IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

UNITED THERAPEUTICS CORPORATION,
Plaintiff,
v.
LIQUIDIA TECHNOLOGIES, INC.,
Defendant.

C.A. No. 20-755-RGA-JLH

Volume IV

J. Caleb Boggs Courthouse
844 North King Street
Wilmington, Delaware

Thursday, March 31, 2022
9:00 a.m.
Bench Trial

BEFORE: THE HONORABLE RICHARD G. ANDREWS, U.S.D.C.J.

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For the Defendants

*** PROCEEDINGS ***

DEPUTY CLERK: All rise. Court is now in session. Honorable Richard G. Andrews presiding.

THE COURT: Good morning, everyone. Please be seated.

09:00:14 So we're here for the closing arguments and,
09:00:23 Mr. Jackson, are you presenting for your side.
09:00:25 MR. JACKSON: Yes, Your Honor.
09:00:25 THE COURT: And you are -- you're ready?
09:00:27 MR. JACKSON: Yes, Your Honor.
09:00:27 THE COURT: And, Mr. Sukduang, you're presenting
09:00:30 for your side?
09:00:30 MR. SUKDUANG: Yes, Your Honor.
09:00:31 THE COURT: And you're ready?
09:00:32 MR. SUKDUANG: Yes, Your Honor.
09:00:33 THE COURT: All right. Well, then, let's go
09:00:36 ahead, Mr. Jackson.
09:00:37 MR. JACKSON: May I approach?
09:00:39 THE COURT: Sure.
09:00:51 MR. JACKSON: Good morning, Your Honor.
09:00:57 THE COURT: All right. Good morning,
09:00:58 Mr. Jackson.
09:00:59 MR. JACKSON: First on behalf of United
09:01:00 Therapeutics, I'd like to thank you for your time and
09:01:02 attention as we put in the evidence over the past several
09:01:05 days, including a number of individuals who testified by
09:01:09 deposition. Not always great to watch a video.
09:01:13 So, this case, obviously, involves two patents,
09:01:16 the '066 and the '793. I'm going to take them one by one.
09:01:19 '066 is the synthesis patent, and the '793 is the treatment

patent or dry-powder inhaler patent.

So on the '066, the defendants have two bases of argument for why they're saying the patent is invalid. First is this product-by-process argument. And the second is a written description argument.

The product by process, the first, it's unclear what they are actually comparing the new product to. There was some testimony about the Chicago process and there was some testimony about the Moriarty process. But it was -- it was going back and forth, and it wasn't really clear. In any event, Dr. Winkler is their expert -- was their expert for invalidity on the '066, and he never really established that the prior product is actually the same as current product. He failed to establish that there was -- that the product in the public domain was structurally and functionally the same as the old -- as the new product. And you'll recall at the pretrial conference, Liquidia disclaimed an on-sale bar argument. And it is also precluded from arguing obviousness based on the '393 patent.

So Dr. Winkler gave his conclusory opinion about -- based on the purity that the product -- that the old process and the new process are the same. But the problem is that the claims of the new process of the '066 patent don't analyze purity as a whole. It analyzes specific types of impurities, impurities that are reduced

between the starting batch and the pharmaceutical composition, and those impurities have to come from the alkylation and hydrolysis steps in the process. So, it only looks at very specific impurities, not overall impurity numbers.

On Claim 2, Dr. Winkler does not analyze anything about the crystallinity of the salt formation of the isolated salt. Dr. Winkler does not address or analyze how any prior art of the -- about the Treprostinil salt could be stored at ambient temperature. And on Claim 8, the last claim, there is -- the product-by-process principles don't apply at all because it's a process claim, not a product claim.

So, as the Court heard testimony, Dr. Winkler kept focusing on the -- saying the products are the same, but he kept focusing on the molecules, just the BTO molecule, not the -- actually a comparison entire batch and the entire synthesis process, which is described there.

And as the Court heard, all the experts agree that the synthesis process includes all the impurities that come with the various pieces and various batches that you -- that are moved through the -- that are moved through synthesis.

When we came back on -- in response, Dr. Walsh talked through the exact -- the structural and functional

differences between the old process and the new process. And this is his slide right here. This is his slide right here. So the old process, again, he talked about this old process being the -- testing the impurities at six months for the impurity of 3AU90. And that's at 5 degrees C, so that blue, that's old process refrigerated. Whereas the new 3AU90, that's the new process at 25 degrees C. So, comparing the old process refrigerated and the new process at 25 degrees C, that's a big difference. It's showing that there's much less impurities after six months even though it's at 25 degrees C as opposed to refrigerated.

Likewise, the total related substances. This was the old process refrigerated. This is the new process, not refrigerated. Those show structural and functional differences in the two processes. That was important to United Therapeutics in how they were synthesizing the molecule or synthesizing the batches that they were doing and getting approval from the FDA and was selling. So, as you heard from Dean Bunce, he testified that United Therapeutics had to change the specification with the FDA because the new process was reportedly a consistently better product and it was too pure, based on the specification. It was 102 percent, too pure in comparison to the specification. And as Dr. Walsh said, he had never seen a more pure product in his 40 years of API production. Right.

09:06:21 So those show the structural and functional differences.

09:06:24 The next argument Defendants make is that it's a
09:06:30 written description argument and that the inventors, they
09:06:33 argue the inventors didn't actually possess the invention
09:06:37 that's described in the patent. And in particular, the
09:06:41 impurities limitations. But all experts agree that the
09:06:45 reactions in this process -- that all reactions, in fact,
09:06:50 generate impurities. And in fact, the patent itself
09:06:55 describes the exact steps -- exact steps in the process, so
09:07:01 it starts with the BTO, which includes the impurities. And
09:07:04 then Example 1 talks about the alkylation process. That's
09:07:08 at Column 10 lines 35 and 36. Talks about it being a light
09:07:12 brown liquid. As you heard from UTC's experts and
09:07:17 Dr. Scheidt, that color indicates an impurities to him, and
09:07:22 a POSA would know that as well.

09:07:23 The next step is Example 2, that turns to
09:07:29 yellow, pale yellow color, and that's found in Column 11 at
09:07:33 47 through 49. And that's the end of the hydrolysis steps.
09:07:37 Those are the -- that shows that the inventors -- that there
09:07:41 were -- inventors understood there were impurities in the --
09:07:45 in the batches that they were making and describing in the
09:07:47 patent.

09:07:48 And then the last step is the alkylation and
09:07:51 hydrolysis, and it turns -- after the salt formation step,
09:07:55 it turns white and -- or off-white, and that's in Example 5.

09:07:59 And so as a result -- at 14, column 14, line 47. So, the
09:08:05 inventors knew and understood what they were doing. That's
09:08:08 why they identified, for example, the colors. Those
09:08:10 indicate the impurities.
09:08:12 At bottom, the POSA would have understood the
09:08:19 inventors actually possessed what they claim to have
09:08:23 invented, and they -- the words in the patent describe it.
09:08:26 It's within the four corners of the specification. That's
09:08:28 the test for written description.
09:08:30 So, next, Liquidia actually infringes. Now, as
09:08:38 you know, we had a hard time getting actual samples so we
09:08:42 could test in the various intermediates, so instead, we went
09:08:45 and looked at the data in their DMF, in Yonsung's DMF, on
09:08:49 which Liquidia's relying. And the data in Yonsung's DMF
09:08:53 showed that the starting batch -- that's the TN02. That's
09:09:00 the TN02 right here. That's the starting batch. It
09:09:03 reduced -- the impurities are reduced. That's in the
09:09:06 pharmaceutical composition. That's TN; right? These are --
09:09:09 if you just look at percent impurities, that's here. .2 to
09:09:14 .03. So it's a reduction, and we have to show that those
09:09:18 impurities come from the alkylation and hydrolysis steps.
09:09:21 Well, they do.
09:09:22 BTO, that's the -- that's at the start of it.
09:09:25 That's pre the alkylation and hydrolysis. And then it jumps
09:09:30 up in TN01 at .59. That shows the impurities are coming

09:09:34 from the alkylation and then in TN02 at .2, in the
09:09:39 hydrolysis steps. So if you look at either the percent
09:09:42 impurities, and the same story as in the number of
09:09:45 impurities. That shows that the impurities that are
09:09:47 generated from the alkylation and hydrolysis steps are
09:09:50 reduced in the -- between the starting batch and the
09:09:53 pharmaceutical composition.
09:09:55 Alternatively, if you just say let's look at one
09:09:59 impurity, the 15-epi-Treprostinil. There is no
09:10:04 15-epi-Treprostinil in BTO. There's -- it was not detected.
09:10:08 And so, Dr. Dean Toste looked at that and said, okay, let's
09:10:14 look at what it is in the -- after the in -- so he starts in
09:10:21 the starting batch at TN02 and then he looks at the final
09:10:26 pharmaceutical composition and in TN. And each of those
09:10:30 yellow bars drops down to the blue bar. That's the
09:10:33 comparison of the epi, 15-epi-Treprostinil, and TN02 in the
09:10:38 yellow and then dropping down to the 15-epi-Treprostinil in
09:10:41 the TN, in the blue. That shows that they infringe.
09:10:45 The next thing that Liquidia argues is that it
09:10:49 didn't -- it doesn't store the Treprostinil sodium in the
09:10:56 process at ambient temperature. Now, there's actually
09:10:59 multiple places where they stored at ambient temperature,
09:11:02 and we focused on three. So, first, here, it's stored at
09:11:07 ambient temperature for 43 days when it's being held after
09:11:12 it's being -- after it's been isolated but before it's

accepted into the warehouse. 43 days of storage under any test is storage.

Next, it's stored at ambient temperature at -- during that transit from Korea to the United States. And I'm going to come back to that in a minute. I'll show that in the next slide. And then it's also stored at ambient temperature after it's in the -- when it's actually here in the United States, they put it in the dry box before it's -- while it's in the process and while they're in the process of moving it through the -- their manufacturing process to create the final pharmaceutical composition.

THE COURT: So when does it become a pharmaceutical composition?

MR. JACKSON: So, I think it becomes a pharmaceutical composition -- for purposes of this, I believe it's after the -- I think -- if I'm not mistaken, didn't -- I believe Dr. Nuckolls said it was after -- there was a step in the PRINT Process. I think it was Step 3 in the PRINT Process, but can I check.

THE COURT: PRINT Process occurs in the United States; right. >

MR. JACKSON: Correct.

THE COURT: So it's not a pharmaceutical composition before then?

MR. JACKSON: It's not a pharmaceutical

09:12:23 composition before then, correct.

09:12:31 As I said, the Court heard a number -- a bunch
09:12:35 of testimony about various batches and the transit of those
09:12:37 various batches, and I wanted to focus on exactly what those
09:12:40 batches show. So again, Liquidia's talking about, well, our
09:12:44 specification and the thing we say to the FDA is it's
09:12:47 between 2 to 8. Well, that's not what they've actually --
09:12:51 they are able to, and they do store it, at a variety of
09:12:56 other temperatures. And they are -- they are seeking
09:12:59 approval to infringe, and in the Hatch-Waxman case, that's
09:13:04 sufficient. As the *Sunovion Pharma v Teva*, which is 731
09:13:11 F.3d 1271 at 1280, which is a Federal Circuit case from
09:13:16 2013, the Court says, "Simply saying but I won't do it is
09:13:32 not enough to avoid infringement." And that's the test
09:13:35 we're applying.

09:13:35 So, my colleagues did me the generous help of
09:13:41 providing me additional insight on the answer to the Court's
09:13:45 question. It's the pharmaceutical composition at the time
09:13:50 of manufacture. And then it's a pharmaceutical product
09:13:53 after the PRINT Process.

09:13:55 THE COURT: All right. So it's a pharmaceutical
09:13:57 composition in Korea?

09:13:59 MR. JACKSON: Yes. Yes. So, I was confused
09:14:03 between pharmaceutical product and pharmaceutical
09:14:05 composition, so I apologize.

09:14:06 The -- so these -- this is the data about how
09:14:12 they ship it. So the first TN, so TN115E010, they use in
09:14:19 the clinical phase. They had no temperature data. All the
09:14:23 green boxes on this slide show times when they had no
09:14:26 temperature data for the --
09:14:28 THE COURT: And actually, just sorry to
09:14:30 interrupt. But the question on infringement here, I'm
09:14:36 predicting what they will do with the product in the future;
09:14:39 right?
09:14:39 MR. JACKSON: Right. Right.
09:14:42 THE COURT: Okay.
09:14:43 MR. JACKSON: And so it's helpful to see what
09:14:44 they've done with the product in the past and their ability
09:14:47 to -- what -- whether they're going to infringe in the
09:14:49 future. So, here, all the green boxes show they shipped it
09:14:55 without any temperature log. So we have no idea what the
09:14:59 temperature -- whether it was kept at any particular
09:15:01 temperature or what the temperature was.
09:15:02 And those were ones that they used in the
09:15:07 clinical -- in clinical trials, and that was in 2016. Then
09:15:10 the blue are the ones 116J010 and 117I010. Those -- the
09:15:20 PTXs are listed on this slide. Those both came in, and
09:15:23 those were -- showed temperatures that although they say
09:15:26 it's 2 to 8, it dropped down to negative 50, stayed below 0
09:15:31 for the entire -- for a big, long chunk, multiple days, and

then jumped up on the late in the -- late in the time graphs to well above 2 to 8.

So and by the way, every single batch that they shipped, every one with -- that is in evidence, which are all on this slide, every one, none of them stayed within 2 to 8 the entire time. They are outside the 2 to 8 zone, so while they said say they stayed within 2 to 8, it's just not true. So these are the two that dropped down to negative 50. They did not at the time have any information that -- any confirmation that those temperatures dropping down to negative 50 would be stable and would be appropriate for human use, but they did it. They used it nonetheless.

Then they have two more batches here or two more sets of batches here that they got that were transported without any temperature logs. Then on November 14th of 2019, they asked, they sent an email and said can you give us confirmation that it's going to be stable? And the PTX 2020 said Yonsung has no stability data below 0. So no stability for freezing. And nonetheless, the very next day Yonsung issued that declaration quote/unquote guaranteeing that it would be okay. Even though they obviously did not have any stability data. They didn't get -- gain stability data in a day.

And then they have these batches that went up to as high as 16.7 degrees C for an extended period of time,

but they quarantined it when it got to the -- to the facility in the United States. And they held it in quarantine through the depositions in this matter, and only at trial did we learn that it's now been released to the R & D group.

Now, you'll recall there was also some testimony that when they got it, they knew it had come up to 16 degrees C, and they could have sent it back. But the documentation said, don't worry. This Treprostinil sodium, this Treprostinil salt, is stable and safe at above -- at ambient temperature. So that's why they took it in. They could why have just said we're sending it right back. We're getting a credit. Let's get another batch because we want that for GMPs, but no, they didn't. They accepted it. That shows they knew it was acceptable and appropriate.

Next, they -- also on the 79 -- moving to the '793 patent, they have two arguments. One is written description, and the other is enablement. And their two arguments on that are -- involve the dry-powder and the scope of pulmonary hypertension. I'll take those in turn.

First, dry-powder is described and enabled in the patent. The standard for written description is after reviewing the four corners of the specification, the POSA would understand the inventors were in possession of the claimed invention. The '793 patent satisfies the standard.

09:18:37 The language is actually in the patent. The inhalation
09:18:41 device can also be a dry-powder inhaler, and in such case
09:18:44 it's inhaled in solid formulation, usually in the form of a
09:18:47 powder with particle size less than 10 micrometers in
09:18:51 diameter or less than 5 micrometers in diameter. It's
09:18:57 expressly described in the patent. They had possession of
09:18:58 the -- they knew what they were inventing, and they had
09:19:02 possession of the invention.

09:19:03 And even Dr. Gonda admitted that the patent
09:19:06 describes in written form a dry-powder inhaler and
09:19:10 formulation. And that's in the trial transcript at 770
09:19:13 lines 9 through 25. Liquidia's failed to carry its burden
09:19:19 that they lacked -- that it lacks written description by
09:19:23 clear and convincing evidence. First, Gonda wrongly says
09:19:26 that there's no evidence that they were in possession in the
09:19:29 patent. That's wrong. It's right there.

09:19:31 Second, Dr. Gonda relies on irrelevant evidence
09:19:35 outside the four door corners. He focused on whether the
09:19:38 inventors made a dry-powder formulation or whether there are
09:19:41 dry-powder formulations on the market today. But the
09:19:44 relevant question is not that. The relevant question is
09:19:47 whether the POSA, after reviewing the four corners of the
09:19:50 patent, would conclude that the inventors actually possessed
09:19:54 the invention, and they did. That's why it's described.
09:19:57 Their complaint is, in essence, that the patent didn't walk

a POSA through the very detailed steps of how to make a dry-powder, but that's not necessary.

On enablement, Liquidia's assertion is that a person of ordinary skill couldn't do -- prepare a powder formulation without undue experimentation. But that's refuted by both by Dr. Clark's testimony, Dr. Gonda's admissions, and Dr. Smyth's testing.

First, Dr. Clark explained that in each step in preparing a dry-powder -- that each step in preparing a dry-powder was known in the art at the time. And in fact, he says by 2006, "The processes and the issues around developing dry-powder inhalers were actually well-known, and the process of developing formulation usually used pretty routine techniques, both in terms of analysis and in terms of manufacturing."

Dr. Gonda claimed that it would have been impossible, but he didn't even try. He also claims that a person of ordinary skill would have had to do extended stability studies before making a formulation, but that's actually not the case, as evidenced by Liquidia's own actions. They picked this product and just started testing on it. They didn't go through a whole bunch of stability studies. And Dr. Smyth, you saw him talk through. I tried to make -- I tried to figure out how to make a dry-powder. It took me three weeks. The three weeks, and then there

might have been -- he might have needed additional time to do routine experimentation in order to bring that product further forward. But this is all it took for him to get to things that fell within the scope of the claim.

Next, the patent describes and enables pulmonary hypertension. Pulmonary hypertension is a condition associated with an elevation of the pulmonary arterial pressure over normal levels. That's what the patent says, and both experts -- both experts, Dr. Waxman and Dr. Hill, agree, and it's undisputed that under this definition, Treprostinil can be used to treat conditions that arise for any precapillary forms of pulmonary hypertension in all five groups. And it's undisputed, also, that a POSA -- a person of ordinary skill would not use Treprostinil to treat a patient in a single subcategory under group two, which is the isolated and pure solely postcapillary pulmonary hypertension. A person of ordinary skill would have known not to do that. And, in fact, Dr. Gonda said he thought it would be -- I asked him whether he thought it would be -- or excuse me. Dr. Hill. I asked him, and he said he thought it would be stupid to do. "I'm usually very cautious about referring to any of my colleagues in that way, but in this particular situation, that's probably apt." That was his testimony.

And it's also -- I also note that Liquidia's own

patent itself uses the same language about pulmonary hypertension, treating of pulmonary hypertension with Treprostinil.

Next, Liquidia infringes the '793 patent. And I'm only going to spend a minute on this because I think it's pretty clear. The test -- the two things they're challenging about whether or not they infringe the patent are "therapeutically effective" and "single-event dose." And Dr. Hill testified that he thought that it wasn't -- there wasn't sufficient information for therapeutically effective. And that a dosing would not -- would not -- would have to -- could not be done more than once a day. But the patent itself at line -- at Column 8 lines 1 through 2 says Treprostinil can be administered a single time per day or several times per day. The patent also says in the application an effective amount of Treprostinil in only a few breaths or even a single breath was achieved. So the patent says an -- look at the data and look at the hemodynamics. An effective amount of Treprostinil and an effective -- an effective amount of Treprostinil was achieved. The application was achieved. A POSA looking at that would understand that an effective amount, a therapeutically effective amount, was detailed in the hemodynamic data.

Second, Dr. Hill argued that the therapeutically

09:24:32 effective dose can only be measured by primary clinical
09:24:35 endpoints, such as how a patient feels, functions, or
09:24:38 survives, and not the hemodynamics. But that's not
09:24:41 nonsensical. As I said, the patent itself says
09:24:46 "therapeutically effective" or it says "effective." And
09:24:50 the -- Dr. Hill even admitted that the patent has data
09:24:55 showing that it has -- that Treprostinil results in a
09:24:59 hemodynamic response. So, that's just not the case.
09:25:03 And then finally, it's not on a slide, but in
09:25:07 preparing for this, the -- I note, so this is -- this was
09:25:14 Dr. Winkler's -- the presentation he did; right? And so, he
09:25:21 -- these were -- he was the only expert they had on
09:25:24 invalidity of the '066. And this was his page showing that
09:25:30 it was -- asserting his ideas about why it was invalid. So,
09:25:35 product-by-process claims, that applies to 1, 2, 3, 6, and
09:25:39 9.
09:25:40 Lack of written description of reduction of
09:25:43 impurities applies to 1 and dependent Claims 2, 3, and 6.
09:25:47 And indefiniteness of storage limitations, applies to
09:25:51 Claim 8. Or 6, 8 and dependent 9. So, as a result -- but
09:25:55 the Court will recall that it granted the Rule 52(c) on
09:26:01 this. So, as a result, Claim 8, there is no argument that
09:26:06 Claim 8 -- there's no argument now that Claim 8 is invalid.
09:26:10 So the only question is whether or not that claim, for
09:26:15 example, is infringed. If it's infringed, we already know

it's valid, so that means that the United Therapeutics should prevail.

My colleagues also just helpfully gave me more detail on the pharmaceutical composition. Pharmaceutical composition is prepared when starting -- is prepared starting when the TN -- let's go back to that. Oh, yeah that's an easier way of doing it.

So, I'm showing back -- this is, again, Dr. Winkler's slide. A pharmaceutical composition is prepared when the TN is mixed with excipients in PRINT Step 1, and at -- which is the LIQ861 bulk powder. The pharmaceutical product is prepared starting at the PRINT Step 5, but the PRINT Process in between, you'll recall that along the way, they take that starting batch, and they do various things in the PRINT Process. But the -- that PRINT Process has no impact on the alkylation or hydrolysis impurities. And that's what Dr. Nuckolls specifically said on -- in response to questions on direct.

THE COURT: So, wait. The -- did I just understand you to say that your position now is that the pharmaceutical composition is made through PRINT Process Step 1?

MR. JACKSON: So, it's --

THE COURT: Mr. Jackson, I think Mr. Carsten wants to speak to me for a second.

09:28:20 MR. JACKSON: Thank you.
09:28:21 MR. CARSTEN: If I may.
09:28:21 THE COURT: It's his argument, but he can speak
09:28:23 with you for a second.
09:28:24 MR. CARSTEN: He won't even -- you won't even
09:28:26 see his lips move.
09:28:28 Yes, the pharmaceutical composition is prepared
09:28:31 at the end of the salt formation step in Korea. It remains
09:28:36 a pharmaceutical composition from that time during the
09:28:39 transit to the United States up until it's received at
09:28:43 Liquidia and Liquidia begins its PRINT Process. And I think
09:28:49 it's actually after Step 1 when they start to mix it with
09:28:54 other stuff. At that point, it's no longer an isolated salt
09:28:58 as required by some of the claims. And at that point, it
09:29:02 becomes a pharmaceutical product.
09:29:05 THE COURT: Okay. All right.
09:29:07 MR. CARSTEN: Thank you, Your Honor.
09:29:09 I apologize Mr. Jackson.
09:29:10 MR. JACKSON: No. No, thank you.
09:29:12 THE COURT: All right. So, Mr. Jackson, you're
09:29:14 done?
09:29:15 MR. JACKSON: Yeah, unless the Court has any
09:29:16 other questions.
09:29:16 THE COURT: I might have some questions after
09:29:18 I've heard from the other side, but thank you for what

09:29:23 you've said.

09:29:24 And let me hear from the other side.

09:29:26 MR. JACKSON: Thank you.

09:29:43 MR. CHEEK: May I approach?

09:29:44 THE COURT: Sure.

09:29:50 Go ahead.

09:30:01 MR. SUKDUANG: Good morning, Your Honor. Sanya Sukduang on behalf of Liquidia Technologies. I'm going to start out with the invalidity of the '066 patent.

09:30:10 Now, at the opening of this trial, I showed you a slide. It was a copy of the Moriarty JOC paper from 2004, and I compared it to the product process claims of the '066 patent. That is the basis for product by process. Mr. Jackson and UTC want to muddle it. The fact of the matter is from the very beginning of this case, what Dr. Winkler testified to and what I'm going to tell you know now is the same argument.

09:30:37 Treprostinil, UT-15, the Treprostinil free acid, was made in a public disclosure, Moriarty 2004. That reference tells you that when you alkylate a triol, you conduct hydrolysis on that triol, and you end up with UT-15, and that's DTX 258 is Moriarty.

09:31:02 If you go to the very last page of the Moriarty reference, it tells you that the purity of that product is the 99.7 percent pure. The public knew how to make

09:31:11 Treprostinil. The public knew what the purity of that
09:31:13 Treprostinil was. That's in the public domain.
09:31:16 The '066 patent, you heard testimony from
09:31:19 Dr. Winkler, from Dr. Nuckolls, and from Dr. Toste that the
09:31:23 claim -- the product of the '066 patent can either be
09:31:27 Treprostinil, which is UT-15, or Treprostinil salt or a
09:31:30 pharmaceutically acceptable salt of Treprostinil. The fact
09:31:33 that the Claim 1 of the '066 patent and all the
09:31:37 product-by-process claims claim Treprostinil. That is the
09:31:42 same product as the Moriarty product. The same exact
09:31:46 product. The chemical structure is the same. The purity is
09:31:50 the same.
09:31:51 And why do we know the purity is the same?
09:31:53 Claim 1, as you heard from Dr. Winkler and Dr. Toste, does
09:31:57 not include a purity limitation. It does not say that the
09:32:01 Treprostinil or the Treprostinil salt needs to be 99 percent
09:32:05 pure, 99.5 percent pure, 98 percent pure. It just has to be
09:32:10 Treprostinil. The only comparison is between the starting
09:32:14 batch and a final composition later in the claim, but
09:32:17 there's no dispute that the claim doesn't require any
09:32:20 specific purity.
09:32:21 When you go to the '066 patent, Example 5, at
09:32:25 the end of Example 5, at the bottom right, I believe it's
09:32:28 Column 14, they tell you that the purity of the
09:32:32 Treprostinil, the same Treprostinil as Moriarty, can be

09:32:35 1 99.7 percent. Those product are the same. That is the
09:32:40 2 comparison that needs to be made.
09:32:43 3 Now, UT doesn't want to make that comparison.
09:32:46 4 They bring up Mr. Bunce. Mr. Bunce was a fact testimony
09:32:50 5 witness. He never said that the products were different.
09:32:53 6 He never testified that there were they were structurally
09:32:57 7 different. He never testified that they're functionally
09:32:59 8 different. What he testified to is when they submitted this
09:33:02 9 information to the FDA using the new process, the new
09:33:07 10 process -- and this is DTX 07 -- 070 at Page 3 -- that that
09:33:13 11 product was the same, both in terms of quality and purity.
09:33:18 12 Dr. Walsh came to testify. He's an inventor on
09:33:22 13 the patent, but not an expert in this case, and he showed
09:33:25 14 you, and he showed you on the slide today from UTC, an old
09:33:28 15 process in blue and a new process in green. What UTC and
09:33:33 16 what Dr. Walsh was comparing -- and he testified to this --
09:33:36 17 that he was comparing Treprostinil free acid to Treprostinil
09:33:42 18 diethanolamine salt. Those aren't the products that you
09:33:45 19 compare for a product by process. Those are two different
09:33:48 20 compounds, and Dr. Walsh confirmed that those are two
09:33:51 21 different compounds.
09:33:53 22 In terms of stability and storage that you
09:33:55 23 heard, Claim 1 does not include storage -- storage of
09:34:00 24 Treprostinil salt. It does not include stability of
09:34:03 25 Treprostinil salt. And we know from the record and from

09:34:07 Dr. Winkler's testimony and Dr. Gonda's testimony that
09:34:10 Treprostinil free acid is not stable at ambient temperature.
09:34:13 It forms dimers.
09:34:16 We also know that not all salts of Treprostinil
09:34:19 are stable at ambient temperature. That's Dr. Smyth's own
09:34:22 testing based on the Treprostinil sodium, not that Liquidia
09:34:25 sent him, not that Yonsung sent him, but UT sent in cold
09:34:29 package. And when he opened it up and tried to use it, it
09:34:32 was hygroscopic. It wasn't physically stable. He testified
09:34:36 to that.
09:34:37 So when you look at the actual comparison for
09:34:39 product by process, remember, it doesn't matter what the
09:34:42 process is. If the product is not novel, it is not valid.
09:34:46 It's Moriarty and the '066.
09:34:50 THE COURT: Is this an obviousness argument or
09:34:55 an anticipation argument?
09:34:56 MR. SUKDUANG: Sure. So product by process --
09:34:58 the way product-by-process claims could work, if the product
09:35:00 is not novel or non-obvious, it's not valid. Our argument
09:35:05 is it's disclosed literally in Moriarty, so it would fall
09:35:09 into the first can. It's not novel, so we didn't argue --
09:35:12 we did not have to argue the process because it's a
09:35:16 product-by-process claim. You only consider the product.
09:35:19 Moriarty discloses that explicitly.
09:35:21 THE COURT: So when you say "not novel," you're

saying it's anticipated?

MR. SUKDUANG: It's anticipated, yes. I'm sorry. To be more clear, it's anticipated. I apologize if I was unclear.

So, again, Dr. Walsh made the wrong comparison. The claims don't require the Treprostinil free acid to be stable or stored. When you look at Claim 6, which is another product-by-process claim, it's only the -- it's only the Treprostinil salt that is stored. And then you take that Treprostinil salt and make a pharmaceutical composition. So, again, the pharmaceutical composition, the product of Claim 6, is Treprostinil, not the Treprostinil salt. So, when you look at all of those documents, it's clear, clear and convincing, that the product is not novel and, therefore, it's invalid.

Now, UT -- you heard testimony they tried to ask Dr. Winkler you're relying on all these internal documents, these confidential documents, from United Therapeutics? That's your basis? Dr. Winkler was very clear. He's like, no. It's Moriarty. He pointed to those internal documents to show that even if you looked within UT, when you do the comparison of the average purity of all the batches in Chicago, it's 99.7 percent pure. That's the same as what Moriarty disclosed. And when you looked at the average of all of the batches made at Silver Spring up that point, the

same purity, 99.7 percent pure.

And importantly, UT offered no expert to refute Dr. Winkler's testimony. Dr. Walsh didn't refute it. He did not refute that testimony. Mr. Bunce did not refute that testimony. And none of those witnesses said that there is a structural or functional difference between the Treprostinil made according to the '066 patent and the Treprostinil made according to the Moriarty process. The only time you ever heard that is attorney argument, and attorney argument does not satisfy -- save validity of the claims.

Moving to written description, Your Honor. Written description is interesting because the claim, as you recall, and we've talked a lot about this with respect to the impurity profile and infringement, the claim requires that the impurities resulting from alkylation BTO and hydrolysis, that those impurities in the starting batch are higher than the final pharmaceutical composition. And UTC, on the argument of what a final pharmaceutical composition is in terms of infringement, is fluctuating. We'll get to that in a minute. But that's the comparison; right?

There is no dispute, all of the experts in this case, Dr. Winkler, Dr. Toste, testified that there is no data, Dr. Scheidt testified, that there's no data in the '066 patent that provides the purity of that starting batch,

09:38:11 which is the Treprostinil starting batch that you make after
09:38:14 Example 2 of the '066 patent. No purity at all. If you
09:38:20 don't have the purity to compare from the starting batch to
09:38:24 the final pharmaceutical composition, you cannot have
09:38:27 written description support.
09:38:29 And why do you need -- why do we know you need
09:38:31 that data? UT filed a 295 motion says we need that data.
09:38:35 We don't have enough. Then UT's experts, Nuckolls and
09:38:39 Dr. Toste, on infringement, they did not rely on color
09:38:42 change. They said we need actual data to try to do this
09:38:45 comparison. POSAs know that you need the data to make this
09:38:51 comparison. Because there is no data, there is no written
09:38:54 description support.
09:38:55 The inventors testified, Dr. Batra testified as
09:38:58 an inventor and as a 30(b)(6) witness, Dr. Tuladhar
09:39:04 testified, that during the process -- both of them
09:39:06 testified -- that during the process of making Treprostinil
09:39:08 salt at UT according to their invention of the '066 patent,
09:39:13 they did not measure the impurities of the intermediate.
09:39:17 Why? Because their real invention is not comparing impurity
09:39:21 in the middle and the impurity at the end. Their real
09:39:23 invention is, as Dr. Batra said, is this beautiful process
09:39:27 that you can clean everything up at the end at the salt
09:39:31 formation step; right? So they never had to measure this
09:39:35 impurity. And inventor testimony concerning what they did

and did not do is highly relevant to the issue of written description. That's the Biogen case from the Federal Circuit from 2021, Biogen, and also this Court's, *Noven v. Amneal*, District of Delaware 2020. Nonetheless, when you look at the four corners of the patent, the patent itself, there is absolutely no evidence of any data to do the comparison.

Dr. Scheidt, knowing that there's no evidence of any data, wants to rely on color changes. He testified that BTO is colorless, but he was shown documents that BTO is not colorless. It could be pale yellow. He also testified that color change does not tell you what impurities were formed, when they were formed, and what impurities were removed. All you can see is that went from light brown to light yellow; right? That doesn't tell you that there was an actual change in impurity profile.

He also relied on TLC, thin layer chromatography. The patent expressly says that thin layer chromatography is done to measure the progress of the reaction. That means, and Dr. Batra testified to this and Dr. Scheidt testified to this, that you're measuring to make sure that my starting material, it could be BTO or it could be the intermediate, is exhausted and I get the final product that I want out of that reaction. That's what TLC is used for; right?

Dr. Scheidt said that you could use, you could use, TLC to measure impurities. You heard from Dr. Winkler that the amount of impurities we're talking about here are so small that they're not going to show up on TLC. But importantly, again, looking at written description within the four corners of the patent, the inventors did not, in that patent, use TLC to measure impurities, either quantitatively by number or qualitatively. And they testified to that effect in their depositions.

THE COURT: Isn't it the case that if a patent specification says at the beginning, I have more impurities. At the end, I have less impurities, isn't that written description support for the proposition that you had less impurities at the end than you did at the beginning?

MR. SUKDUANG: Sure. If the claims -- if that's what the specification says, but then have you to look at what the claim requires. The claim isn't just I have more impurities and less impurities. It's -- and this goes to the infringement issue. It's alkylation of BTO and hydrolysis and what happens with those impurities. So, again, I agree, Your Honor. If the claim -- if Claim 1 just simply said impurities resulting from alkylation and hydrolysis are reduced in the final composition, then yes. What they have in this specification, sure. It would meet that. But the claim doesn't say that. It says have you to

alkylate a specific compound, and those impurities, you have to look at those specific impurities.

THE COURT: Isn't this kind of a claim construction issue because it says it talks about the steps? It suggests something broader than what you've been arguing throughout.

MR. SUKDUANG: No, alkylation and hydrolysis are steps. We're not changing that. You have an alkylation step. You have a hydrolysis step. Those are steps. But what are you doing in those step? You're not just alkylating anything. And the claim says expressly you're alkylating, within the alkylation step, BTO. So, again, I would agree if the claim said alkylation steps and hydrolysis steps, they would have written description support. But you can't read out -- and this is what UTC is trying to do. They're trying to read out that there's an alkylation of a specific compound, the BTO. And you cannot read that out. And that is not a new claim construction argument. That's literally written within the claim. And I'll go to that point now with respect to infringement, because it comes up in that context.

When you look at the infringement, again, Dr. Winkler testified that the claim says expressly you -- alkylation -- you have impurities resulting from alkylation and hydrolysis steps. And the claim also says at the

bottom, when the alkylation is of BTO, benzidine triol, you cannot ignore that limitation. That is when the alkylation is happening.

We are not contesting or arguing, and neither is Dr. Winkler, that -- and you asked this question of Dr. Winkler. Are you saying that you're just saying it's a single molecule of BTO that you say the claim requires and all of a sudden makes this giant batch? He said no. We all know that you have a batch of BTO. And Dr. Nuckolls and Dr. Toste acknowledged that in that batch of BTO, you have other impurities, one of them being 15-epi-BTO. The claim says you're talking about alkylation of BTO. When you go to the examples, Example 1 is telling on this. Example 1 says you're alkylating BTO. The patent doesn't tell you which impurities are formed. They don't mention any specific impurity. They don't tell you which impurities are reduced, what specific impurity. But the issue is in the claim they could have taken that limitation out at the end. They didn't need it. But they put it in, and when you put it in, it has to have meaning.

So, when you look at the issue of total impurities, or you look at the issue of 15-epi-BTO, those are out -- those are impurities that do not result from alkylation of BTO. Dr. Nuckolls -- Dr. Toste testified, and Dr. Winkler confirmed, that 15-epi-BTO is a compound that is

different from BTO. So, that is not alkylation of BTO. Total impurities includes solvents, reagents, other reaction materials that do not result from the alkylation of BTO.

And finally, when you look at the numbers that were involved here and the numbers that Dr. Toste and Dr. Nuckolls and Dr. Winkler looked at, they're so small, the changes are so small. You saw batches presented by UTC's experts where in TN02, the starting batch, there is 15-epi present, and then in some batches it goes down in the pharmaceutical composition TN. Then you've also seen batches from their experts where, in the starting batch, TN02 doesn't have any 15-epi-Treprostinil detected but then all of a sudden it shows up in TN. That can't happen.

The reason why you see that variability is because the numbers are so small. The HPLC methods have limits of detection. They have limits of quantification. When you're on the borderline of that limited detection and limited quantification, a number value change does not mean that there was an actual change or an actual reduction. In fact, the examples where 15-epi-TNO2 is not there, not detected, and all of a sudden shows up in TN is the perfect example that it is not an actual reduction in Yonsung's -- the process. It is just a variability, the natural variability in HPLC, which all the experts have agreed to does occur.

09:46:53 Moving on to storage, again, storage requires
09:46:59 that you actually store the material. Okay. Not use the
09:47:03 material. Your question to counsel was aren't I supposed to
09:47:07 be looking at what happens moving forward? The -- you heard
09:47:12 testimony from Mr. Kindig, a Liquidia employee, and
09:47:18 deposition testimony from Mr. Battistoni. They have a raw
09:47:23 material specification that requires that Liquidia to store
09:47:26 the Treprostinil sodium at 2 to 8 degrees. That is an FDA
09:47:31 requirement. In fact, you heard from Mr. Fuson that the
09:47:35 FDA, in conducting their pre-approval inspection of
09:47:39 Liquidia's facilities, actually went to the refrigerator to
09:47:43 ensure that, one, it meets that 2 to 8 requirement, and they
09:47:48 said it's an average 6 degrees Celsius.
09:47:51 And, two, they saw the Treprostinil sodium in
09:47:53 there. You heard from Mr. Fuson that if the Treprostinil
09:47:57 sodium was not stored at 2 to 8 degrees according to the raw
09:48:01 material specification, that would have been -- that would
09:48:04 have been -- I'm sorry.
09:48:10 Well, whatever. We don't need the slides. You
09:48:13 and I are talking.
09:48:14 That would have been a violation of the FDA.
09:48:18 That would have been the issue the FDA would have had a
09:48:20 problem with. Mr. Matto said, oh, no, the FDA wouldn't have
09:48:24 cared because you've got this one data point from Yonsung.
09:48:26 No. Mr. Fuson did the investigations for the FDA. He

testified to that. He was part of those investigations. He prosecuted what those investigators found. That was the issue. At Liquidia -- at Yonsung, they have a label, and they have specifications, and they have certificates of analysis that we saw from before the patent issued and even up to after the patent issued that that material is stored at 2 to 8 degrees.

Dr. Nuckolls testified that, oh, and you heard from counsel, that for three or four months, this material is somehow sitting in a warehouse at ambient temperature? That's not true. There's a document. It's -- -- -- I think it's DTX -- well, I'll get you the DTX, but it's a document that shows at Yonsung -- it's a 2017 document -- they have they have a list of all their APIs and raw materials, and it says explicitly for Treprostinil sodium, refrigerated. That's not ambient temperature.

And just common sense dictates. Why would Yonsung keep material at ambient temperature then spend all the money to cold-pack it and ship it across the world to Liquidia under cold temperatures when that stuff was sitting for months at ambient temperature? Logic doesn't dictate that. They store it at ambient -- excuse me -- at non-ambient temperatures.

Let's talk about shipping. Shipping to -- from Korea to the United States. That is done at temperatures

below ambient temperatures; right? Counsel wants to point to below freezing. That's not ambient. That doesn't meet the claim limitation. And Yonsung in 2019 knew that their material was going below because they had to ship it that way, guaranteed the quality of it.

They have the stability data at 25 degrees. Mr. Matto points to that. Despite that stability data, if you could use that material at 25 degrees, why wouldn't Yonsung want to provide -- why wouldn't Yonsung want to provide a guarantee of that material? If they can make their material good at 0 degrees and they can make their material quality good at 25 degrees, don't you think they would want to get paid no matter what temperature this stuff gets at? Because remember, Yonsung makes Treprostinil for sale; right? It doesn't make any sense.

Now, it goes to LGM. LGM is the intermediary for Yonsung and Liquidia. LGM testified, Mr. Lenox testified, that they store the Treprostinil sodium that they receive from Yonsung before they ship it to Liquidia in Kentucky at refrigerators that are GMP 2 to 8 degrees. He testified that moving forward, Liquidia has requested temperature data loggers from the time it leaves the Yonsung all the way to the time it goes to Liquidia. They're going to monitor this temperature.

THE COURT: My impression was that they were not

09:51:29 shipping directly to Liquidia.

09:51:30 MR. SUKDUANG: There's instances where it goes
09:51:32 directly to Liquidia, and there's instances where it goes to
09:51:35 LGM, so moving forward, Your Honor -- there are instances
09:51:38 where sometimes the material would have to go to LGM, so I'm
09:51:42 not trying to -- whether it goes to LGM or straight to
09:51:46 Liquidia, the issue is the same. Temperature data loggers
09:51:49 moving forward keeping it at 2 to 8 degrees.

09:51:52 Then we talk about the PRINT Process. And this
09:51:55 is where the confusion is as to where a pharmaceutical
09:51:59 composition and a pharmaceutical product. Both claims are a
09:52:02 pharmaceutical composition or a pharmaceutical product. I
09:52:04 don't know what the difference is. They haven't really
09:52:07 identified that. Claim 8 is to the pharmaceutical product.
09:52:11 Claim 1 is to the pharmaceutical composition.

09:52:14 The fact of the matter is a pharmaceutical
09:52:16 composition or pharmaceutical product, we have not heard any
09:52:19 testimony that those are any different, and Claim 1 as a
09:52:23 comprising claim. You can have other stuff with the
09:52:26 Treprostinil sodium or the Treprostinil free acid. How does
09:52:29 that all of a sudden not become a pharmaceutical product?

09:52:34 Counsel told me that the Yonsung document that
09:52:37 shows they store at the warehouse in 2017, that's DTX 043.

09:52:43 But that PRINT Process, that PRINT Process is
09:52:51 use. That's use of Treprostinil sodium. Dr. Nuckolls put

this glove box up and he said, oh, Step 2.2 at a certain time, 8:00 a.m., and then he skips all the steps in between and shows you Step 2.17, three hours later, and says, oh, that material is stored at ambient temperature for three hours. What he skips is that there are 15 steps in between. That material is in the glove box so you can take some material out, put it into water so you can start making the stock solution to make the PRINT Process. That material is not sitting in a dry box or a glove box for three hours. It's taken out, used, and put away. Use is not storage. And so, during the PRINT Process, Your Honor, that is not storage of Treprostinil sodium.

Moving to the '793 patent, again, the witnesses, Dr. Winkler, Dr. Waxman, both agreed that the claim is to a method of treating pulmonary hypertension. They agree that the claim covers all five groups. And remember, this was filed back in 2006. This patent -- and UT wants to overlook this -- this patent was the first patent or the family of this patent was the first patent of using inhaled Treprostinil. The other failures were with different compounds, so a skilled artisan looking at this patent family, says, oh, did the inventors somehow figure out that you can use inhaled Treprostinil now, not only to treat the other groups, but actually group two? And so when you look at the patent, there's no written description support for

that. They have no examples of actually treating group two inhaled Treprostinil.

There's also no enablement. Dr. Hill testified that it would require undue experimentation, undue experimentation, to use inhaled Treprostinil to treat group two. And what UT and Dr. Waxman says is, oh, nobody would -- everybody would know never to use this, never to use this, in that group. Well, they have a patent that they filed that expressly says pulmonary hypertension with inhaled Treprostinil. When a POSA reads that claim, are they supposed to ignore what the claim says?

They're looking at the claim and says, hey, they're covered -- they're saying somehow they figured out how to treat group two, but I look at the specification, and I don't see that they did this. I don't see any examples. It doesn't cover the concerns that other people had. There's no written description, and it would require undue experimentation in order to achieve that result.

And in fact, when you looked at some of the studies, there was a -- it's called a FIRST study, the acronym that Dr. Hill testified. That's DTX 358. They tried a different compound, not Treprostinil, but a different compound, similar to it. It didn't work. Again, there's no enablement, no written description support for treating the full scope of Claim 1.

09:55:59 Again, on written description enablement, now
09:56:02 focusing in on the dry-powder formulations, there is --
09:56:06 Dr. Gonda testified and he acknowledged that there are two
09:56:08 sentences in the '793 patent talking being dry-powder. A
09:56:13 dry-powder inhaler, a dry-powder formula. But the words are
09:56:16 not enough. If simply having the words in the specification
09:56:20 is enough, then probably 95 percent of all written
09:56:24 description cases would go away because those patents have
09:56:28 the words. The issue is whether those words convey to a
09:56:33 person of skill in the art whether the inventors had
09:56:35 possession of that invention.
09:56:39 Dr. Gonda testified that they do not. Why?
09:56:43 There's no description of a dry-powder formulation in the
09:56:46 patent. There's no description of what excipients you would
09:56:48 use. There's no description of what specific dry-powder
09:56:52 inhaler would work for pulmonary arterial hypertension
09:56:55 patients. And importantly, there's no description or
09:56:58 example of how you take that dry-powder formulation and
09:57:01 actually use it in a method to treat pulmonary hypertension.
09:57:05 Remember, this is not a claim. This is not a claim to a
09:57:09 method of preparing a dry-powder formulation. It's a method
09:57:13 of treating pulmonary hypertension with a dry-powder
09:57:16 formulation. You need both. The inventors, Dr. Seeger and
09:57:22 Dr. Rubin, testified they never worked on a dry-powder
09:57:24 formulation with UT. So, there's no written description

support that that the dry-powder formulation of inhaled Treprostinil to treat pulmonary hypertension.

Enablement, Dr. Gonda. He put up the chart. There's three things you need to look at: What API I'm going to use, what carriers I'm going to use, and when I combine those, are they stable? And then I need to put it into a proper DPI device, a dry-powder inhaler. Can that dry-powder inhaler be used in a patient with pulmonary hypertension? That's going to take a lot of work. A lot of experimentation, a lot of time. Not routine. Because it's not predictable. How do we know it's not predictable? This patent was -- filed 16 years ago. It was filed 16 years ago. UT had all the resources in the world. They make nearly a half a billion dollars a year just on TYVASO. They have the money to do it. 16 years later, no dry-powder formulation.

THE COURT: Yeah, they have monopoly right now; right?

MR. SUKDUANG: They have a monopoly right now.

THE COURT: So why would they be motivated to fool around with a monopoly?

MR. SUKDUANG: And that's interesting, Your Honor. Why would you fool around with monopoly? Then would why would UT -- why would UT spend $95 million to enter a collaboration with Mannkind back in 2018 and pay

09:58:43 1 double-digit royalties to get a dry-powder?
09:58:45 2 The reason why, Your Honor, is because patients
09:58:48 3 need this. Patients need this. TYVASO, while it's
09:58:56 4 handheld -- as I told you, you've got to carry it in a
09:58:59 5 little dog carrier. The inhaled device -- you've got to
09:59:02 6 think about the patients -- it's this small. They carry
09:59:04 7 around some blister packs. So why fool around with
09:59:08 8 monopoly? Because you've got patients that you really want
09:59:09 9 to care for. And they want to do that. They're trying to
09:59:13 10 do it, but he they couldn't do it with their own work.
09:59:16 11 On enablement, Dr. Smyth. He said I did this in
09:59:19 12 three weeks. Treprostinil sodium, the compound exemplified
09:59:24 13 in the patent, did not work. It was too hygroscopic. He
09:59:28 14 could not get a dry-powder formulation to work. He said it
09:59:31 15 was too humid in his lab. His notebook tells other
09:59:34 16 otherwise. It's DTX 600. He put down the humidity in
09:59:38 17 there. He used a dry box or a glove box to control
09:59:41 18 humidity. It still didn't work. So one of the salts
09:59:43 19 covered by the claim simply does not work.
09:59:46 20 Treprostinil free acid, Treprostinil
09:59:50 21 diethanolamine salt, he tried to put in a dry-powder
09:59:53 22 inhaler. That dry-powder inhaler he used inhaled volumes
09:59:55 23 and inspiration efforts that were of a normal, healthy
10:00:00 24 individual.
10:00:02 25 Dr. Waxman's paper. Dr. Waxman's paper from

10:00:06 2021. He said this is the first time this has ever been
10:00:10 reported about how to use DPI inhalers in PAH patients.
10:00:15 It's nearly half the inspiratory effort and the volume that
10:00:19 Dr. Smyth used.

10:00:20 And importantly, in terms of enablement,
10:00:21 Dr. Smyth testified that even though he made a dry-powder,
10:00:26 and even though he thinks he put in a dry-powder inhaler and
10:00:29 got it to come out of that dry-powder inhaler, he would not
10:00:32 give it to a pulmonary hypertension patient without more
10:00:36 testing. And remember, the claim is not what dry-powder
10:00:39 inhalers -- making a dry-powder inhaler or dry-powder
10:00:42 formulation. It's a dry-powder formulation to treat
10:00:45 pulmonary hypertension.

10:00:46 And the issue of non-infringement, the last
10:00:50 issue, Your Honor, Dr. Hill testified that therapeutically
10:00:54 effective single-event dose is a single dose. Dr. Waxman
10:00:58 didn't disagree with that. The parties agree that it's a
10:01:01 single dose. Okay.

10:01:02 The label does not tell you to give a single
10:01:06 dose of LIQ861, Yutrepia. It tells you to administer three
10:01:11 to five times a day. Doctors and patients will use
10:01:14 Yutrepia, LIQ861, three to five times a day. The
10:01:18 instructions tell you that. There's no direct infringement.
10:01:21 Remember, this is a method claim. There's no direct
10:01:24 infringement; therefore, there can be no inducement.

10:01:26 Then there's also no inducement because UT has
10:01:30 not pointed to any evidence that Liquidia instructs doctors
10:01:34 or patients to use this drug one time a day.
10:01:37 On therapeutic efficacy, Dr. Hill and Dr. Waxman
10:01:40 have different views of that word. Dr. Hill says it has to
10:01:44 be how you feel, function, or survive. Dr. Waxman says it's
10:01:50 hemodynamics. Dr. Hill said patients don't care if their
10:01:54 hemodynamic values change. If they can't walk further, if
10:01:57 they can't climb a set of stairs without feeling better,
10:01:59 they don't care.
10:02:00 But under either interpretation, whether you
10:02:04 look at hemodynamic data or Dr. Hill's construction of what
10:02:09 much therapeutically effective is, there is no data in the
10:02:12 label on hemodynamic data for LIQ861. There is no
10:02:17 information in the label from Liquidia to doctors or
10:02:21 patients to say measure hemodynamic data to determine if
10:02:24 you've been therapeutically effective -- whether that drug
10:02:27 is therapeutically effective. There is -- you saw no data
10:02:30 on hemodynamics of LIQ861 at all.
10:02:34 Dr. Waxman pointed to bioavailability data. He
10:02:38 confirmed that bioavailability data, one, does not prove
10:02:42 therapeutic efficacy. He established that. Dr. Waxman also
10:02:46 testified that, two, hemodynamic -- bioavailability data is
10:02:52 not hemodynamic data; right? So even if you look at
10:02:56 hemodynamic data, there's nothing in the label, no

inducement, and no actual evidence that a hemodynamic change results in therapeutic efficacy.

And again, I circle back to the testimony of Dr. Hill. There are patients that receive drugs like Treprostinil, that obtain a positive hemodynamic effect. When I say positive, it's -- you want to see the pressure change. Those patients, it's the first study, those patients got sicker and some died. That that establishes that a hemodynamic effect does not equate to therapeutic.

So, Your Honor, I know I went over my time. I appreciate the indulgence. I do have one more thing to say. We do appreciate your time and your staff. Liquidia appreciates your time and your staff. I have a lot of members on my team that I have literally not met until we showed up for trial this week because of COVID. And we have several members of our team that this was the first time that they had a standup role at trial. And we appreciate the opportunity that you provided to them to allow them to speak, and I know Liquidia does. And we appreciate your time. Thank you.

THE COURT: All right. Thank you. Let me just follow up on one or two things with you.

So I presume the reason why Liquidia wanted to get in this business is because they believe that the label instructions do recommend a therapeutically effective

treatment; right?

MR. SUKDUANG: Yes. Well, the FDA -- you could not sell the drug if it wasn't therapeutically effective.

THE COURT: Right. And I take it that if they are instructing through the label to take this -- to inhale this three or four different times a day -- which is what the label says; right?

MR. SUKDUANG: Yes.

THE COURT: Then that's necessarily, if you break the day down into four different parts, telling them to do it, you know, once in the morning, once in the afternoon, once in the evening, and once before bed or whatever it works out to, that telling them to do it four times is also if you measure it in -- that each time they're also telling them do it each individual time; right?

MR. SUKDUANG: Yeah, you have to take it four times a day or three to five times a day depending on how you -- patients need different amounts, so it could be three times or five times.

THE COURT: Right. But the point is, you now you know, if I tell you to take four pills a day, I'm necessarily also telling you to take a pill; right?

MR. SUKDUANG: Yes, but I'm telling you to take four pills because if I tell you to take one pill, it's not going to work.

10:05:46 THE COURT: So, in -- -- hold on a second. I
10:05:55 lost my thought.
10:05:56 And so, the -- it's not the case that the patent
10:06:01 claims are limited to taking one therapeutically effective
10:06:09 single-event dose; right?
10:06:10 MR. SUKDUANG: It is. When you look at the
10:06:12 claim, when you look at the claim, it's a single-event dose
10:06:15 is therapeutically effective.
10:06:17 THE COURT: Well --
10:06:17 MR. SUKDUANG: And you look --
10:06:18 THE COURT: -- that's true, but it doesn't
10:06:19 prevent you from taking multiple single effective doses;
10:06:22 right?
10:06:23 MR. SUKDUANG: I think when you look at the
10:06:24 claim, and you look at the specification, that's the
10:06:27 instruction. And the reason for that is twofold.
10:06:30 When you look at the examples, Examples 1 and 2,
10:06:33 Examples 1 and 2 are only a single dose, not multiple
10:06:40 dosing. And Examples 1 and 2, look at hemodynamics and say
10:06:44 on a single dose, that's what you need. The patent also has
10:06:50 that language, and I think you saw it today and you saw it
10:06:52 during some testimony that says you can use it a single time
10:06:55 or multiple times per day; right?
10:06:57 THE COURT: Right.
10:07:00 MR. SUKDUANG: That's indication in the language

10:07:01 of the patent that the inventors knew how to say -- how to
10:07:04 teach how to take something once or how to take things
10:07:07 multiple times, but they chose not --
10:07:09 THE COURT: But the patent itself --
10:07:10 MR. SUKDUANG: I'm sorry.
10:07:11 THE COURT: But the patent itself says a method
10:07:13 of treating by administering a therapeutically effective
10:07:19 single-event dose.
10:07:20 MR. SUKDUANG: Correct.
10:07:20 THE COURT: Doesn't that mean one or more?
10:07:22 MR. SUKDUANG: No. "A" is one. There's case
10:07:24 law and we can brief that for you. "A" is one. There's
10:07:27 case law that says one or more. There's case law that
10:07:30 says --
10:07:31 THE COURT: Yeah, but one or more is simply the
10:07:34 prefer reading; right?
10:07:35 MR. SUKDUANG: Of "A"?
10:07:36 THE COURT: Yes.
10:07:36 MR. SUKDUANG: I'm not sure that's the case.
10:07:38 THE COURT: I am sure that's the case.
10:07:40 MR. SUKDUANG: Okay. Yes. But when you look at
10:07:41 "A," you have to look at the rest of the patent. Look at
10:07:44 the examples. The examples are single dose studies. Single
10:07:47 dose. And they got a patent. They got a patent on a method
10:07:51 of treating --

10:07:52 THE COURT: Although -- you say examples, but as
10:07:55 you as also pointed out and as your opponents pointed out,
10:07:58 the actual written description says a single dose or
10:08:01 multiple dose.
10:08:02 MR. SUKDUANG: That's -- yeah, you can take a
10:08:03 single dose or multiple dose.
10:08:05 THE COURT: So, they could, notwithstanding the
10:08:08 examples because we know claims are not limited to examples,
10:08:12 they could claim one or more doses?
10:08:15 MR. SUKDUANG: They could have, but they didn't.
10:08:17 I mean, that's the problem that we're having. I understand
10:08:20 the issue, Your Honor.
10:08:20 THE COURT: You're going to have to convince me
10:08:23 of that.
10:08:23 MR. SUKDUANG: I understand the issue, Your
10:08:25 Honor.
10:08:25 THE COURT: Hold on. Let me see if there's
10:08:27 something else that I want to ask you about.
10:08:30 So, I hate to be dense on this point, but your
10:08:35 argument in terms of the product being the same for the
10:08:50 product-by-process claims, which I think are Claims 6 and 9;
10:08:50 right?
10:08:57 MR. SUKDUANG: The product-by-process claims are
10:08:59 Claims 1 -- Claim 1 is a product-by-process claim I think
10:09:04 all asserted claims except Claim 8 a product-by-process

claim.

THE COURT: Hold on just a minute.

Okay. So, just going to Claim 8, one of the points that your opponent said was that because I knocked out the indefiniteness argument, that there's no actual --

MR. SUKDUANG: Invalidity.

THE COURT: -- invalidity -- thank you -- argument still standing on that. Is that right?

MR. SUKDUANG: Right. So now with respect to Claim 8, based on your ruling it's the storage limitation, and the storage -- because Claim 8, also like Claim 6, includes the storage limitation. It says it has to be stable at ambient temperature and then stored before you make the pharmaceutical product.

THE COURT: Right. So in other words, what you say is the written description, then, presumably --

MR. SUKDUANG: No. No, Your Honor. It's the non-infringement now on Claim 8.

THE COURT: Oh, okay. All right. So there's no invalidity claim on Claim 8?

MR. SUKDUANG: Correct. It's non-infringement of Claim 8.

THE COURT: Got it. Okay. Thank you.

And so, on the -- and just to go back, I think maybe I asked you about this while you were arguing, but --

your written description arguments relating to impurities is, essentially, they don't provide any data that shows what they say is happening is true; is that right?

MR. SUKDUANG: It's twofold. It's, one, there's no data to do the actual comparison; right? So it's not just a matter of is it true. The claim requires comparison.

THE COURT: Or that they have it.

MR. SUKDUANG: Or that they have it, they have possession. So there's no data that they have possession of it. And then when you look at the patent as a whole, when you look at what they did, it's not just that there's no data. It's that they -- there's just never a comparison. They never say compare starting batch to final pharmaceutical composition. That only shows up in the claim.

So, and the reason for that is because when you look at the process -- and I bring up inventor testimony not in terms of what they did but just to explain what the invention was. I'm sorry. What they did was eliminate column chromatography. So when you eliminate column chromatography, you have to eventually purify the product. And what they did was they added a salt step at the end. So you made Treprostinil, and then in the example of the patents, they used a diethanolamine base to make Treprostinil diethanolamine salt. And the patent says when

you perform the carbon and salt treatment steps, you can remove the impurities at the very end.

So when you look at the process itself, as you flow through the examples, Example 1, 2, 3, Example 1 is making -- is alkylating the BTO.

Example 2 is you take that product, and in the patent it's called the benzidine nitrile. You take that benzidine nitrile, and you conduct hydrolysis to form Treprostinil.

When you read the examples, the end of Example 1 says you take the crude material and you move it to the next step. And then when you look at the end of Example 2, it says you take that crude material and you move to the next step, which is Step 3, which is the formation of the diethanolamine salt or any salt, but the example is the diethanolamine salt.

So, when you look at the process, not only is there no data, but I view it as kind of like a one-flow process that you take a solution out of Step 1, and you take that solution and you use it as part of Step 2, and you take that solution and then you use it as part of Step 3 or Example 3 to make the salt.

So it's twofold. No data. They didn't actually measure data because they didn't have to. And, two, in how in how you do the process, according to UT, they don't need

to do it. And the inventors testified we don't need to do it. We don't need to measure those intermediary impurities because we don't care about what the purity is in the middle. How do we know that if we removed chromatography? We care what we end up with at the end.

And so for written description, you've got to have possession. You've got to have -- the POSA has to understand you have possession. Not of impurities, and not of just generally removing impurities, but comparing what the impurities look like in your intermediate and what those impurities look like in your final product. Again, if the claim just said I'm reducing impurities, then when you don't have column chromatography, your stuff is going to be less pure, and you form salts, and okay. It's going to be more pure. But that's not what the claim says. It says you have to measure it. You have to measure it at two specific points, and then I bring back that you have to actually alkylate the specific compound.

THE COURT: Do -- based on the testimony at trial or including, I guess, the thousand exhibits, is there any way to synthesize Treprostinil that doesn't involve starting with benzidine triol?

MR. SUKDUANG: You know, I wish I was a better chemist, Your Honor. I was --

THE COURT: Well, I'm not asking you as a

chemist. I'm asking you as somebody.

MR. SUKDUANG: I don't know. I don't -- I personally -- I don't know if there's another way to synthesize Treprostinil without going through benzidine triol. I don't know the answer to that. I do know that --

THE COURT: And I take it that part of that is you don't know whether there's anything in the record that would answer that?

MR. SUKDUANG: Well twofold. I don't know if there's anything in the record, but also I just don't know if there's another process out there for -- I know there's -- there's -- and Dr. Winkler testified to this.

Before Dr. Moriarty got involved with United Therapeutics, Pharmacia Upjohn made Treprostinil, and I think you heard that from Mr. Poisson. UT licensed in the compound Treprostinil from Pharmacia Upjohn. Pharmacia Upjohn had a process of making Treprostinil, and I think there's a patent, or something like that -- and, again, Dr. Winkler testified to that. It's not an exhibit. It's not an exhibit.

THE COURT: Okay.

MR. SUKDUANG: I can't tell you whether those processes go through a process separate from BTO, so I don't want to say yes there is or no there isn't, but I know that there's testimony that there are other processes out there

before the Moriarty process that were used to make this compound.

THE COURT: Okay. Let me think for a minute.

And I know you said this. I just -- I should have -- I want to make my notes better on this, but your product-by-process anticipation and validity argument, what you want to compare -- what you have compared is the claim in the patent as to whatever the product is and the something that existed as a result of the -- that you called the Moriarty or Chicago process. What exactly is the thing that is the comparison to the patent claim in this patent that you're comparing it to?

MR. SUKDUANG: Sure. So, the patent -- the first step is what does the patent claim? It's a product. That patent is a Treprostinil -- Treprostinil, sometimes, you -- sometimes it's referred to in the record as Treprostinil. Sometimes it's referred to in the record as Treprostinil free acid. Those two are the same things. Sometimes it's referred to as UT-15. So Treprostinil, Treprostinil free acid, and UT-15 are nomenclature for the same compound.

THE COURT: But the UT-15 is an actual product out in the real world as compared to the other two, which are in the patent; right?

MR. SUKDUANG: Right. So UT-15 is a product out

10:18:31 in the real world. UT-15C, which is Treprostinil
10:18:34 diethanolamine salt, so, again, just for nomenclature,
10:18:39 UT-15C is a salt of Treprostinil. It's a specific salt,
10:18:45 Treprostinil diethanolamine salt, that's not sold anywhere.
10:18:49 That's a --
10:18:51 THE COURT: But --
10:18:51 MR. SUKDUANG: But the product we're comparing
10:18:53 is Moriarty.
10:18:53 THE COURT: You might be giving me too much
10:18:56 information here. The thing that you're trying to say is
10:19:00 anticipated is not UTC 15 or UTC 15C or anything else. It's
10:19:07 what is described in the patent claim; right?
10:19:09 MR. SUKDUANG: Yes, what's described in the
10:19:11 patent claim is Treprostinil. Is Treprostinil. Claim 1 is
10:19:15 Treprostinil.
10:19:16 THE COURT: So the actual -- so I guess for your
10:19:23 anticipation claim, does the -- is the purity of the actual
10:19:34 UTC product in the real world, is that relevant?
10:19:40 MR. SUKDUANG: No, because twofold. One, the
10:19:43 claim, as the experts testified, don't require purity. It
10:19:48 doesn't say 99 percent pure. It just says Treprostinil,
10:19:52 right. So the purity of what Remodulin is or what the
10:19:54 Chicago process -- and that's why we're focusing in on it,
10:19:59 and what we're trying to center what I did in my opening and
10:20:02 tried to do here is that you have to look at what the

compound is. The compound in the claim is Treprostinil. The compound in the prior art, Moriarty, is Treprostinil; right? They are literally the same molecule. Structurally the same. They -- there is no dispute that the compound Treprostinil in both places is the same.

The reason why purity comes in to play is because UTC argues that they're structurally and functionally different; right? That's how a product-by-process claim can survive, if there's a -- if the product is known out there, if they can say that it's structurally or functionally different. How UT is trying to establish structural or functional difference is through purity, and that's where Dr. Walsh comes in. He's the only person who talks about that, but he didn't compare the correct compounds.

THE COURT: Well, I guess that's what I was trying to get fixed in my mind here, is the -- and I guess it's fair to say, from your point of view in trying to invalidate these claims, the broader the scope of the product that's claimed in the '066 patent, at least for invalidity purposes, the happier you are. And to some extent, I guess what I'm trying to figure out is all the talk in the, say, Claim 1 of the '066 patent about, you know, having more or less impurities, the alkylation and hydrolysis, for your invalidity purpose, I'm supposed to

10:21:56 ignore all of that; right?
10:21:57 MR. SUKDUANG: Correct. It's just the product.
10:21:58 THE COURT: And so, the product -- is the
10:22:06 product, in your opinion -- is this what I'm going to see in
10:22:09 your brief -- the product is "Treprostinil or a
10:22:14 pharmaceutically acceptable salt thereof, no further
10:22:19 description"?
10:22:20 MR. SUKDUANG: Yes, that is -- from a
10:22:22 product-by-process claim and that specific
10:22:25 product-by-process claim, that is the product. There's
10:22:28 actually no dispute between the parties on that. That is
10:22:31 what the product is.
10:22:32 THE COURT: And so, then for example, for then
10:22:35 the dependent Claim 2, the product is going to be that but
10:22:41 the salt -- actually, I can't tell whether this is a --
10:22:49 yeah, because it says the salt is isolated in crystalline
10:22:54 form. It's going to be something where the Treprostinil has
10:22:57 to have -- and I may not be getting this exactly right, but
10:23:03 an isolated crystalline form or at least a crystalline form;
10:23:07 right?
10:23:07 MR. SUKDUANG: Right.
10:23:07 THE COURT: Okay. Hold on a minute. And so --
10:23:17 MR. SUKDUANG: But Your Honor --
10:23:18 THE COURT: Let me just finish my thought --
10:23:19 MR. SUKDUANG: Sure. Sure. Sure.

10:23:20 THE COURT: -- and then can you go ahead.

10:23:24 So, basically, is your brief going to tell me
10:23:29 that if I conclude that the Moriarty process made
10:23:36 Treprostinil or pharmaceutically acceptable salt thereof,
10:23:40 the details of that product don't actually matter other than
10:23:44 as long as it's one or the other of those things?

10:23:48 MR. SUKDUANG: Yeah, under the case law, under
10:23:50 the prevailing case law. That's the issue. It's whether
10:23:52 the product is the same. It's essentially -- if you look at
10:23:57 a product-by-process claim, let's just -- and I know you've
10:23:59 dealt with cases like this. It's a compound claim; right?
10:24:03 It's just a compound. If that compound is disclosed in the
10:24:07 prior art, that compound is not novel. That's what a
10:24:11 product-by-process claim is.

10:24:13 THE COURT: And then so the argument about the
10:24:16 functional or structural differences, perhaps the
10:24:23 plaintiffs' argument is -- and I'm just asking you if this
10:24:26 is your understanding of your argument, not why you disagree
10:24:29 with it -- but if they say the products that's made by the
10:24:41 process is, you know, more pure Treprostinil or Treprostinil
10:24:46 salt, that that's a structural difference?

10:24:51 MR. SUKDUANG: That's my understanding of their
10:24:53 argument.

10:24:54 THE COURT: Okay. You wanted to say something.

10:24:57 MR. SUKDUANG: Yeah. And you mentioned Claim 2.

Claim 2 is part of the process. It's not the product. So if you look at Claim 1, Claim 1 says, well, you have to isolate the Treprostinil salt. And I know you don't want to look up at slides, but it's up there.

THE COURT: Well, no I have it.

MR. SUKDUANG: It says isolate the Treprostinil salt, and then you make the pharmaceutical composition. Claim 2 just says, hey, when I'm in the middle of this process, I have an isolated salt that's in crystalline form. So, again, you've got to come back. Those are all part of the process and you jump back.

THE COURT: Well, and so I get what you're saying there, and I take it you say the same thing for dependent Claim 3, because it's talking about the basis of the product.

MR. SUKDUANG: Correct. Correct.

THE COURT: And claims --

MR. SUKDUANG: Claim 5 has not been asserted.

THE COURT: Right. Right. Okay. I take it -- I don't want to spend much time on this. In terms of the argument about enablement in terms of the formulation, and this is the '793 patent, and I think it was your expert, not Dr. Smyth, but the other one, who said you have to pick the API, and he had other two other boxes. I mean, in this case, the picking the API, you start with what the patent

says.

MR. SUKDUANG: Treprostinil, yes.

THE COURT: And so --

MR. SUKDUANG: And he acknowledged that.

THE COURT: Yes. Okay. Well, I just wanted to make sure.

MR. SUKDUANG: He's not arguing that you have to --

THE COURT: Because your other expert seemed to have spend a lot of time about talking about picking the API.

MR. SUKDUANG: Doctor?

THE COURT: Not Dr. Smyth, but the other guy whoever that was.

MR. SUKDUANG: Dr. Gonda? Oh, sure. Our expert was Dr. Gonda, and he did. He had three boxes, and the API. And --

THE COURT: Right.

MR. SUKDUANG -- if you looked at the box, it said Treprostinil underneath it. So it's --

THE COURT: But still spent a lot of time like acting like that was a big deal and it was what the API was.

MR. SUKDUANG: And actually, it is a big deal because you've heard testimony from this case that there's multiple forms of an API.

10:27:29 THE COURT: Right, but we're talking about undue
10:27:32 experimentation. And so if you have a limited universe of
10:27:35 what you're picking from, in a general -- because I don't
10:27:38 think undue experimentation is really a question of how long
10:27:42 does it take, because sometimes routine experimentation --
10:27:45 MR. SUKDUANG: Takes a long time.
10:27:46 THE COURT: -- takes a long time.
10:27:48 MR. SUKDUANG: Sure.
10:27:48 THE COURT: I think the question is, you know,
10:27:51 how many different choices are out there. You know, are the
10:27:56 choices unpredictable, things like that. And so, at least
10:27:59 on enablement, it seemed to me, okay, the API's got a big
10:28:06 arrow pointing to it. One of the things Dr. Smyth said that
10:28:10 I didn't really hear any challenge to was, you know, the
10:28:16 most common excipient is -- I forget.
10:28:19 MR. SUKDUANG: Lactose.
10:28:20 THE COURT: Whether it was lactose or mannitol
10:28:22 or something, and so, yeah, so that seemed to me like pretty
10:28:27 routine formulation kind of stuff. I mean, you've got to
10:28:30 find out, you know, we got to test it. But it's not like
10:28:33 you can't test. It's just, as you know, total shots in the
10:28:37 dark. And so it seemed like a third box, the third box
10:28:41 maybe was -- but in any event.
10:28:44 MR. SUKDUANG: So on the API issue, so just so I
10:28:47 can solidify that point, or try to at least, Treprostinil --

10:28:52 Treprostinil is the starting point. Right. But there are
10:28:57 different forms of Treprostinil, just like there are
10:29:00 different forms of API. And we're talking about a powder
10:29:03 formulation; right? So you have to look at do I want to use
10:29:07 Treprostinil free acid, or if you look at what Dr. Smyth
10:29:11 did, do I want to use Treprostinil sodium? And that's what
10:29:14 Liquidia did. Or do I what than to use Treprostinil
10:29:17 diethanolamine salt, or do I want to use, as counsel from UT
10:29:19 argued to Dr. Gonda, aren't there any other possible salts?
10:29:23 So, the selection of the API is the selection of
10:29:27 the Treprostinil form that would be suitable. And in order
10:29:31 to do that, and we saw from Dr. Smyth's testing, certain
10:29:35 forms of Treprostinil won't work. The sodium didn't work.
10:29:41 He said he got the diethanolamine to work. He said he got
10:29:45 the free acid to work. There are other issues with those.
10:29:48 But the selection of the API is not simply, oh, it's
10:29:51 Treprostinil, boom, I'm ready to go. You've got to look at
10:29:55 I'm not making a solution. I'm not making an injection.
10:29:58 I'm not making something that I'm inhaling up my nose like
10:30:01 in a soft mist or something like that. I am making a
10:30:05 specific formulation, Treprostinil dry-powder.
10:30:08 And when I look at what formulation I want to
10:30:11 make, I have to do investigations as to the form that I'm
10:30:16 choosing of Treprostinil, like you pointed out, that would
10:30:20 be appropriate. Which salt or free acid? Or if I'm not

going to use a salt, am I going to use a different form? And have I to determine, hey, is that going to be stable when I jet mill it like Dr. Smyth tried to do or combine it with another active -- excuse me another excipient? Or when it's in the blister pack, or something like that. So, all of that is not routine.

We agree, and the patent says, you start here, Treprostinil, but that just tells you, hey, I'm in New York City and I want you to go to San Francisco. I'm telling you where you start and where you end. And you think about the pioneer days when they said I want to get out there; right? I want to go West. All the perils and the hardships and the things to get there, that's the undue experimentation because they knew where they started from and they knew why where they wanted to go.

That's not the issue here. We know where we want to start from, Treprostinil. We know where we want go, a dry-powder formulation of Treprostinil. It's how you get there that's the undue experimentation. And when you start here, it's which form do I use? And Dr. Gonda testified to that, and Dr. Smyth used more than one form. Why? Because it's not simply just picking Treprostinil, go.

THE COURT: Okay. Thank you.

MR. SUKDUANG: Thank you.

THE COURT: Let me just check.

10:31:49 Okay. I think that's all I have for you at this
10:31:52 time.
10:31:52 MR. SUKDUANG: Thank you, Your Honor.
10:31:54 THE COURT: Is there anything -- because of my
10:31:59 questioning or anything else, Mr. Jackson, you'd like to
10:32:12 say?
10:32:12 MR. JACKSON: I just went back and checked, and
10:32:14 you asked me earlier about the pharmaceutical composition.
10:32:16 I found this. We got the exact cites, so I figured I'd help
10:32:20 you out with that.
10:32:21 THE COURT: Okay.
10:32:22 MR. JACKSON: So if you look at transcript
10:32:24 Page 93, Line 16 through 22, that's Dr. Nuckolls. He
10:32:31 says -- it's on the screen now. It says "Does Liquidia's
10:32:35 pharmaceutical composition meet the limitations referencing
10:32:37 a pharmaceutical composition?"
10:32:39 Yes, it does. It shows this shows material from
10:32:43 the NDA which shows Liquidia 861, the bulk inhalation
10:32:49 powder, is one of the ingredients listed in the composition
10:32:51 of the drug product. So it's the Liquidia 861 bulk
10:32:54 inhalation powder that's the pharmaceutical composition.
10:32:57 And if you go to Page 101 --
10:32:59 THE COURT: Wait. Sorry. The bulk inhalation
10:33:03 powder, maybe that trial transcript makes clear what's meant
10:33:10 by that. But what do you think that means?

10:33:12 MR. JACKSON: Sure. The Treprostinil sodium
10:33:13 gets shipped over from --
10:33:15 THE COURT: Well, so in other words, Liquidia
10:33:17 861 is essentially what Yonsung sends in?
10:33:23 MR. JACKSON: No, they send Treprostinil sodium,
10:33:25 and then when it gets into the United States, it gets mixed
10:33:28 and they create the bulk inhalation powder.
10:33:32 THE COURT: So, the pharmaceutical composition
10:33:35 is when they make the bulk inhalation powder at Liquidia?
10:33:39 MR. JACKSON: Yes, Your Honor.
10:33:40 THE COURT: Okay. So -- so the Claims 6 and 8
10:34:38 of the '066 patent that require storage and the '066 patent
10:34:45 or the Claim 6 of the isolated salt, and in Claim 8, of the
10:34:52 Treprostinil -- Treprostinil salt -- and by the way, are the
10:34:58 Treprostinil salt and the isolated salt the same thing?
10:35:02 MR. JACKSON: The Treprostinil salt and the
10:35:04 isolate salt, the isolated salt is a subset of the
10:35:07 Treprostinil salt. It's -- it has to be isolated. Whereas
10:35:10 the Treprostinil salt --
10:35:12 THE COURT: But I mean, do they exist at the
10:35:14 same time?
10:35:15 MR. JACKSON: Well, let me put it this way: The
10:35:21 claim that uses the word "Treprostinil salt" without the
10:35:24 word "isolated" can exist later than when it's just the
10:35:28 isolated salt.

10:35:30 THE COURT: So in terms of the steps,
10:35:35 alkylation, hydrolysis, form a salt, at the time that you
10:35:38 form a salt, is that the isolated salt?
10:35:41 MR. JACKSON: Yes.
10:35:42 THE COURT: Okay. And when does it become the
10:35:45 Treprostinil salt?
10:35:45 MR. JACKSON: That's -- you form the
10:35:48 Treprostinil salt.
10:35:49 THE COURT: So the isolated salt and the
10:35:51 Treprostinil salt are the same thing?
10:35:52 MR. JACKSON: Yes, but later, if you mix the
10:35:54 Treprostinil salt with other things, it's still the
10:35:57 Treprostinil salt.
10:35:59 THE COURT: Okay.
10:36:00 MR. JACKSON: So it's no longer isolated. If
10:36:04 the claim requires isolated, you're only looking at isolated
10:36:07 part if the claim just requires the Treprostinil salt
10:36:09 without the isolate the requirement.
10:36:11 THE COURT: And so the Treprostinil salt is
10:36:14 formed in Korea; right?
10:36:17 MR. JACKSON: Yes.
10:36:18 THE COURT: And it continues through until such
10:36:21 time as Liquidia starts doing its PRINT Process; right?
10:36:25 MR. JACKSON: Actually, it continues all the way
10:36:28 through. It's still Treprostinil salt in the product.

10:36:31 THE COURT: Oh, okay. All right.

10:36:33 MR. JACKSON: And then you also asked or we
10:36:36 discussed the pharmaceutical product. I just wanted to give
10:36:39 you the citation for that since the claim -- some of the
10:36:41 claims also require pharmaceutical product.

10:36:44 Could you pull up the transcript at 101, lines
10:36:48 12 through 16. Again, this is Dr. Nuckolls.

10:36:53 "What do you consider to be the pharmaceutical
10:36:55 product in this case?"

10:36:56 "The pharmaceutical product, I think, would be
10:36:58 the LIQ861 drug product after it's been packaged and
10:37:02 prepared and ready to be sold."

10:37:04 THE COURT: So really, that's the final product
10:37:06 a consumer would buy?

10:37:08 MR. JACKSON: Right.

10:37:09 THE COURT: Okay. Hold on a minute.

10:37:47 So on the question of the product-by-process
10:37:53 argument, the purity of the product of the composition --
10:38:19 actually, let me just go back.

10:38:20 Do you agree that all of the asserted claims in
10:38:24 this '066 patent other than Claim 8 are product-by-process
10:38:28 claims?

10:38:29 MR. JACKSON: I believe so, yes, Your Honor.

10:38:34 THE COURT: Okay. And do you agree that the
10:38:44 product that's claimed is Treprostinil -- Treprostinil or a

10:38:51 pharmaceutically acceptable salt thereof?

10:38:53 MR. JACKSON: I believe it's more narrow than
10:38:55 that. Yes, it has to be Treprostinil. It can't be
10:39:00 acetaminophen; right? So it has to be Treprostinil, but it
10:39:03 has to be the Treprostinil that claims the impurities --
10:39:08 that has the impurities limitation that is identified in
10:39:11 there.

10:39:11 THE COURT: What is the impurities limitation
10:39:14 that's identified?

10:39:15 MR. JACKSON: That the impurities have been
10:39:16 reduced between -- the impurities that were generated in the
10:39:20 alkylation and hydrolysis steps were reduced in between the
10:39:24 starting batch and the --

10:39:26 THE COURT: That sure sounds like a process
10:39:28 limitation.

10:39:29 MR. JACKSON: But it's -- you go, but there are
10:39:31 actual -- the results of that -- can we pull up --

10:39:36 THE COURT: The results only make sense as a
10:39:38 process limitation.

10:39:39 MR. JACKSON: But if there's structural and
10:39:41 functional differences in how -- in what the products are --
10:39:44 can we pull up my first slide again.

10:39:46 If there are structural and functional
10:39:50 differences between the products, that's me -- that means
10:39:57 it's no longer -- it isn't invalid under the

product-by-process principles or case law. And that's why I focused here on the old process. That's what they were focusing on. It's not clear whether it's Chicago or Moriarty or whatever, but the old process had these -- this was the --

THE COURT: So, but you say the most pure API seen in 40 years. Is that what the patent claims?

MR. JACKSON: Well, the patent claims the product that goes -- that -- in which the -- there is those steps of the alkylation and hydrolysis, and then the impurities resulting from that are then taken out between the -- are reduced between the starting batch and the final Treprostinil sodium.

THE COURT: But the testimony about what the actual product looks like, as a result of this, that's not what's claimed; right? I mean, that's -- you know, that's a product. The claim is to a -- is a patent claim, so it covers whatever the patent actually says.

MR. JACKSON: Correct. And I think the patent describes a product that is -- results from that process, right, product by process. It's the product that results from those various reduction in impurities during the alkylation and hydrolysis steps. And that's why this is -- this was the slide that's so important. It shows that the product, the new product, is not functionally and

structurally the same as the old product. The new product. After six months --

THE COURT: And so these things that Dr. Walsh, you know, has old and new, is that in the patent?

MR. JACKSON: The new process -- the new product is the result of the patent.

THE COURT: Right, but the measurements of AU 3 -- 3AU90, is that in the patent?

MR. JACKSON: So these -- these details were six-month stability studies later, so no those aren't --

THE COURT: So they're not claimed?

MR. JACKSON: Well, this -- I thought you were asking if this example, this data itself, is in the patent. I thought you were asking if this was an example.

THE COURT: Right. So the data, if it's not in the patent, it's not claimed.

MR. JACKSON: Correct, but the -- it's the product --

THE COURT: What somebody tells the FDA months later that's interesting, but it's not what the patent is.

MR. JACKSON: Right. But we were trying to show that there was structural and functional differences between the new and the old. And this is the structural and functional differences that we identified. The -- it had -- it's not exactly the same Treprostinil.

10:42:44 THE COURT: But well, right. That would be kind
10:42:46 of the point is, you know, saying here's -- or maybe it's
10:42:52 the point, I don't know. But if you have a patent that says
10:42:56 here we do some stuff and we make a product, and now you're
10:43:02 trying to say, well, what are the -- is the thing that we
10:43:06 claim there the product, is it functionally or structurally
10:43:12 different from the prior art? It's not a direct comparison
10:43:21 to say here's some stuff that we made using this process and
10:43:24 it has this property or that property. Maybe, I don't know.
10:43:30 I'll have to think about this probably. Maybe it's
10:43:33 something from which I could draw a conclusion about whether
10:43:36 what's claimed is functionally or structurally different,
10:43:39 but just because something that was actually made was
10:43:44 functionally or structurally different if, in fact, that's
10:43:47 what it is, that's not a comparison; right?
10:43:53 MR. JACKSON: So let me see if I can answer --
10:43:55 be helpful and answer the question. I think -- what I think
10:43:58 what you're getting at. So, in a product-by-process claim,
10:44:02 it's the composition that matters. And -- and it's a
10:44:06 composition claim. And so, the impurities in that
10:44:09 composition are part of that composition, and they matter.
10:44:13 And as I've said, the impurities are expressly claimed. So
10:44:18 if the impurities, the composition, it's not just the
10:44:21 molecule of Treprostinil. The -- it's the pharmaceutical
10:44:25 composition that is the product of that process. So, you

have to go through that process and see whether -- see the result of that process and then compare whether they're structural or functional differences to the prior product.

And the -- what I'm trying to show you is that we know -- they knew that there were structural and functional differences. The fact that they can show this later data is consistent with they knew there were structural and functional differences in terms of the purity -- not purity numbers, but purity profile. But that's also what kicked their numbers, their purity numbers, overall up and caused Dr. Bunce or Dean Bunce to say to the FDA, we're going to increase our specification because we're getting too pure.

THE COURT: Well, so, you know, I understand, I think, why one could say fewer purities are a structural difference. Is there any evidence that it's a functional difference?

MR. JACKSON: Well, to the degree you're saying functional, the -- the impurities in your body, right, the function Dean -- Dr. Toste did say small -- a bunch of this is about this 15-epi-Treprostinil or other things that are similar, very close to Treprostinil that they're trying to weed out to make sure they don't get -- because those products could be bioavailable. You'll recall, I believe it was Dr. Toste who talked about the --

10:46:06 THE COURT: Well --

10:46:08 MR. JACKSON: -- thalidomide.

10:46:10 THE COURT: Yeah, I remember thalidomide. Honestly, I thought the thalidomide was in the late 1950s, not the early 1960s, but I don't know.

10:46:31 But isn't the -- who has the burden of proof on whether there's functional or structural difference?

10:46:43 MR. JACKSON: My colleagues can correct me. I think they have to establish that they're the same and then it shifts to us to show structural and functional differences. That might be --

10:46:52 MR. CARSTEN: I think that's right.

10:46:53 MR. JACKSON: I believe that to be the case.

10:46:55 MR. SUKDUANG: Yeah.

10:46:56 THE COURT: Okay.

10:46:57 MR. SUKDUANG: Yes.

10:46:57 THE COURT: So, to show a functional difference, wouldn't you have to do more than say it could have an effect?

10:47:07 MR. JACKSON: Well, as I was starting to say, there are two ways you can look at functional differences. One is that we're worried about bioavailability. FDA is worried about bioavailability of any impurities. Let's make sure we get those out.

10:47:20 The second is storage. That's the whole point

of the being able to store at ambient temperature as opposed to having -- being required to keep it refrigerated. That was the whole reason why they realized, hey, this is going to be safe and can be stored at ambient temperatures; right? That's why that storage is written into the claims. That's a functional difference.

THE COURT: Okay. All right. I think I'm done with questions.

But, let's do this. Let's take a short break and then I'll come back. Possibly, I will think of a question or two in the interim. But we'll just come back and talk about whatever it is you decided in terms of briefing, et cetera.

So, why don't we take a ten-minute break. Okay?

MR. JACKSON: Thank you, Your Honor.

DEPUTY CLERK: All rise.

(Recess was taken.)

DEPUTY CLERK: All rise.

THE COURT: All right. So, I do have one more question for you, Mr. Jackson, which has to do with product-by-process claims and the argument that we've just been recently addressing.

You said the new product, the product that gets made by the claimed process, that it has the functional difference that the new product can be stored at room

temperature, and, in fact, it claims being stored at room temperature, so let's assume that's true for the Treprostinil salt. Is there any evidence that that's true for the Treprostinil acid?

MR. JACKSON: I don't believe so, Your Honor. Or at least I'm not aware of it. I can go back and check, but standing here --

THE COURT: Okay. Well, you know, if it turns out to be something else, that's the reason why we're going to have, I'm sure, lots of briefing here.

MR. JACKSON: Right. I just wanted to on that exact question. What I think you and I were discussing and debating, I think -- I wanted to just be clear. I think that the way you were asking the question to me, it sounded like you were asking about this being a compound question, the Treprostinil compound. But what I was trying to say and, I didn't know whether I got this across, is that it's a pharmaceutical composition. It's a composition claim. So it's all the stuff in the composition. And that includes the various impurities and that result from the process. Does that make sense?

THE COURT: Let me think about that. Okay. Well, in any event --

MR. JACKSON: Thank you.

THE COURT: All right. Well, who do you -- what

thoughts do you have about briefing?

MR. JACKSON: So, let me get -- just before I get to briefing, I think the first thing we talked with your deputy clerk and sorting out exhibits, what exhibits are, making sure there aren't duplicates, we proposed -- we discussed and proposed a joint list that we would get you the exhibits and we have a table that includes if they're duplicates. It's PTX 6 and DTX 43. And on that list when you get down to DTX 43, you'll see PTX 6, so you get all the cross-references. And we propose doing that in three weeks and then having from six weeks from tomorrow, having the first round of briefing. Then six weeks later having the responsive briefing, and then together, the opening and the response is each side gets a total of 100 pages to be split up as they see fit. And then reply three weeks after that limited to ten pages.

THE COURT: I'm guessing perhaps Ms. Keller had something to do with that idea.

MS. KELLER: Mr. Flynn had insight, too.

THE COURT: I couldn't remember whether he was here last week.

MS. KELLER: Yeah. I don't know if this was clear, but I think the hundred pages would be for findings of fact and the briefing.

THE COURT: Okay. Well, so, let me just think

for a second.

I'm sorry. And how long did you say for this reply brief?

MR. JACKSON: So, six weeks -- three.

THE COURT: Six weeks.

MR. JACKSON: Six, six, three. Sorry.

THE COURT: It's all right. All right. So that's 15 weeks. I'm going to probably want to chop that down just a little bit. But before we talk about that -- and actually, does that mean, then, that the hundred pages that's being talked about is a total of 200 pages all together?

MR. JACKSON: 220.

THE COURT: 220. Okay. Okay. All right. Well then the amount of pagination sounds fine to me. When -- I can't remember. Is there a 30-month stay or something else that's in this case?

MR. JACKSON: There is. It's middle to late October. I think it's like October 18th, but I can check the exact date. But it's October, Your Honor.

THE COURT: Okay. Well, October 18th is close enough for my purposes. Today is March 31st. Is -- yeah, that schedule is not going to work so well for me, the timing. So, I guess a couple things. I just want to remind you all that in terms of the transcript, you have -- if

you've got any corrections to that, you need -- you've got two weeks from today to do that.

MR. JACKSON: Yes, Your Honor.

THE COURT: I guess I'm wondering why -- and I appreciate, probably, that almost everybody in the room has been working real hard on this case, probably for quite a while, but particularly this week, I guess I'm wondering: Do you really need three weeks to -- actually, that's not so important to me.

Hold on. Let me just think about the math here. I -- so I think I would like to have the briefing done by about around June 15th. You want to just talk?

MR. JACKSON: Including the replies, Your Honor?

THE COURT: Yeah, including everything. You want to just spend a minute or two talking to each other and see whether you can figure out how that would work out in way that is fair to both sides and --

MR. JACKSON: Sure. I mean can we -- rather than just doing it right now, can we just say it will be done June 15th per Your Honor's request and then we can negotiate.

THE COURT: That is -- that will be fine. Is June 15 a day of the week?

MR. CARSTEN: It's a Wednesday.

MR. SUKDUANG: It is always a day of the week.

11:07:53 It's also a day of the workweek.

11:07:55 THE COURT: You're a wiseguy. But it's a day of
11:07:58 the workweek. That was the -- that was the construction
11:08:00 that I wanted.

11:08:02 Okay. That will be fine. So, why don't you
11:08:06 work out a schedule. I think it would probably be better
11:08:10 for both of you or both sides to try to get the exhibit list
11:08:16 at least completely finalized and then the other thing is --
11:08:22 or finalized sooner than three weeks from now, but the other
11:08:26 thing is, then I will want --

11:08:36 MS. KELLER: Hyperlinked briefs, Your Honor?

11:08:38 THE COURT: Yes, hyperlinked briefs. I couldn't
11:08:40 think of the word.

11:08:41 THE COURT: So is there anything else for today?

11:08:44 MR. JACKSON: Not from the plaintiffs, Your
11:08:46 Honor.

11:08:46 MR. SUKDUANG: No, Your Honor.

11:08:47 MR. JACKSON: Thank you for your time.

11:08:49 MR. SUKDUANG: I do appreciate the seriousness
11:08:50 of the case to both sides, and as far as I -- oh, I did want
11:08:53 to just talk off the record with lead counsel for a second
11:08:58 or Mr. Jackson -- I don't want an argument, but Mr. Sukduang
11:09:03 and you, but we're through, and everyone else can go about
11:09:08 their business. I don't need a court reporter.

11:09:13 (Court was recessed at 11:08 a.m.)

I hereby certify the foregoing is a true and accurate transcript from my stenographic notes in the proceeding.

/s/ Heather M. Triozzi
Certified Merit and Real-Time Reporter
U.S. District Court.