the ordinary course of business and that's Exhibit 2118 at paragraph 3. Dr. Cassella's declaration does not describe how Exhibit 2083 itself was accessed or how it was purportedly stored and maintained within Concert. Concert does not contest that Exhibit 2083 was prepared for this PGR and the metadata for Exhibit 2083 states that it was prepared "for Goodwin, Concert's counsel in this matter."

Exhibit 2083 should be excluded for three reasons, 1)

Concert has not asserted any exception to the double hearsay under FRE 805, 2) Exhibit 2083 was indisputably prepared for this PGR and thus cannot qualify as a Concert business record under FRE 803(6) and 3) even if Exhibit 2083 was eligible under 803(6) Dr. Cassella's declaration fails to show that the exception applies.

So as to the first point, the document itself, Exhibit 2083, is hearsay under FRE 803 as an out-of-court statement by an unknown author. Presumably someone at Concert prepared the document for Goodwin which is offered for the truth of the matter asserted. Additionally, the data contained in the document are double hearsay under FRE 805 as they are statements by the unknown individuals that actually conducted the study and compiled the data which are also relied upon for the truth of the matter asserted.

JUDGE POLLOCK: Counsel, this is Judge Pollock. Forgive me for not being familiar with this part of the record but can you explain the accorded relevance of these exhibits you're trying to exclude. What does Petitioner assert that they're proving? Why are they before us is the question?

MR. CHRISTIE: Sure. So Patent Owner, they both relate to the unexpected results the Patent Owner's asserting in this case, 2083 relates to the clinical trial data for their first unexpected result which is allegedly unexpected superior efficacy and Exhibit 2084 is a report on the drug-drug interaction

study which they also rely on for unexpected results.

JUDGE NEWMAN: Thank you. Please continue.

MR. CHRISTIE: Sure. So as I was saying, the Exhibit 2083 contains hearsay and double hearsay and as the Federal Circuit explained in Wilson v. Zapata Off-Shore, Co.,

"Double hearsay in the context of a business record exists when the record is prepared by an employee with information supplied by another person. If the source of the information is an outsider, the outsider's statement must fall within another hearsay exception to be admissible."

And that's exactly what's happened here. Concert sponsored an outsider to conduct its clinical study and took that data and compiled in its own document for this PGR. As a result, in order to admissible Concert had to show that both the hearsay and double hearsay were subject to their own business record exceptions, that is the document Exhibit 2083 itself was a Concert business record and the data in it was a business record of the entity that actually conducted the study. In this case, Concert has only asserted a business record exception for the document Exhibit 2083 itself but has not offered any exception for the double hearsay data and this failure to offer any exception is a basis to exclude on its own.

Second, Concert cannot show that even the document itself is subject to a business record exception. To qualify as a business record under FRE 803(6) requires that the record was

kept in the course of a regularly conducted activity of a business and that making the record was a regular practice of that activity. Exhibit 2083 cannot meet this basic requirement as it was prepared for this PGR and thus not prepared in the regular course of Concert's business. As noted, Concert does not dispute that Exhibit 2083 was prepared for this matter and metadata states that the document was in fact prepared "for Goodwin." Recently just last year 2021 Federal Circuit explained in Wi-LAN, Inc. v. Sharp Electronics, Corp., that documents that are created and prepared for the purposes of litigation are outside the scope of the business record exception and that's 992 F.3d at 1372.

And finally, on Exhibit 2083 even if it hadn't been prepared for litigation and was eligible for the business record exception, Dr. Cassella's declaration does not meet the standard under 803(6)(d) for a qualified witness. Dr. Cassella does not offer any explanation of how Exhibit 2083 was accessed or how it was purportedly stored and maintained within Concert. Accordingly, Exhibit 2083 should be excluded.

If we could please move to slide 75 to discuss Exhibit 2084. Exhibit 2084 is a draft synopsis of a clinical report containing patient data for Concert's drug-drug interaction study that it sponsored. The exhibit appears to be an undated draft extracted from a larger report. Exhibit 2084 is the only evidence that Concert relies on for its alleged drug-drug interaction unexpected results. As with Exhibit 2083 Concert supports

Exhibit 2084 with Dr. Cassella's declaration, Exhibit 2118. Dr. Cassella does not contend that he personally prepared Exhibit 2084. His declaration does not identify who prepared Exhibit 2084 itself or who actually conducted the drug-drug interaction study, recorded the patient data or compiled the data in the exhibit.

Also like Exhibit 2083, Exhibit 2084 is both hearsay and double hearsay. The document itself is hearsay under FRE 803 as an out-of-court statement by an unidentified individual offered for the truth of the matter asserted. Additionally, the data in the document is double hearsay under FRE 805 as a statement by the declarant that actually carried out the study and reported the data also offered for the truth of the matter asserted. Now Concert has not offered any exception for either hearsay or double hearsay for Exhibit 2084. I'll direct you to their opposition at pages 10 to 13. It does not even mention the word hearsay.

JUDGE NEWMAN: Mr. Christie, you have one minute remaining in the primary time. You can go into your rebuttal time should you like.

MR. CHRISTIE: Okay. So as with Exhibit 2083, even if Concert had established a business record exception for Exhibit 2084 the document itself, this would not cure the issue with the double hearsay and likewise the Cassella declaration is insufficient to support Exhibit 2084 for the same reasons that it's

insufficient to support Exhibit 2083, and with that I'll save the rest of my time for rebuttal.

JUDGE NEWMAN: Thank you. Counsel, at this point I think we'd like to take a, want to say five minute break, ten minute break? Five should work. Okay. So let's say we'll be back on the record at 11:15, I'm sorry which is -- I'm on the west coast so add three hours to that for the east coast.

(Break.)

JUDGE NEWMAN: All right. The panel is ready to go. Please proceed.

MR. CEDRONE: Good afternoon, Your Honors. Gerard Cedrone for Patent Owner Concert Pharmaceuticals. Petitioner has failed to carry its burden to show that the claims of the '659 patent are obvious. In fact, as my colleagues and I will address there are several independent reasons why the Board should reject Petitioner's arguments.

First, I'll spend about 15 minutes addressing the threshold issue. As I'll discuss in a minute both of Petitioner's asserted grounds depend on disclosures that do not qualify as prior art. Next my colleague Emily Rapalino will spend about 35 minutes addressing motivation and reasonable expectation and she'll explain Petitioner's focus on oral JAK inhibitors and how Compound (1) specifically rests on pure hindsight. A person of ordinary skill would not have substituted Compound (1) for Ruxolitinib to treat AA at the claimed doses. Finally my

colleague Daryl Wiesen will spend about ten minutes addressing objective indicia of nonobviousness including the claimed invention's unexpected ability to resolve harmful drug-drug interactions, the unexpectedly superior (audio interference) efficacy (phonetic) profile and its ability to satisfy a long felt need for AA treatment.

I'm going to begin with a directional issue which we've outlined in slide 3 because it really has the potential to resolve this entire case. Both of Petitioner's asserted grounds depend on Petitioner's argument that Silverman disclosed Compound (1) and that Silverman in the 2015 declaration of Dr. Vinita Uttamsingh disclosed the metabolic stability of Compound (1) and several other compounds vis-à-vis Ruxolitinib. The relevant portions of those documents fall within exception to the prior art set out in Section 102(b) and before making our affirmative arguments let me proceed directly to the two counter arguments that Incyte has made that we can't satisfy these exceptions either because we're not entitled to the May, 2016 priority date or because Dr. Uttamsingh is not an inventor, named inventor. Let me address both of those counter arguments.

Before doing so I'd like to make clear and I think it's important to be precise about this. Incyte keeps saying Patent Owner has not established, Patent Owner has not established, but the burden of proof on this issue -- the burden of persuasion on this issue rests with Incyte, rests with Petitioner. If you turn to

slide 5 we've reproduced language from the Dynamic Drinkware case which makes clear that as to some of the questions related to this affirmative defense, the burden of production may at times shift to us but the burden of persuasion always rests with Incyte. Incyte has never managed to shift the burden of production to us on these questions and it has not satisfied its burden of persuasion and to the extent Incyte has shifted the burden of production to us we've more than met it.

So let me walk through both of these counter arguments and to set the stage a little bit counsel for Petitioner referred to the Institution stage and the Board at Institution decision and I think what happened at the Institution stage is telling. In our preliminary response we raised our 102(b) defenses. In Incyte's preliminary reply it never challenged Dr. Uttamsingh's inventorship, it never raised the question of (indiscernible) --

JUDGE POLLOCK: Counsel, counsel, this is Judge Pollock. We're having issues with your video and your audio has become quite difficult to follow. Can we pause a moment and see if we can fix that?

MR. CEDRONE: Yes, Your Honor.

JUDGE NEWMAN: We're getting a (indiscernible) bandwidth connection --

JUDGE POLLOCK: Yes, from your end.

JUDGE NEWMAN: -- from your end.

(Pause, due to technical difficulties.)

JUDGE NEWMAN: Okay, counsel. Are you ready to proceed?

MR. CEDRONE: I am, Your Honor. I'm sorry, I thought I was and I was muted.

JUDGE NEWMAN: Oh, no. Okay.

MR. CEDRONE: I apologize and I thank you so much for bearing with us because after two years of doing this we somehow still run into these issues, so thank you so much and what I had been saying apparently only to myself is I'll try and start over and just recap because I'm not exactly sure where I lost everyone, and thank you again for bearing with us.

JUDGE NEWMAN: Much better sound. We appreciate your work on that.

MR. CEDRONE: Thank you, and I apologize again. The point I want to emphasize at the outset is that for these 102(b) exceptions while the burden of production shifts to us for some questions in some instances the burden of persuasion always remains with the Petitioner and that's made clear from the Dynamic Drinkware case that we cite at slide 5 and I wanted to also emphasize some of the backdrop of this issue and how it arose. Counsel for the Petitioner mentioned the Institution stage and the Board's Institution decision and I think what happened at the Institution stage is telling. We raised our 102(b) defense in our preliminary response and Petitioner in its reply never challenged Dr. Uttamsingh's inventorship, never challenged our

entitlement to the May 4th, 2016 priority date and so in the Board's Institution decision which was modified by paper 25, the rehearing decision, the Board made clear that if Dr. Uttamsingh's declaration was to be believed it might well be that the 102(b) exceptions were satisfied but that there were certain factual issues that required further development about the disclosures in the references and the conveyance of certain information. But tellingly the Board did not identify either inventorship or the priority question as live questions and that's because it was not something that was raised in Petitioner's preliminary reply even as it objected to other elements of the 102(b) defense. So petitioner has never shifted the burden to us on these questions. To the extent they have we've satisfied them and Petitioner certainly hasn't satisfied its burden of persuasion on these issues. So let me move into the two specific issues of priority and inventorship.

If I can direct the Board's attention to slide 30 we've excerpted some language from the Lupin, Ltd. v. Pozen, Inc. case there and there are several others along similar lines that we cite in our surreply that make clear that not only does the Petitioner have to raise the issue of priority but they have to point to specific claims that allegedly lack written description support and I think as became clear through some of the questioning with Mr. Feldstein, not only did they not raise the issue at all until their substantive reply they have never pointed to specific claims

that lack written description support and so the burden of production has never shifted to us on this issue. Even if it had we satisfied it. The burden of production requires us to produce either evidence or argument, it's disjunctive, to establish our entitlement to the May 4th, 2016 priority date. We've done that. Along with our preliminary response we submitted Exhibit 2004, the priority application. It's been in the record since our first submission to the Board and you can see from the face of that application compared to the claims in suit that there is written description support. So we have satisfied that burden of production.

In their slides Petitioner cites cases where something more was needed but those cases -- I think one of the examples is Apple, Inc. v. Qualcom, Inc. -- were cases where it was not clear from the face of the priority application that there was written description support. This is not that kind of case. You can compare, you know, the Board is quite adept at reading, you know, these types of documents and it's clear from the face that there is written description support.

Moving on to the question of inventorship and just to close out that point, again, the burden of persuasion is always with the Petitioner so they have to convince the Board that we are not by a preponderance of the evidence entitled to written description support. They haven't come close to doing that, and so that leaves this question of inventorship. Here too this was not

something that was raised until Petitioner's reply. The burden of production I think has never shifted to us but even if it has we've more than satisfied it and so I would direct the Board's attention to our slide 34 where we've included evidence in the record related to Dr. Uttamsingh's inventorship. I'm sorry, I have the wrong slide. It's slide 32 of our slides where we've included evidence relevant to Dr. Uttamsingh's inventorship.

First and most importantly, Exhibit 1001 at code 72 Dr. Uttamsingh is a named inventor on an issued patent. As the Board is well aware there's a presumption that an inventor named on an issued patent is an inventor. But that's not all. We also have here her sworn inventorship oath, Exhibit 1047. We have testimony relating to her supervision and conduct and analysis of certain assays at Exhibit 1172, all of which speak to her inventive contributions and if I could emphasize the standard of inventorship which sort of remarkably Incyte never discusses in its brief, never discusses I think in its slides or here today the standard of inventorship which we've reproduced at slide 31 from the Trovan Ltd. v. Sokymat SA, Irori case and the Ethicon, Inc. v. U.S. Surgical Corp. case from the Federal Circuit make clear that a joint inventor has to generally contribute to the conception of the invention or perform part of the task that produces the invention.

The evidence on slide 32 more than meets the burden of production on that question and Incyte has produced nothing in

response, nothing to disprove Dr. Uttamsingh's inventorship because again, that's what Petitioner would have to do to convince this Board by a preponderance of the evidence that this inventor named on the face of the patent who contributed to assays that Incyte relies on to prove obviousness, was not a properly named inventor and I want to be very clear. Our argument is not that this evidence is the only contribution that Dr. Uttamsingh made, our argument is not that these assays and her analysis of them were the only contributions she's made, it's simply that Incyte has never asked her any questions directed to any other contributions.

Dr. Uttamsingh from 2015 to 2017 was the director of clinical pharmacology at Concert, yet Incyte never asked her in relation to this patent about the surprising clinical properties of a compound what her role was in selecting the assays, what her role was in selecting the compound for further development, what her role was in selecting the doses that were used for this compound and that's a critical failure because, again, it's Incyte's burden of proof on these issues and so unless the Board has further questions on the counter arguments I'll move into our affirmative discussion of why we think these three disclosures that Incyte relies on should be excluded.

There are two ways that Incyte could argue that Silverman and the 2015 declaration are prior art. It could assert that they're prior art under (a)(1) which covers printed publications or (a)(2)

which covers certain patents. We've put in evidence reproduced at slides 7 and 8 dealing with the common ownership exception to (a)(2). Incyte has never responded to that either in its papers or here today. We don't understand (a)(2) to still be in dispute so I'm going to rest on our papers on that unless there are further questions because I think the parties' dispute really has to do with whether Silverman and the Uttamsingh declaration from 2015 qualify as prior art under subsection (a)(1) and really we're talking about three specific disclosures.

So there's the disclosure of Compound (1) itself in Silverman, there's the disclosure of the metabolic stability data for Compound (1) from the 2015 Uttamsingh declaration and there's the disclosure of the metabolic stability data for other compounds but not Compound (1) from Silverman. Each of those disclosures is an inventor disclosure that's exempt from prior art under either subsection 102(b)(2)(a) or 102(b)(2)(b), excuse me, (b)(1)(a) and (b)(1)(b) and let me walk through each of those disclosures in turn.

So first Petitioner relies on Silverman for its disclosure of Compound (1) itself and if you turn to slide 12 we have several examples from the petition pages 12, 26, 33 and 71 where it's clear that Silverman is the only reference that Petitioner is citing for the disclosure of Compound (1). That last box on the page from page 71 is Petitioner's claim chart which makes clear that Silverman is the only reference that Petitioner identifies to

disclose Compound (1). But before Silverman disclosed Compound (1) Dr. Uttamsingh did and that's key because, as we've just discussed, Dr. Uttamsingh is an inventor of the '149 patent. On slide 13 we've -- excuse me, the '659 patent.

On slide 13 we've put the language of the relevant inventor disclosure exception and the timeline of the relevant events with the language of the statute color coordinated to the relevant events showing that within a year of our priority date Silverman issued and before that the Uttamsingh declaration became public and so anything that is in both the 2015 Uttamsingh declaration and Silverman is not prior art.

Incyte's counsel raised an argument today that Dr. Uttamsingh has to be an inventor as to the disclosure or that there's some sort of claim-by-claim analysis in the exception. It's clear from the face of the statute there is no such exception. Incyte is reading language into the statute that's not there. The question is was Dr. Uttamsingh an inventor? She was, and did she make a disclosure before the disclosure that Incyte's now relying on? She did, and so Compound (1) in Silverman is excluded as prior art and again, I can't emphasize enough Silverman is the only reference that Incyte relies on in its petition for the disclosure of the compound.

The next disclosure that Incyte relies on is metabolic stability data from Dr. Uttamsingh's 2015 declaration so at slide 15 we've reproduced examples from the petition where Incyte

relies on that 2015 declaration pages 15 to 34 and 40, for example, of the petition. But again the 2015 Uttamsingh declaration, and here we're talking about the whole declaration, is not prior art. So if you turn to slide 16 which lays out the other inventor disclosure exception in subsection (b)(1)(a) because Dr. Uttamsingh's declaration came within one year of the effective filing date of the '659 patent it's not prior art and so Incyte can't rely on anything in that declaration including most importantly the metabolic stability data related to Compound (1) in Silverman or anywhere else, excuse me, not in Silverman, in support of its obviousness combination and we've reproduced at the next two slides, slide 17 and 18 the specific metabolic stability data that we're talking about which critically is the only data that Incyte has pointed to anywhere demonstrating that Compound (1) or Compound 111 as it's sometimes known is more metabolically stable than Ruxolitinib.

The final example, or rather the final disclosure excuse me, that's excluded as prior art is example 4 from Silverman. At slide 19 we've laid out the relevant timeline. The key point here is that the information in example 4 came directly or indirectly from Dr. Uttamsingh. There's a lot of back and forth in the papers about exactly how that information was conveyed but as you can see from the language of the statute itself the question is whether it was a direct or indirect disclosure and at slides 22 to 24 we have Dr. Uttamsingh's declaration in this case, which is

Exhibit 2069, and at slide 25 or rather slides 26 to 28 we have Exhibits 2070, 2071 and 2072 from several of the Silverman inventors, all of which make clear that the only way this information would have been conveyed to the Silverman inventors was through Dr. Uttamsingh.

When you take all of these disclosures together and exclude them from the case, Incyte's obviousness grounds, both of them, cannot survive. I have a procedural point and a substantive point. The procedural point is one that we've already touched on. As is clear from their claim chart which we've reproduced at slide 12, the only source that Incyte relies on for the disclosure of the compound is Silverman. There is nothing else and so when that compound is excluded from Silverman, neither of its obviousness grounds can survive and more substantively we have the declaration of Dr. Ortiz De Montellano reproduced, excuse me --

JUDGE NEWMAN: Counsel, I'm going to interrupt you for a second. How would you respond to Petitioner's point about all of the compounds in Silverman leading to the idea that proceeding with a deuterated a 2- 3-position compound would have been obvious regardless of whether Compound 111 was specifically disclosed?

MR. CEDRONE: So I mean I think my first argument would be that that is simply not in the petition but putting aside that procedural point that this is again another argument that's

been raised late in the day, there's two points that I would make.

As I understand their argument they rely on two sources to make that argument. They rely on a line from Silverman itself that talks about active metabolites at the 2- and 3-position. If you go back and read that paragraph it doesn't discuss deuteration at hotspots or anything that would motivate a POSA. It simply talks about the fact that there were active metabolites stemming from those 2- and 3-positions.

The other point I would make is they cite in their slides the IPR decision discussing deuteration generally but the IPR was about synthesis of a compound. The question in this case is not synthesis of a compound, would there have been motivation to deuterate a compound because maybe it would have superior metabolic properties? The question in this case is would you select a particular compound from a genus of 60 plus compounds to treat a specific disease with specific side effects at specific doses and there's nothing in Silverman that gets you there once the compound is excluded and especially once the metabolic stability data is excluded.

A related question or related argument that Incyte has raised I think at slide 57 is they point to a list of, I think it's nine things where they argue that even if the compound is excluded there are other disclosures that would not be excluded and I've got two responses to that. The first is that several of the things on those slides are just not in fact disclosed in Silverman. To

take just one example and I think Ms. Rapalino may speak to this shortly, nothing in Silverman would have directed a person of ordinary skill to use Compound (1) at the 5 to 25 milligram range. So those purported disclosures at slide 57 examples 1 through 9, many of them simply aren't in the patent but even if we take them at face value a lot of those disclosures, most of them in fact have Compound (1) built in either expressly or implicitly and the point is that once you remove Compound (1) from those disclosures Incyte doesn't have anything to stand on as to those disclosures.

And so for this reason, unless the Board has further questions, I'm happy to rest on our papers because we believe that we have easily satisfied our burden of production to the extent it's even shifted to us. Incyte has not come close to satisfying its burden of persuasion on these 102(b) issues and without these disclosures, as Dr. Ortiz De Montellano made clear in his declaration Exhibit 2068, paragraphs 47 to 48 which we reproduce at slide 34, without these disclosures the Silverman patent is essentially gutted of the central points that Incyte uses it for.

Unless the Board has further questions on this threshold issue I'm happy to turn it over to Ms. Rapalino to discuss motivation and reasonable expectations. Thank you, Your Honors.

MS. RAPALINO: Good afternoon, Your Honors. Emily

Rapalino on behalf of Patent Owner Concert Pharmaceuticals. Can you all hear me okay?

JUDGE NEWMAN: Yes. This setup is much better. We appreciate your help in getting this new setup going.

MS. RAPALINO: We appreciate your patience in letting us do that, so thank you. We just heard Mr. Cedrone explain why certain disclosures in the Silverman reference and the entirety of the Uttamsingh declaration are disqualified as prior art. Even if those disclosures were considered prior art to the '659 patent Petitioner has failed to meet its burden to show that the challenged claims are obvious.

Before I launch into the substance I want to take just one moment to provide some background on Patent Owner's invention here. Patent Owner Concert developed and patented a novel method of treating AA, a condition for which at the time there were no evidence-based effective treatments available. That novel method involved using a low dose of a deuterated form of a JAK inhibitor drug called Compound (1). AA is one of the most prevalent autoimmune diseases in the U.S. and it causes these recurrent episodes of hair loss that can be extensive. While the physical symptoms are not life threatening, patients can suffer terrible psychosocial and emotional impact and impairment.

The cause or pathogenesis of the disease was not well understood and still isn't today but it was thought to result from

a combination of a number of complex factors including both external stressors as well as genetic predisposition and a complex series of signaling molecules in the body. Because the precise relationship between all of those factors wasn't clearly understood, there was no consensus at the time as to which therapeutic approach or strategy would be successful in treating the disease.

Now I want to focus on four general arguments that undermine Petitioner's obviousness challenges here and those four general points are set forth on Patent Owner's slide 37. First, Petitioners focus on oral JAK inhibitors is hindsight driven. Now, you heard Petitioner argue that in fact the art was focused on JAK inhibitors and that there was no hindsight involved and they point in Petitioner's slide 19 to a handful of references that mention the study, I think as Mr. Feldstein put it the future research possibility of using JAK inhibitors for AA. But those references don't support a focus on JAK inhibitors for this disease. One of the references on their slide, Exhibit 1140, actually talks about seven or eight different treatment options that were under study at the time and that's at pages 2 to 3.

Another reference on their slide, Exhibit 2063, actually talks only about topical use of JAK inhibitors for AA and discusses JAK inhibitors -- it really focuses on JAK inhibitors not for AA but for other autoimmune diseases and the third reference on their slide, while it discusses JAK inhibitors and

talks about their study in AA it notes that considerations of safety and dose have not yet been addressed, very important points, and as I'll discuss in a moment the prior art as a whole taught that many different treatment strategies were being studied but that no treatment had yet shown evidence-based efficacy and the importance of that is that means that a POSA would not have put a lot of stock in isolated anecdotal observations of hair regrowth for Ruxolitinib of the type that Petitioner relies on here. They would have known about the phenomenon of spontaneous remission and again, although Mr. Feldstein tried to dismiss the phenomenon of spontaneous remission, there was ample evidence in the record that spontaneous remission was in fact very common and interfered with the ability to accurately assess the efficacy of a drug intervention without a proper control.

The evidence is also that a POSA would have known about prior drugs that had shown initial promise in isolated or anecdotal case reports but then had failed to show efficacy when tested in a controlled clinical trial and there's evidence of that on Patent Owner's slide 50 which I will talk about in a moment.

The second general point on slide 37 that I want to raise is that even if a POSA were focused on JAK inhibitors the prior art teaching was in favor of JAK1/3 inhibitors like Tofacitinib and away from JAK1/2 inhibitors like Ruxolitinib or Compound (1) and this was both because of efficacy and safety reasons. Now,

you heard Petitioner argue that this is just a case of alternatives and that the law is that the existence of alternatives doesn't teach away. But this is not just the disclosure of equivalent alternatives, there are prior art teachings that raise serious questions about the safety of JAK1/2 inhibitors. I believe that Mr. Feldstein referred to those concerns as abstract metaphysical possibilities of toxicity. In fact, as I'll discuss in a moment, there was very substantial evidence of a great degree of concern with toxicity from JAK1/2 inhibitors like Ruxolitinib including the existence of black box warnings regarding safety on each and every JAK inhibitor that had been approved for an autoimmune condition. So those again were not hypothetical concerns, those were very real concerns expressed by persons of ordinary skill at the time.

The third general point I want to talk about on slide 37 is that even in treating Alopecia Areata at the time, the art very clearly taught a preference for topical treatments for AA rather than oral treatments. As a result, the focus on topical treatments there was simply no motivation to focus or use a deuterated compound. Deuteration, to the extent that it has an impact, it has an impact on metabolism, on metabolism in the liver and Petitioner never disputes that for the topical route there's simply no relevance to a deuterated compound because the drug reaches its site of action on the skin through topical use before there is any liver metabolism for which deuteration would potentially be

relevant.

Now, the fourth point on slide 37 that I want to focus on is that even if a POSA were focused on oral Ruxolitinib and on oral JAK inhibitors for AA, there's simply nothing in Petitioner's references that would motivate a person of skill in the art to use these claimed low doses in the '659 patent and no reasonable expectation that using those claimed low doses would provide a reasonable expectation of success in having both a safe treatment for Alopecia Areata and an effective treatment and although this is the fourth bullet point on our slide 37 I'd actually like to start with the discussion of dose because I think it's important to respond to some of the arguments that Petitioner made related to the claimed doses.

So if I could direct the Board's attention to Patent Owner's slide 85 where our discussion of the nonobviousness of the claimed doses begins. Now, you heard Petitioner argue that this is simply a range case like the DuPont case or like the Galderma case where the prior art discloses a range of doses and Patent Owner has simply claimed a range or claimed doses within that range and the first point I want to make I want to be very clear that this case is not a range case like DuPont or like Galderma. In each of those cases the prior art teaching was to the use of a particular compound or a particular process in the case of the DuPont case to achieve a particular result. So in the case of DuPont it was to make a specific compound. It was a process for

oxidizing one compound to make another compound where the range was a temperature range and the prior art taught that you could practice this process anywhere within that temperature range and then the claims in that case were to practicing the very same process to get the very same results in the very same compound just using a narrower temperature range within the prior art range.

That is nothing like what we have here. Here there is no prior art disclosure of a range of doses for Compound (1) which is what the '695 patent is directed to, there is no range of doses for Compound (1) that was taught to be safe and effective for treating Alopecia Areata.

You heard Petitioner argue that Silverman is where this disclosure comes from. The Silverman reference, Exhibit 1002, discloses a range and they put on their slide -- I believe it was slide 35 or I'm sorry, not slide 35, it was slide 8 -- if you look at Petitioner's slide 8 they have a range on their slide from 5 to 50 milligrams that they say comes from Silverman. I want to look at what Silverman actually says about dose and what it teaches and what it does not teach.

So if we turn to Patent Owner's slide 86 we've reproduced at the top of the slide the paragraph from Silverman Exhibit 1002 on dose and this is at column 20, lines 9 through 19. So what Silverman actually says is that there is a broad range of effective amount of a compound of this invention can range from 1

milligram to 500 milligrams. So it discloses a broad range of doses and it's not specific to Compound (1). This is about compounds of the invention. Then it discloses a dozen narrower ranges and there is nothing in this paragraph that directs the POSA to Alopecia Areata as the use of the compound at these doses and so when it talks about an effective amount it's not talking about Alopecia Areata.

In fact, at slide 87 Patent Owner's slide 87, we have the testimony from Patent Owner's expert Dr. Ko at Exhibit 2059, paragraph 90 where he talks about the fact that the Silverman reference lists a long laundry list of diseases for which the compounds of the invention may be useful and none of those is Alopecia Areata and in fact, Petitioner's expert Dr. Patterson at his deposition Exhibit 2055 at page 198, he agreed that none of the examples of diseases that can be treated by the compounds of this invention include Alopecia Areata.

So nothing in the paragraph in Silverman directs the POSA or provides guidance on which of those doses, if any, is effective for Alopecia Areata nor does anything in this paragraph direct the POSA as to which of the 60 plus compounds specifically disclosed in Silverman would be effective at which doses and for which diseases. It strains credulity to think that a POSA would read this paragraph -- this generic disclosure of a range of 100 to 500 milligrams for the compounds of the invention which includes 60 plus compounds and a laundry list of diseases at

column 23 of Silverman -- it strains credulity to think that what this teaches a POSA is that every single dose within that range would be an effective amount of any of those 60 plus compounds to treat any of the dozens of diseases listed in the patent. That's simply not what Silverman teaches.

And as we see on Patent Owner's slide 88 Silverman itself tells us that that's not what Silverman intends to teach. So if we look at, again, this reproduces Silverman Exhibit 1002 at column 20 lines 19 through 21. Silverman itself actually teaches that the dose will vary depending on the disease. So there's no teaching in Silverman here that the specific doses, any of the specific ranges that are disclosed in Silverman are relevant to AA and it in fact tells the POSA that this is going to vary depending on the disease.

So in light of these disclosures, in light of the generic nature of this paragraph, it's only with hindsight that Incyte can cherry pick one narrow range, the 5 to 50 milligram range, and then try to argue that that is somehow applicable to AA and applicable to Compound (1) and this really takes us outside the scope of those range cases. The DuPont case itself says that where the prior art range is broad it does not invite optimization and that makes sense. When you think about what those cases teach they teach that where the prior art suggests that a process or method is workable across a broad range or across a narrow range, it invites optimization to figure out which value within

that range is optimal at best. But where a prior art reference merely generically discloses a broad range without suggesting that the process or method would work across that whole range, it's simply not an invitation to optimize and to routinely optimize and find the correct dose.

JUDGE POLLOCK: Counsel, this is Judge Pollock. Is there evidence of record suggesting that the underlying mechanism for treating AA with a JAK inhibitor is different from the underlying mechanism of using that same JAK inhibitor for treating another disease responsive to JAK inhibitors?

MS. RAPALINO: Yes, Judge Pollock, there is in fact such evidence. So one of the things that you heard Petitioner try to do was to say well, there are JAK inhibitors that are used for other diseases at particular doses and so a POSA would use that teachings because of potentially a common mechanism and use those same doses to learn about the dose for AA. But in fact what the record here shows is that the doses in fact do vary from one disease to another even for the same drug in this class and that as a result, not only do they vary but it varies as to whether there is even any safe and effective dose for using the same drug that treats one disease to treat another disease and if I could point the Board to --

JUDGE POLLOCK: I'm sorry. I seem to hear you're conflating doses with mechanisms. I'm asking about are you suggesting there are multiple mechanisms underlying the use of a

JAK inhibitor, not that the doses might vary?

MS. RAPALINO: Okay. I apologize, Judge Pollock. I think I misunderstood your question. So if we turn to Exhibit 1071 and this is the Clark reference and that is reproduced at Patent Owner's slide 53. This is the Exhibit 1071 the Clark reference at figure 3. It shows the complexity of the JAK pathways and it shows that JAK proteins are actually responsible for a great variety of bodily functions and that therefore the precise mechanism by which a JAK inhibitor might impact one disease, there's a high likelihood that that may differ as compared to its mechanism in treating another disease and so -- and I was going to point to the slide again to show that if we look at the JAK2 inhibitors, the JAK2 dimers all the way on the right side of figure 3 in Exhibit 1071, you can see that JAK2 is particularly important for blood related bodily functions. So this like Erithropolesis, Myelopolesis, all of the functions that make blood cells the JAK2 is particularly important for those processes and so inhibition of JAK2 there would be great concern by a POSA in using a JAK inhibitor to treat what is essentially a physically benign disease like AA, there would be great concern by the POSA in using an inhibitor of a JAK2 to do that because of the tremendous interference that would likely have all of these mechanisms set forth on slide 53.

JUDGE NEWMAN: Counsel, this is Judge Newman. Wouldn't that be influenced however by the references that

Petitioner has shown us about success with Ruxolitinib?

MR. RAPALINO: So I'd like to address those next. So Petitioners argue that there were these "successes" or that Ruxolitinib was already in use to treat AA and so let me just be clear that Ruxolitinib itself is only FDA approved for treating a very serious form of cancer, Myelofibrosis, and so if we're talking about the concern about side effects the evidence was that side effects in a very serious condition, physical condition like cancer are much more highly tolerated than in a physically benign disease like AA and so its use in cancer doesn't speak to whether the side effects would have been tolerable and whether POSAs would have used Ruxolitinib or for that matter Compound (1) in treating a disease like AA. But I'd like to address those references that Petitioner relies on as purportedly showing the successful use of Ruxolitinib and AA. If I could point the panel to starting at Patent Owner's slide 43.

JUDGE POLLOCK: Counsel, one quick question before we move on. This is Judge Pollock. Are the JAK inhibitors of record specific to the different JAK proteins?

MS. RAPALINO: Yes. So Tofacitinib, one of the JAK inhibitors of reference that's Xeljanz, that's specific to JAK1/3 whereas Ruxolitinib is specific to JAK1/2 or has a higher affinity for JAK1/2.

JUDGE POLLOCK: Thank you.

MS. RAPALINO: So I want to turn for a moment to talking

about what Petitioner calls these purported successful uses of Ruxolitinib in AA and if we start with slide 43 this is an excerpt from Dr. Ko's testimony at paragraph 68 of Exhibit 2059 and he notes that these case reports. All of these references are case reports with no controls and a POSA would not have been able to conclude that the benefit reported was caused by Ruxolitinib rather than by spontaneous remission or fluctuation due to the natural disease course. He also notes that in each of these references or in three of these references the patient had a different co-morbid condition that made them not a typical AA patient. But in any event, none of these had a control, these were all anecdotal case reports and what the POSA would know about anecdotal case reports in general, even if we set AA aside for a moment, on Patent Owner's slide 46 Exhibit 2080 was a review about the value and limitations of these anecdotal case reports about a single patient, a handful of patients and what that review concluded after doing a study of the results in these anecdotal case reports was that causality cannot be inferred from uncontrolled observations, that cause effect relationships require planned studies that include controls and this is a particularly challenging issue in a disease like AA where the evidence was that there was the phenomenon of spontaneous remission.

If we look at slide 41, this comes from Exhibit 2008. It notes that the majority of AA patients experience some baldness which spontaneously resolves within a year and so the level of

spontaneous remission was quite high. It's not on this slide but we also have Exhibit 1145 in the record at page 1 and in the summary bullet points on the very first page of that reference, that reference notes that objective assessment of treatment efficacy is very difficult due to the high but unpredictable rate of spontaneous remission. So it was well known by POSAs in the art that this phenomenon of spontaneous remission would have prevented the POSA from drawing conclusions about whether the hair regrowth that was seen in these isolated case reports was due to the drug intervention itself or whether it was simply a result of a natural course of a disease which is cyclical and has spontaneous remission as part of the disease progression.

Now, if I could go back for one moment to talk about dose, these case reports -- the other issue with the Petitioner's reliance on these isolated and anecdotal case reports is that in none of these case reports was a dose lower than 30 or 40 milligrams per day used in AA and the claims at issue, claim doses of 16 milligrams per day and 24 milligrams per day and there is simply nothing in the record that would have motivated the POSA to use that lower dose of Compound (1) and to expect that at a lower dose they would have both a safe and effective treatment and I want to note in this regard that again I began, Judge Pollock, when I misunderstood your question to note this that in this class of drugs JAK inhibitors it was well known that the pharmacokinetic -- pharmacodynamic relationship and the

relationship of that to therapeutic efficacy was unpredictable and that a drug that was effective at a particular dose in one disease may not be effective when given for a different disease and may not be safe and effective.

So, for example, if I could point the Board's attention to Patent Owner's slide 110 it was well known that for Xelganz which is Tofacitinib, another drug in this class a JAK1/3 inhibitor, that the dose of Tofacitinib that was safe and effective in ulcerative colitis was 10 milligrams twice a day. This comes from Exhibit 1066 at page 1 while the dose of that same drug that was safe and effective in psoriatic arthritis was half that dose, 5 milligrams twice daily and importantly what was also known about Tofacitinib was that there was no dose that was both safe and effective for use of this drug in psoriasis, and so Petitioner's reliance on the use of JAK inhibitors in one disease as evidence that a POSA would have been motivated with a reasonable expectation of success of using that dose or a different dose in another disease simply would not carry water with a POSA and so if we look back at Petitioner's slide 8 where they put these different points on their range between the 5 and 50 milligram dose where those points come from references that talk about treatment of diseases other than AA using doses of Ruxolitinib. So for example, they talk about the Zeiser and Williams references that relate to treatment of Graft versus Host disease and rheumatoid arthritis. Those simply wouldn't be

relevant and wouldn't provide a reasonable expectation, not only that you could use that dose for treating AA but they wouldn't provide a reasonable expectation that there would be any dose that would necessarily be both safe and effective for the treatment of AA.

Now, I'd like to go back to slide 37 and now that I've talked about dose I'd like to just go back and talk through the other three general points I wanted to make that undermine Petitioner's obviousness argument. So I'd like to go back and talk about the notion that this focus on oral JAK inhibitors is hindsight driven. If we look at slide 39 it just highlights that there was no evidence-based efficacy for any drug as of the priority date. Exhibit 2058 reproduced on slide 39 is a review published right around the priority date for the '659 patent and it reported that a review of randomized trials concluded that there was no effective evidence-based treatment for AA and as Dr. Ko explains, and this is on slide 40 and it comes from his testimony Exhibit 2059 at paragraph 27, he explains that the difficulty of finding this evidence-based efficacy for AA comes from two phenomenon. One is the phenomenon of spontaneous remission that we just talked about and the other is that there was resistance in the prior art to the use of drugs that had serious side effects because of the nature of AA, because AA is a relatively physically benign disease. There was a resistance to using drugs like JAK inhibitors that cause serious side effects.

I've covered already some of the evidence about spontaneous remission and I'd like to just talk about the issue of the serious side effects. So on slide 42, Patent Owner's slide 42, we have reference 2037 that talks about the fact that AA is a benign lifelong genetic predisposition and that as a result safety aspects will have to be carefully considered. We also have other evidence of the serious nature of the side effects, particularly from JAK1/2 inhibitors and so if we look at slide 63 this is Exhibit 1004.

It's one of Petitioner's primary references Exhibit 1004 and this is the Ruxolitinib label and it shows the incidence of these serious blood related toxicities and you can see that for each of thrombocytopenia, anemia and neutropenia the rate of side effects is extremely high. Petitioners try to argue that this isn't relevant data for a non-cancer population because patients in this cancer population tend to have a predisposition towards these side effects and while that is true and you can see that by looking at the placebo group that the rate of these side effects is high, you can see that the drug effect here is even higher and makes these side effects much higher and even more so, if we look at slide 64 we see that the use of JAK inhibitors -- this comes from Exhibit 1074 -- and this is a study of the use of JAK inhibitors in a non-cancer population and psoriasis population. We see that there too the incidence of these serious side effects was also extremely high.

If we look at, turning to slide 65 and we looked at this slide earlier or a version of this slide earlier, this is Exhibit 1071 and it reproduces a figure from the Clark 2014 paper figure 3 that talks about and diagrams the complexity of the JAK pathways and it shows that it's not surprising that JAK1/2 inhibitors in particular cause this array of serious blood-related side effects. Again, the panel all the way on the right shows that JAK2 proteins are involved in a variety of important blood cell producing functions and that inhibiting this pathway can lead to some of those very serious side effects.

The other thing that a POSA would have known here is that there were prior drugs, again that had shown some promise in initial case reports like these anecdotal case reports that Petitioner points to but that they had ultimately failed to show any efficacy in clinical trials. So if we look at Patent Owner's slide 50 we see two examples of these and these would have been important and they would have factored prominently in the mind of a POSA. In Exhibit 2101 there was a case report of the use of a drug called Alefacept in treating AA and noted that it showed promise in the treatment of AA and then in Exhibit 2102 when the drug was actually subjected to a controlled clinical trial it failed to show efficacy.

Likewise Exhibit 2103 talks about the promise of anti-TMF agents as a treatment for AA and then in Exhibit 2104 talks about the fact that again when tested in controlled clinical trials

these agents did not show any efficacy in the treatment of AA. All of these things, all of these prior failures and the concerns about both spontaneous remission and side effects mean that this laser focus on oral JAK inhibitors as the promise for AA is simply an exercise in hindsight, that this isn't where the mind of the POSA was at the relevant time.

I'd like to turn now -- oh, I want to talk for a moment about the JAK1/3 versus JAK1/2 preference. You heard Mr. Feldstein argue that there was no evidence of any difference in efficacy between JAK1/3 and JAK1/2 and that's simply not the case. There was evidence in the record of differences in both efficacy and most importantly in safety.

So if we look at Patent Owner's slide 59 one of those references is one of Petitioner's primary references, the Christiano reference. That reference talks about and focuses on the efficacy of JAK3 inhibition in preventing AA. The only data in the Christiano reference is data on JAK3 inhibition for the prevention of AA.

Likewise on Patent Owner's slide 60 from Exhibit 1016, this is an in vitro test testing the inductivity of both Tofacitinib, a JAK1/3 inhibitor and Ruxolitinib, a JAK1/2 inhibitor on a particular type of hair follicle cell showing that Tofacitinib performed better in this assay and I will note that the only data that Mr. Feldstein pointed to from that Xing reference was pre-clinical data, mouse data. There is no human clinical data

showing any equivalent efficacy for Tofacitinib and Ruxolitinib.

Mr. Feldstein also talked about the clinical use by dermatologists of JAK inhibitors in the prior art. What he failed to mention was that -- well he mentioned that the dermatologist, their own dermatologist Dr. Shapiro said that dermatologists didn't use Ruxolitinib and they only used Tofacitinib. So the only JAK inhibitor that was even in anecdotal use in the clinic for AA was Tofacitinib, not Ruxolitinib and for good reason. Again, Ruxolitinib only had cancer indications as its approved indications whereas Tofacitinib had autoimmune indications rather than those cancer indications.

I'd like to talk last about the issue of topical versus oral treatment and this starts at Patent Owner's slide 67. The evidence was that POSAs at the time had a strong preference for topical treatment for AA rather than oral treatment. This was again both for efficacy reasons and for safety reasons.

If we look at Patent Owner's slide 68 we see evidence again, this comes from the Christiano reference, one of Petitioner's primary references at Exhibit 1005. Christiano herself calls the topical route the more clinically convenient route of delivery and elsewhere calls it the more clinically relevant route of delivery and talks about the fact that topical Tofacitinib was highly effective.

Likewise Exhibit 1016 also talks about topical treatment with JAK inhibitors resulting in more robust hair regrowth than

did systemic treatment in AA and so you heard Petitioner's counsel argue that Dr. Shapiro said that only if there was efficacy in the topical route would a POSA prefer the topical route over the oral route because of safety reasons and here there is evidence in the record that the topical route was in fact the more efficacious than the systemic route.

Likewise on Patent Owner's slide 69 we see in Exhibit 2037 the notion that these JAK inhibitors are interesting for topical treatment and we also see that the note here that targeted delivery by using the topical route applying to the drug directly to the affected organ may help increase local drug concentration and efficacy and this again not only shows a preference for topical treatment, but it shows that efficacy was impacted by the local concentration of drug meaning that there was a teaching away from using a systemic drug at a lower dose which is what is claimed in the '659 patent, systemic being less effective and lowering the dose meaning you would have less drug concentration at the site of action.

There are also multiple references that talk about both the efficacy and safety benefit of the topical route over the systemic route and again these are at slides 70 and 71. Again, if we look at slide 71 we see that Exhibit 1027 talks about the risks of serious adverse events from systemic therapy and that these may be avoided if topical therapy were an option and in this particular patient declined systemic therapy in favor of topical

therapy precisely for those reasons, for the safety reasons and for the intolerance to side effects when given orally. I would also note that Ruxolitinib itself when given topically in a clinical trial that Incyte conducted failed to achieve efficacy in Alopecia Areata.

I think I'm coming close to the end of my time. I will conclude just on this issue of the topical versus oral route. I'll just conclude with the fact that there was no dispute, again, in the record that there was no motivation for a POSA to use a deuterated drug like Compound (1) when given topically. This was explained by Dr. Ortiz De Montellano and this is at Patent Owner's slide 77. It comes from his declaration 2068 at paragraphs 16 and 18 and also from Dr. Ko's testimony at 2059, paragraph 73. They explain that the relevance of deuteration to the topical route and Petitioner Incyte has not disputed that there simply isn't any relevance because of the lack of metabolism before it reaches the site of action.

So unless the panel has any further questions, I'm going to turn it over to my colleague, Mr. Wiesen, who will talk about the objective indicia.

JUDGE NEWMAN: There's about six minutes to go before we head into time for rebuttal.

MR. WIESEN: Thank you, and my goal will be to stick to that six minutes but we'll see whether I meet that goal.

JUDGE NEWMAN: I'll give you a one minute warning.

MR. WIESEN: Thank you. I appreciate it. Daryl Wiesen on behalf of the Patent Owner and I want to start with the argument concerning the Motion to Exclude that focused on Exhibits 2083 and 2084 which are underlying data concerning the secondary considerations, given 2083 is the clinical trial results, Exhibit 2084 is the report on the drug-drug interaction study and I will note that Petitioner's argument is fundamentally is that it's not a standard business practice for a pharmaceutical company to hire doctors or a contract research organization to run a clinical trial and then to rely on that data and I think it's fair to say that when you think about that those are standard business practices and that would address the hearsay objections that Petitioner is making.

But I don't think the panel needs to get to that question because the other issue that comes up here is can experts rely on this data because we have in Exhibit 2059 Dr. Ko in paragraphs 99 to 107 and Dr. Ortiz De Montellano in Exhibit 2068 paragraphs 20 to 29 analyze this data and as the Monsanto, Co. v. David case that we've cited from the Federal Circuit states experts can rely on inadmissible hearsay data and Monsanto was specifically about exactly the type of data at issue here, clinical trial data, and there is no reason to doubt based on Exhibit 2118, the Cassella declaration, that these documents are authentic. These are the data that Concert had and that Concert relied on and once we hit that then it's reasonable for the experts to rely

on it and the declaration testimony explaining why these data support unexpected results is admissible and the panel need not reach the question of whether the underlying documents come under or not because as we'll see, the analysis from the experts is more than sufficient to establish the unexpected results.

Let me turn to that data now very briefly and if we turn in Patent Owner's slides first to slide 117 is where we start on unexpected results and simply set out the legal standard from the Millenium Pharamaceutical, Inc. v. Sandoz, Inc. case. If we look at slide 118 what we see is an excerpt from Exhibit 1004 which is the Ruxolitinib label and this is what Ruxolitinib says. If you are giving Ruxolitinib in combination with a strong CYP3A4 inhibitor you have to adjust the dose of Ruxolitinib and the label lists specific strong CYP3A4 inhibitors that require an adjustment and one of this is Itraconazole as we've highlighted here on slide 118.

If we look at slide 119 and we look at the conclusion that Dr. Ortiz De Montellano draws based on the study that we'll look at in a second in Exhibit 2068 Concert would not need such a dose modification language. It would be to Mr. Feldstein's argument of a difference in kind. Modified for Ruxolitinib, don't modify for CTP543 and that is an unexpected result. Why? Because one would expect Ruxolitinib and deuterated Ruxolitinib CTP543 to have the same drug-drug interaction.

Petitioner's entire theory in this case is that people would

expect these things to be the same and suddenly here they're now arguing they would expect them to be different because we've established a difference. But for this attribute, as Dr. Ortiz De Montellano explained one would expect them to be the same, but they're not. How do we know that? If we jump to slide 125 we see a comparison of the data Exhibit 1004, on the top is the study with Ruxolitinib which shows a 33 percent change in Cmax and a 91 percent change in the AUC, the area under the curve when the strong CYP3A4 inhibitor is given with Ruxolitinib and as Dr. Ortiz De Montellano explains in his declaration at Exhibit 2068 in paragraph 26 you can see there's only a 27 percent change in the AUC and a 13 percent change in the Cmax and that reduced change, that difference is an unexpected result that resulted not requiring a label change, and that lack of modification is an unexpected result and as Dr. Ko explains, if we see slide 126, we have Dr. Ko's statement in paragraph 107 of Exhibit 2059 to a doctor that's important. For someone who's receiving chronic treatment to be able to knock dosage off that's an important distinction that will matter to the doctors who give these drugs and that result is unexpected and there's no real explanation for the arguments that Petitioner makes are mainly to try and argue that there's no nexus or the unexpected results are not commensurate in scope.

But the evidence establishes that CTP543 as an example falls within the scope of the claim and that the case law is clear,

if you look at the cases we've cited in our petition, that the precise matching up that Petitioner is asking you to find is simply not legally required.

JUDGE NEWMAN: Sir, you have one minute left.

MR. WEISEN: Great. Thank you. So with that I want to turn very briefly to the other unexpected results and we've established the efficacy of CTP543 through the clinical trials and through the evidence that Dr. Ko discusses in his declaration, Exhibit 2059. There's also in the record evidence of the improvement over a placebo in Exhibits 1168 and 1169 as we've reproduced on exhibits 129 and 130 showing there are safe and efficacious results at the specific low doses of 16 and 24 milligrams per day.

The last thing I think I want to respond to is the argument that we haven't compared to the appropriate comparator to show unexpected results. I'll note that the case law suggests that while the preferred thing to do is to compare to the closest prior art it's not always required if there isn't a sufficiently comparable study in the prior art and we'll note, as Ms. Rapalino pointed out, there was no evidence-based proof of efficacy in AA, no placebo controlled clinical trial in the prior art to compare it to. The only thing that could be compared to was something like the Mackay-Wiggan reference. If you look at slide 136 that's in fact what Dr. Shapiro did. He did that comparison with Ruxolitinib and if we look at slide 136 we see that even if the result is the

same the patients that were in Concert's study had more severe Alopecia Areata and achieving the same result but with more severe patients is an unexpected improvement as even Dr. Shapiro had to agree -- Judge Pollock, are you trying to ask a question? I apologize.

JUDGE POLLOCK: No, no.

MR. WIESEN: Dr. Shapiro admitted as we have on slide 138 in his deposition Exhibit 2054 that it's more difficult to treat these patients with more severe Alopecia. With that, I'm going to wrap up so that we can preserve some of our time for the surrebuttal unless there are any other questions.

JUDGE NEWMAN: No questions right now. Let's take another five minute break and we'll be back on at 35 after the hour.

MR. WIESEN: Thank you.

(Break.)

JUDGE NEWMAN: We're back on the record. Mr. Feldstein, to begin would you mind addressing Patent Owner's argument regarding the reduced drug-drug interactions as an unexpected result.

MR. FELDSTEIN: So, sure Your Honor. Their slide, Concert's slide 125 is where they presented part of that and in Concert's slide 125 copies from the Ruxolitinib label at the top and from Dr. Ortiz De Montellano at the bottom. The top study is the inhibition of Rollatini with an inhibitor called

ketoconazole. The study at the bottom is with CTP543 or whatever they're calling it here in a different inhibitor itraconazole. There's nothing to show. They didn't show less drug-drug interaction with the same inhibitor and so it's apples and oranges comparison and moreover what we had established in our evidence on slide 52, Incyte slide 52, is that itraconazole is what Concert used is a significantly weaker inhibitor than ketoconazole and there's nothing unexpected about less inhibition with a weaker inhibitor and in terms of the difference in kind that they're trying to squeeze out of this they're speculating what the FDA might do in the future if Concert passes its stage 3 trials, if Concert files for an NDA, if Concert gets approval. It's all speculation. There's nothing to -- there's no unexpected result. There's unexpected speculation but there's no unexpected result. It's less inhibition with a weaker inhibitor and in the context of whether it's written in the claim it was a 12 milligram dose they tested, it's not in the claim. The claims require a dosage of 16, 24, it was not a claimed dose. It was not of the claim population. It has no nexus with the claim method of treatment.

JUDGE NEWMAN: Thank you.

MR. FELDSTEIN: If there are no further questions on that I'll go back to the 102 issue and much of the issue, and I'd point us back again to Incyte's slide 57. There's a slew of disclosure that's not challenged. I think Concert fundamentally misreads

how to apply 102(b). They don't really discuss the first (indiscernible) guidelines in the Federal Register. What they seem to be suggesting is that you take Silverman, if they can establish a 102(b) exception, and take a pair of scissors or a sharpie and cross out every time that it refers to Compound (1). That's not the point. The point is you can only cross out the identical disclosure. The disclosure of Silverman is not identical to what they're pointing to from Dr. Uttamsingh either internally or not. Dr. Uttamsingh doesn't teach using Compound 111 to treat diseases by Ruxolitinib. You can't excise that from Silverman because she didn't teach it. You can't excise using Compound (1) at 95 percent deuterium incorporation because she didn't teach it, and so their idea that you can take a pair of scissors or a sharpie and then you're left with some blank statement of use blank to treat diseases is not consistent with the first inventor to file guidelines for apply 102(b) which requires identical subject matter effectively an anticipation. If it's not anticipated effectively, the whole thing comes in. The use of Compound (1) to treat diseases was not disclosed by Dr. Uttamsingh. It cannot be excluded under 102(b) even if they could establish the 102(b) prerequisites.

I'd like to note that the whole line of cases they rely on in their surreply like Lupin, they rely on an early PTAB case Focal Point that predated Dynamic Drinkware. Lupin doesn't address Dynamic Drinkware and Lupin addresses a factually -- all the

cases they rely on address a factually different circumstance where petitioner had to challenge priority in the first place because they were relying on some intervening disclosure. They were relying on a prior art that was intervening between two other priorities claimed on the face of the patent and to establish that it was prior art they had to initially argue that it wasn't entitled to an earlier priority date.

For us to establish basically a prima facie case that Silverman is prior art, we didn't need to do that. It's a factually different case. On our slide 62 we cite the Apple, Inc. v. Qualcom, Inc. case which is more factually analogous where it was the Patent Owner had the burden to show 112 support and that was the issue that was no reason for Apple to concretely challenge 112 support and I'll note also they talk about their clear answer that they met their burden on establishing 112 support in their surreply by a compare cite. To analyze written description it needs to be from the perspective of a person of ordinary skill in the art. They're devoid of their burden of production on that and again, they don't address enablement which is also part of 112 requirement for priority.

I think that on inventorship I'd like to point to Concert's slide 32. They point to evidence of Dr. Uttamsingh's inventorship but they don't point to inventorship of anything in particular. Did she invent the formulation that's disclaimed now? Did she invent claim 21? There's no evidence that she is

inventor of any challenged claim much less any remaining claim in the patent and we do in fact, you know, they suggest that we didn't carry our burden to rebut what they allegedly prove but if you look for example at Incyte's slide 65 we did ask Dr. Uttamsingh about conception and the question was from Exhibit 1172,

"Q. You -- before Ms. Wagner came up with the idea of using 4 to 50 milligrams per day of Compound (1) for the treatment of hair-loss disorder in a mammal, you didn't yourself conceive of that idea, correct?"

"A. As far as I remember, that's correct."

And so in terms of this is merely the subject matter of claim 1 just narrowed basically by dose and the 95 percent deuteration which she also didn't contribute to based on the deposition testimony, we actually have affirmative evidence that the method that's claimed is not something that she conceived of and conception is obviously the touchstone of invention.

JUDGE PAULRAJ: Mr. Feldstein, this is Judge Paulraj. So on the question of inventorship, have you cited any case law for the proposition that inventorship is determined on a claim-by-claim basis as opposed to the specification as a whole or the patent as a whole?

MR. FELDSTEIN: Thank you, Your Honor. Actually on slide 64 of our deck we cite in Egenera, Inc. v. Cisco Sys. Inc. Federal Circuit 2020,

"Like validity, inventorship is a claim-by-claim question."

And Irion IP, LLC v. Hyundai Motor Am., Federal Circuit 2010,

"Although §102 refers to 'the invention' generally the anticipation inquiry proceeds on a claim-by-claim basis."

And so it does need to be a claim-by-claim basis for inventorship for priority for all of anticipation.

JUDGE NEWMAN: This is an obviousness inquiry though. You're saying this is an anticipation-type inquiry for what was disclosed?

MR. FELDSTEIN: In terms of going and, I mean obviousness inquiry would also have to proceed on a claim-by-claim basis and here we're merging in the inventorship. The inventorship is a claim-by-claim basis. If they were going to claim an exception based on inventor, the inventor has to be an inventor of that claim. If they're going to claim an earlier priority date and earlier effective filing date, that claim that they're defending has to have an earlier effective filing date. It's not uncommon that in a patent some claims may have different inventive filing dates. Some claims may have different inventors and that's why it has to be done on a claim-by-claim basis when you're starting to rely on priority dates and inventorship.

JUDGE NEWMAN: And is there any statutory basis for this or you're relying entirely on case law?

MR. FELDSTEIN: I think the language -- we have

language summarized honestly on slide 60 but it has to be disclosure from an inventor of a claimed invention and so it's not inventor of the patent, it's inventor of a claimed invention and the 102(b) exception applies to the claimed invention and claim 1 is one claimed invention, claim 21 is a different claimed invention and we read, in the statute, we read inventor of a claimed invention to refer to of a specifically claimed invention, not inventorship of a patent as a whole with --

JUDGE NEWMAN: It's inventor or joint inventor though, isn't it?

MR. FELDSTEIN: Correct. But it has to be inventor or joint inventor of a claimed invention. It's not inventor or joint inventor of a patent.

JUDGE NEWMAN: Joint inventor of a claimed invention. Okay. I understand. Please continue.

MR. FELDSTEIN: Yes. Thank you. I want to move to a different point on toxicity concerns, especially because I may have misunderstood a question in my opening about the toxicity concerns. Concert made much of toxicity concerns over using Ruxolitinib or JAK inhibitors for the treatment of Alopecia Areata pointing, as they recognized what we say as improperly pointing to blood cancer patients, myelofibrosis patients (indiscernible) effects.

If we look to Incyte's slide 21 the Teva Pharms. Int'l GmbH v. Eli Lilly & Co. case from last year makes clear that potential

safety concerns did not outweigh evidence of actual studies. Then what we have on the right hand side of slide 21 are actual studies in Alopecia Areata. Dr. Mackay-Wiggan reporting no serious adverse effects, that's with Ruxolitinib and Pieri also Ruxolitinib, no side effects. Higgins, also Ruxolitinib, no adverse effects and so they're hypothesizing by relying on other drugs. They rely on Baricitinib in one of their slides, I think slide 64, they're relying on Baricitinib not Ruxolitinib and they rely on adverse event profile in blood cancer patients. Here we don't have to speculate. The evidence on slide 21 shows that what was reported in the art and what a POSA would have known is that there were no serious side effects reported for the use of Ruxolitinib with AA.

A question that came up from Judge Pollock to Concert whether there's a common mechanism or not or JAK mediated autoimmune disorders and I'd, in the record, I'd point you to the Patterson declaration. He's one of our experts, Exhibit 1007 paragraph 60 where Dr. Patterson explains the common mechanism that is taught by Dr. Christiano.

The last point I'd like to make, unless there are questions, is on unexpected results. There was a statement that the law states and I may be paraphrasing -- I am paraphrasing, but I believe it was in some substance that the law states there's no need to compare to the closest prior art if there's not a study available to compare it to. Concert's argument is there wasn't a

ready made available study to compare their drug to, therefore they didn't have to compare it to Ruxolitinib. There's no law whatsoever that says you are only able to pick and choose what's already available in terms of existing clinical studies. If they wanted to establish unexpected results in the same patient population with Ruxolitinib they'd run a clinical trial comparing Ruxolitinib to CPT543 in a comparable population and then they analyze it. You don't go and analyze a completely separate drug because you just didn't do the work. You don't go and rely on a study with a population that is more sick that you say is not comparable and in terms of what happened --

JUDGE NEWMAN: You're about one minute left, counsel.

MR. FELDSTEIN: -- thank you. I'll turn my last slide, slide 38. Slide 38 is the data comparing CPT543 to Ruxolitinib. The Ruxolitinib bars are the first three bars. They're not as numerically strong as Ruxolitinib and so their argument that somehow even this comparison of the CPT543 to Ruxolitinib shows some unexpected benefit, that's not what it shows. This is exactly what you'd expect to see Dr. Shapiro explains that Ruxolitinib and CTP have similar activity. Thank you, Your Honors.

JUDGE NEWMAN: Thank you.

MR. CEDRONE: If I may proceed, Your Honor?

JUDGE NEWMAN: Yes, we are ready for you.

MR. CEDRONE: Thank you, Your Honor. I'd like to make

four points on the 102(b) and then I may turn to one or two remaining issues. First, Mr. Feldstein argued that the disclosure we're seeking to exclude is not identical to the disclosure in Silverman. So rather than use our words let's use Petitioner's words. On our slide 12 we cite exactly how Petitioner describes the disclosure in Silverman. Compound (1) is disclosed and claimed in Silverman. A POSA would have been motivated by Silverman's teaching of Compound (1). The POSA would have been motivated to use Compound (1), the deuterated analog of Ruxolitinib from Silverman, and then an example from the claim chart where they describe a compound represented by the following structure or formula and point to example 1002. Dr. Uttamsingh's declaration contained that same disclosure of Compound (1) that's excluded and the Board can simply strike that entry from the claim chart. That's the fourth box on slide 12 which is page 71 of the petition.

The second point I'd address is the lack of written description support and the burdens and I just want to reiterate that on this issue of priority the burden of persuasion is always with Incyte and they have never, including today during either of their representations provided any evidence of any claim for which there is no support. They haven't met their burden of persuasion. I think Mr. Feldstein said we're relying on a footnote in our surreply. We make the argument in our surreply but that's not the only thing we rely on. We have the Exhibit

2004, the priority application itself, that we produced. That's why it's called the burden of production. We produced this exhibit during our first submission in this case and Incyte has never rebutted it, never rebutted the fact that on its face it provides written description support.

The third point I'd like to address is Incyte points to our slide 32 and says that we never established Dr. Uttamsingh's inventorship. Again, respectively that's flipping the burden on this issue. They have the burden of persuasion and it's particularly clear here because, as the Board is well aware, for an issued patent an inventor named on the face of the patent is presumptively a properly named inventor. Just one example citation is JEP Power Products, that's IPR 2016-01388, the final decision on December 5th, 2017. There's a presumption of inventorship. We have more than that as we've provided here.

Now Mr. Feldstein points to his own slide 65 and says that they asked Dr. Uttamsingh questions during her deposition in which she, Mr. Feldstein says, acknowledged that she didn't conceive the invention. The question they asked her does not match up with the actual legal standard for inventorship. Mr. Feldstein asked her during her deposition,

"Q. You didn't yourself conceive of that idea, correct?"

There were several other similar questions in the deposition where they asked questions along the lines of,

"Q. Did you originally conceive of this invention or was

this claim your original idea?"

Respectfully that's not the task. The question is did you contribute to the conception of the idea, did you perform part of the task that led to the invention? Incyte's counsel never asked Dr. Uttamsingh questions along those lines. Never asked if she performed part of the task that led to the claimed doses. Never asked if she contributed to the conception of the use of Compound (1) for the treatment of AA orally at these claimed doses. They asked a question that is very different.

"Q. Did you yourself originally conceive of this claim?"

That's just a different question and it doesn't match up with the legal standard. The final point I'd make is that Mr. Feldstein raised this claim-by-claim argument, the idea that 102(b) is applied on a claim-by-claim basis.

I think, Judge Newman I believe it was your question, highlights the problem with that argument. If you look at the language of the statute, for example on our slide 13 we have one of the inventor disclosure exceptions, the statute says the disclosure is excluded if it was publicly disclosed by the inventor or joint inventor. Mr. Feldstein answered Your Honor's question by saying something along the lines of that language means inventor or joint inventor of a claimed invention. I think it's telling that Incyte can only answer the question by reading into the statute language that's not there. His response to the question required him to read in the words of a claimed

invention. Congress knows how to write these statutes and if it had wanted it to proceed on a claim-by-claim basis it could have drafted language along those lines. The case that Mr. Feldstein cites about claim-by-claim, the language claim-by-claim comes from the case law.

Simply if Your Honors read that case and the cases it in turn cites, they simply stand for the proposition that if somebody contributes to one of the claims of an invention, they are a properly named inventor on the patent. Then when you turn to 102(b)(1) the question is just is this person just an inventor? Dr. Uttamsingh is an inventor and for the reasons we've already gotten into, these exceptions are satisfied.

I think the final point I'd like to address is just briefly Mr. Feldstein during his rebuttal pointed to slide 21 and to argue that there were actual studies showing no side effects from Ruxolitinib. The three references on that slide, we should be clear they're not studies, they're anecdotal reports that would not have, you know, outweighed the actual data from studies in the record.

Unless Your Honors have further questions, I believe we are -- unless Your Honors have further questions I believe that, you know, for all the reasons we've explained the Board can finish its analysis at the 102(b) issue and find that the disclosures that are key to Incyte's two asserted grounds are not prior art. But as we've explained regardless even if those

disclosures come in, a person of ordinary skill in the art simply would not have selected this compound for treatment at the claimed doses for this disease without the benefit of hindsight and even if they would have the objective indicia of nonobviousness confirm that this invention was not obvious as of the priority date. Unless Your Honors have any further questions, we thank you.

JUDGE NEWMAN: We do not. Thank you very much to counsel for the time and effort that you put into this matter. We've had a great and very helpful argument today and will take it under advisement. Thank you.

MR. CEDRONE: Thank you, Your Honors.

MR. FELDSTEIN: Thank you, Your Honor.

(Whereupon, at 3:58 p.m., the oral hearing was concluded.)

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