

UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE PATENT TRIAL AND APPEAL BOARD
PATENT NO. 10,131,682

SYNAFFIX B.V.,)
Petitioner,)
vs.)
HANGZHOU DAC BIOTECH CO., LTD.,)
Patent Owner.)

DEPOSITION OF RAVI CHARI, called
as a witness by and on behalf of the Patent Owner,
Hangzhou DAC Biotech pursuant to the applicable
provisions of the United States Patent Trial and
Trademark Appeal Board, before P. Jodi Ohnemus,
RPR, RMR, CRR, CA-CSR #13192, NH-LCR #91, MA-CSR
#123193, and Notary Public, within and for the
Commonwealth of Massachusetts, at Foley Lardner,
111 Huntington Avenue, Boston, Massachusetts, on
Wednesday, April 16, 2025, commencing at 9:33 a.m.

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I N D E X

TESTIMONY OF:

PAGE

RAVI J. CHARI

(By Ms. Lou)

5

(By Mr. Houston)

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E X H I B I T S

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1 RAVI J. CHARI, PhD, having
2 satisfactorily been identified by
3 the production of a driver's license,
4 and being first duly sworn by the Notary
5 Public, was examined and testified as
6 follows to interrogatories

7 BY MS. LOU:

8 Q. Good morning, Doctor Chari.

9 A. Good morning.

10 Q. Could you please state your full name for
11 the record.

12 A. Ravi Chari.

13 Q. Okay. My name is Jihong Lou. With me
14 here today is my colleague, Catherine Mattes.
15 We're attorneys from the law firm called Quinn
16 Emanuel. We represent patent owner Hangzhou DAC
17 Biotech in inter partes review filed by Synaffix.
18 And in today's deposition I will refer to inter
19 partes review as IPR.

20 Is that okay with you?

21 A. That's fine.

22 Q. Thank you.

23 And you understand that in this IPR
24 Synaffix challenged certain claims of US Patent No.
25 10,131,682; is that right?

1 A. That's correct.

2 Q. So in today's deposition I will refer to
3 US Patent No. 10,131,682 as the '682 patent.

4 Is that okay with you?

5 A. That's fine. I'll do the same. If that's
6 okay -- I was going to ask you how should I refer
7 to the patent. '682 is good.

8 Q. Perfect.

9 A. I remember the number.

10 Q. Perfect. Same here.

11 So have you testified in deposition or in
12 court in any case?

13 A. Only this -- twice: Once, this one, about
14 a couple of months ago -- was it?

15 And then once on some traffic -- something
16 to do with signs.

17 Q. I see.

18 So -- yeah. So you mentioned -- you may
19 remember that we've met before in our first
20 deposition that was November the 14th of last year.

21 A. Oh, wow.

22 Q. So last year.

23 A. That's long ago. Six months ago. Wow. I
24 thought a few months ago.

25 Q. Yeah. So in that November 14th deposition

1 my colleague Frank Calvosa explained to you the
2 ground rules for the deposition; right?

3 A. Yeah. Right.

4 Q. So for today I will -- to refresh your
5 memory, I will go over some of the ground rules for
6 deposition again.

7 Is that okay with you?

8 A. Sure.

9 Q. Okay. So first of all, I will ask
10 questions, and you will answer the questions I
11 asked. It's very important that we do not talk
12 over each other so that we will have a clean record
13 for the court reporter.

14 So please let me finish my question before
15 you answer, and then I will let you finish
16 answering before I ask the next question.

17 Is that okay with you?

18 A. That's fine.

19 Q. Okay. You must give verbal answers. So
20 that you cannot either nod your head or shake your
21 head, and then you must say something on the record
22 so that the court reporter can write down your
23 answer.

24 Is that okay with you?

25 A. That's fine.

1 Q. And please keep your voice up, and, then,
2 speak slowly and clearly -- and I will do the same
3 -- so that the court reporter can write down
4 everything we said here today.

5 A. Okay.

6 Q. Is that okay with you?

7 A. I will try my best.

8 Q. If you don't understand the question I
9 asked, could you please let me know; and I will try
10 to clarify the question if it's unclear to you.

11 A. Sure.

12 Q. If you answer the question I asked, I
13 would assume that you understand the question.

14 Is that fair?

15 A. That's fair.

16 Q. I will be taking breaks throughout the
17 deposition at regular intervals -- roughly every
18 hour -- but if you need a break at any time in
19 between, please just let us know.

20 A. Sure.

21 Q. And I only ask that you let me finish
22 asking the pending questions before we take the
23 break.

24 Is that okay with you?

25 A. That's fine.

1 Q. And you understand that you are under oath
2 here today and your answers are given under the
3 penalty of perjury; is that correct?

4 A. That's correct; right.

5 Q. Is there any reason you cannot provide the
6 most accurate and complete answers today?

7 A. No.

8 Q. Is there any reason you cannot provide
9 your answers truthfully today?

10 A. No.

11 Q. And you understand that Synaffix filed two
12 declarations from you in this IPR; right?

13 A. That's correct.

14 Q. And I'm handing you the first declaration
15 filed in this IPR.

16 A. (Witness reviews document.)

17 Q. And that is previously marked 1003.

18 A. Okay.

19 (Exhibit 1003, previously marked.)

20 Q. Do you recognize Exhibit 1003 as the first
21 declaration you've submitted in this IPR; right?

22 A. (Witness reviews document.) Yes, I think
23 it sounds right.

24 Q. Okay. Please turn to page 108 of Exhibit
25 1003.

1 A. Okay. 108?

2 Q. Yes, 108.

3 A. Okay.

4 Q. And do you see -- is that your signature
5 on that page?

6 A. That's correct, yes.

7 Q. And you signed -- signed the declaration
8 on February the 9th, 2023; right?

9 A. Yeah, that's correct. That sounds right.

10 Q. Yeah, it's been a while.

11 When you signed the declaration in
12 February 2023, you confirmed that what you stated
13 in the declaration is true and correct; right?

14 A. That's correct.

15 Q. In today's deposition I will refer to this
16 declaration as your first declaration.

17 Is that okay with you?

18 A. That's correct. That's fine.

19 Q. You can put that away for now.

20 A. Oh, okay. That's good. It's big.

21 Q. We'll come back to it.

22 I'm handing you your second declaration
23 filed in this IPR previously marked as Exhibit
24 1076.

25 (Exhibit 1076, previously marked.)

1 A. (Witness reviews document.)

2 Q. Do you recognize Exhibit 1076 as the
3 second declaration you submitted in this IPR?
4 Right?

5 A. Yes, I do.

6 Q. Please turn to page 28 of Exhibit 1076.
7 That's the last page.

8 A. Yeah.

9 Q. Is that your signature?

10 A. That's correct, yes.

11 Q. You signed the declaration on March 14th,
12 2025; right?

13 A. That's correct.

14 Q. When you signed this declaration on March
15 14th, 2025, you confirmed that what you stated in
16 the declaration is true and correct; right?

17 A. Yes.

18 Q. In today's deposition I'll refer to this
19 declaration as your second declaration.

20 Is that okay with you?

21 A. That's fine.

22 Q. As you sit here today, is there anything
23 in the second declaration that you would like to
24 correct?

25 A. Only one thing I remember on paragraph 23

1 is this one. This label area (indicating).

2 (Court Reporter comment.)

3 A. This one. This label here, "tertiary
4 amine," is usually an amide, a-m-i-d-e, instead of
5 amine. Something I noted when I reviewed it again.
6 Said, Wait a minute. Means there's not an amide.
7 We used an amine. Should be amide.

8 Q. So you're talking about on top of page 17
9 of your second declaration?

10 A. Yeah. Yeah. Exactly. The label should
11 say tertiary amide.

12 Q. Did the --

13 A. The red label.

14 Q. The label that said tertiary amine should
15 be corrected to amide?

16 A. Exactly. It's only there I could find
17 when I'm studying this declaration.

18 Q. So is there anything else you'd like to
19 correct in this second declaration?

20 A. I don't think, no.

21 (Discussion off the record.)

22 Q. And you recall that you were deposed on
23 November 14th of 2024 for this IPR; right?

24 A. That's correct -- I mean, yes.

25 Q. And you understand that in that November

1 14th deposition you answered questions under oath;
2 correct?

3 A. Yes.

4 Q. And during the November 14th deposition
5 you understood that you were obligated to tell the
6 truth; right?

7 A. Yes.

8 Q. And during that November 14th deposition
9 you testified truthfully and accurately to the best
10 of your knowledge and belief; right?

11 A. Yes.

12 Q. And I'm sure your counsel told you that
13 you had an opportunity to review the transcript of
14 your November 14th deposition and submit errata to
15 correct any errors in your answers; right?

16 A. Yes.

17 Q. And you did not submit any errata for your
18 November 14th deposition; is that right?

19 THE WITNESS: Did we?

20 A. A small thing, I don't -- yeah. Okay.
21 That's fine.

22 Q. But you did not submit any errata sheet;
23 right?

24 MR. HOUSTON: They may have -- to clarify,
25 Jihong: They may have been submitted to us, but I

1 think it was after it got filed in the proceeding.

2 A. Very minor -- minor type, most --

3 MR. HOUSTON: So no errata were filed in
4 the proceeding.

5 MS. LOU: I see.

6 MR. HOUSTON: So that was why he's
7 confused. I think he did prepare some after the
8 fact, but they weren't submitted.

9 A. And they were minor things like typos or
10 things like that I thought maybe wasn't very
11 important enough to fix; right?

12 Q. Right.

13 So you don't -- so the corrections were
14 typographical --

15 A. Yeah.

16 Q. -- not substantive.

17 A. Pretty much.

18 Q. Okay.

19 MS. LOU: Counsel, would you please make
20 sure to send -- send us a copy of that errata? I'm
21 not sure if we have a copy of that.

22 MR. HOUSTON: Okay. I can agree to do
23 that. Sure.

24 MS. LOU: Thank you.

25 Q. And you understand that in today's

1 deposition you must testify truthfully and
2 accurately to the best of your knowledge and
3 belief; correct?

4 A. Yes.

5 Q. Thank you.

6 Now turning to your second declaration,
7 Exhibit 1076.

8 A. Yes.

9 Q. On page 3, paragraph 3, here you have a
10 table where you listed additional documents you
11 reviewed when you prepared this second declaration;
12 right?

13 A. That's correct, yes.

14 Q. And here you cite to paragraph 13 of your
15 first declaration; is that right?

16 A. Okay. Yes.

17 Q. And I see that you have paragraph 13 of
18 your first declaration also in front of you.

19 A. Right.

20 Q. So in paragraph 13 of your first
21 declaration you provided the list of documents you
22 reviewed when you prepared the first declaration;
23 right?

24 A. That's correct.

25 Q. So the two lists of documents -- one in

1 paragraph 13 of your first declaration, one in
2 paragraph 3 of your second declaration -- are the
3 complete set of documents you reviewed and
4 considered in preparing your first and second
5 declarations; correct?

6 A. That's correct.

7 Q. You did not list any declarations from
8 Doctor Tumey filed in this IPR as materials you had
9 considered; right?

10 A. Right.

11 Q. Correct?

12 A. Correct.

13 Q. And you did not consider any declarations
14 from Doctor Tumey filed in this IPR when preparing
15 your own declarations; right?

16 A. Correct.

17 Q. And in the list of materials considered
18 you did not list the prosecution history of the
19 '682 patent as materials you considered; right?

20 A. Correct.

21 Q. So you did not consider the prosecution
22 history of the '682 patent; right?

23 A. That's correct.

24 Q. And in this IPR you are not offering any
25 opinions on the construction of any claim terms;

1 right?

2 A. Correct.

3 Q. So one of the invalidity grounds you
4 analyze in this IPR is based on the reference
5 authored by Morales-Sanfrutos; right?

6 A. That's correct.

7 Q. And Morales-Sanfrutos is spelled
8 M-o-r-a-l-e-s-S-a-n-f-r-u-t-o-s; right?

9 A. That's correct. Yes.

10 Q. And I will refer to this reference as
11 Morales for today's deposition.

12 Is that okay with you?

13 A. That's fine. Good.

14 Q. And Morales described a Michael addition
15 reaction of an electrophilic vinyl sulfone with an
16 amino or thiol group; right?

17 A. That's correct. You have a copy of
18 Morales that I can have it in front of me?

19 Q. Of course.

20 A. And, then, I want to make sure I see.

21 Q. Yeah.

22 A. Thank you. Appreciate it.

23 Q. So I just handed over Morales Exhibit 1005
24 that was previously filed in this IPR.

25 (Exhibit 1005, previously marked.)

1 A. Yeah. Thank you.

2 Q. So Morales described the Michael addition
3 reaction of the electrophilic vinyl sulfone with an
4 amino or thiol group; right?

5 A. Yeah, he does.

6 Q. And thiol is spelled t-h-i-o-l; right?

7 A. Yeah.

8 Q. Okay. And in Morales a compound
9 containing a vinyl sulfone was reacted with a
10 horseradish peroxidase; right?

11 A. That's correct.

12 Q. So I will refer to horseradish peroxidase
13 as HRP in today's deposition.

14 Is that okay with you?

15 A. That's good. Sure.

16 Q. In Morales the reaction of the vinyl
17 sulfone with HRP involve a Michael addition
18 reaction; right?

19 A. That's correct.

20 (Discussion off the record.)

21 Q. So in Morales the reaction of the vinyl
22 sulfone with HRP involved a Michael addition
23 reaction; right?

24 A. That's correct.

25 Q. And when vinyl -- when the vinyl sulfone

1 compound of Morales reacted with HRP, the reaction
2 that took place was a Michael addition reaction;
3 right?

4 A. That's correct.

5 Q. In Morales the adjacent sulfone in the
6 vinyl sulfone group activates the vinyl to make it
7 reactive; right?

8 MR. HOUSTON: Objection. Form.

9 A. That's how I think it does, but it, you
10 know --

11 (Court Reporter comment.)

12 A. That is what I think it does, activates
13 the vinyl for reaction.

14 Q. So the adjacent sulfone in the vinyl
15 sulfone group activates the vinyl to make the
16 reaction going; right?

17 (Court Reporter comment.)

18 A. That is correct.

19 Q. And without the adjacent sulfone, the
20 Michael addition reaction would not proceed with
21 just the vinyl group; right?

22 A. I don't think it does.

23 Q. There's no reason for you to think it
24 does; right?

25 A. Right. Correct.

1 Q. And in the Michael addition reaction a
2 vinyl group needs something else to activate the
3 carbon to make it reactive; right?

4 A. That's correct.

5 Q. For example, a sulfone can be used to
6 activate the carbon in the vinyl group to make it
7 reactive; right?

8 A. That's correct.

9 Q. And you had previously stated that the
10 vinyl group cannot react by itself and the adjacent
11 sulfone is necessary to activate the vinyl to
12 enable the Michael addition reaction; right?

13 A. That's correct. Yes.

14 Q. And you would agree that your opinions
15 with respect to whether vinyl in the context of a
16 Michael addition reaction can react by itself have
17 not changed; correct?

18 A. Not changed, no.

19 Q. And the Michael addition reaction
20 described in Morales only involves mixing the vinyl
21 sulfone compound with HRP in the buffer solution
22 for the reaction to proceed; right?

23 A. That's correct.

24 Q. And the Michael addition reaction
25 described in Morales does not need any catalyst to

1 catalyze the reaction; right?

2 A. I will check that. Let me check that.
3 Make sure that...

4 (Witness reviews document.)

5 Q. Yeah, so I would direct your attention
6 to --

7 A. The section?

8 Q. -- page -- page 8 of Morales. And on the
9 top right it says "Labeling HRP --"

10 A. Yeah. Yeah.

11 Q. -- "with vinyl sulfone."

12 A. (Witness reviews document.) So 8, 8.5
13 buffer, consider that a base catalyst reaction or
14 something to correctly be catalyzed. 'Cause 8.5 is
15 a high pH for normal reaction. If we look at the
16 paragraph you mention, use pH 8.5 -- is it 8.5?
17 Yeah. (Witness reviews document.) Yeah, 8.5.

18 I would call that a base catalyst reaction
19 because 8.5 is high. You need thiol...

20 (Court Reporter comment.)

21 A. ...you need thiol to be nucleophilic,
22 n-u-c-l-e-o-p-h-i-l-i-c.

23 Q. So for the Michael addition reaction to
24 take place, Morales used a buffer that has a pH of
25 8.5.

1 A. That's correct.

2 Q. And the pH 8.5 buffer is relatively more
3 basic than the neutral condition.

4 A. That's correct.

5 Q. But here in Morales it did not add any
6 other reagent to the reaction besides the pH 8.5
7 buffer; correct?

8 MR. HOUSTON: Objection. Form.

9 A. 37 degrees, which is normal temperature.
10 People usually use room temperature.

11 (Court Reporter comment.)

12 A. 37 degrees for one day. Normal room
13 temperature for one day. 37 degrees is a little
14 bit higher. Does it contribute to the reaction
15 speed? Maybe it does. Probably does. So
16 temperature and pH: two things that are higher
17 than normal.

18 Q. Right.

19 So Morales used a condition that has a pH
20 of 8.5 and also a temperature of 37 --

21 A. Exactly.

22 Q. -- degrees?

23 A. Yeah.

24 Q. Which is higher than normal.

25 A. Yeah.

1 Q. Normal is room temperature?

2 A. Exactly.

3 Q. But the reaction could proceed at room
4 temperature in the same buffer; right?

5 MR. HOUSTON: Objection. Form.

6 A. It would take much longer. Takes one day
7 here. I just think -- may take it much longer.
8 Just don't know how much longer, but could take
9 much longer.

10 Q. Right. So if I --

11 A. I mean, could happen. I just don't know.

12 Q. Right. Okay.

13 So -- but if you look at the description
14 here in Morales, besides the pH 8.5 buffer and the
15 temperature of 37 degrees, the reaction did not
16 require anything else to take place; right?

17 A. That's correct. From what I can read,
18 yes; that's correct.

19 Q. So you don't need to add a strong base to
20 this reaction?

21 MR. HOUSTON: Objection. Form.

22 A. No. A strong base is -- a definition 8.5
23 -- to me -- base, but not strong, but, you know...

24 Q. Right. So it's an aqueous buffer of pH
25 8.5, but it did not require adding organic base --

1 A. That's correct.

2 Q. -- to push the action forward?

3 MR. HOUSTON: Objection. Form.

4 A. But, again, just one day, maybe it will
5 help. I just don't know. Could have helped to add
6 base? One day is a long time of reaction to take
7 place, one day.

8 Q. But here the reaction took place after 37
9 degrees for one day. The author did not say
10 whether the one day was needed or whether in 12
11 hours would be enough; right?

12 A. Yeah, they don't say it.

13 Q. Right. So -- but if you look at the
14 actual conditions used in Morales, the reaction
15 proceeded at the -- in the aqueous buffer with a pH
16 of 8.5 at a temperature of 37 degrees for one day;
17 correct?

18 A. That's correct. I'm trying to see one
19 more thing. Just hold on. (Witness reviews
20 document.)

21 Trying to figure out the excess of reagent
22 they used, but they don't say the HRP's
23 concentration in molar. You know, 20 millimolar,
24 is compound...

25 (Court Reporter comment.)

1 A. 25, compound No. 10, but HRP 2 milligrams
2 per mil, much lower -- lower concentration.

3 Q. So another condition you noticed is there
4 could be a molar excess --

5 A. High excess.

6 Q. -- of a small molecule relative to the
7 protein.

8 A. That's correct. Much larger excess.

9 Q. But besides the pH, the temperature, and
10 the molar excess, do you see anything else that
11 required this reaction to go forward?

12 A. No, I don't see anything else.

13 Q. So for Morales' Michael addition to
14 proceed, you reacted HRP with a linker and the
15 reaction took place at 37 degrees with a pH -- in
16 the pH buffer of pH 8.5; correct?

17 A. That's correct.

18 Q. And you don't need to add any catalyst to
19 this system; right?

20 MR. HOUSTON: Objection. Form.

21 A. Define "catalyst."

22 You can call pH a catalyst. You can call
23 temperature a catalyst. But you don't add a
24 catalyst, you are right. But base is a catalyst.

25 Q. Right. So catalyst is usually a reagent

1 that accelerates a reaction but itself is recycled
2 in the system; correct?

3 A. So base catalyst reaction is base
4 catalyzed; right? So call it a catalyst, but it's
5 all, you know, how you define a catalyst.

6 Q. Okay. So setting aside the buffer, is
7 there anything else that you would think could be
8 catalyzing this reaction?

9 MR. HOUSTON: Objection. Asked and
10 answered.

11 A. The main thing is the pH that helps
12 the thiol react.

13 Q. The only thing is the pH that helps the --

14 A. And the temperature.

15 Q. -- and the higher temperature; correct?

16 A. (Witness nods.)

17 Q. Okay. And you don't see Morales use UV
18 light to activate the vinyl for it to react; right?

19 A. Yeah. He doesn't do it, no.

20 Q. And in your second declaration you cited a
21 reference authored by Dondini; right?

22 A. Dondoni.

23 Q. And prior to this case were you aware of
24 the Dondoni reference?

25 A. No, I wasn't.

1 Q. When did you become aware of the Dondoni
2 reference?

3 A. After the -- think the vinyl sulfone --
4 said do we need a sulfone? I looked up to see can
5 vinyl react by itself without sulfone being
6 present.

7 (Cour Reporter comment.)

8 Q. And you said in paragraph 8 of your second
9 declaration that Dondoni discloses a photoinduced
10 thiol-ene reaction; correct?

11 A. Right.

12 Q. And the photoinduced reaction described in
13 Dondoni is not a Michael addition reaction; right?

14 A. No. No. Right.

15 Q. No, it's not; right?

16 A. No, it's not.

17 Q. In paragraph 8 of your second declaration
18 you included a reaction from Scheme 3 of Dondoni;
19 right?

20 A. Scheme 3?

21 Q. Right.

22 A. Yeah.

23 Q. And Scheme 3 of Dondoni is the only
24 example of a photoinduced thiol-ene reaction you
25 discussed in your declaration; right?

1 A. That's only one I discussed, yes.

2 Q. And in paragraph 6 of your second
3 declaration you stated that there are other
4 reaction schemes where vinyl alone can serve as a
5 functional group that can link to cell-binding
6 agent.

7 Do you see that?

8 A. Which paragraph did you say?

9 Q. Paragraph 6.

10 A. 6. Yes, that's correct.

11 Q. The only example you provide in your
12 declaration is Scheme 3 from Dondoni; right?

13 A. That's correct.

14 Q. Let's turn to paragraph 8 of your second
15 declaration. Below this paragraph it shows Scheme
16 3 from Dondoni; right? I asked you that question
17 previously.

18 A. Paragraph 8; right?

19 Q. Paragraph 8.

20 A. (Witness reviews document.) 6 and 8? 9.
21 Where's 8? I don't see 8 in my --

22 Q. Oh, 8. It's...

23 MR. HOUSTON: (Indicating.)

24 A. Oh, 8. Sorry. Not 6; right. Never mind.
25 6 is over here. 6 is...

1 MR. HOUSTON: Oh, I see. That's figure 6.
2 That's what you're seeing.

3 A. Oh, 6. Okay. I've got it now. I saw it.
4 That's fine. 8, yeah.

5 Q. Okay.

6 A. 6. Where is the 6? That's fine. Sorry.

7 Q. Okay. Yeah. So we are looking at
8 paragraph 8 on pages --

9 A. Yeah, I see it.

10 Q. -- 6 and 7 of your declaration.

11 A. I got it, yeah.

12 Q. And in this scheme you excerpted from
13 Dondoni compound 1a is a substituted sugar with the
14 vinyl group attached; right?

15 A. Do you have the Dondoni paper just so I
16 have it?

17 Q. So...

18 A. I want to make sure that I -- before we
19 tell you what I...

20 Thank you. So you say 1a.

21 Q. So I'm handing you the exhibit that was
22 previously marked as 1064 in this IPR --

23 (Exhibit 1064, previously marked.)

24 A. Okay.

25 Q. -- the Dondoni reference.

1 And if you turn to Scheme 3 of the
2 reference --

3 A. Yeah.

4 Q. -- you will see that's the scheme that you
5 excerpted in your declaration; right?

6 A. Yeah, except for the circles, the red
7 circles.

8 Q. Right. You provided some annotation of
9 that scheme.

10 A. Yeah. Yeah.

11 Q. And in Scheme 3 you see there is a
12 compound labeled 1a; right?

13 A. Let me see.

14 Q. It's in the next -- next to that arrow in
15 the middle of the scheme.

16 A. Oh, yeah. Yeah. Okay. Yeah.

17 Q. And compound 1a is -- has a substituted
18 sugar ring with a vinyl group attached; right?

19 A. That's correct.

20 Q. And in compound 1a the vinyl group is
21 attached via a CH2 linker to the sugar ring; right?

22 A. That's correct.

23 Q. And compound 1a does not contain a
24 sulfone; right?

25 A. That's correct.

1 Q. And compound 1a does not contain any vinyl
2 sulfone; right?

3 A. That's correct.

4 Q. And compound 1a does not contain any
5 fluorophore; right?

6 A. That's correct.

7 Q. And compound 1a does not contain any
8 alkyne; right?

9 A. That's correct.

10 Q. Scheme 3 of Dondoni does not disclose any
11 compound containing a vinyl sulfone group; correct?

12 A. That's correct.

13 Q. In Scheme 3 bovine serum albumin was
14 reacted with compound 1a; correct?

15 A. That's correct.

16 Q. And bovine serum albumin is depicted as
17 native BSA on top of the scheme; right?

18 A. That's correct.

19 Q. So I will refer to bovine serum albumin as
20 BSA in today's deposition.

21 Is that okay with you?

22 A. That's fine.

23 Q. The reaction between compound 1a and BSA
24 requires UV light with a wavelength of 368
25 nanometers; right?

1 A. That's correct.

2 Q. Sorry. I just want -- I misspoke.

3 A. 365; right?

4 Q. So 365.

5 A. I -- checking to make sure. Sorry. Thank
6 you. 365.

7 Q. Right.

8 So the reaction between compound 1a and
9 BSA required UV light with a wavelength of 365
10 nanometer; right?

11 A. That's correct.

12 Q. What does the UV light do here in this
13 reaction of compound 1a?

14 A. The free radical formation.

15 (Court Reporter comment.)

16 A. Helps free radical formation.

17 Q. So the UV light is necessary to generate
18 free radical for the reaction to proceed.

19 A. That's correct. That's my understanding.

20 Q. And this reaction between compound 1a and
21 BSA also requires a compound called DPAP; right?

22 A. Let me look it up. What is the compound
23 called?

24 Q. So next to the arrow, to the other side of
25 the arrow you see "DPAP" above "DMSO"; right?

1 A. DPAP. DPAP.

2 Q. And if I direct your attention to page 2
3 of Dondoni, in the left column --

4 A. Yeah.

5 Q. -- about near the bottom you will see
6 "2,2-dimethoxy-2-phenyl-acetophenone (DPAP)" as a
7 sensitizer.

8 Do you see that?

9 A. Okay. I see it, yeah.

10 Q. So DPAP is included in this reaction as a
11 sensitizer; correct?

12 A. I don't know what the role of DPAP is, but
13 it is -- let me see make sure it says DPAP. If it
14 does. (Witness reviews document.)

15 Yes, I -- sensitizer, okay. DPAP is a
16 sensitizer.

17 Q. Right. And, then, the DPAP is needed for
18 the reaction; right?

19 MR. HOUSTON: Objection. Form.

20 A. In that paragraph it said that it needed.
21 I do not know whether without it it would work so
22 well.

23 (Court Reporter comment.)

24 A. I don't know that it works as well without
25 it. They didn't disclose whether they did it

1 without it. I don't see it here.

2 Q. So let me direct your attention to the
3 line you just read. (As read):

4 "So the reaction proceeded at room
5 temperature with irradiation of UV light with a
6 wavelength of 365 nanometer under argon in the
7 presence of 10 mole percent of DPAP."

8 Do you see that?

9 A. Which are you talking about?

10 Q. The line you were just reading about --

11 A. DPAP.

12 Q. -- what DPAP mean.

13 A. Very good yield, okay.

14 Q. And here the author described a reaction
15 between compound 1a and compound 2 using DPAP as a
16 sensitizer; correct?

17 A. That's correct.

18 Q. And I want to -- and just see that in this
19 sentence it says 10 percent -- 10 molar percent of
20 DPAP was used; right?

21 A. Yeah.

22 Q. And that if you look at the bottom of this
23 column, it says (as read):

24 "The amount of sensitizer was key to
25 reaction efficiency as in a control experiment the

1 use of 5 mole percent of DPAP resulted in a low
2 conversion of 1a."

3 Do you see that?

4 A. Yes.

5 Q. So from that can you infer that DPAP is
6 necessary for the reaction?

7 MR. HOUSTON: Objection. Form.

8 A. No, I think the -- the conversion is
9 pretty good.

10 (Court Reporter comment.)

11 A. The conversion is 75 -- sorry. (Witness
12 reviews document.) Yeah. Yes, that's pretty good
13 75 percent. I wouldn't call that low.

14 (Witness reviews document.) It says "Low
15 conversion...1a, 75 percent, entry 9." (Witness
16 reviews document.)

17 So maybe could work without DPAP. Just 75
18 percent pretty high.

19 (Court Reporter comment.)

20 A. We worked without DPAP. 75 percent is
21 pretty high yield for a reaction chemistry.

22 Q. So the 70 percent is in the reaction that
23 has 5 percent mole percent of DPAP; right?

24 A. Yeah, it's a much smaller amount. If you
25 had, like, 1, maybe it takes longer. It's not

1 known how long -- what would do without DPAP,
2 whether it be quicker, slower, or maybe still
3 complete. It's not disclosed in this paper, at
4 least.

5 Q. So you don't know one way or another
6 whether without DPAP the reaction would proceed or
7 not.

8 A. For the proceed, but how slow it proceed,
9 I do not know. 'Cause the other paper -- you
10 mentioned earlier Morales took over one day. Just
11 like this one is very quick. They said minutes.
12 So question is how long will it take without DPAP.

13 (Witness reviews document.)

14 Q. For a photoreaction, if you irradiate a
15 system for one day, would the photo UV light
16 destroy the reagent?

17 A. Depends -- no, not necessarily. 'Cause
18 you know, the protein is pretty stable; and, then,
19 the reagent makes a radical. You need a little bit
20 of a radical formation. Question -- I don't know
21 how much is formed without DPAP. Is it small
22 amount? Does it happen at all?

23 Q. Are you saying that if you shine a UV
24 light on the protein for a day the protein would
25 remain stable?

1 A. It could. Depending on the protein, I
2 guess. I mean, somebody, this PSA, other --
3 somebody disclosed in '682 it is small molecules,
4 probably stable as a rock.

5 (Court Reporter comment.)

6 Q. No. I'm asking you about protein.
7 Because Dondoni describes reaction between --

8 A. PSA.

9 Question is does it need long light -- or
10 not? Does it need light for a long time or just
11 have light for a few minutes and start the
12 reaction. Takes much longer to complete because
13 you don't make enough radical -- we don't -- we're
14 not sure you need light overnight, do we?

15 Q. So you don't know one way or another
16 whether the reaction after shining five minutes of
17 light --

18 A. Yeah.

19 Q. -- whether the reaction would still be
20 going after a day?

21 A. Exactly. Paper doesn't say anything about
22 duration of light and how long it takes.

23 Q. So you don't know one way or another what
24 would happen after five minutes of UV, the system,
25 whether the system will...

1 A. That's correct. May take longer, but
2 still finish without DPAP.

3 Q. So you don't know one way or another --

4 A. That's correct.

5 Q. -- whether that is the case or not.

6 But in -- going back to Dondoni, the
7 author described using DPAP and UV light in the
8 reaction between compound 1a and PSA; correct?

9 A. That's correct.

10 Q. Because Dondoni describes a photoinduced
11 reaction, the UV light is necessary for the
12 reaction to proceed; correct?

13 A. That's my understanding; that's correct.

14 Q. Have you -- strike that.

15 Do you know what does DPAP do in this
16 reaction?

17 A. Pardon me. The question?

18 Q. Do you know what DPAP does in this
19 reaction?

20 A. It says sensitizes. That's what it says
21 right here. But I don't -- I've not used it
22 myself. It says sensitizes...

23 (Witness reviews document.)

24 Q. So you have not used a sensitizer for a
25 photoinduced reaction yourself.

1 A. That's correct.

2 Q. So without the UV light the vinyl group in
3 compound 1a will not react with BSA; right?

4 A. That's what I think. You need some
5 radical catalyst. Radical catalyst.

6 Q. So you need something --

7 A. To form a radical. To initiate the
8 reaction.

9 Q. Okay. You need something to generate a
10 radical species to initiate --

11 A. Exactly. That's correct.

12 Q. -- the reaction?

13 A. Yes.

14 Q. And UV light does that in the system.

15 A. Yeah.

16 Q. Dondoni does not describe any photoinduced
17 reaction that reacts any compound containing a
18 vinyl sulfone with a cell-binding agent; right?

19 A. That's correct.

20 Q. And let's turn to page 5 of Dondoni,
21 Exhibit 1064.

22 A. Okay.

23 Q. If you look at the last column toward the
24 bottom and you see a sentence that starts with
25 "However," about -- where the No. 7 in the

1 reference list is to the left side of column -- I
2 just wanted --

3 A. Oh.

4 Q. The sentence that starts with "However."

5 A. Oh, yeah. Additional cys, yeah.

6 Q. So here Dondoni says (as read):

7 "However, in addition to cysteine 34 --"

8 A. Yeah.

9 Q. -- glycosylation of SH groups arising from
10 75-91 disulfide bridge cleavage was observed."

11 A. Okay.

12 Q. So here Dondoni is saying that the
13 photoinduced reaction conditions used in Scheme 3
14 cleaved open the disulfide bond in BSA; right?

15 A. That's correct.

16 Q. And Dondoni is reporting that once the
17 disulfide linkage is cleaved open, 2 molecules of a
18 compound 1a was added to each of cysteine 75 and
19 cysteine 91; right?

20 MR. HOUSTON: Objection. Form.

21 A. (Witness reviews document.) Let me see.
22 Let me read this a little bit. Very likely were
23 able to do...

24 (Witness reviews document.) Sorry. What
25 was the question again? Sorry.

1 Q. So Dondoni is describing this disulfide
2 bridge between cysteine --

3 A. Right, yeah.

4 Q. -- 75 and cysteine 91?

5 A. Yeah.

6 Q. That's been cleaved open right?

7 A. Yeah.

8 Q. So once a disulfide bridge is opened up
9 you expose the thiol group in the cysteine; right?

10 A. Yes.

11 Q. And then Dondoni observed 3 molecules of
12 compound 1a being added to BSA; right?

13 A. Okay.

14 Q. Right?

15 A. Right.

16 Q. And then the 3 molecules of compound 1a
17 was added to cysteine 34, cysteine 75, and cysteine
18 91; right?

19 A. Yes. But we don't know the ratio -- how
20 much of each one anyway. Yeah. They didn't say
21 how much of the new disulfides react to thiol.
22 Anyway. Okay.

23 Q. But the -- because 3 molecules of compound
24 1a are added to BSA, that means there are 3
25 attachment sites --

1 A. The question is --

2 Q. -- from cysteine; right?

3 A. The question is a new -- what's the
4 percent of each thing? Maybe 3 molecule of maybe 1
5 percent. Therefore it's not clear from this paper
6 how much of this was called side product. Is it 1
7 percent? Is it 10 percent? Is it 80 percent?

8 So it's not known how much of the 3
9 molecules are being added for the other thiols that
10 are being created.

11 Q. So let me understand your answer.

12 Are you saying that how -- you don't know
13 where the compound 1a is added?

14 A. No. No, I don't know how much.

15 Q. But the -- the author described in Scheme
16 3 this product where you have the sugar attached to
17 3 cysteine residues, right, at the bottom of Scheme
18 3.

19 A. Scheme 3, yeah.

20 But what it doesn't say is what the
21 percent of each of the new sites; is it -- show a
22 picture. Could be, like, trace amount; right? I
23 don't know how much is being formed on the new
24 sites percent-wise.

25 You know, it all depend like how exposed

1 the disulfide is in BSA compared to some other
2 cell-binding agent -- be exposed. All the -- many
3 factors involved in this information.

4 The solvent exposure of the disulfide and
5 what percent of it reacts and what percent being
6 converted to the reaction. Right.

7 Q. So the reaction may not be that clean. It
8 could involve many side products?

9 A. I don't know.

10 MR. HOUSTON: Objection. Form.

11 A. Could be -- could be 99 percent. Maybe
12 even there's small amount of side product. It's
13 easy to remove by separation. We don't know how
14 much is being formed -- the sites.

15 Q. So you don't know how efficient and
16 effective the reaction was.

17 A. No, I don't know how effective reaction in
18 the -- in the new site, talking about in the
19 cysteine cleavage sites.

20 (Court Reporter comment.)

21 A. Cysteine cleavage, c-y-s-t-e-i-n-e.

22 So in the regular reaction they said these
23 are very good, the thiol all in the BSA.

24 The side reaction -- I don't know how
25 efficient side reactions are. Is it small amount?

1 Trace amount? Doesn't say how much.

2 Q. So when you say "side reaction," are you
3 referring to the product that's shown as -- in the
4 bottom of Scheme 3, the product here is a product
5 of a side reaction?

6 Is that what you're saying?

7 A. This is the final product; right. So the
8 side reaction is a cleavage of the disulfide. You
9 said 70 -- let me see the number.

10 (Witness reviews document.) You said it's
11 a disulfide, right? 74 and 90. (Witness reviews
12 document.)

13 They say here quantitative formation of
14 10 --

15 (Court Reporter comment.)

16 A. Quantitative formation of 10 --
17 quantitative formation of 10 was verified by MALDI
18 whatever -- MALDI-TOF analysis.

19 Q. So (as read):

20 "The quantitative formation of 10 was
21 verified by MALDI-TOF analysis --"

22 A. Right.

23 Q. -- "which revealed peaks at masses 6 -- 66
24 --" sorry -- "66,652, and 67,601 --"

25 A. Yeah.

1 Q. -- "amu for a native BSA and glycosylated
2 BSA 10 respectively, a shift corresponding to the
3 addition of 3 molecules of galactoside 1a per
4 protein, figure 2."

5 Is that what you're reading from?

6 A. That's what it is. That's correct.

7 Q. So from this sentence the author is
8 reporting the addition of 3 molecules of compound
9 1a to BSA; right?

10 A. But he said that the amount of
11 quantitative -- how was the 3 -- it doesn't say
12 what percent is 3.

13 If you look at the MALDI-TOF picture, for
14 example...

15 (Witness reviews document.) Anyway, he
16 said 10 is quantitative. And how do you get --
17 quantitative means greater than 99 percent in my
18 mind. So if you get a little bit of the tri
19 reactive molecule, quantitative minus -- 100 minus
20 1 percent, .1 percent? Could be a small amount of
21 the tri -- 3 cysteines reacting.

22 Q. I see.

23 So you're saying, even though MALDI-TOF
24 mass spectrometry detected compound 10 with 3
25 molecules of compound 1a added to BSA, the amount

1 of compound 10 could be very small.

2 A. Yeah, because they say it's quantitative
3 reaction to give 10, which is -- which is a mono --
4 mono reactive compound; right? Compound 10?
5 (Witness reviews document.)

6 Q. So compound 10 is labeled as the 3 sugar
7 added to BSA, that product at the bottom of Scheme
8 3.

9 A. Quantitative -- let's see. (Witness
10 reviews document.)

11 So the question is, they say one hour, the
12 reaction...

13 (Court Reporter comment.)

14 A. For the reaction. They say happened in a
15 few minutes. So question is are they going too
16 long.

17 Trying to see how many minutes the
18 reaction take.

19 Q. Right. So you were trying to figure out
20 how long the reaction took?

21 A. Exactly.

22 Q. And the author seems to indicate that the
23 reaction could be taking too long?

24 A. Yeah. I'm thinking one hour maybe too
25 long. The question is how long does it actually

1 take to get the mono...

2 (Witness reviews document.) Supporting
3 information -- need supporting information for
4 critical details, how long it takes to get -- if
5 you look at table 2 here, compounds....

6 (Witness reviews document.)

7 Q. So the table 2 is describing preparation
8 of glycosol cystines 5a through c; right?

9 A. Yeah, but glutathione, okay, a smaller
10 molecule in table 2 --

11 (Court Reporter comment.)

12 A. -- glutathione glycoconjugate.

13 Q. But table 2 does not describe the reaction
14 in Scheme 3; right? Table 2 does not describe any
15 reaction with the BSA.

16 A. That's -- table just the control they did
17 with glutathione to show the efficiency of reaction
18 and how long it takes. The time is not given here.

19 (Witness reviews document.)

20 I'm trying to see how long the BSA
21 reaction takes to get the mono. I don't see.

22 Q. But where do you see that Dondoni reports
23 the reaction producing the mono labeled BSA?

24 I don't see it myself.

25 A. I'm trying to find it. (Witness reviews

1 document.)

2 Q. So you don't see it anywhere in Dondoni
3 that -- the product of adding just one molecule
4 compound 1a to BSA; right?

5 A. Yeah, they only mention 3 molecules, but
6 doesn't -- doesn't mean that other cell-binding
7 agents would have exposed disulphides. All depends
8 on how exposed the disulphide is.

9 (Court Reporter comment.)

10 Q. Okay. So going --

11 MR. HOUSTON: Are you finished?

12 Were you finished?

13 THE WITNESS: Yeah.

14 MR. HOUSTON: Okay. Sorry. I thought you
15 were --

16 THE WITNESS: No I'm saying -- she's
17 writing down.

18 A. You know, with other cell-binding agents,
19 disulfide might be unaffected by the light because
20 they're not exposed.

21 So the BSA, this particular disulfide
22 seemed to go off --

23 (Court Reporter comment.)

24 A. This particular disulfide seems to re --
25 seems to be reduced and reacts.

1 Q. So you cited Dondoni as the only reference
2 in your declaration to support your viewpoint that
3 vinyl could be -- alone could be a functional group
4 that reacts.

5 A. The reason -- the reason is, the
6 cell-binding agent list in 6a2 is very broad.
7 Three small molecules. I cited the reference
8 because considered mild. During the heat -- other
9 reaction known to cause -- called --
10 cross-metastasis reaction need heat. With this
11 particular -- but other small molecules described
12 in 6a2, the cell-binding agents can be heated. A
13 small molecule can be heated. But not a protein.
14 That's why I cited this reference for the
15 particular -- my condition for protein.

16 Q. Yeah. So you're -- I don't think you're
17 answering my question. I asked you in your
18 declaration you filed in this IPR you cited only
19 Dondoni --

20 A. Exactly. Exactly.

21 Q. -- to support your view.

22 A. That's correct.

23 Q. Correct; right?

24 You did not cite any other reference --

25 A. No.

1 Q. -- to support what you just said --

2 A. That's correct.

3 Q. -- right?

4 So going back to what I was asking about
5 Dondoni, so you cited Scheme 3 of Dondoni in your
6 declaration; right?

7 A. Yes.

8 Q. So I'm asking you in Scheme 3 the product
9 is described as the compound 1a being added to 3
10 cysteine residues; correct?

11 A. That's correct.

12 Q. And the 3 cysteine residues are cysteine
13 34, cysteine 75, and cysteine 91; correct?

14 A. That's correct. Yes.

15 Q. So if you look at the bottom of page 2 on
16 the right column and the top of the left column on
17 page 5, Dondoni here says that -- unfortunately --
18 sorry -- I mean, strike that. (As read):

19 "Identification of a reaction window for
20 selective cysteine 34 glycosylation was next
21 addressed by considering shorter irradiation times
22 and --"

23 A. Reading? Are you on page 2 now?

24 Q. Page 4.

25 A. Page 4.

1 Q. So if you look at the bottom --

2 A. Yeah.

3 Q. -- Dondoni says (as read):

4 "Identification of a reaction window for
5 selective cysteine 34 glycosylation was next
6 addressed by considering shorter irradiation
7 times..."

8 And then Dondoni listed a set of reaction
9 times. And when -- and it says (as read):

10 "...and/or aerobic conditions.

11 Unfortunately, this goal could not be achieved by
12 these experiments."

13 Do you see that?

14 A. Yeah.

15 Q. So here Dondoni describes an attempt to
16 selectively attach just 1 sugar molecule to
17 cysteine 34 without cleaving out the disulfide
18 linkage; right?

19 A. That's correct.

20 Q. And Dondoni reports here that their
21 attempt to do so was not successful; right?

22 A. What he doesn't say, Dondoni, does he do
23 it out of catalyst, the whatever catalyst? Does he
24 do the -- does he do that -- we don't know what he
25 tried.

1 Under those conditions, you're right that
2 you cannot get selective thiol reaction.

3 Q. Right.

4 A. But we don't know what they tried.

5 Q. So my question was a yes-and-no question.
6 Dondoni reported here that their attempt
7 to do so was not successful; right?

8 A. That's right. That's correct.

9 Q. Thank you.

10 Dondoni reports that they observed the
11 addition of 3 sugar molecules to cysteine 34,
12 cysteine 75, cysteine 91 of BSA; right?

13 A. That's correct.

14 Q. And Dondoni reports here that occurred
15 after only 5 minutes of light irradiation; right?

16 A. (Witness reviews document.)

17 Q. So you can read on in top of column --
18 left column on page 5.

19 A. Oh, page 5. Okay.

20 Q. Here Dondoni says (as read):

21 "We demonstrated that BSA could be -- the
22 BSA glycoconjugate 10 can be synthesized in a
23 reproducible manner, even under aerobic conditions,
24 in 5 minutes only"; right?

25 A. Yeah, 5 minutes.

1 Q. So they were able to reduce a reaction
2 time to 5 minutes only.

3 A. That's correct.

4 Q. But then they still could not produce the
5 product where you only have one sugar molecule
6 added to just cysteine 34; right?

7 A. Under the conditions, yes.

8 Q. Under the conditions they tried; correct?

9 A. Yes.

10 Q. And then, in all of this experiment, the
11 disulfide linkage was cleaved open and 3 sugar
12 molecules are attached to the BSA; right?

13 A. That's correct.

14 Q. And Dondoni analyzed the glycosylated BSA
15 compound 10 using mass spectrometry in figure 2;
16 right?

17 A. That's correct.

18 Q. And mass spectrometry provides information
19 on the molecular weight of the glycosylated BSA
20 compound 10; right?

21 A. That's correct.

22 Q. And then Dondoni used mass spectrometry to
23 confirm that the glycosylated BSA compound 10 has a
24 molecular weight corresponding to the glycosylated
25 BSA having 3 sugar molecules; right?

1 A. That's correct.

2 Q. And you don't know whether -- one way or
3 another whether the photoinduced thiol reaction you
4 relied on on Dondoni would cause disulfide bond
5 cleavage in HRP or not; right?

6 A. BSA you mean?

7 Q. HRP.

8 A. The HRP, I don't know.

9 Q. Right.

10 And you don't know one way or another
11 whether the photoinduced thiol reaction relied on
12 in Dondoni would cause denaturation of HRP or not;
13 right?

14 A. That's correct.

15 Q. And Morales does not describe any
16 photoinduced reaction that reacts a vinyl group
17 with HRP; right?

18 A. He does a vinyl sulfone, doesn't he,
19 Morales?

20 Q. Right.

21 Morales describes a Michael addition
22 reaction involving vinyl sulfone; right.

23 A. That's correct, yes.

24 (Discussion off the record.)

25 (Recess was taken.)

1 Q. So let's go to your first declaration,
2 Exhibit 1003.

3 A. Okay.

4 Q. Paragraph 82. That's on page 46.

5 A. Yeah.

6 Q. So here you rely on compounds 1, 2, 4, and
7 5 from Morales to analyze the patentability of
8 claim 1; right?

9 A. Right. Yeah.

10 Q. And each of compounds 1, 2, 4, and 5 of
11 Morales has a vinyl sulfone functional group with
12 the sulfone adjacent to the vinyl; right?

13 A. That's correct.

14 Q. And compound 1 of Morales has two vinyl
15 sulfone groups; right?

16 A. Yes.

17 Q. And in addition to vinyl sulfone, compound
18 2 of Morales has an alkyne group; right?

19 A. That's correct.

20 Q. And in addition to vinyl sulfone, compound
21 4 of Morales has an alkyne and a fluorophore;
22 right?

23 A. That's correct; yes.

24 Q. In addition to vinyl sulfone, compound 5
25 of Morales has an alkyne and a fluorophore; right?

1 A. That's correct.

2 Q. And you agree that each of compounds 1, 2,
3 4, and 5 of Morales contains additional functional
4 groups that are not present in compound 1a of
5 Dondoni; right?

6 A. 1a of Dondoni, you said?

7 Q. Right. If you look at Scheme 3 of
8 Dondoni.

9 A. (Witness reviews document.)

10 Q. On the next page.

11 A. (Witness reviews document.) Okay. 1a,
12 yeah. Okay.

13 Q. So that's a yes to the question I asked;
14 right?

15 A. What was the question again?

16 Q. So you would agree that each of compounds
17 1, 2, 4, and 5 of Morales contains additional
18 functional groups that are not present in compound
19 1a of Dondoni; right?

20 A. That's correct; yes.

21 Q. And you do not cite any reference
22 reporting of photoinduced reaction using the
23 condition described in Scheme 3 of Dondoni and
24 involving the reaction of a compound with a vinyl
25 sulfone group; right?

1 A. That's correct.

2 Q. And you did not cite any reference
3 reporting of photoinduced reaction using the
4 condition described in Scheme 3 of Dondoni and
5 involving the reaction of a compound with
6 additional functional groups such as vinyl sulfone,
7 alkyne, and the fluorophore; right?

8 A. That's correct.

9 Q. And let's turn to your second declaration,
10 Exhibit 1076.

11 A. Okay.

12 Q. And if you please go to paragraph 14 on
13 page 11.

14 A. Okay.

15 Q. Here you said your analysis identified C
16 as the propargylamine group; right?

17 (Court Reporter comment.)

18 A. Okay. Yes, that's correct.

19 Q. And so you depicted with red dotted circle
20 on page 10 the propargylamine group; right?

21 A. That's correct, yes.

22 Q. And this shows that -- your mapping of the
23 propargylamine group to the Z variable; right?

24 A. Yeah, Z. Yeah.

25 Also Y variable up at the top.

1 (Court Reporter comment.)

2 A. Y and -- yeah, a Y and the Z, 4 composite
3 amine A and B, 4a, 4b.

4 Q. So you matched variable Z to the
5 propargylamine moiety in compound 2 and then you
6 labeled those mapping as 2a and 2b; right?

7 A. (Witness reviews document.) 2a and 2b?
8 Okay. Yeah.

9 Q. Okay. And then for compound 4 you matched
10 this alkyne-containing moiety to the Z variable
11 under 4a; right?

12 A. Yes.

13 Q. And for compound 5 you mapped the
14 alkyne-containing moiety to variable Z under 5a;
15 right?

16 A. That's correct.

17 Q. So in each of these instances -- 2a, 2b,
18 4a, and 5a -- you mapped the alkyne-containing
19 moiety to C; right?

20 A. That's correct.

21 Q. And correspondingly in each of 2a, 2b, 4a,
22 and 5a, you mapped Y to a vinyl group; correct?

23 A. That's correct.

24 Q. And that vinyl is part of the vinyl
25 sulfone group in Morales compound; right?

1 A. That's correct.

2 Q. Okay. Let's turn to paragraph 18 of your
3 second declaration. That's on page 13 of the
4 second declaration.

5 A. Paragraph 13, yeah.

6 Q. Paragraph 18. And here you stated (as
7 read):

8 "When Morales-Sanfrutos' propargylamine is
9 considered for Y in the claims, a POSA would also
10 have appreciated that propargylamines are capable
11 of linking to CBAs."

12 Do you see that?

13 A. (Witness reviews document.)

14 Q. Right?

15 A. Yeah. That's correct, yes.

16 Q. Okay. And here in paragraph 18 on the
17 next page you cite to Exhibit 1072; right?

18 A. That's correct. I...

19 Q. And you cited Exhibit 1072 for its
20 disclosure of a reaction with a propargylamine
21 moiety that is catalyzed by a copper catalyst;
22 correct?

23 A. That's correct.

24 Q. And the copper catalyst is CuAAC depicted
25 in your declaration; right?

1 A. That's correct.

2 Q. And in the next paragraph, paragraph 19 of
3 your second declaration, you are citing to Exhibit
4 1070 at the end of that paragraph; right?

5 A. That's correct.

6 Q. And here you cited Exhibit 1070 for its
7 discussions of a reaction using a copper catalyst,
8 CuAAC, to catalyze a reaction between an amide --
9 sorry, strike that. Let me redo that question.

10 A. Which page are you on?

11 Q. Let me re-ask that question. I messed it
12 up.

13 So here in paragraph 19 you cited Exhibit
14 1070 for its discussion of a reaction between an
15 azide and an alkyne that is catalyzed using a
16 copper catalyst, CuAAC; right?

17 A. Yeah, that's correct.

18 Q. And you also cite Exhibits -- sorry,
19 strike that.

20 In the next paragraph, in paragraph 20,
21 you cite Exhibit 1069 in the declaration; right?

22 A. That's correct.

23 Q. And 1069 involves using copper catalysts
24 to catalyze a reaction between azide and the
25 propargylamine; right?

1 A. That's correct.

2 Q. And in this reactions described in
3 Exhibits 1069, 1070, and 1072, copper catalyst was
4 necessary for the reaction between an azide and an
5 alkyne; right?

6 A. Yeah, that's what they disclose; that's
7 correct.

8 Q. And without the copper catalyst azide
9 would not react with the alkyne; right?

10 A. That was an assumption, I suppose.

11 Q. Right. So let's go to your first
12 declaration, Exhibit 1003.

13 A. What page?

14 Q. At paragraph 87 on page 52.

15 A. Okay.

16 Q. Actually, paragraph 87 is on page 51 and
17 52 --

18 A. Okay.

19 Q. -- of your first declaration.

20 And here you started the paragraph by
21 analyzing claim 1 of the '682 patent; right?

22 A. That's right.

23 Q. And then on the next page, on page 52,
24 towards the end, six lines from the bottom you
25 started analyzing claim 2 of the '682 patent;

1 right?

2 A. Yeah. Claim 2, yeah. Yes.

3 Q. So here you said on page 52 of your first
4 declaration that claim 2 is met because compound 2
5 of Morales has an amino group that can be mapped to
6 Z; right?

7 A. That's correct.

8 Q. And here you are citing table B1 of the
9 first declaration; right?

10 A. Which page is that table? Sorry.

11 Q. But you are citing table B1 on page 52;
12 right?

13 A. Yeah. Yeah. B1. That's right.

14 Q. So if you go to table B1 that's on page 46
15 to 47 of your first declaration.

16 A. Okay.

17 Q. So you can see that in table B1 that you
18 cite, compound 2 has the propargylamine on the
19 left-hand side and the vinyl sulfone on the
20 right-hand side; right?

21 A. That's correct. Yes.

22 Q. So for claim 2 your analysis maps Z to the
23 propargylamine on the left and the Y to the vinyl
24 on the right of compound 2; right?

25 MR. HOUSTON: Objection. Form.

1 A. I'm confused. Can you -- can you repeat
2 the question, please?

3 Compound 4?

4 Q. So your analysis of claim 2 of the '682
5 patent, you are mapping Z to the propargylamine on
6 the left-hand side of compound 2 and you are
7 mapping vinyl on the right-hand side of compound
8 2 --

9 A. Okay.

10 Q. -- to Y; right?

11 A. Okay.

12 Q. So propargylamine mapped to Z; vinyl
13 mapped to Y; correct?

14 A. That's correct, yes.

15 Q. And, actually, just to confirm: You can
16 turn to page 48 of your first declaration. Here it
17 shows your mapping.

18 So to meet claim 2 you are mapping
19 compound 2 under either 2a or 2b, right, where you
20 have the propargylamine mapped to Z?

21 A. That's correct.

22 Q. And just let's go back to page 52 of the
23 same declaration.

24 A. 52, you say?

25 Q. Yeah, 52.

1 A. All right.

2 Q. And here you are only citing compound 2 in
3 your analysis of claim 2; right?

4 A. Okay.

5 Q. And you're not citing any other compounds
6 from Morales to support your analysis of claim 2;
7 right?

8 A. That's correct.

9 Q. So for claim 2 you are assuming that vinyl
10 alone could be Y; right, in your analysis?

11 So we can go back to page 48 of your
12 mapping.

13 MR. HOUSTON: Objection. Form.

14 Q. Let me restate that question just in case
15 you forget.

16 So for claim 2 you're assuming that vinyl
17 alone could be Y; right?

18 MR. HOUSTON: Objection. Form.

19 A. Vinyl alone could be Y...

20 What about 2c where the propargyl is also
21 Y? 2 -- compound 2c?

22 Q. But I'm asking you about claim 2. For
23 claim 2 you said claim 2 required Z to be
24 containing an amino, so you relied on the mapping
25 of 2a and 2b for claim 2; right?

1 A. What about 2c, the vinyl?

2 Q. So for 2c if you map the vinyl to Z then
3 it does not meet claim 2's requirement that Z
4 contains an amino group; right?

5 A. Why not?

6 'Cause you look at structure of compound 4
7 and 5, the amine group is just comprising. It says
8 that's the tertiary group. Doesn't react when it's
9 comprising.

10 (Court Reporter comment.)

11 A. Let me find the structure you're talking
12 about. Hold on. Hold on a minute.

13 So look at the section 2.

14 Q. So you can see the language of claim 2.
15 Is that what you're looking for?

16 A. Exactly, comprising.

17 Q. So it's to the -- but let me first direct
18 your attention to your analysis of claim 2 in the
19 first declaration. And we just went over that.
20 That's on page 52; right?

21 A. Yeah. Okay.

22 Q. And you did not rely on any other compound
23 than compound 2 of Morales in your analysis for
24 claim 2; right?

25 A. Let me see. 52. (Witness reviews

1 document.) Well, which one are you looking at?

2 What section are you looking at on page 52?

3 Q. So page 52, if you look at the sentence
4 starting with the word "Claim 2," it says (as
5 read):

6 "Claim 2 further specifies --"

7 A. Comprising, yeah, disulfide.

8 Q. "-- that Z comprises a thiol, disulfide,
9 amino --"

10 A. Yeah.

11 Q. And then you bolded the "amino" -- word
12 "amino"?

13 A. Yeah.

14 Q. "-- carboxy, aldehyde, maleimido --"

15 A. Yeah.

16 Q. "-- haloacetyl, hydrazine or hydroxyl
17 group."

18 Then you go on to say (as read):

19 "As shown in table B1, Morales-Sanfrutos's
20 compound 2 has an amino group.

21 A. That could be.

22 Q. So I'm asking you: Your analysis
23 basically just point to claim 2 of Morales because
24 claim -- sorry. Strike that.

25 Your analysis pointed -- points to

1 compound 2 of Morales for claim 2 of the '682
2 patent; right?

3 A. Compound 2, Morales. (Witness reviews
4 document.) That's correct, yes.

5 Q. And you're not citing any other compound
6 here when you analyze claim 2; right?

7 A. No, not any other compound.

8 Q. Right. And then you're analyzing claim 2
9 for its requirement that Z contains an amino group;
10 right?

11 A. That's correct, yes.

12 Q. And you pointed to compound 2 of Morales
13 because in your mapping the group that you mapped
14 to Z contains an amino group; right?

15 A. That is correct, yes.

16 Q. So going back to page 48, then, of the
17 same declaration --

18 A. Yeah.

19 Q. -- and if you look at the mapping for
20 compound 2 which you relied on for analyzing claim
21 2, 2a and 2b has a propargylamine mapped to Z;
22 right?

23 A. 2a and 2b -- yes.

24 Q. But 2c you do not have a group that
25 contains an amino group that's mapped to Z; right?

1 A. That's correct.

2 Q. So for purposes of claim 2, the mapping of
3 2c does not apply; correct?

4 A. 2 there's only one amino group, yes.

5 Q. Right. In order to map compound 2 to the
6 requirement of claim 2, you need to map the
7 propargylamine to Z and map the vinyl to Y; right?

8 A. That's correct.

9 Q. And here in your mapping you are assuming
10 that vinyl alone can be Y; right?

11 A. Yes.

12 Q. Okay. Let's go to your second
13 declaration, paragraph 28 -- 25.

14 A. Paragraph 25, you say?

15 Q. Yes, paragraph 25 of the second
16 declaration on page 17.

17 A. Yeah.

18 Q. So here your analysis is about claim 1;
19 right? You ended the paragraph by saying this
20 compound cited in your paragraph satisfied claim 1;
21 correct?

22 A. That's correct, yes.

23 Q. And here you cite compounds 2c, 4b, and
24 5b; right?

25 A. Yes.

1 Q. So if you keep that page in front of you
2 and then turn to your first declaration on pages 48
3 and 49 -- and remember that in paragraph 25 of the
4 second declaration you cited 2c, 4b, and 5b, and --
5 which is shown on pages 48 and 49 of your first
6 declaration; right?

7 A. Yes.

8 Q. So in each of the mapping 2c, 4b, and 5b,
9 the Z group is mapped to a vinyl; right?

10 A. That's correct, yes.

11 Q. So this mapping of 2c, 4b, and 5b would
12 not meet requirement of claim 2; right?

13 A. Wait. Let me understand that a little
14 bit.

15 Can you -- there's too many numbers.

16 Can you start again with the -- you are
17 talking about table page 46; right -- page 49?

18 Q. Yeah. So page 48 and 49.

19 A. Yes.

20 Q. So you analyze compound 2, 4, and 5.

21 A. Okay.

22 Q. So for each of compound 2, 4, and 5 you
23 mapped them in two different directions to the
24 claimed formula; right?

25 A. Yeah.

1 Q. So compound 2a, 2b, 4a, and 5a you mapped
2 in such a direction that the Y maps to a vinyl and
3 then Z maps to a group containing an alkyne; right?

4 A. That's correct, yes.

5 Q. And the group containing an alkyne also
6 contains either an amino group or a nitrogen
7 attached to a fluorophore; right?

8 A. Yes.

9 Q. And additionally you also mapped those
10 three compounds, compounds 2, 4, and 5, in the
11 other direction by mapping the vinyl group to Z in
12 -- in 2a -- sorry. Strike that. Let me start over
13 again.

14 And additionally you also mapped those
15 three compounds, compounds 2, 4, and 5, in the
16 other direction, as shown in 2c, 4b, 5b, by mapping
17 Z to a vinyl group; right?

18 A. 2c -- what was the other one? 4, yeah. I
19 mapped, yeah, 2c.

20 Q. And in these mappings, 2c, 4b, and 5b, the
21 Z group does not contain an amino; right?

22 A. (Witness reviews document.) 2c, 4b --
23 what was the other?

24 Q. 2c, 4b, and 5b.

25 A. Under Y or Z?

1 Under Z.

2 Q. Right. For Z you are mapping the vinyl to
3 Z here; right?

4 A. I'm confused. This is making me dizzy.
5 Start again, please, if you don't mind.

6 Q. Right. I'm just trying -- actually, let
7 me go back to do -- go over this again.

8 So in your -- in your second
9 declaration --

10 A. Yeah.

11 Q. -- in paragraph 25 --

12 A. Yes.

13 Q. -- so here you analyzed compounds 2, 4,
14 and 5 with certain mapping to show that they
15 satisfied claim 1; right?

16 A. Okay.

17 Q. And you did not say anything about claim
18 2; right?

19 A. That's correct.

20 Q. So I'm trying to establish that you did
21 not -- you're not saying that compounds 2c, 4b, and
22 5b would satisfy claim 2; correct?

23 A. 2b -- let me see. Let me look at 2b.
24 What I'm looking at, 2b, 4b, and 5b?

25 Q. Yeah.

1 So your analysis as shown in your
2 declaration is on page 48 and 49 of your first
3 declaration. That's what I'm relying on when I'm
4 asking you questions here.

5 So here you are mapping Z to a vinyl
6 under 2c, 4b, and 5b; right?

7 A. (Witness reviews document.) 5c -- wait a
8 minute. 2b.

9 Q. Let me -- strike that. Let me make it
10 easier.

11 So for compound 2c -- let's do one at a
12 time.

13 A. Okay. What page is 2c?

14 Q. 2c on page 48 of your first declaration.

15 A. Okay. 2c.

16 Q. And here you are mapping the
17 propargylamine to Y; right?

18 A. That's correct, yes.

19 Q. And then you are mapping the vinyl to Z;
20 right?

21 A. That's correct.

22 Q. So your mapping of vinyl to Z shows that Z
23 would not contain an amino group; right?

24 A. That's correct, yes, but -- yeah, compound
25 to a low amino group.

(Court Reporter comment.)

Q. Same question for your analysis under 4b.

A. Okay. 4b.

Q. And here you are mapping the alkyne with the nitrogen attached to a di, that group, to Y; right?

A. Yes.

Q. And then you are mapping the vinyl group to Z; right?

A. That's correct, yes.

Q. And so again your mapping of the vinyl to Z shows that Z will not contain an amino group; right?

A. Okay. That's correct.

Q. And let's do that for the mapping of 5b. Here again you are mapping the group with the alkyne and the nitrogen attached to a di to the Y moiety; right?

A. Yes.

Q. And then you are mapping the vinyl group to Z; right?

A. That's correct.

Q. And your mapping of vinyl to Z shows that the Z would not contain an amino group; right?

A. 5Z -- 5b has amino group -- is not -- it

1 is like a tertiary amino group. 5b?

2 Q. Right.

3 So the tertiary amino group of 5b is
4 attached to the di. And you -- I just showed to
5 you the di portion of the molecule is mapped to Y;
6 right?

7 A. Di portion of the molecule is...

8 (Witness reviews document.)

9 Q. If you go back to page 49, under 5b.

10 A. Okay. 5b.

11 Q. So there is this shape, weird shape, and
12 then it says "DNS." That's the di containing an
13 amino; right?

14 A. Right.

15 Q. So you are mapping that part of the
16 molecule to Y; right?

17 For 5b.

18 A. 5b. 5b, yeah. Map to Y.

19 Q. So in your mapping of 5b, Z does not
20 contain any amino group; right?

21 A. 5b -- Z -- Z is vinyl; right?

22 Q. Right.

23 A. Yeah. Okay.

24 Q. So you are mapping vinyl to Z; right?

25 A. Yeah.

1 Q. So in each of 2c, 4b, and 5b you are
2 mapping a vinyl to Z; correct?

3 A. That's correct in the first declaration,
4 yes.

5 Q. Right. And then let's go to page 52 of
6 your first declaration.

7 A. Okay.

8 Q. In that part of paragraph 87 you talk
9 about claim 2, you said claim 2 requires Z to
10 comprise a: "Thiol, disulfide amino, carboxy,
11 aldehyde --"

12 A. Wait.

13 Q. Let me finish.

14 A. Which paragraph again? Sorry.

15 Q. Sorry. Yeah. So in paragraph 52.

16 A. Oh, paragraph --

17 Q. Sorry. Page 52.

18 A. Page 52.

19 Q. Page 52, paragraph 87.

20 A. Okay. I want to make that -- sorry. I
21 want to make sure I follow what you're saying here.
22 Okay.

23 Go ahead. Sorry.

24 Q. And in that sentence starting with the
25 word "Claim 2 --"

1 A. Yeah.

2 Q. Do you see that?

3 Yeah. And it says (as read):

4 "Claim 2 further specifies that Z comprise
5 a thiol, disulfide, amino, carboxy, aldehyde,
6 maleimido, haloacetyl, hydrazine or hydroxyl
7 group."

8 Do you see that?

9 A. Yeah.

10 Q. So a vinyl group would not mean this
11 requirement of Z; right?

12 A. Mine doesn't -- ah, Z, you say? Okay,
13 (Witness reviews document.) Depends. Its -- if
14 you look at compound, for example --

15 Q. No, I'm asking you a yes-or-no question:

16 A. Yeah.

17 Q. So if Z is vinyl, does that meet the
18 requirement of claim 2 for Z?

19 A. So you're talking about claim 2. Want to
20 make sure I understand your question. (Witness
21 reviews document.) Table 1.

22 So -- sorry. Can you rephrase the
23 question again, please?

24 Q. So assuming Z is a vinyl --

25 A. Yeah.

1 Q. -- without any further substitution.

2 A. Yup.

3 Q. Does that vinyl meet the requirement of Z
4 as specified by claim 2?

5 A. (Witness reviews document.) Yes. Okay.

6 Q. Is that a yes or no?

7 A. That's correct. That's correct, yes.

8 Q. No. Let me ask -- I think you are -- are
9 you saying that a vinyl would meet the requirement
10 of claim 2?

11 A. (Witness reviews document.) For reaction
12 with --

13 Q. So --

14 A. -- Z?

15 Q. Claim 2 requires Z to comprise this list
16 of functional groups; right?

17 A. Right.

18 Q. And if Z is a vinyl group, does the vinyl
19 meet the requirement of Z as set forth in claim 2?

20 A. (Witness reviews document.) I'm still not
21 clear with the question. Was claim 2 -- oh,
22 compound 2; right? Compound 2 has a vinyl and has
23 an amine.

24 Q. No. I'm asking, Doctor Chari -- let me
25 focus you on my question, please; right?

1 A. Okay. Yeah.

2 Q. So I'm asking you if Z is a vinyl group,
3 the vinyl does not have any further substitution,
4 does that vinyl group meet the requirement of Z as
5 set forth in claim 2?

6 A. Yes, it will be; yes.

7 Q. How does that satisfy the requirement of Z
8 for claim 2? Can you explain?

9 A. So claim 2 says you need a -- comprising
10 amino group; right? And compound 2 has an amino
11 group next to the propargylamine. It doesn't say
12 if could react. It says comprising.

13 To my mind, the amino group in compound 2
14 has amino group, just amino propargyl.

15 Q. Okay. So I don't think you're answering
16 my question.

17 I'm asking you in some of your mapping
18 that we just went through in the mapping of 2c, 4b,
19 and 5b, you are mapping a vinyl group to a Z;
20 correct?

21 Yes or no.

22 A. That's correct, yes.

23 Q. So when you were mapping Z to the vinyl,
24 how does that vinyl satisfy the requirement of
25 claim 2?

1 A. So claim 2 says that you need -- you
2 comprise an amino group; right? Compound 4 and 5
3 are amino groups in their structure, they are not
4 reactive. They are amino group which are tertiary;
5 right? Compound 4 and 5.

6 Q. Yes. So let's go to compound 4 and 5 on
7 page 49 of your mapping.

8 A. 49.

9 Q. So the question I asked you was your
10 analysis of 4b and 5b; correct, where you map a
11 vinyl to Z.

12 A. Okay.

13 Q. And when you mapped the vinyl to Z, you
14 mapped the di linked to a nitrogen and then
15 attached to a propargyl group --

16 A. That's correct.

17 Q. -- to Y; correct?

18 A. That's correct.

19 Q. So you're not mapping the di linked to a
20 nitrogen with the propargyl group attached to Y --
21 to Z; correct? Let me start over again.

22 So you are not mapping the moiety
23 containing a di linked to a nitrogen and then
24 linked to a propargyl group to Z for analysis 4b
25 and 5b; correct?

1 A. That's correct; yes.

2 Q. So you needed to map that moiety to Y in
3 order to meet the requirement for Y for analysis 4b
4 and 5b; correct?

5 A. That's correct, yes.

6 Q. So when you map vinyl to Z, the vinyl
7 would not satisfy the requirement for claim 2;
8 right? I'm asking your analysis for 4b and 5b, not
9 4a and 5a.

10 A. 4b and 5b.

11 Let me -- structure of 4b and 5b.

12 Is structure somewhere of 4b and 5b? Oh,
13 yeah. It's right there. Okay. 4b and 5b.

14 Your question is 4b and 5b. (Witness
15 reviews document.) The vinyl reaction's for Z;
16 right?

17 What is the question?

18 Q. That is your analysis; right? Vinyl is
19 mapped to Z.

20 A. Vinyl is mapped to Z. So you say it won't
21 satisfy the requirement for claim 2, is what you're
22 saying.

23 (Court Reporter comment.)

24 Q. Pardon me?

25 A. 4b and a 5b have the amino group in the

1 top; right?

2 Q. Right.

3 A. Under Y.

4 Q. Yes.

5 So once you mapped the amino group to Y,
6 as shown on top for 5b and 4b, the vinyl that's
7 mapped to Z would not meet the requirement for
8 claim 2; right?

9 A. If it mapped that way; that's correct --
10 well, even if it mapped that way, the amino group
11 present -- presented in the molecule, right,
12 comprise the amino group.

13 Say 4b and 5b are mapped to Y, they react
14 with the alkyne. You still have an amino group
15 left behind. Remember claim 2 has comprised an
16 amino group. And if you look at the way it's
17 drawn, 4b and 5b react in Y; correct?

18 (Court Reporter comment.)

19 Q. Right. So for 4b and 5b your analysis, in
20 order to show compound 4 and 5 meet the claims
21 requirement for Y, you mapped that portion of
22 compound 4 and 5 containing the di, the amino, and
23 the propargyl group to Y; correct?

24 A. That's correct.

25 Q. Once you mapped those groups to Y, you

1 cannot use that group again to map it onto Z;
2 correct?

3 A. That's correct. Yes.

4 Q. So under the mapping of 4b and 5b, you
5 used a vinyl group to map that to Y -- to Z;
6 correct?

7 A. Yes.

8 Q. And then, once you do that, the vinyl
9 group would not meet the requirement for claim 2;
10 correct?

11 A. Why not? Claim 2 says comprised amino
12 group. Still have an amino group left from Y. 4b
13 from Y; right? Amino still present. It's still
14 there, amino group.

15 Q. So let me understand your opinion.

16 Are you using the di containing the amino
17 group twice in your mapping in order to satisfy the
18 claim analysis here? Is that your analysis
19 throughout the declaration?

20 A. No, I'm not -- I'm just saying that you
21 say that 4b -- does the requirement of the vinyl
22 group for Z; right?

23 Are you saying it doesn't satisfy the
24 requirement of the Z for the vinyl. The di still
25 has an amino also. Di, not just a di, it has an

1 amino group sitting it on it. Where is the di?

2 Morales di...

3 (Witness reviews document.) So compound
4 4b and 5b again, please. Sure. So Compound 4b and
5 5b? Is that what you said?

6 Q. No, 4b and 5b is your designation that you
7 use in your first declaration on page 49. That's
8 the analysis you provided; correct?

9 A. Page 47?

10 Q. Yes, 49.

11 A. 49. Okay. (Witness reviews document.)
12 Yeah. Okay. That's correct.

13 Q. And it is your opinion that when you
14 analyzed 4b and 5b you mapped the moiety of the
15 molecule containing the di, the amino, and the
16 propargyl group to Y; correct?

17 That's the box --

18 A. Yeah.

19 Q. -- on top --

20 A. That's correct.

21 Q. -- of each --

22 A. That's correct; yes.

23 Q. -- column.

24 You are not pointing that group to Z
25 anywhere in your declaration; correct? -- for 4b

1 and 5b.

2 A. That's correct.

3 Q. So in your analysis of 4b and 5b you are
4 mapping the vinyl to Z; correct?

5 A. Yeah, that's correct.

6 Q. And in that analysis, mapping vinyl to Z,
7 the Z would not meet the requirement for claim 2;
8 correct?

9 A. Why not? 'Cause remember 4b and 5b have
10 an amino group in their ring structures; right?
11 They're a tertiary amine. They don't react to --
12 comprising an amine. It has an amine.

13 Q. But isn't it true that under 5b, that's
14 the dansyl group, you're including that dansyl
15 group in the role for Y, not for Z?

16 A. Yeah, because you're mapping 5b. So we
17 have to include the whole structure; right?

18 You're mapping 4b and 5b with the
19 dansyl --

20 (Court Reporter comment.)

21 A. To those two groups. It include the whole
22 group. You don't map 4b, 5b. You are mapping the
23 whole group; right? 4b and 5b is being mapped.

24 Why -- why wouldn't the dansyl group?
25 'Cause you're mapping the whole structure; isn't

1 it?

2 Q. Yeah. So let me direct your attention to
3 claim 2.

4 A. Claim to comprise the amino group --

5 Q. No. No. Let me go to claim 2 for you
6 right now.

7 A. Okay.

8 Q. So that's part of your declaration on page
9 111, the first declaration.

10 A. 111. Page 111 or --

11 Q. Page 111.

12 A. Okay. Claim 2. Linker -- yeah.

13 Q. So it says (as read):

14 "The hydrophilic linker of claim 1 wherein
15 Z comprises --" this list of functional group.

16 Do you see that?

17 A. Yeah. Yeah.

18 Q. And then going -- because claim 2 refers
19 to claim 1, I want to direct your attention to
20 claim 1, which is on page 109 of your declaration.

21 A. Okay.

22 Q. And claim 1 begins with "A hydrophilic
23 linker of formula 1."

24 A. Yeah.

25 Q. Do you see that?

1 A. That's correct.

2 Q. And on formula 1 you see it's a molecule
3 with Y on one end of the molecule and Z on the
4 total opposite end of the molecule.

5 Do you see that?

6 A. Yeah. Yeah. Yeah. That's correct.

7 Q. So if you map a group to Y, how can the
8 part of that group also be used to map to Z?

9 A. So Z functional reacts to enable linkage;
10 right, with vinyl -- Z could react to the vinyl
11 sulfone, right?

12 (Court Reporter comment.)

13 A. Z could react to the vinyl sulfone; right?
14 And you're saying that -- you're saying Y has
15 already reacted with...

16 (Witness reviews document.) I think they
17 are two separate thing: One is the reaction, Z
18 reaction with the vinyl group; other is comprising
19 that the -- one comprises an amine; right?

20 Q. So are you reading claim 2 to just say
21 requiring this hydrophilic linker of claim 1 to
22 comprise this functional group --

23 A. Yeah.

24 Q. -- not wherein Z comprises.

25 A. Comprising the -- comprises an amino

1 group; right?

2 (Court Reporter comment.)

3 A. So your point is that this -- tell me your
4 point.

5 Q. Yeah. I'm trying to understand your
6 analysis for claim 2, how that works. So are you
7 saying if a molecule contains an amino group
8 anywhere in the molecule and that molecule is a
9 hydrophilic linker, that molecule would meet the
10 requirement for claim 2 even though the Z
11 functional group itself does not contain --

12 A. That's correct.

13 Q. -- an amino?

14 A. If it's comprising, it's comprising. If
15 you have the amino somewhere in the molecule --
16 satisfy the -- of 2; right? That's my
17 understanding of -- something it's comprising an
18 amino group even in the molecule should meet the
19 requirement.

20 Q. I see. So anywhere in the molecule --

21 A. Exactly.

22 Q. -- regardless of where it is --

23 A. Exactly.

24 Q. -- how you use that amino to map into any
25 of the variables of amino 1 --

1 A. Exactly. Comprising mean it's just there.
2 My understanding. You know, legally, I don't know.
3 But comprising means -- comprise has amino
4 somewhere in the molecule, the dansyl, and the
5 rhodamine. There was --

6 (Court Reporter comment.)

7 Q. Rhodamine.

8 A. Rhodamine.

9 Q. So anywhere in the molecule for example a
10 dansyl or rhodamine either contains or attached to
11 an amino, it will meet the requirement for claim 2?

12 A. That's my understanding. Comprising to me
13 means that somewhere in the molecule is the amino
14 group.

15 Q. I see. So the claim says "Wherein Z
16 comprises," you didn't think it requires the Z
17 group to comprise this functional group; right?

18 A. The functional group Z separate at the
19 vinyl sulfone. The vinyl sulfone acts as the Z,
20 right; and then the -- molecule, there's an amino
21 somewhere in the molecule.

22 Does that make sense?

23 Q. Okay. So that's how you analyze claim 2
24 throughout your two declarations; correct?

25 A. That's correct.

1 Q. Okay. We can move on.

2 So, Doctor Chari, I'm going to ask you
3 some chemistry questions: So when you mix a
4 compound containing N-hydroxysuccinimide ester with
5 a protein containing an amino group in a buffer
6 solution, that N-hydroxysuccinimide ester would
7 react with the amino group; right?

8 MR. HOUSTON: Objection. Beyond the
9 scope.

10 A. Which -- refer to which page?

11 Q. Oh, no, I'm just asking.

12 A. General -- general question, okay.
13 General question, okay.

14 Q. General question, yes.

15 A. Would react, yes; correct.

16 Q. Because you're an organic chemist.

17 A. I've used an NHS ester before and know it
18 reacts with amino group.

19 (Court Reporter comment.)

20 A. N-hydroxysuccinimide ester before,
21 N-hydroxysuccinimide ester.

22 Q. So N-hydroxysuccinimide ester is also
23 called NHS ester?

24 A. N-H-S, yes.

25 Q. And you don't need another reagent to push

1 that reaction to occur; right?

2 MR. HOUSTON: Objection. Form.

3 A. Well, the ester goes fast a higher pH.
4 All depends on what, you know, definitely pH
5 catalyzed.

6 Q. Right.

7 A. Low pH won't happen. High pH will be
8 faster. But both hydrolyze pretty quickly.
9 There's a balance.

10 Q. So if you use, say, a pH buffer of pH 8.5,
11 that would happen? That reaction would happen?

12 A. That would have a very quick hydrolysis.

13 Q. Okay. And then the NHS ester would react
14 with the amino group; right?

15 A. Yeah. It would react.

16 Q. Right.

17 So how about a compound containing a
18 P-nitrophenyl ester? Would that react with an
19 amino group from a protein?

20 MR. HOUSTON: Objection. Beyond the
21 scope.

22 A. That should react with a protein too as
23 well.

24 Q. Right. And that reaction would happen in
25 the pH buffer without additional reagents; right?

1 MR. HOUSTON: Same objection.

2 A. Yeah, my understanding, if you have the
3 right pH for it to react; maybe a higher pH than
4 NHS, but...

5 Q. Like a pH 8.5, for example?

6 A. Yeah, could -- could -- yeah. Could be
7 good.

8 Q. Okay.

9 A. A short time, 'cause you don't want to
10 have a protein at pH 8.5 for too long.

11 Q. Right. But for that reaction to take
12 place you can use a pH buffer for the reaction to
13 occur; right?

14 A. That is correct.

15 Q. Okay. And then how about dinitrophenyl
16 ester?

17 MR. HOUSTON: Objection.

18 Q. Would that react with an amino group from
19 a protein?

20 MR. HOUSTON: Objection. Beyond the
21 scope.

22 Q. You may answer.

23 A. It should be a faster reaction.
24 Dinitrophenyl --

25 (Court Reporter comment.)

1 A. Faster reaction.

2 Q. And that reaction would happen in the pH
3 buffer solution; correct?

4 A. Should happen.

5 Q. All right. How about pentafluorophenyl
6 ester? Would that group react with an amino group
7 from the protein?

8 MR. HOUSTON: Objection. Beyond the
9 scope.

10 A. It could react with a high pH, I think.
11 Don't know if as reactive as NHS ester.

12 Q. Right. So here for this functional group
13 you could use a pH 8.5 buffer, for example, for the
14 reaction to take place; right?

15 MR. HOUSTON: Objection. Beyond the
16 scope.

17 Q. You may answer.

18 A. I think so, yes.

19 Q. All right.

20 MR. HOUSTON: Just pause long enough to
21 let me get in my objection. Okay.

22 Do you understand, Doctor Chari? You need
23 to pause and let me get in my objection before you
24 answer.

25 THE WITNESS: Yeah, you're right. Sorry.

1 Thank you. I answered too quickly.

2 Sorry.

3 Q. And what about pentafluorophenyl ester?
4 Would that react with amino group from a protein?

5 MR. HOUSTON: Objection. Beyond the
6 scope.

7 Q. You may answer.

8 A. It's been reported that it does react to
9 the protein.

10 Q. Right. And that reaction could happen in
11 a buffer solution; correct?

12 MR. HOUSTON: Objection. Beyond the
13 scope.

14 Q. You may answer.

15 MR. HOUSTON: Objection. Form.

16 A. You mean buffer solution? What pH?
17 (Court Reporter comment.)

18 Q. Let's see. A pH8.5 --

19 A. She asked buffer solution. I asked what
20 she meant by buffer solution. Buffers are so
21 different pHs, you know?

22 Q. How about pH 8.5 buffer solution?

23 MR. HOUSTON: Objection. Beyond the
24 scope.

25 A. Should react, but I don't know the speed.

1 Q. Right. Okay. It should -- could react;
2 right? It should react?

3 A. That's correct.

4 Q. And, then, what about pyridyldisulfide?
5 Would that react with a thiol group from a protein
6 in a buffer solution?

7 MR. HOUSTON: Objection. Beyond the
8 scope.

9 Q. You may answer.

10 A. Buffer solution all -- be much faster
11 reaction, but lower pH would react -- pH 7 -- very
12 nicely; sulfide exchange. Don't need high pH --
13 don't want high pH for that reaction for
14 pyridyldisulfide.

15 Q. So you -- you can -- the reaction can go
16 forward with a lower pH like pH 7.4, for example?

17 A. I don't know if pH 5.4 [verbatim] -- pH 7
18 is good for that reaction.

19 Q. pH 7.

20 (Court Reporter comment.)

21 Q. Okay. How about nitropyridyldisulfide?
22 Would that functional group react with a thiol
23 group from a protein in buffer solution?

24 MR. HOUSTON: Objection. Beyond the
25 scope. Form.

1 Q. You may answer.

2 A. It should react faster. I know it reacts
3 faster than pyridyldisulfide.

4 Q. It would react faster than
5 pyridyldisulfide in a buffer solution.

6 A. That's correct.

7 Q. I see.

8 What about maleimide, m-a-l-e-i-m-i-d-e?
9 (Court Reporter comment.)

10 Q. Would that functional group react with a
11 thiol group from a protein in a buffer solution?

12 MR. HOUSTON: Objection. Beyond the
13 scope. Form.

14 Q. You may answer.

15 A. It would react much faster. We know it
16 reacts much faster even at lower pH.

17 Q. Right. So the reaction would take place
18 much faster in a buffer solution at lower pH;
19 correct.

20 MR. HOUSTON: Same objections.

21 A. When I mean lower pH, I don't mean 4, but,
22 I mean 6, 6.5, 7.

23 Q. I see.

24 A. You don't want 8.5 hydrolyzed amide. It
25 has to be neutral pH or lower.

1 Q. I see. Neutral or lower. Around 6.5 or 7
2 pH.

3 A. Yeah.

4 Q. Okay. How about haloacetate? Would that
5 functional group react with thiol group from a
6 protein in a buffer solution?

7 MR. HOUSTON: Objection. Beyond the
8 scope. Form.

9 A. That needs a high pH.

10 Q. How?

11 A. Probably 8.5, 9 even.

12 Q. Okay. So pH 8.5 or 9 could be used as a
13 buffer solution for a reaction between haloacetate
14 and the thiol group from protein; correct?

15 MR. HOUSTON: Same objections.

16 A. That's correct. Yes.

17 Q. What about carboxylic acid chloride?
18 Would that functional group react with a thiol
19 group from a protein in a buffer solution?

20 MR. HOUSTON: Objection. Beyond the
21 scope. Form.

22 A. Carboxyl chloride, you said?

23 Q. Carboxylic acid chloride.

24 A. Yeah, that --

25 MR. HOUSTON: Same objections.

(Court Reporter comment.)

A. I -- that, I don't know about. I think it's very sensitive to hydrolysis, but -- be soluble, I just don't --

(Court Reporter comment.)

A. Sensitive to hydrolysis, I said.

MR. HOUSTON: You said something about soluble, didn't you?

A. It may not be soluble. I just don't know what --

Q. Right.

A. It is -- compared to --

Q. I see.

A. Compared with --

Q. I see. So you don't know for sure about carboxylic acid chloride?

A. I don't know the nature of the carboxyl chloride whether it will dissolve or hydrolyze faster, you know.

Q. I see. Let's go to your second declaration. Paragraph 27.

MR. HOUSTON: I'm sorry. Which paragraph?

MS. LOU: 27.

Q. So paragraph 27 on page 18.

A. Yeah.

1 Q. And here you said that (as read):

2 "Singh identifies maleimide,
3 haloacetamide, and vinyl sulfone as a
4 thiol-reactive functionality"; right?

5 A. That's correct, yes.

6 Q. So in paragraph 27 you also stated that
7 "...vinyl sulfone were not included in the
8 experimentally validated ADCs in Singh pursued for
9 commercialization because our specifically
10 contemplated drugs at the time were not very
11 hydrophobic; and inclusion of PEG alone in our
12 tested linkers was able to address our water
13 solubility/drug aggregation concerns"; right?

14 A. That's correct, yes.

15 Q. So you agree that Singh does not disclose
16 any experimental examples of ADCs with a linker
17 that includes a sulfone moiety, correct?

18 A. That is correct.

19 Q. And Singh does not disclose any
20 experimental examples of a linker with a vinyl
21 sulfone as a thiol reactive functional group;
22 right?

23 A. That's correct.

24 Q. And you agree that Singh discloses vinyl
25 sulfone only as one of the thiol reactive

1 functional groups; right?

2 MR. HOUSTON: Objection. Form.

3 A. One could try vinyl sulfone if you want to
4 increase solubility.

5 (Court Reporter comment.)

6 Q. I'll get to that.

7 So in Singh the vinyl sulfone is -- if it
8 is selected as a thiol reactive functional group --
9 would be included on either end of the linker to
10 react with the drug or cell-binding agent; right?

11 MR. HOUSTON: Objection. Form.

12 A. Yes.

13 Q. Right?

14 So it's a reactive functional group to
15 react with a drug or cell-binding agent that
16 contains a cell group; right -- thiol group; right?

17 A. That's correct.

18 Q. So you would not add the vinyl sulfone to
19 the middle part of the linker; correct?

20 MR. HOUSTON: Objection. Form.

21 A. Why not? I mean, if you have a different
22 reactive group -- if you have maleimide, you need a
23 vinyl sulfone to react. It all depends on where
24 the -- what the reactive species is.

25 (Court Reporter comment.)

1 A. In Singh we have maleimide and a PEG;
2 right? Okay.

3 (Court Reporter comment.)

4 A. Maleimide reacts with a cell-binding
5 agent.

6 (Court Reporter comment.)

7 A. And the PEG. Maleimide and the PEG;
8 right? The maleimide is the binding agent. The
9 PEG has -- succinimide reacts with the -- well, PEG
10 can react -- no, wait a minute. Sorry. I take it
11 back.

12 In Singh the maleimide reacts with thiol
13 on the drug; right?

14 (Court Reporter comment.)

15 A. Maleimide reacts on the -- the PEG -- the
16 succinimide reacts with the antibody or
17 cell-binding agent; right?

18 Now, vinyl sulfone can be anywhere in the
19 molecule to make it more soluble. Could be in the
20 middle. Could be anywhere. Doesn't have to react.
21 Doesn't have to react to species.

22 Q. So let me ask you this: The only place
23 Singh talks about vinyl sulfone is in paragraph
24 134; right?

25 A. That's correct, yes.

1 Q. So when Singh talked about vinyl sulfone
2 in paragraph 134, it describes vinyl sulfone as a
3 thiol-reactive functionalities; right?

4 A. That's correct, yes.

5 Q. So Singh does not describe vinyl sulfone
6 as part of the linker; right?

7 MR. HOUSTON: Objection. Form.

8 A. That is -- yeah. That's correct, yes.

9 Q. Right. So if you put vinyl sulfone in the
10 middle of the linker, it -- not react with a
11 cell-binding agent or a drug; right?

12 MR. HOUSTON: Objection. Form.

13 A. That's correct, yes.

14 Q. And Singh does not say that sulfone by
15 itself should be added to the linker; right? I'm
16 asking about Singh. Singh does not say you should
17 add sulfone to the linker; right?

18 A. What does it -- doesn't say it
19 specifically; that's right. That is correct.

20 Q. Right. And then you said in paragraph 28
21 of your second declaration --

22 A. Yeah.

23 Q. -- that Harris teaches that (as read):
24 "Sulfone groups have a particularly
25 advantageous impact on water solubility";

1 right?

2 A. That's correct.

3 Q. But you don't cite any specific portions
4 of Harris to support this statement; right?

5 A. If you look at Harris, the reason they put
6 the sulfone is to make the PEG more soluble. They
7 said PEG wasn't enough, so they put the sulfone on
8 top of the PEG to make it more soluble.

9 Q. Where does Harris say that?

10 A. Harris says -- I don't know why the
11 sulfone -- they say -- if you look at their
12 rationale why they make molecule, do you have it in
13 front of you?

14 Q. Oh, yeah. We can give you Harris.

15 A. I guess I can read what it says there.

16 MR. HOUSTON: Actually, can we take a
17 break soon?

18 MS. LOU: Can we finish the question about
19 Harris since we just got into it?

20 MR. HOUSTON: Yes.

21 A. (Witness reviews document.)

22 Q. So Harris describes PEG with active
23 sulfone on the end that's used to modify other
24 molecules; right?

25 A. Let me read it. Let me see Harris.

1 (Witness reviews document.) So what was the
2 question about it?

3 Sorry. Would you --

4 Q. I haven't seen anywhere in Harris that
5 says sulfone is added to the molecule because
6 sulfone would increase solubility. Harris, to me,
7 seems like it describes a PEG linker that was
8 active sulfone functionalities on either end of
9 them. And that PEG linker is used to modify other
10 molecules. I want you to point me to where Harris
11 talks about sulfone providing the additional
12 solubility.

13 A. Okay. Okay. Hold on one second. Let me
14 find that. (Witness reviews document.)

15 So where he had mentioned, he mentioned
16 "Provides water soluble --"

17 Q. Which page are you reading from?

18 A. Page 6 of Harris.

19 Q. I'm sorry. Which line?

20 A. Mentioned line No. 7, 8.

21 Q. Okay.

22 A. Mentions (as read):

23 "Provides water soluble hydrolytically
24 stable derivatives of polyethylene glycol polymers
25 having --"

1 (Court Reporter comment.)

2 MR. HOUSTON: Let's clarify which number.

3 Top or bottom?

4 A. See that?

5 Those four lines. I'm just citing those
6 four lines. That's where sulfone makes it water
7 soluble.

8 Q. But this -- that sentence that begins "The
9 invention provides water soluble and hydrolytically
10 stable derivatives of polyethylene glycol, PEG,
11 polymers and related hydrophilic polymers having
12 one or more active sulfone moieties."

13 Is that the sentence you were reading
14 from?

15 A. That's correct, what I'm reading, yes.

16 Q. So here the sentence talks about both "PEG
17 polymers and related hydrophilic polymers having
18 one or more active sulfone moieties."

19 You see that?

20 A. That's correct; yes.

21 Q. So wouldn't a POSA understand that the PEG
22 polymers, the PEG functionality in those PEG
23 polymers provides the water solubility and
24 hydrophilic stability?

25 MR. HOUSTON: Objection. Form.

1 A. I think POSA would say it's not enough
2 solubility like by a PEG alone.

3 (Court Reporter comment.)

4 Q. But the sentence says "polyethylene
5 glycol, PEG, polymers and related hydrophilic
6 polymers having one or more active sulfone
7 moieties."

8 Do you see that?

9 A. Yes.

10 Q. So they are saying both two entities here
11 right? No. 1, polyethylene glycol, PEG,
12 polymers --

13 A. That's correct.

14 Q. -- No. 2, "related hydrophilic polymers
15 having one or more active sulfone moieties";
16 correct?

17 A. That's correct.

18 Q. And both are water soluble and
19 hydrophilically stable; right?

20 MR. HOUSTON: Objection. Form.

21 A. The PEG polymers aren't water soluble
22 enough. Sulfone -- direct product --

23 (Court Reporter comment.)

24 MR. HOUSTON: Okay. Everybody slow down.
25 Court reporter needs to get this down.

1 A. The PEG polymer may not be water soluble
2 enough. You asked me how I know it. A POSA would
3 know that. POSA works on PEGs all the time. They
4 say, You'll need something more soluble, including
5 me and Singh.

6 So if you add an active sulfone moiety to
7 it, it will make it more soluble.

8 Q. But here Harris does not say that the PEG
9 polymers are not soluble enough in the sentence you
10 point to; right?

11 A. I read that. Let me see where I read
12 that. Hold on a second. (Witness reviews
13 document.) Give me a minute. (Witness reviews
14 document.)

15 Q. So sitting here today, you haven't been
16 able to find any disclosure in Harris --

17 MR. HOUSTON: Hold on, Jihong. He's still
18 looking.

19 MS. LOU: Okay.

20 A. (Witness reviews document.) All I can see
21 from here is page 9, line 23.

22 MR. HOUSTON: Doctor, just to clarify.
23 Again, are you using the numbers at the top?

24 THE WITNESS: Yeah. Page 9 -- I'm sorry.
25 Page 7 at top. Sorry. Page 7 at top. Page 9 at

1 the bottom.

2 MR. HOUSTON: Just to clarify: Which page
3 number? Top or bottom page number?

4 THE WITNESS: Bottom -- top page 7.

5 Sorry.

6 MR. HOUSTON: Okay. Thank you.

7 A. Line 23 it says (as read):

8 "Water soluble sulfur-activated PEG
9 polymer," in line 27.

10 Q. Right. But here going back to the
11 sentence we just saw on page 6 -- with 6 on top of
12 the page, the page number on top of the page -- the
13 sentence you just pointed to on page 6 at lines 8,
14 9, 10, and 11 --

15 A. Yeah.

16 Q. -- there it does say that the polyethylene
17 glycol, PEG, polymers are water soluble and
18 hydrolytically stable; right?

19 A. Sulfone-activated PEG polymer is water...

20 (Witness reviews document.)

21 (Court Reporter comment.)

22 Q. Right, but this sentence -- we just went
23 over this; right? This sentence provides two
24 things; talks about two things: No. 1, the PEG
25 polymers; No. 2, the related hydrophilic polymers

1 having one or more active sulfone moieties. Both
2 are described as water soluble and hydrolytically
3 stable; right?

4 I want you to focus on page 6, the lines 8
5 to 11 that we just -- you just pointed out.

6 A. Page at the top; right?

7 Q. Page 6 at the top.

8 MR. HOUSTON: Jihong, could you clarify
9 what the question for the witness, please.

10 MS. LOU: Yes.

11 Q. So my question is this sentence you are
12 directing us to initially, this sentence describes
13 two things; right: One is the PEG polymers; two is
14 the related hydrophilic polymers having one or more
15 active sulfone moieties; correct?

16 MR. HOUSTON: Objection. Form.

17 A. So line 6 --

18 Q. Answer me yes or no. Just --

19 MR. HOUSTON: He's trying to answer you.
20 Just give him a chance.

21 A. So page 6, line -- page on the top; right?

22 Q. Uh-huh.

23 A. Line 8 says (as read):

24 "The invention provides water soluble and
25 hydrolytically stable derivatives of PEG polymer."

1 To me it means PEG alone not water
2 soluble, can't --

3 (Court Reporter comment.)

4 A. PEG alone is not water soluble enough.
5 Need sulfone to make it water soluble. They don't
6 say water soluble hydrolytically stable. They
7 still say -- you know what I mean? When you say a
8 statement to mention water soluble and derivatives
9 of PEG polymer, my understanding is that PEG
10 polymer is not water soluble. You need to have a
11 sulfone to make it soluble.

12 Q. Okay. So let me direct your attention to
13 page 11, 11 being the number on top of the page.

14 A. Okay.

15 Q. And you see a paragraph that starts on
16 line 25 on page 11?

17 A. Yeah.

18 Q. It says (as read):

19 "Polyethylene glycol --" which is also
20 called PEG -- "is used in biological applications
21 because it has properties that are highly desirable
22 and is generally approved for biological or
23 biotechnical applications."

24 And the next sentence says (as read):

25 "PEG typically is clear, colorless,

1 odorless, soluble in water."

2 Do you see that?

3 A. Yes.

4 Q. So here it describes PEG as having good
5 water suitability; correct?

6 A. PEG by itself.

7 If you attach a PEG to something you
8 attach to it is not soluble, may be not soluble
9 enough.

10 Q. But here in Harris it does say PEG has
11 good water solubility; right?

12 A. By itself.

13 MR. HOUSTON: Objection. Form.

14 A. PEG by itself is water soluble.

15 Q. Right. And then -- but it does not say
16 once you attach the PEG to another group together
17 the product will not be water soluble; correct?
18 You don't see anywhere here it says --

19 A. Both know that, depending on whatever you
20 are attaching it to, the PEG won't be water soluble
21 enough. Stay hydrophobic. Whatever molecule it is
22 -- drugs, cell-binding agent. It's not soluble
23 enough -- not water soluble enough. I need
24 something more.

25 Q. So --

1 A. Harris doesn't say it. You're right.

2 (Court Reporter comment.)

3 Q. Harris doesn't say that; right?

4 A. Yeah, exactly.

5 Q. And then in Singh, for which you are a
6 co-inventor, Singh describes ADCs use PEG as the
7 linker; correct?

8 A. That's correct.

9 Q. And then Singh does not say the PEG linker
10 there was not enough for water solubility; correct?
11 In Singh the --

12 A. Yeah, PEG -- PEG was enough for -- for
13 whatever -- in Singh PEG was enough. Didn't need
14 anything else.

15 Q. Okay.

16 MR. HOUSTON: At this point the court
17 reporter is asking for a break.

18 MS. LOU: Yeah, we should take a break.

19 (Recess was taken.)

20 Q. Welcome back. Let's go to paragraph 29 of
21 your second declaration.

22 A. What page is that, please?

23 Q. Page 19.

24 A. Page 19, yes.

25 Q. So I just want you to take a moment to

1 read paragraph 29.

2 A. Yeah. (Witness reviews document.) Okay.

3 Q. So here you cite Singh, which is Exhibit
4 1008, figure 36; correct?

5 A. Okay.

6 Q. So I can show you Singh, which is Exhibit
7 1008.

8 (Exhibit 1008, previously marked.)

9 Q. Okay. So I just handed you Singh.

10 A. Page 36, you said?

11 Q. Figure 36.

12 A. Which page is that? Let me see.

13 Q. So it's at the front of the --

14 A. Yes, I see.

15 Q. And here you cite figure 36 and then in
16 figure 36 it's a figure "Surviving Fraction" data
17 for 6 molecules; correct?

18 A. That's correct.

19 Q. And I just want to go a few pages back to
20 page 4 of this patent application.

21 A. Page 4.

22 Q. After the figures.

23 MR. HOUSTON: Would you refer to the page
24 number at the bottom?

25 MS. LOU: Oh, you're right.

1 Q. The page number at the bottom is 57.

2 A. Okay.

3 Q. And I want to direct your attention to
4 paragraph 58.

5 Do you see that?

6 A. Page 57? No.

7 Q. Page 57 on the bottom, you see the number
8 page 57; right?

9 A. 58 --

10 Q. Paragraph 58, to the left column?

11 A. Yeah.

12 Q. And it says "Figure 36 shows in vitro
13 potency of anti-CanAg antibody --"

14 A. Yeah.

15 Q. And then -- mean -- "conjugates with 4 to
16 17 D/A toward multidrug-resistant --"

17 A. Yup.

18 Q. -- "multidrug-resistant cells"; correct?

19 A. Yeah.

20 Q. So I just want to confirm figure 36
21 describes the biological data --

22 A. That's right.

23 Q. -- for the six compounds; right?

24 A. That's correct.

25 Q. So figure 36 does not really say what's

1 the solubility of these compounds; correct?

2 A. That's correct, yes.

3 Q. And none of the linkers of the six
4 compounds described in figure 36 includes a
5 sulfone --

6 A. That's correct.

7 Q. -- linker; right?

8 A. That's correct, yes.

9 Q. And so, Doctor Chari, do you know what
10 LogP is?

11 A. What is what?

12 Q. LogP.

13 (Court Reporter comment.)

14 A. Log -- LogP?

15 Q. LogP.

16 A. Yeah, solubility. That's correct. Yeah.

17 MR. HOUSTON: Objection. Form.

18 (Court Reporter comment.)

19 A. Measure of solubility. Water solubility.

20 Q. Right. And do chemists -- does a chemist
21 use software to calculate LogP?

22 A. All they can measure they can also measure
23 -- physically measure it or through software.

24 Q. Yeah. So you can either experimentally
25 measure LogP --

1 A. That's correct.

2 Q. -- or use a software.

3 A. Exactly.

4 Q. Do you yourself calculate LogP of a
5 compound you designed?

6 A. No. We just look it -- look it up. If we
7 can find it. Either look it up in the chemical
8 literature, chemical abstract you can have LogP
9 calculated. Sometimes measure it. But we often
10 don't measure it.

11 Q. Right. And LogP is an indicator for
12 hydrophobicity --

13 A. That's correct.

14 Q. -- or hydrophilicity of a molecule; right?
15 (Court Reporter comment.)

16 A. Oh, sorry.

17 Q. That's right, right?

18 A. That's correct.

19 Q. Yeah. So you did not provide any LogP
20 calculation for any of the compounds containing
21 maleimide or vinyl sulfone in your declaration;
22 correct?

23 A. That's correct.

24 Q. Okay. And you did not provide any data to
25 show vinyl sulfone will have better solubility than

1 maleimide in your declaration; correct?

2 A. That's correct.

3 Q. And let's go to your first declaration.

4 A. Okay.

5 Q. In paragraph 133 --

6 A. Page?

7 Q. I'm getting there.

8 Paragraph 133 on page 74.

9 A. Okay.

10 Q. And here you analyzed dependent claim 2
11 for ground 3; correct?

12 A. Yeah.

13 Q. Again you reproduced language from claim 2
14 requiring Z to comprise at least one of the
15 functional group listed in the claim; right?

16 A. Yeah.

17 Q. And -- and this paragraph is the only
18 paragraph where you discussed claim 2 for ground 3;
19 right?

20 (Court Reporter comment.)

21 A. This is correct.

22 Q. And let's go to your -- so Doctor Chari,
23 when the POSA designs linkers for antibody drug
24 conjugates, they would try to design linkers that
25 are stable; right?

1 MR. HOUSTON: Objection. Form.

2 A. Stable in what?

3 Q. That's chemically stable.

4 MR. HOUSTON: Objection. Form.

5 A. Well, you know, sometimes you could say
6 less stable, some of the approved conjugates are
7 less stable. So it's not known the requirement.
8 You are right. For example, there is one antibody
9 ADC approved --

10 MR. HOUSTON: Can you say that more
11 slowly?

12 A. -- ADC approved with a half-life of six
13 hours in patients. Six hours. Very short. But it
14 works. So you cannot say POSA will say longer is
15 better. Not necessarily. May be also toxic. You
16 just don't know. Rules doesn't reach -- rules are
17 different for each component that would not
18 conjugate. Sometimes the drug requires it to be
19 water stable.

20 (Environmental sounds.)

21 (Discussion off the record.)

22 Q. Did you say water stable?

23 A. Yes, sometimes a drug can be less stable.

24 Q. Less stable?

25 A. Less stable. Doesn't have to be highly

1 stable.

2 Q. Would a POSA include a sulfonic ester as
3 part of a linker for ADC?

4 MR. HOUSTON: Objection.

5 A. Sulfonic ester?

6 Q. Sulfonic ester.

7 MR. HOUSTON: Objection. Form.

8 A. Sulfone ester...

9 Q. So it's the structure where you have an
10 oxygen attached to a sulfur and the sulfur has two
11 other oxygens attached to it and then another
12 valency to --

13 A. So --

14 MR. HOUSTON: Objection. Form.

15 A. -- may be unstable.

16 THE WITNESS: Oh, sorry.

17 MR. HOUSTON: When I'm doing this
18 (indicating), let me object.

19 Objection. Form. Beyond the scope.

20 A. May be unstable. Sulfone esters are
21 typically unstable.

22 Q. So sulfonated esters are not stable.

23 A. Might be unstable depending on condition,
24 where the sulfone ester is in the molecule.

25 Q. Okay. And then would the POSA include a

1 sulfonic ester as part of the linker in the middle
2 of the linker?

3 MR. HOUSTON: Objection. Form. Beyond
4 the scope.

5 A. Where -- what -- would it make it more
6 soluble?

7 Q. For any reason.

8 A. The problem is the way it's linked. If
9 linked via O, sulfones as are not --

10 (Court Reporter comment.)

11 A. -- known to be stable. Hydro --

12 Q. So let me understand what you just said.

13 The problem is the way it linked. If
14 linked via a -- via a -- oxygen, it is known to be
15 stable or known to be unstable?

16 A. Unstable.

17 Q. Unstable. So if oxygen is attached to a
18 sulfur and then that sulfur has two other oxygens
19 attached to it --

20 A. Would be unstable.

21 Q. -- then it will be unstable.

22 MR. HOUSTON: Objection. Same. Same
23 objections.

24 THE WITNESS: You want to tell beyond the
25 scope; right?

1 MR. HOUSTON: My objections are beyond the
2 scope and form.

3 You may answer if you can.

4 THE WITNESS: Okay.

5 Q. So a sulfonic ester would be unstable;
6 correct?

7 MR. HOUSTON: Same objections.

8 A. Yes, depending on the pH and depending on
9 what -- many factors, you know, like condition,
10 buffer, pH.

11 Could be anything.

12 Q. Okay. And would the POSA be motivated to
13 include a sulfonic ester as part of the linker?

14 MR. HOUSTON: Same objections.

15 A. The linker...

16 If it confers the right properties, makes
17 it --

18 (Court Reporter comment.)

19 A. -- right properties, it gives them
20 solubility and stability, yes. But all depends on
21 the structure of the molecule that they design and
22 properties.

23 Q. I see.

24 So -- but you just said sulfonic esters
25 are not stable; right?

1 A. But I also mentioned to you earlier
2 stability may not be important for an ADC. People
3 don't know what's important. It's a balance of
4 stability and activity and toxicity. Many factors
5 that come into play -- stability, activity,
6 toxicity.

7 Q. Okay. What's the -- another physiological
8 pH, like pH 7.4, how long would a sulfonic ester
9 stay a sulfonic ester without breaking apart?

10 MR. HOUSTON: Objection. Beyond the
11 scope. Form.

12 A. Depends on, like I said, the molecule
13 where it's located, how it's linked. But -- but I
14 can't tell you without looking at a structure of a
15 molecule how stable it would be. Maybe it's
16 enough.

17 Like I said, people have used esters,
18 carbonate esters, carbonate; half-life six hour on
19 patients. Approved drug.

20 (Court Reporter.)

21 A. Half-life six hours patient.

22 MR. HOUSTON: Half-life of six hours.
23 Correct me if I'm wrong.

24 Can you say it more clearly for the court
25 reporter?

1 A. Half-life of six hours in patients with
2 approved ADC. ADC is an antibody drug conjugate.

3 (Court Reporter comment.)

4 Q. Do you have an estimate of the half-life
5 for a sulfonate ester?

6 MR. HOUSTON: Objection. Beyond the
7 scope. Form.

8 A. Again, like I said, depending on where
9 it's located, the structure and what half-life and
10 what, I don't like to say no.

11 (Court Reporter comment.)

12 A. I don't like to say no without looking at
13 structure, and can't predict half-life.

14 Q. But the half-life could be as short as a
15 few hours; right?

16 MR. HOUSTON: Same objections.

17 A. I have no -- I have no idea. Could be six
18 hours. Could be 24 hours. Just don't know.

19 Q. Are you aware of any ADC drug that
20 contains a sulfonate ester as part of the linker?

21 A. No, I'm not aware. Nobody disclosed it
22 anyway.

23 MS. LOU: So we'll just take a quick
24 five-minute break and I will come back. Is that
25 okay?

1 (Recess was taken.)

2 MS. LOU: We have nothing further for now.

3 Thank you, Doctor Chari.

4 MR. HOUSTON: So we'll take a break and
5 consider redirect. Maybe we should go off the
6 record.

7 (Recess was taken.)

8 (Whereupon the deposition recessed at
9 12:29 p.m.)

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AFTERNOON SESSION (1:20 PM)

EXAMINATION

BY MR. HOUSTON:

Q. Doctor Chari, could you try to find the Singh exhibit that you were asked about earlier today. That might be it right in your hand, actually.

A. This one (indicating).

Q. Is that Exhibit 1008?

A. Yeah, page -- figure 36, you said; right?

Q. Well, is that -- first of all, is that Exhibit 1008 that you have?

A. Yeah, that's right. Figure 36.

Q. Okay. If you could turn to figure 36.

A. Yeah.

Q. Do you recall being asked about figure 36 earlier --

A. Yes.

Q. -- today?

Could you explain what figure 36 shows?

A. Figure 36 shows we have the drug-to-antibody ratio, D-A-R, the same, is always 4. Longer PEG is less active. Why is it not active? Because they're biologically not as exposed to put into a -- into -- where it has to go

1 basically. Biologically less active. Not
2 necessarily better, but it's less active. Shows
3 here in this figure it's less active in vitro.

4 Q. So a longer PEG makes the drug less
5 active.

6 Is that what you're saying?

7 A. Exactly. Doesn't get to a target because
8 it's too hydrophilic. It stays inside the -- it
9 doesn't get into a target.

10 Q. Okay. Okay. You can set that exhibit to
11 the side.

12 A. Okay.

13 Q. And see if you can find the Harris
14 exhibit, which should be 1007.

15 A. Harris? What patent? Okay.

16 Which page did you want to go to in this
17 one?

18 Q. Well, first do you recall being asked
19 about what Harris teaches?

20 A. Let me make sure this is...

21 Q. Okay. Yes, please.

22 A. Sorry. That's not Harris. Sorry. Wrong
23 one. How many papers are you going to give me?
24 That's Harris here.

25 Q. Do you have Exhibit 1007?

1 A. Yeah. That's correct, yes.

2 Q. Okay. Do you recall -- and that's the
3 Harris reference; correct?

4 A. Yeah. Yeah.

5 Q. Okay. Do you recall being asked where
6 Harris teaches that sulfone adds to the
7 hydrophilicity of the linker?

8 A. That's correct, yes.

9 Q. Okay. Could I ask you to turn to -- I'll
10 use the page numbers at the bottom --

11 A. Okay.

12 Q. -- page 21.

13 A. Are you -- are you -- page 21. Yes.
14 Okay.

15 Q. Let me know when you're there.

16 A. Yeah.

17 Q. I want to direct your attention to the
18 very bottommost paragraph.

19 Do you see that?

20 A. Yeah.

21 Q. There it's talking about the polymer
22 derivative timeframes; correct?

23 A. Yes.

24 Q. And you understand that to include
25 sulfones?

1 A. Yeah, active -- said active polymer,
2 active means sulfones, yeah.

3 Q. Okay. And it goes on to say that they (as
4 read):

5 "...are considered infinitely soluble in
6 water or as approaching infinite solubility."

7 A. That's correct.

8 Q. Do you see that?

9 A. That's correct, yes.

10 Q. And then it says and they can enhance --
11 they (as read):

12 "...can enable otherwise insoluble
13 molecules to pass into solution when conjugated
14 with the derivative."

15 Do you see that?

16 A. That's correct, yes.

17 Q. Would a POSA have understood that PEG
18 alone could exhibit those same properties?

19 MS. LOU: Objection. Form.

20 A. I don't think -- I don't think a POSA
21 would --

22 (Court Reporter comment.)

23 A. I don't think a POSA would agree that a
24 PEG alone would increase solubility like to
25 infinite solubility, infinite solubility --

1 hydrophobic molecule.

2 Q. Does that discussion in the paragraph at
3 the bottom of page 21 suggest to a POSA that the
4 sulfone is contributing to those properties?

5 A. Absolutely, yes.

6 Whatever this paragraph...

7 Q. When vinyl sulfone reacts to form a
8 linkage with a cell-binding agent or a drug, does
9 that lead to the creation of sulfone carbonates?

10 MS. LOU: Objection to form.

11 A. Sulfone carbonate...

12 No.

13 Q. Does it lead to the creation of sulfone
14 esters?

15 MS. LOU: Objection to form.

16 A. No.

17 Q. If you have a linker that has a vinyl
18 sulfone group in the middle of the linker, would
19 that vinyl sulfone group still be reactive?

20 A. I don't see why not. Yes, it should be.
21 If sulfone vinyl is available for reaction, it
22 should react.

23 Q. Could you find in your stack of papers
24 your first declaration, which should be Exhibit
25 1003.

1 A. Okay.

2 Q. 1003.

3 A. Which page are you looking?

4 Q. If you have that exhibit, then I'll ask
5 you to turn to pages 48 and 49, which is where your
6 table B2 is.

7 A. Yeah. Yes.

8 Q. Let me know when you're there.

9 A. Yeah.

10 Q. Okay. Do you see in table B2 -- yes,
11 table B2, in various boxes for the Y or the Z you
12 show a vinyl group --

13 A. Right.

14 Q. -- correct?

15 A. Yes.

16 Q. When undergoing a Michael addition type
17 reaction, would you expect the vinyl alone to be
18 what -- to cause the reaction?

19 A. No. You need a -- Michael reaction would
20 require something besides a vinyl.

21 Q. What in Morales-Sanfrutos -- what is
22 helping the vinyl react in that case?

23 A. The sulfonate group is helping the vinyl
24 react in the Michael reaction.

25 Q. Is the sulfone group itself actually

1 reacting in the Michael-addition-type reaction?

2 MS. LOU: Objection to form.

3 A. No, double-bonded reaction.

4 (Court Reporter comment.)

5 A. Double-bonded react -- vinyl group reacts
6 with the -- with the molecule to reacting...

7 Q. Are there other reaction schemes where the
8 vinyl alone can react?

9 MS. LOU: Objection to form.

10 A. Yes, like a -- like I showed before, there
11 is the free radical reaction. Those are reaction
12 which are more harsh conditions, but --

13 (Court Reporter comment.)

14 A. Given the right cell-binding agent that
15 can tolerate the harsh conditions, one could get
16 reaction by, for example, heat-induced, you know,
17 reaction.

18 Q. Are there -- does a POSA -- is a -- sorry.
19 Let me start again.

20 Is a POSA aware of cell-binding agents
21 that can survive those types of reaction
22 conditions --

23 A. Can --

24 Q. -- where -- let me finish, please.

25 A. Sorry.

1 Q. -- where the vinyl alone is doing the
2 reaction?

3 MS. LOU: Objection to form. Leading.

4 A. Cell binding is a widely known -- among
5 small molecules, small molecule, that could survive
6 any conditions you asked them to survive.

7 Proteins are more sensitive, but small
8 molecules can survive harsh conditions.

9 Q. Do all cell-binding agents contain
10 disulfide bonds?

11 MS. LOU: Objection to form. Leading.

12 A. Many don't. Many don't.

13 Very few do, actually.

14 Q. How would a POSA go about connecting a
15 cell-binding agent to a vinyl group when you want
16 just the vinyl group by itself to be what's
17 reacting?

18 MS. LOU: Objection to form.

19 A. You could introduce thiol on the
20 molecule --

21 (Court Reporter comment.)

22 Q. Doctor Chari, did you say introduce?

23 A. Yeah.

24 Q. Okay.

25 A. Introduce a thiol in a site away from the

1 binding of the cell-binding molecule. Okay.

2 That's one way to do it.

3 You can also do a double bond and have the
4 heat reaction, but that's specific cases. But
5 thiol is widely applicable for the radical
6 reaction.

7 (Court Reporter comment.)

8 Q. Would a POSA have known how to modify a
9 cell-binding agent as needed to get that reaction
10 to occur?

11 MS. LOU: Objection to form. Scope.

12 A. You can -- a thiol on any molecule --

13 (Court Reporter comment.)

14 A. -- any molecule you want as long as it
15 doesn't affect binding. You have to find the right
16 site --

17 (Court Reporter comment.)

18 A. -- any molecule you want as long as
19 they're the right site the thiol goes in.

20 Q. And a POSA would know how to do that?

21 A. Absolutely. Yes.

22 MR. HOUSTON: Okay. I have no further
23 questions, Doctor Chari. Thank you.

24 MS. LOU: We'll take a five-minute break,
25 five-, 10-minute break and then come back here.

1 (Recess was taken.)

2 MS. LOU: So we have no more questions.

3 Thank you.

4 COURT REPORTER: PDF? I have an order for
5 Monday delivery.

6 MS. LOU: If we can get a rough by Friday?

7 COURT REPORTER: Yes.

8 MS. LOU: And Monday the final.

9 (Whereupon the deposition ended at
10 1:42 p.m.)

SYNAFFIX B.V. vs. HANGZOU DAC BIOTECH CO., LTD.

4/16/2025 - RAVI J. CHARI, PhD

ACKNOWLEDGEMENT OF DEPONENT

I, RAVI J. CHARI, PhD, do hereby declare that I have read the foregoing transcript, I have made any corrections, additions, or changes I deemed necessary as noted on the Errata to be appended hereto, and that the same is a true, correct and complete transcript of the testimony given by me.

RAVI J. CHARI, PhD

Date

*If notary is required

SUBSCRIBED AND SWORN TO BEFORE ME THIS

_____ DAY OF _____, 20____.

NOTARY PUBLIC

Commonwealth of Massachusetts
Middlesex, ss.

I, P. Jodi Ohnemus, Notary Public
in and for the Commonwealth of Massachusetts,
do hereby certify that there came before me on the
16th day of April, 2025, the deponent herein, who
was duly sworn by me; that the ensuing examination
upon oath of the said deponent was reported
stenographically by me and transcribed into
typewriting under my direction and control; and
that the within transcript is a true record of the
questions asked and answers given at said
deposition.

I FURTHER CERTIFY that I am neither
attorney nor counsel for, nor related to or
employed by any of the parties to the action
in which this deposition is taken; and, further,
that I am not a relative or employee of any
attorney or financially interested in the outcome
of the action.

IN WITNESS WHEREOF I have hereunto set my
hand and affixed my seal of office this
19th day of April, 2025, at Waltham.



P. Jodi Ohnemus, RPR, RMR, CRR,
CSR, Notary Public,
Commonwealth of Massachusetts
My Commission Expires:
3/3/2028

SYNAFFIX B.V. vs. HANGZOU DAC BIOTECH CO., LTD.

4/16/2025 - RAVI J. CHARI, PhD

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RAVI J. CHARI, PhD

Date

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Federal Rules of Civil Procedure

Rule 30

(e) Review By the Witness; Changes.

(1) Review; Statement of Changes. On request by the deponent or a party before the deposition is completed, the deponent must be allowed 30 days after being notified by the officer that the transcript or recording is available in which:

(A) to review the transcript or recording; and

(B) if there are changes in form or substance, to sign a statement listing the changes and the reasons for making them.

(2) Changes Indicated in the Officer's Certificate. The officer must note in the certificate prescribed by Rule 30(f)(1) whether a review was requested and, if so, must attach any changes the deponent makes during the 30-day period.

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VERITEXT LEGAL SOLUTIONS

COMPANY CERTIFICATE AND DISCLOSURE STATEMENT

Veritext Legal Solutions represents that the foregoing transcript is a true, correct and complete transcript of the colloquies, questions and answers as submitted by the court reporter. Veritext Legal Solutions further represents that the attached exhibits, if any, are true, correct and complete documents as submitted by the court reporter and/or attorneys in relation to this deposition and that the documents were processed in accordance with our litigation support and production standards.

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