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UNITED STATES PATENT AND TRADE OFFICE
BEFORE THE PATENT TRIAL AND APPEAL BOARD

CONJUPRO BIOTHERAPEUTICS,	)	
INC.,	)	
	)	
Petitioner,	)	
	)	
vs.	)	Case No. PGR2025-00057
	)	Patent No. 12,234,236
ASCLETIS PHARMA CHINA	)	
CO. LTD.,	)	
	)	
Patent Owner.	)	

DEPOSITION OF MICHAEL C. PIRRUNG, Ph.D.
THURSDAY, FEBRUARY 26, 2026
LOS ANGELES, CALIFORNIA

Reported by: Adele C. Freeman, CSR No. 9690, RPR, CRR, RMR

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UNITED STATES PATENT AND TRADE OFFICE
BEFORE THE PATENT TRIAL AND APPEAL BOARD

CONJUPRO BIOTHERAPEUTICS, INC.,	)	
	)	
Petitioner,	)	
	)	
vs.	)	Case No. PGR2025-00057
	)	Patent No. 12,234,236
ASCLETIS PHARMA CHINA CO. LTD.,	)	
	)	
Patent Owner.	)	

DEPOSITION OF MICHAEL C. PIRRUNG, Ph.D., taken on behalf of
the Ascletis Pharma China Co., Ltd., Patent Owner, with some
parties appearing remotely, at 10250 Constellation Boulevard,
Suite 900, Los Angeles, California, commencing at 9:08 a.m.
and terminating at 1:32 p.m., on Thursday, February 26, 2026,
before Adele C. Freeman, Certified Shorthand Reporter No.
9690 for the State of California, pursuant to Notice.

1 APPEARANCES OF COUNSEL:

3 For Petitioner:

4 FOX ROTHSCHILD
5 BY: JOE CHEN, Ph.D., ESQ.
6 ZIN ZHU, Ph.D., ESQ. (Remote)
7 212 Carnegie Center, Suite 400
8 Princeton, New Jersey 08540
9 609-844-3024
10 joechen@foxrothschild.com

9 For Patent Owner Ascletis Pharma China, Co., Ltd.:

10 COOLEY, LLP
11 BY: GEOFFREY D. BIEGLER
12 ISHA AGARWAL
13 1299 Pennsylvania Avenue, NW, Suite 700
14 Washington, DC 20004-2400
15 Gbiegler@cooley.com
16 Iagarwal@cooley.com

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1 LOS ANGELES, CALIFORNIA; THURSDAY, FEBRUARY 26, 2026

2 9:08 A.M.

3 -000-

4
5 THE REPORTER: Before I swear in the witness, I
6 would like to state for the record that I am a Certified
7 Shorthand Reporter licensed by the State of California,
8 California License No. 9690.

9
10 MICHAEL PIRRUNG, Ph.D.,
11 having been first duly sworn, testified as follows:

12
13 EXAMINATION

14 BY MR. BIEGLER:

15 Q. Sir, could you please state your full name
16 for the record.

17 A. Michael Craig Pirrung.

18 Q. I introduced myself off the record. My
19 name is Geoff Biegler. I'm an attorney at Cooley
20 representing the patent owner in this case. I'm
21 going to ask you some questions today, obviously.

22 Have you been deposed before?

23 A. I have.

24 Q. Okay. How many times, approximately?

25 A. A dozen.

1 Q. And you understand that you are now under
2 oath?

3 A. I do.

4 Q. And you understand that that means you have
5 to testify truthfully, accurately, and completely
6 today?

7 A. Yes.

8 Q. Is there any reason you can't do that
9 today, whether for a medical reason or any other
10 reason?

11 A. There's no reason I can't testify
12 truthfully.

13 Q. Okay. Great.

14 And if that changes during the course of
15 the deposition, will you let me know right away?

16 A. I will do that.

17 Q. Okay. Great.

18 You understand that the deposition today is
19 being recorded, transcribed by the court reporter,
20 correct?

21 A. I do.

22 Q. Okay. And you understand that the
23 transcript of the deposition might be shown to the
24 judges in this proceeding, correct?

25 A. Yes, I do.

1 Q. Okay. Probably, as you're used to, we can
2 take a break about every hour, but if you need a
3 break at any time, just let me know.

4 A. Yup.

5 Q. So you're currently a professor of
6 chemistry at the University of California Riverside,
7 correct?

8 A. That's right.

9 Q. And I think you were telling me off the
10 record that you also have an appointment at U.C.
11 Irvine; is that right?

12 A. That's correct.

13 Q. Okay. And you have a Ph.D. in organic
14 chemistry, correct?

15 A. I do.

16 Q. You have experience in small-molecule drug
17 discovery?

18 A. I do.

19 Q. Have you, over the course of your career,
20 undertaken efforts to discover or design a new
21 small-molecule drug?

22 A. I have.

23 Q. Approximately how many times have you been
24 involved in those sorts of efforts?

25 A. I guess I've worked on a dozen or so

1 small-molecule drug projects.

2 Q. And in those projects -- those 12 projects,
3 were you actually involved in the discovery of the
4 small-molecule or the development or both?

5 A. In some cases, there was a discovered
6 compound that was the basis of the project that we
7 were working on, and in some cases, the project was
8 focused on discovering a compound that would be the
9 basis of a drug development project.

10 Q. Okay. So I think -- let me see if I got
11 this right.

12 You're saying in some of those cases, there
13 was already a drug discovered, and you were doing
14 some additional work on it, and in other cases, the
15 project was focused on discovering the compound
16 itself --

17 A. Correct.

18 Q. -- is that right?

19 Okay. I know you have a lot of experience
20 in the synthesis of organic compounds, correct?

21 A. That's right.

22 Q. So what I want to get at is, in how many of
23 those approximately dozen instances you testified
24 about were you actually involved in discovering the
25 new small-molecule?

1 MR. CHEN: Objection. Form.

2 THE WITNESS: So I'd like to hear the question
3 again.

4 BY MR. BIEGLER:

5 Q. Yeah, I can probably state it better.

6 How many times have you been involved in an
7 effort to actually discover a new small-molecule?

8 A. Approximately five.

9 Q. Okay. And in some instances where you're
10 working to discover a new small-molecule, you might
11 do screening, correct?

12 A. Right.

13 Q. And in other instances, you might have a
14 known compound that you attempt to modify; is that
15 fair?

16 A. So the two scenarios you describe are not
17 either/or. Screening is -- I mean, screening is just
18 a test, right, some sort of test of biological
19 activity, and so, yeah, in some cases, there is a
20 molecule that has some identified biological
21 activity, and one wants to turn that into an actual
22 drug, and in some cases, you're looking for that
23 molecule that has some biological activity that could
24 be the basis for being turned into a drug.

25 Q. Fair enough. Thank you for that

1 explanation.

2 So what I want to ask, then, is this, in
3 how many instances have you attempted to modify or
4 improve an existing molecule that you knew had some
5 sort of biological activity?

6 A. Right. Yeah, at least three.

7 Q. Okay. And you refer in your declaration,
8 in part of it, to structure-based drug design; is
9 that familiar?

10 A. It is familiar, but if you want me to
11 comment on my declaration, I should probably look at
12 it.

13 Q. Yeah, I can give it to you in a second. I
14 want to just ask some general questions --

15 A. Okay.

16 Q. -- if you can, if you want to see the
17 declaration, that's fine, too --

18 A. All right.

19 Q. -- but I just wanted to ask you what is
20 structure-based drug design in your experience?

21 A. So in some cases, one works on developing
22 active compounds without knowledge of the
23 three-dimensional structure of the target --

24 Q. Uh-huh.

25 A. -- but there has been a very significant

1 effort over the past many decades in determining the
2 structures of many biomolecules, some of which are
3 drug targets.

4 And so when you have the structure of your
5 drug target, and in some cases, with small-molecule
6 drug candidates bound to them, that can be very
7 informative to chemists who are aiming to make
8 structural changes their drug candidates in order to
9 come up with their best compounds.

10 Q. Okay. And have you been involved in
11 efforts to discover or to modify a small-molecule
12 using that sort of information, structure-based drug
13 design?

14 A. The projects that I worked on haven't
15 usually had a structure of the drug target, but in
16 the 25 years of the scholarship that I've practiced
17 in pharmaceutical and medicinal chemistry, I've been
18 very familiar with the literature of that -- of that
19 field and the practice of practitioners who I have
20 worked with as consultants, and I have taught that in
21 classes to graduate students.

22 So I'm still very familiar with the field
23 of structure-based drug design, even if that has not
24 been a modality that I can use in the projects that
25 I've pursued myself.

1 Q. Okay. And so let me just back up a little
2 bit. I think I just want to make sure I get one
3 thing clear.

4 You testified that you had been involved in
5 approximately five efforts to actually discover a new
6 small-molecule, and then we talked about your
7 involvement in efforts to modify a known drug with
8 biological properties. You said you'd done that
9 about three times.

10 Are those two things -- those two -- let me
11 see how I can say this.

12 Are the five times and the three times, are
13 those exclusive, or is it -- how should I say this?

14 Were those -- do those projects overlap at
15 all?

16 MR. CHEN: Objection. Form.

17 THE WITNESS: Probably -- I mean, there really is a
18 difference when you're -- when you have a structure to begin
19 with that came from other people's efforts or whatever versus
20 trying to discover a new compound, and, in fact, the
21 development of methods to find new compounds was something
22 that I spent a significant amount of my time on, and so
23 they -- they do tend to be exclusive --

24 BY MR. BIEGLER:

25 Q. Okay.

1 A. -- in -- I mean, I wouldn't make an
2 absolute statement about that, but like I said, about
3 three, about five, it could have been more --

4 Q. Yeah.

5 A. -- so that's...

6 Q. So just -- let me see if I can ask the
7 question a little bit better.

8 Is it correct that there was approximately
9 five projects you were involved in to actually
10 discover a new small-molecule, and then three --
11 approximately three separate projects where you
12 worked to modify a known compound?

13 A. Fair. Fair enough, yes.

14 Q. Okay. And in none of those eight --
15 approximately eight total instances, were you able
16 to -- let me strike that and start over.

17 In none of those eight projects or
18 instances did you actually apply structure-based drug
19 design; is that true?

20 MR. CHEN: Objection. Form.

21 THE WITNESS: Structure-based drug design was not
22 available in the projects that I've worked on because the
23 structures of the targets were not available.

24 BY MR. BIEGLER:

25 Q. Right.

1 So the answer's no, correct?

2 A. Right.

3 Q. Okay. And are you familiar with the
4 concept of a target compound profile?

5 MR. CHEN: Objection. Form.

6 THE WITNESS: I'd like to hear a definition of
7 that.

8 BY MR. BIEGLER:

9 Q. Yeah.

10 MR. BIEGLER: Let me just mark an exhibit,
11 actually. Can you give me the worksheet, please.

12 Do we know what exhibit number we're on?

13 MS. AGARWAL: Yes, 2032.

14 MR. BIEGLER: Can we mark that 2032.

15 (Exhibit 2032 identified.)

16 BY MR. BIEGLER:

17 Q. I've handed you what I've marked as
18 Exhibit 2032, and on its face, it's an article
19 titled, Accelerated Drug Discovery by Rapid Candidate
20 Drug Identification. The first author is Fredrik
21 Bergstrom.

22 Have you ever seen this paper before?

23 A. Never.

24 Q. Okay. Well, let me just see if this sort
25 of gets us anywhere on this concept of a compound

1 target profile.

2 So the second sentence, it says, "To
3 facilitate the rapid identification of a potential CD
4 and CD," and CD is defined earlier as candidate drug,
5 "a thoroughly worked-out CD target profile (CDPT)
6 with criteria acceptable for the disease target
7 product profile (TPP) is required at the start of
8 lead generation (LG)."

9 Do you see that?

10 A. Sure.

11 Q. And so is that concept of having a
12 thoroughly worked out candidate drug target profile,
13 is something that's familiar to you?

14 MR. CHEN: Objection. Form.

15 THE WITNESS: It's not familiar at all.

16 BY MR. BIEGLER:

17 Q. Okay. So in the projects that you've
18 undertaken to discover or modify a small-molecule,
19 did you have a target profile in mind?

20 MR. CHEN: Objection. Form.

21 THE WITNESS: So the -- this -- this publication,
22 which lays out this idea of the candidate drug target
23 profile --

24 BY MR. BIEGLER:

25 Q. Uh-huh.

1 A. -- is new to me, and it is, I note, a
2 perspective, so it's not like a peer -- well, it
3 probably is peer reviewed, but it is the opinion of
4 these -- these authors about how they prefer to
5 conduct their drug discovery efforts.

6 And so, you know, I -- I don't think I can
7 answer any questions based on the -- the assumptions
8 and the world view that these particular authors put
9 out.

10 Q. Okay. That's fair. Let's put that aside.
11 I just want to ask you more generally. I was hoping
12 this might make the discussion easier.

13 A. Okay.

14 Q. But in your -- your approximately eight
15 efforts to discover or modify a small-molecule `drug,
16 did you have a profile in mind for what you were
17 trying to achieve, what properties the drug would
18 have?

19 A. Sure. Sure.

20 Q. Why is that?

21 A. Well, there are important criteria that we
22 apply to drug candidates that tell us how we're doing
23 in the drug discovery process.

24 Q. Okay. What are some examples of those?

25 A. They're metrics, right, so they're -- they

1 are -- depending on the exact type of -- of target
2 that we're working on, these metrics could include
3 inhibition constants for enzymes, binding constants
4 for proteins, affinities for nucleic acids, some sort
5 of measurement that one can make that is indicative
6 of the mode of action of the drug on its target site.

7 Q. And in the instances that you were
8 attempting to modify a known compound with some
9 biological activity, did you have a specific property
10 you were seeking to improve?

11 MR. CHEN: Objection. Form.

12 THE WITNESS: We were aiming, in one instance, to
13 make structural modifications that would make compounds more
14 drug-like, as well as maintain activity on their target site.

15 BY MR. BIEGLER:

16 Q. What do you mean by "drug-like"?

17 A. So there are a number of criteria that have
18 been developed over decades as to the sorts of
19 properties that most marketed drugs possess, and
20 there is, sort of -- there's some rules that have
21 been applied in this area, as well as there's just
22 the practice of the field as to what -- what a drug
23 looks like, and that would mean in a structural
24 sense.

25 So there's some metrics that fit the rules,

1 as well as structural things that are familiar to
2 someone who's -- who looks at a lot of drug
3 structures.

4 Q. What are the -- you mentioned the
5 properties that most marketed drugs possess, what
6 kind of properties were you referring to?

7 A. So.

8 MR. CHEN: Is that a question? Sorry, Counsel, is
9 that a question, or are you just talking to yourself?

10 BY MR. BIEGLER:

11 Q. Read the question.

12 MR. CHEN: Go ahead.

13 THE WITNESS: Should you read the question again?

14 THE REPORTER: Would you like it?

15 THE WITNESS: Yes.

16 MR. BIEGLER: I can ask it again.

17 BY MR. BIEGLER:

18 Q. When you mentioned that marketed drugs
19 possess certain properties, what properties were you
20 referring to?

21 A. So the most common codification of this is
22 in something that is familiar to -- to most
23 practitioners called Lipinski's Rules, and these
24 rules identify structural and physical chemical
25 features. The log of the octanol-water partition

1 coefficient; the number of NHs and OHs in the
2 compound; the number of Ns and Os in the compound;
3 and the molecular weight of the compound.

4 These are all important features for --
5 specifically for orally active drugs.

6 Q. But you'd agree that the purpose of
7 modifying an existing drug is to ultimately improve
8 some property of the drug to make it better, correct?

9 MR. CHEN: Objection. Form.

10 THE WITNESS: A goal in a drug development program
11 can be to make a compound better, but that's not the only
12 possible goal.

13 BY MR. BIEGLER:

14 Q. Okay. Have you been involved in the
15 discovery of salts of new small molecules?

16 MR. CHEN: Objection. Form.

17 THE WITNESS: I have not done that research in my
18 own lab.

19 BY MR. BIEGLER:

20 Q. Okay. When you say you haven't done it in
21 your own lab, have you done it in any other context?

22 A. I am familiar with the concepts of forming
23 salt derivatives of drug substances and different
24 crystalline forms of drug substances and other
25 matters that go beyond the -- sort of the first stage

1 of drug discovery where one is simply identifying
2 what the molecule that you're going to be using as a
3 drug is.

4 Q. So you're familiar with the concepts, but
5 you've never actually undertaken an effort to make a
6 salt of a new small-molecule --

7 MR. CHEN: Objection. Form.

8 BY MR. BIEGLER:

9 Q. -- is that right?

10 A. It would be intrinsic to the use of any
11 molecule that will form a salt in a biological assay
12 to form that salt. So I mean, numerous times in my
13 discovery program, we have prepared compounds that --
14 that do have salt-forming abilities, and we did that
15 in the course of our analysis of them.

16 Q. Sure. But -- okay, let me try to be more
17 specific.

18 Have you ever run a salt screen?

19 A. I'd have to know what you define as a "salt
20 screen".

21 Q. Trying to form salts for a small-molecule
22 with a number of different counterions.

23 A. I haven't done that in my lab, but it's a
24 very obvious thing that a chemist knows how to do to
25 form salts from compounds.

1 Q. And so since you haven't conducted a salt
2 screen yourself, you wouldn't know how often a
3 particular counterion might actually form a salt with
4 a new small-molecule; is that right?

5 MR. CHEN: Objection. Form.

6 THE WITNESS: On the basis of my understanding of
7 organic chemistry, I believe that the success rate of forming
8 salts from compounds is very high.

9 BY MR. BIEGLER:

10 Q. And so if you took a new small-molecule and
11 screened it with, let's just for round numbers' sake,
12 say 100 counterions, do you have an estimate of, on
13 average, how many would form salts?

14 A. So the premise of your question is faulty
15 because there's not 100 counterions available to make
16 salts from compounds.

17 Q. Okay. Well, in a typical salt screen --
18 let me back up. You asked me what I thought a salt
19 screen was.

20 What do you understand a salt screen to be?

21 A. I am not familiar with the concept, and I
22 can understand that one might want to make a number
23 of salts out of a drug development candidate, but the
24 purpose of making those salts is not -- would not be
25 simply to determine if they could be made.

1 Chemically, it would be expected that you
2 could make those salts, and there must be some other
3 purpose to having those salts to evaluate them for
4 desirability.

5 Q. When you say, "Clinically, it would be
6 expected that you could make those salts," you mean
7 that you could form some salt with some counterion
8 with a molecule; is that right? Did I understand
9 that correctly?

10 A. Did that question include the word
11 "clinically"?

12 Q. I don't think so.

13 A. I did hear that word.

14 Q. Hang on. Let me try again. I must have
15 misspoke.

16 MR. BIEGLER: I'd appreciate if you don't show the
17 witness the realtime.

18 THE WITNESS: Okay. No problem.

19 MR. BIEGLER: Sorry. Hang on a second. The word
20 was "chemically," so let me re-ask my question.

21 THE WITNESS: Okay.

22 MR. BIEGLER: I don't know if I said it wrong or
23 what happened --

24 THE WITNESS: Yes, please.

25 MR. BIEGLER: -- but that's what I did.

1 BY MR. BIEGLER:

2 Q. You said, chemically, it would be expected
3 you could make those salts.

4 Did you mean by that that you could form
5 just a salt with some counterion with a
6 small-molecule; is that what you're saying?

7 A. I believe, chemically, that I could form
8 salts of a compound that's a salt-forming compound
9 with the counterions that are available, which is --
10 you know, there are compounds that chemists identify
11 as alkaline metals and alkaline earths, and those are
12 common counterions that we encounter in chemistry,
13 and we would expect that we would be able to form
14 salts with those counterions.

15 Q. You'd agree that it's impossible to know in
16 advance whether a particular small molecule will form
17 a salt with a particular counterion without actually
18 running the experiment, right?

19 MR. CHEN: Objection. Form.

20 THE WITNESS: I disagree.

21 BY MR. BIEGLER:

22 Q. You think you can predict it ahead of time?

23 A. I do.

24 Q. But you've never actually undertaken that
25 effort, correct?

1 A. I am a chemist who understands the
2 principles of acid-based theory, and given the
3 appropriate reagents, I believe that salt-forming
4 compounds can be converted into their salts with a
5 variety of different counterions.

6 Q. Okay. If you do form a salt and you're
7 looking to develop a drug candidate, what properties
8 would you look at to determine if that salt is a
9 good -- a good form to move forward with?

10 MR. CHEN: Objection. Form.

11 BY MR. BIEGLER:

12 Q. Let me ask that question a little more
13 clearly.

14 What properties would you look at to
15 determine if a particular salt is a good candidate
16 for drug development?

17 MR. CHEN: Again, objection to form.

18 THE WITNESS: I don't know.

19 BY MR. BIEGLER:

20 Q. You've never worked on GLP-1R agonist
21 before this proceeding, correct?

22 MR. CHEN: Objection. Form.

23 THE WITNESS: My knowledge and experience in
24 25 years of practicing research in medicinal chemistry,
25 studying literature in medicinal chemistry, and teaching

1 medicinal chemistry is what I rely on in evaluating the art
2 in this case and forming my opinions. And specific
3 information relevant to this particular target is not
4 necessary to do that.

5 BY MR. BIEGLER:

6 Q. Fair enough, but that was not my question.
7 My question was quite simple, you've never
8 worked on GLP-1R agonist prior to this proceeding,
9 correct?

10 MR. CHEN: Objection. Form.

11 THE WITNESS: I have not done research on GLP-1R
12 receptor agonists.

13 BY MR. BIEGLER:

14 Q. Okay. So you've never attempted to
15 discover a new GLP-1R agonist, right?

16 MR. CHEN: Objection. Form.

17 THE WITNESS: That has not been a project that I've
18 worked on.

19 BY MR. BIEGLER:

20 Q. You've never attempted to modify an
21 existing GLP-1R agonist, correct?

22 A. That's correct.

23 Q. You had never worked with Orforglipron
24 before this matter, correct?

25 A. I have not worked with Orforglipron before.

1 Q. You had never studied the interactions of
2 Orforglipron with the GLP-1R receptor before this
3 matter, correct?

4 MR. CHEN: Objection. Form.

5 THE WITNESS: So I read the published literature
6 extensively and relevant literature in this area certainly is
7 something that I have read before the case -- this case.

8 BY MR. BIEGLER:

9 Q. But you had never actually studied the
10 interactions of Orforglipron with GLP-1 receptor
11 before this case, right?

12 MR. CHEN: Objection. Form.

13 THE WITNESS: I have certainly read relevant
14 articles for this case before I got involved in it.

15 BY MR. BIEGLER:

16 Q. Had you ever looked at the cryo-EM
17 structure, for instance, of the -- sorry, let me try
18 that again.

19 Had you ever looked at the cryo-EM
20 structure of Orforglipron bound to the GLP-1 receptor
21 before this case?

22 A. So I read the journals that most
23 cutting-edge medicinal chemistry would show up in,
24 including PNAS, in which that cryo paper was
25 published. And so I certainly would have seen that

1 paper when it appeared.

2 Q. Okay.

3 MR. BIEGLER: This already has an exhibit number,
4 doesn't it?

5 MS. AGARWAL: Yes, it's Exhibit 1002.

6 (Exhibit 1002 identified.)

7 BY MR. BIEGLER:

8 Q. So this -- I'm going to hand you -- sorry,
9 let me just put the exhibit number on here.

10 MR. BIEGLER: Say it again, 1002?

11 MS. AGARWAL: Yes.

12 THE WITNESS: Okay.

13 BY MR. BIEGLER:

14 Q. Do you recognize -- let me start over.

15 I've handed you what's been marked
16 previously as Exhibit 1002, and the title is the
17 Expert Declaration of Michael C. Pirrung, Ph.D.

18 Do you recognize this document?

19 A. I do.

20 Q. And this is your declaration in this
21 matter, correct?

22 A. Yes.

23 Q. Okay. And if we flip to page 207.

24 A. Yes.

25 Q. You signed this on June 15th, 2025,

1 correct?

2 A. That's correct.

3 Q. And when you prepared your declaration, did
4 you believe everything in it was true and accurate?

5 A. I did.

6 Q. Do you believe everything, sitting here
7 today, in your declaration is true and accurate?

8 A. I do.

9 Q. Have you noticed any errors in your
10 declaration since you submitted it?

11 A. I have not.

12 Q. Okay. And I'm just asking you for a time
13 period or a date here.

14 When were you first contacted about this
15 matter?

16 A. I don't recall.

17 Q. Do you recall roughly how long it was
18 before you submitted or signed this declaration on
19 June 15th, 2025?

20 A. I don't have a specific recollection of
21 being -- of how I was contacted about this.

22 Q. Okay. Do you know if it was a month, two
23 months, a year?

24 A. It was probably not a year, but -- but
25 between one month and six months, I couldn't say.

1 Q. Okay. So let's go to paragraph 20 of your
2 declaration, and I want to -- you see you have in
3 paragraph 20 a list of materials that you considered?

4 A. Right.

5 Q. Or a list of Exhibits it's entitled,
6 correct?

7 A. Right.

8 Q. And how did you select that list of
9 materials?

10 A. So -- I mean, obviously, there's -- well,
11 this list of materials is prior art to which I refer
12 in the declaration, and much of this art was
13 identified based on the structural similarities of
14 the compounds within it to Orforglipron, and then
15 there's other relevant art here that, you know,
16 supports some of the positions that I've taken.

17 Q. And of the prior art you identify in your
18 list of exhibits, what references were identified by
19 you, and which were identified by counsel or provided
20 to you?

21 A. I'm not sure.

22 Q. Okay. Well, let me ask you a baseline
23 question.

24 Were some of the references in this list of
25 exhibits provided to you by counsel?

1 A. Yes.

2 Q. Okay. Did you, yourself, identify any of
3 the prior art references in the list of exhibits
4 yourself?

5 A. Yes.

6 Q. And do you know which of these you
7 identified yourself versus being provided them by
8 counsel?

9 A. Can I hear the question again?

10 Q. Yeah.

11 Which of these exhibits did you identify,
12 as opposed to them being provided to you by counsel?

13 A. One would be Talele.

14 Q. Okay. Sorry, were you done?

15 A. Yes.

16 Q. Sorry, I thought you were still looking.
17 Sorry.

18 So is Talele the only reference here that
19 you recall identifying yourself in this list of
20 exhibits?

21 A. I'm not sure about any others.

22 Q. What about the Su references? Did you
23 identify those yourself?

24 MR. CHEN: I caution the witness, do not disclose
25 any previous communications with attorney.

1 THE WITNESS: Yeah, I -- I'm not sure about that.

2 BY MR. BIEGLER:

3 Q. So you don't remember identifying those
4 yourself?

5 A. I'm just not sure how to answer the
6 question, so.

7 Q. Well, I think the question is
8 straightforward.

9 It's just if you identified Su yourself or
10 it was provided to you by counsel?

11 A. I'm just not sure what freedom I have to
12 discuss that matter.

13 Q. If -- if there is a privilege objection,
14 your counsel will make it, otherwise, you're required
15 to answer my question, so let me just try it again.

16 A. So I thought that my counsel did make a
17 privilege objection.

18 Q. He didn't instruct you not to answer.

19 A. Okay.

20 Q. So my question again is, did you identify
21 Su yourself, or was it provided to you by counsel?

22 A. So counsel had Su.

23 Q. Okay. Let's switch gears a little bit.

24 I want to talk a little bit about the Kawai
25 reference.

1 A. Okay.

2 Q. And I think you start discussing that in
3 paragraph 52 of your declaration?

4 A. Okay.

5 Q. And Kawai discloses a high-resolution
6 cryo-electron microscopy, or cryo-EM, structure of
7 Orforglipron bound to the GLP-1 receptor, correct?

8 A. Yes, it does.

9 Q. Let me just start with this. What is a
10 cryo-electron microscopy structure?

11 A. The cryo part of that means very cold, and
12 so that indicates that in order to get the molecules
13 to be amenable to the analysis by electron
14 microscopy, they are very cold, very cold, and that
15 basically enables electron microscopy to be used to
16 visualize the molecules that are, basically, frozen
17 into place.

18 Q. And what's the output of that sort of
19 experiment?

20 MR. CHEN: Objection. Form.

21 THE WITNESS: So cryo-EM produces the goal of the
22 field generally called structural biology, which can be
23 obtained using a lot of different modalities that is,
24 basically, a three-dimensional view of the interaction
25 between -- well, of a biomolecule, first, that's what makes

1 it structural biology, and in some cases, it also involves
2 molecules that are interacting with the biomolecule.

3 BY MR. BIEGLER:

4 Q. And based on that three-dimensional view,
5 Kawai was able to create a three-dimensional model of
6 the protein ligand interaction; is that right?

7 THE REPORTER: Protein?

8 MR. BIEGLER: Ligand, L-I-G-A-N-D.

9 THE WITNESS: Yes. Kawai did that in his paper.

10 BY MR. BIEGLER:

11 Q. And that -- and to be clear, the protein in
12 ligand -- let me start over.

13 The three-dimensional model discussed in
14 Kawai is Orforglipron bound to the GLP-1 receptor,
15 correct?

16 A. That's correct.

17 Q. And that model was deposited in the Protein
18 Data Bank; is that right?

19 A. It was.

20 Q. What's the Protein Data Bank?

21 A. So there is a tradition of structural
22 biology, that when one determines the structure of a
23 biomolecule, that it's important to make that
24 available to the scientific world for their own uses,
25 and so a Protein Data Bank was created long ago, and

1 however people determine the structures that they
2 determined, there's generally, in scientific
3 publications, what's called a deposition requirement
4 that is after the publication appears, the authors
5 have a certain period of time in which they have to
6 make their structure available to the world by
7 putting it in this data bank that has access of
8 anyone without cost.

9 Q. And that thing is -- that data bank is
10 called the Protein Data Bank?

11 A. It is.

12 Q. And once -- once a structure is deposited
13 in the Protein Data Bank, it's accessible to the
14 public, right?

15 A. That's right.

16 Q. And I see that the Kawai model has a
17 Protein Data Bank ID code of 6X0X?

18 A. Yes, that's what their declaration says.

19 Q. What does that mean?

20 A. So -- I'm not sure.

21 Q. Okay. Fair enough.

22 You understand that to be some sort of
23 identification code that is used in Protein Data
24 Bank; is that your understanding?

25 A. I don't know about the Protein Data Bank

1 specifically, but there are other similar data banks,
2 such as the Cambridge Crystallographic Archive, where
3 particular structures are given particular ID
4 numbers, and that facilitates those who want to go to
5 the data bank and access the structures. They can
6 access based on the codes.

7 But I am familiar with that only from the
8 standpoint of Crystallographics structures, and not
9 PDB structures.

10 Q. Did you go to look, as part of your work
11 here, the cryo-EM structure model deposited in the
12 Protein Data Bank?

13 MR. CHEN: Objection. Form.

14 THE WITNESS: I relied on the structure provided in
15 the Kawai paper rather than going to the Protein Data Bank.

16 BY MR. BIEGLER:

17 Q. You agree, though, that -- so the date on
18 the Kawai paper -- so Kawai was published
19 November 11th, 2020, correct?

20 A. That's the publication date that I see
21 here, yes.

22 Q. And Kawai itself indicates that the -- that
23 the Orforglipron GLP-1 receptor interaction model had
24 been deposited in the Protein Data Bank, right?
25 That's in the paper?

1 A. Correct.

2 Q. And so you agree that a skilled artisan, at
3 least as of 2023, would have had access to that
4 three-dimensional protein interaction model that's in
5 Protein Data Bank, correct?

6 A. They would.

7 Q. And the model in the Protein Data Bank
8 is -- it's three-dimensional, right?

9 A. Yes.

10 Q. And you can manipulate it so see sort of
11 different angles, if you will, of the protein ligand
12 interactions; is that true?

13 A. I'm not sure about what functionality the
14 PDB facilitates.

15 Q. Have you ever used the PDB?

16 A. I have not.

17 Q. Do you disagree that a skilled artisan
18 looking to modify Orforglipron in 2023 would have
19 considered the three-dimensional Orforglipron GLP-1
20 receptor model in Protein Data Bank?

21 MR. CHEN: Objection. Form.

22 THE WITNESS: So examining the structure of the
23 receptor with Orforglipron bound is something that anyone
24 could have done in 2023, but it's -- you know, it's an
25 optional thing. You don't have to do that in order to, you

1 know, contemplate the interaction between the protein and
2 this drug.

3 BY MR. BIEGLER:

4 Q. It's something that a skilled artisan could
5 have done, though, if they were seeking to modify
6 Orforglipron, fair?

7 A. They could have done that; that's right.

8 Q. Okay. In your declaration, I'm looking at
9 paragraph 55, you rely on this one image of the
10 Orforglipron GLP-1 receptor interaction, right?

11 MR. CHEN: Objection. Form.

12 THE WITNESS: Well, I -- in my declaration, I
13 include this image, which is taken from the Kawai
14 publication --

15 BY MR. BIEGLER:

16 Q. Uh-huh.

17 A. -- there's -- I rely on the Kawai
18 publication as a whole for teaching about how the
19 drug and the receptor interact.

20 Q. Fair enough.

21 But this is the only image you rely on,
22 right?

23 MR. CHEN: Objection form.

24 MR. BIEGLER: Let me strike and start again.

25 BY MR. BIEGLER:

1 Q. This is the only image of the Orforglipron
2 GLP-1 receptor interaction that you relied on,
3 correct?

4 MR. CHEN: Objection. Form.

5 THE WITNESS: Yeah, this is the only image that
6 reflects that. So for purposes of, like, directing one to
7 areas of interaction and so forth, this is the key way to do
8 that.

9 BY MR. BIEGLER:

10 Q. And this is a two-dimensional image, right?

11 A. It is a two-dimensional image. It's on a
12 page.

13 Q. Fair enough.

14 You can't manipulate it, right?

15 MR. CHEN: Objection. Form.

16 THE WITNESS: That's correct.

17 BY MR. BIEGLER:

18 Q. And in paragraph 58, you talk about the
19 "binding pocket adjacent to the methyl group of the
20 indazole moiety," as is depicted by Kawai, right?

21 A. That's the reference in my declaration,
22 yes.

23 Q. And just so we're all on the same page, if
24 we go back to paragraph 53, there's an image there of
25 Orforglipron, correct?

1 A. That's a chemical structure.

2 Q. Fair enough.

3 Chemical structure of Orforglipron, right?

4 A. Yes.

5 Q. And the portion that is shaded in blue,
6 that's the indazole moiety, correct?

7 A. That's correct.

8 Q. Okay. So just for simplicity for the rest
9 of the day, if we refer to the indazole moiety for
10 Orforglipron, we both understand that's what we're
11 talking about?

12 A. Yes, indeed.

13 Q. Okay. So going back to paragraph 58, you
14 say that "the binding pocket adjacent to the methyl
15 group of the indazole moiety is shown as being
16 surrounded by a spacious hydrophobic environment
17 formed by the side chain of tyrosine at position 205,
18 lysine position 202, and glutamate at position 318,"
19 correct?

20 A. Right.

21 Q. I paraphrased a little bit, there to be
22 fair.

23 A. Right.

24 Q. Okay. So first of all, did you mean the
25 glutamate at position 138, not 318?

1 A. Yeah, I just noticed that this appears to
2 be an error in the declaration, yes.

3 Q. Okay. I think that appears several times,
4 but it sounds like wherever you refer to glutamate
5 318, you actually mean --

6 A. 138, correct.

7 Q. -- 138.

8 Okay. Do you agree that glutamate is
9 considered to be a polar amino acid?

10 A. So glutamate is not only a polar amino
11 acid, it's a charged amino acid, as is the lysine
12 202, but in this context, that glutamate and that
13 lysine are forming a salt bridge. So that means that
14 they neutralize one another's charge.

15 And the region of the interaction of those
16 residues with the indazole is in their carbon chains.

17 Q. And how did you determine that?

18 A. By looking at this image.

19 Q. Okay. And you agree --

20 A. And -- yes. And it's also noted that
21 there's interactions with the tyrosine 205. And this
22 is specifically called out in Kawai, that this is a
23 hydrophobic interaction.

24 Q. Okay. So just to back up a little bit.

25 You do agree, though, that are the

1 carbocyclic acid group on glutamate is polar,
2 correct?

3 A. Yes.

4 Q. And did you attempt to examine how close
5 the carbocyclic acid of the glutamate at position 138
6 is to the methyl group on the indazole moiety?

7 MR. CHEN: Objection. Form.

8 THE WITNESS: I didn't examine that distance.

9 BY MR. BIEGLER:

10 Q. And if that carbocyclic acid group was
11 close to the methyl group on the indazole moiety,
12 that could make that interaction polar, correct?

13 MR. CHEN: Objection. Form.

14 THE WITNESS: In terms of the molecular forces that
15 molecules and groups can have between one another, we don't
16 expect an interaction between a strongly polar and even
17 charged group and a neutral hydrophobic group. So the
18 distance isn't the controlling factor, it's the character of
19 the groups.

20 BY MR. BIEGLER:

21 Q. Yeah, maybe interaction was the wrong word.

22 If the carboxylic acid group on the
23 glutamate was close to the methyl group on the
24 indazole, that could make that environment more
25 polar, correct?

1 MR. CHEN: Objection. Form.

2 THE WITNESS: Well, the environment of the
3 glutamate also pertains to the ability of the -- of the
4 carboxylic acid of the glutamate to influence its
5 surroundings. And there's -- there's no indication that the
6 presence of glutamate 138 is creating a more polar
7 environment.

8 BY MR. BIEGLER:

9 Q. But you didn't attempt to determine how
10 close that carboxylic acid group in the glutamate was
11 to the methyl on the indazole, correct?

12 MR. CHEN: Objection. Form.

13 THE WITNESS: So I did not attempt to make a
14 measurement of the distance of the glutamate to the methyl
15 group of the indazole.

16 BY MR. BIEGLER:

17 Q. Okay. How about the lysine? Is that a
18 polar or non-polar amino acid?

19 A. So lysine is a polar, and, in fact, charged
20 amino acid that frequently appears on protein
21 surfaces and frequently, as in this case appears, is
22 involved in a salt bridge, where there is proximity
23 between a negatively charged amino acid, such as
24 glutamate 138, and the lysine 202.

25 And so these two things have natural

1 affinity for one another based on their charge.

2 Q. And for lysine, it's the ammonium moiety
3 that makes it polar, correct?

4 A. The ammonium group is a charged group, and
5 that's likewise accurately described as a polar
6 group.

7 Q. Okay. And did you attempt to -- to find
8 out how close the ammonium group on the lysine at
9 position 202 is to the methyl group on the indazole
10 moiety?

11 A. I did not make a measurement of that
12 distance.

13 Q. Okay. And you said a couple times now that
14 your belief is that the glutamate at 138 and the
15 lysine at 202 are forming a salt bridge; is that
16 right?

17 A. Correct.

18 Q. What's your basis for saying that?

19 A. This is a common structural motif that I've
20 seen countless times in three-dimensional protein
21 structures, and they're proximately -- they're
22 presented proximately in this image.

23 Q. Does Kawai state that those two amino acids
24 form a salt bridge?

25 MR. CHEN: Objection. Form.

1 THE WITNESS: That formation of a salt bridge of
2 those residues is such a routine element of protein
3 structure, it would not be something that structural
4 biologist would think worthy of comment.

5 BY MR. BIEGLER:

6 Q. So the answer is no?

7 A. So there's no comment about that being a
8 salt bridge.

9 Q. Okay. And did you attempt to determine how
10 close the carboxylic acid group on the glutamate 138
11 and the ammonium group on the lysine 202 are to each
12 other?

13 MR. CHEN: Objection. Form.

14 THE WITNESS: So I did not make a measurement of
15 that, sir.

16 BY MR. BIEGLER:

17 Q. Okay. So the only basis for your opinion
18 that the glutamate and the lysine are forming a salt
19 bridge is by looking at the image on -- in
20 paragraph 55 of your declaration, correct?

21 MR. CHEN: Objection. Form.

22 THE WITNESS: So, I mean, the basis of my
23 conclusion is this structure fitting into my general
24 understanding of protein structures and protein structures
25 that I've seen in the past, where salt bridge formation at

1 the protein surface is a common occurrence.

2 BY MR. BIEGLER:

3 Q. Fair enough.

4 But putting aside your previous experience,
5 the only thing in Kawai that's leading you to that
6 conclusion is the image in paragraph 55, right?

7 A. Right.

8 MR. CHEN: Objection. Form. Give me time to
9 object.

10 MR. BIEGLER: I just have a couple more questions
11 on this, if that's okay.

12 MR. CHEN: Okay. Yeah. Yeah.

13 MR. BIEGLER: Let me just finish up with Kawai.

14 BY MR. BIEGLER:

15 Q. So we haven't talked about the tyrosine
16 yet, and tyrosine is -- I'm going to butcher how to
17 say this -- but amphipathic amino acids; is that
18 right?

19 A. Tyrosine has different sorts of
20 interactions with other molecules is fair.

21 MR. BIEGLER: Amphipathic is A-M-P-H-I-P-A-T-I-C
22 (sic).

23 BY MR. BIEGLER:

24 Q. Tyrosines have both hydrophobic and
25 hydrophilic groups, correct?

1 A. That's a fair description.

2 Q. And the aromatic ring in tyrosine is
3 hydrophobic, right?

4 A. That is the hydrophobic part; that's right.

5 Q. And the hydroxyl group is the hydrophilic
6 part, correct?

7 A. It is.

8 Q. Okay. Did you look to see if the tyrosine
9 at position 205 -- which portion of it is closest to
10 the methyl on the indazole moiety?

11 A. Well, I -- in the image presented, one can
12 easily see the juxtaposition of the aromatic ring of
13 the tyrosine and the indazole methyl group, and Kawai
14 states that there is an interaction between that
15 tyrosine and the methyl group.

16 MR. BIEGLER: Okay. Why don't we take a break
17 there --

18 THE WITNESS: Break, break is good.

19 MR. BIEGLER: -- and come back in 10 -- 5, 10.

20 MR. CHEN: Sounds good.

21 (A brief recess was taken.)

22 MR. BIEGLER: Okay. Welcome back. I'm going to
23 hand you what's been previously marked as Exhibit 1004.

24 (Exhibit 1004 identified.)

25 BY MR. BIEGLER:

1 Q. Do you recognize this as the Kawai paper?

2 A. I do.

3 Q. Okay. If you can turn to page 4 of 25.

4 A. Uh-huh.

5 Q. And in the first column, second full
6 paragraph towards the bottom, it starts, "On the
7 other side."

8 Do you see that?

9 A. Ah, yes.

10 Q. Okay. So it says -- the sentence says, "On
11 the other side of the binding pocket, the
12 4-fluoro-1-methyl-indazole moiety (Figure 1A, blue
13 shading) of" -- I'll say Orforglipron -- "has
14 aromatic interactions with tyrosine 205 and tyrosine
15 145."

16 Do you see that?

17 A. Yes.

18 Q. Okay. And is that the -- is that what you
19 were referring to when you said that Kawai said that
20 the aromatic ring of tyrosine -- sorry, hang on a
21 second, let me try this again.

22 I think you said previously that Kawai said
23 that the interaction between tyrosine 205 and the
24 indazole group was hydrophobic.

25 Do you remember that testimony?

1 A. Right.

2 Q. Okay. Is this what you were referring to,
3 this sentence that we just --

4 A. Yeah, this sentence is what I was -- is one
5 place in Kawai that that interaction is enumerated.

6 Q. Okay. And it says that the
7 4-fluoro-1-methyl-indazole moiety has an aromatic
8 interaction with tyrosine 205, right?

9 A. It does.

10 Q. It doesn't say which portion of the
11 4-fluoro-1-methyl-indazole moiety has that
12 interaction, correct?

13 MR. CHEN: Objection. Form.

14 THE WITNESS: Yeah, it's silent on that, that's
15 true.

16 BY MR. BIEGLER:

17 Q. And did you make any attempt to determine
18 whether that interaction was close to the methyl
19 group on the indazole or further away?

20 A. I did not do any measurements of that sort.

21 Q. Okay. We can put that one aside.

22 Okay. So I want to talk about the Meng
23 reference, just to orient you in case you need it.
24 Your discussion of that starts at, I believe,
25 paragraph 85 of your declaration.

1 A. Okay.

2 Q. So Meng is one of the prior art references
3 you relied on for your arguments that Compound 65 of
4 the patent is obvious; is that right?

5 A. Correct.

6 Q. I'm going to hand you what has been marked
7 as Exhibit 1029.

8 (Exhibit 1029 identified.)

9 BY MR. BIEGLER:

10 Q. Do you recognize Exhibit 1029 as the Meng
11 reference?

12 A. Yes, I do.

13 Q. Okay. And if we can start on page 4, do
14 you see there's a section entitled Summary of the
15 Invention?

16 A. Yes.

17 Q. And following that, Meng discloses a genus
18 of GLP-1 receptor agonist, right?

19 A. Yes. This is Roman numeral 1.

20 Q. Correct.

21 There's numerous positions on that generic
22 chemical structure where you can select the
23 substituent, right?

24 MR. CHEN: Objection. Form.

25 THE WITNESS: There's, you know, at least six

1 positions -- eight positions on that generic structure that
2 are going to be defined by subsequent paragraphs, right.

3 BY MR. BIEGLER:

4 Q. And then the subsequent paragraphs provide
5 the potential substituents for each position, right?

6 A. Yeah, that's their -- that's their purpose.

7 Q. And for each -- each position, there are
8 numerous possible substituents identified, right?

9 MR. CHEN: Objection. Form.

10 THE WITNESS: I'm not sure numerous is the exact
11 word. There are multiple options at each of the R1 through
12 R4 positions and the W1 and W2 positions.

13 BY MR. BIEGLER:

14 Q. And you'd agree that this generic chemical
15 structure, and then the following list of potential
16 substituents, results in many different possible
17 GLP-1 agonists, right?

18 MR. CHEN: Objection. Form.

19 THE WITNESS: Well, this is a broad genus, it would
20 encompass a large number of compounds.

21 BY MR. BIEGLER:

22 Q. And despite that large number of compounds,
23 you focus in your declaration only on Compound II; is
24 that right?

25 A. So I am aware certainly of Compound III,

1 which is another compound whose -- whose structure is
2 explicitly disclosed here.

3 Q. You say in paragraph 87 that, "Notably
4 Compound II, one of only two compounds in Meng that
5 are structurally and functionally characterized."

6 Do you see that?

7 A. Right.

8 Q. I think that's maybe missing a verb, should
9 be Compound II is one of the only two compounds?

10 A. Yes.

11 Q. Okay. Why is it notable to you that
12 Compound II is one of the only two compounds in Meng
13 that are structurally and functionally characterized?

14 A. Well, like many patent applications, large
15 genres are claimed -- are put out there, and it is
16 the responsibility of the inventor to provide a
17 written description that convinces a person of
18 ordinary skill in the art that they were in
19 possession of the specific invention as of the time
20 that they claim to have invented it, right.

21 And so a person of ordinary skill in the
22 art could not, I believe, look at this genus and
23 envision the Compounds 2 and 3 claimed in Meng are
24 the invention.

25 So including those structures in the later

1 paragraphs is, you know, part of the duty of the
2 inventor to define what they invented, and so those
3 two compounds, 2 and 3, fit within that genus, and I
4 take them to be the invention here, even though many,
5 many other structures are disclosed in that genus in
6 paragraph 7.

7 Q. And so when you say "structurally
8 characterized" in your declaration in paragraph 87,
9 do you mean that those two compounds of specific
10 structures are drawn out; is that what you mean by
11 that?

12 A. So --

13 Q. Let me ask you a better question.

14 A. Okay.

15 Q. What do you mean when you say that Compound
16 II is structurally characterized?

17 A. So there are standards of chemical
18 structure that are used in scientific publications,
19 as well as in some patent specifications, and, you
20 know, here -- here in this application, we have what
21 I would call these two working examples, and these
22 working examples include the sorts of information
23 about the compounds themselves, as well as the
24 intermediates in their synthesis that establishes
25 their chemical structure.

1 So the structures that are presented in 2
2 and 3, they could be prophetic. I mean, I can use
3 ChemDraw, and I can draw these structures.

4 Q. Okay.

5 A. And I understand that if those structures
6 have the properties, you know, alleged, the useful
7 properties alleged, I could still obtain a patent on
8 them, right, even if I had never made them.

9 But the evidence in the specification
10 supports that those compounds were actually
11 physically prepared, and that -- that is -- all of
12 that encompasses what I would describe as
13 structurally -- and structurally characterized.

14 Q. Okay. And what do you mean by
15 "functionally characterized" in paragraph 87?

16 A. So at the end of this application, in
17 paragraph 191, there is a table, where the --
18 the activity of these compounds as GLP-1 receptor
19 agonist was determined.

20 Q. Okay. And why does it matter if those --
21 if Compound II is functionally characterized?

22 A. One thing that it does is also establishes
23 that they were in possession of their invention.

24 Q. Uh-huh.

25 A. And since you can't obtain biological

1 activity from that test if you don't have the
2 compound, and -- that's -- that's the main sort of
3 feature of being structurally and functionally
4 characterized that makes these two structures in
5 Meng, you know, of greater interest and higher
6 priority than any other structure one could envision
7 from the genus.

8 Q. Okay. And so let's stick with the data
9 that's on page 23 of Meng.

10 And that table discloses EC50 data for
11 Compound II, Compound III, and what it calls a
12 control drug, which is, in fact, Orforglipron,
13 correct?

14 A. That is my understanding about that data,
15 yes.

16 Q. Okay. What's an EC50?

17 A. So an EC50 -- the EC part stands for
18 effective concentration, and it is a common way to
19 express the efficacy of a drug at its target site.
20 And that -- the way the mathematics of that works
21 out, that EC50 number is provided in units of
22 molecular concentration.

23 So in this table, there is a parenthesis
24 after the EC50 that says NM, so that stands for
25 nanomoles -- that's 10 to the minus -- nanomolar, and

1 that's 10 to the minus 9 molar, that's a
2 concentration.

3 Q. And so the smaller -- the EC50 result, the
4 more potent the compound is, correct?

5 A. So yes, the way -- the way
6 concentrations -- the way these work, logically, you
7 desire compounds that will be effective at lower
8 concentration, meaning that, for example, a lower
9 dose of drug would be effective.

10 Q. And in -- I'm looking at paragraph 88 of
11 your declaration, and in the second sentence, you
12 say, "Specifically, Compounds II" -- I think maybe
13 that's a typo, it should be just be Compound II?

14 A. Right.

15 Q. Okay. So let me start over.

16 "Specifically, Compound II is 1.6 fold more
17 potent than Orforglipron, as evidenced by its lower
18 EC50 value (reflecting the concentration required to
19 achieve half-maximal activation of the GLP-1
20 receptor.)"

21 A. Right.

22 Q. Okay. And let's see here, how did you --
23 so let me -- before I get to the calculations, going
24 back a sentence, that 1.6 fold increase in potency is
25 what you rely on to say that adding a nitrogen atom

1 into the aromatic core of Orforglipron analogs can
2 significantly enhance GLP-1 receptor potency, right?

3 A. Yes. That's the way that's written.

4 Q. Okay. So how did you calculate the
5 significant 1.6 fold increase in activity between
6 Compound II and Orforglipron? How do you get there?

7 A. You divide 1.2, the EC50 of Orforglipron,
8 by 0.75, the EC50 of Compound II.

9 Q. Okay. And you think that that increase in
10 potency is enough to suggest to a person of skill
11 that adding a nitrogen atom into the aromatic core of
12 Orforglipron can significantly enhance GLP-1 receptor
13 potency; is that right?

14 A. That's true.

15 Q. Now, why is that -- in your opinion, why is
16 that increase in potency, what is that important?

17 MR. CHEN: Objection. Form.

18 THE WITNESS: In general, reflecting my earlier
19 testimony, it's desirable to get compounds that have EC50s
20 that have as low of concentration as possible, as that
21 indicates that you can use lower doses of drug, and it also
22 sometimes indicates that molecules will be more specific for
23 their drug targets.

24 There are also other benefits that can come from
25 making that nitrogen -- introduction of that nitrogen.

1 BY MR. BIEGLER:

2 Q. Okay. You don't mention -- I don't see you
3 mention Compound III in your declaration; is that
4 right? You said you're aware of it. I don't really
5 see it discussed.

6 A. That's correct.

7 Q. And you'd agree that Compound III is also
8 structurally and functionally characterized in Meng?

9 A. Compound III is, yes.

10 Q. And Meng discloses that Compound III has an
11 EC50 of 0.50, correct?

12 A. It does.

13 Q. That's lower than the EC50 of Compound II?

14 A. It is.

15 Q. I calculated that Compound III has a
16 2.4-fold increase in potency compared to
17 Orforglipron; does that sound about right to you?

18 A. Yeah.

19 Q. And Compound II -- sorry, strike that.
20 Compound III has approximately a 1.5-fold
21 increase in potency compared to Compound II, correct?

22 A. Correct.

23 Q. And Compound III has -- so just to back
24 up -- Compound II has a nitrogen substitution in the
25 indole moiety in the same location as Compound 65 in

1 the patent, right?

2 A. Correct.

3 Q. Compound III also has a nitrogen
4 substitution in the indole moiety, but in a different
5 location than Compound 65, correct?

6 A. That's correct.

7 Q. Okay. You can put that aside.

8 Let's go to -- I want to talk about Yoshino
9 a little bit, which you start discussing at
10 paragraph 65 of your declaration.

11 I'm going to hand you what's been
12 previously marked as Exhibit 1008.

13 (Exhibit 1008 identified.)

14 BY MR. BIEGLER:

15 Q. Do you recognize Exhibit 1008 as the
16 Yoshino reference?

17 A. Yes, I do.

18 Q. And I'd like to start on page 9 of 166 of
19 Exhibit 1008 in column 3.

20 A. Okay.

21 Q. And Yoshino, in column 3, discloses a
22 generic structural formula for GLP-1R agonist,
23 correct?

24 MR. CHEN: Objection. Form.

25 THE WITNESS: Yes. Yeah, that's what they're

1 disclosing here, yes.

2 BY MR. BIEGLER:

3 Q. And like we saw with Meng, there are
4 numerous positions where -- where a substituent can
5 be selected, correct?

6 A. That's right.

7 Q. And then after the generic structure,
8 Yoshino goes on to provide multiple options for each
9 position where there can be substituent picked,
10 right?

11 A. Correct.

12 Q. And would you agree that there are at least
13 thousands, if not millions, of potential compounds
14 that are encompassed within that genus?

15 MR. CHEN: Objection. Form.

16 THE WITNESS: There are a huge number of variants
17 that would be encompassed within that genus is absolutely so.

18 BY MR. BIEGLER:

19 Q. And in that generic chemical structure, Z2
20 is the position where the indazole moiety of
21 Orforglipron would be, correct?

22 A. So in the course of working on this
23 particular patent, I've really struggled to relate
24 the genus presented here to the actual compounds,
25 including Orforglipron, and I -- it is a mystery to

1 me how these inventors expected this generic
2 structure even to encompass the explicitly enumerated
3 compounds in this patent.

4 So I'm not sure, as I sit here today,
5 exactly how these different groups correspond to
6 groups in the actual claimed compounds.

7 Q. Okay. So you weren't able to determine
8 that Z2 is the position where the indazole moiety on
9 Orforglipron would be?

10 MR. CHEN: Objection. Form.

11 THE WITNESS: I don't have confidence that the Z2
12 position is the indazole.

13 BY MR. BIEGLER:

14 Q. Okay. So let's then -- I want to jump a
15 little bit.

16 So we saw there's a very large number of
17 compounds that are encompassed within the generic
18 chemical structure of Yoshino.

19 In addition to that, there are 159
20 exemplary compounds that are drawn out in Yoshino,
21 correct?

22 A. I am aware of that, yes.

23 Q. And there's 80 compounds that have EC50
24 data, correct?

25 A. Yes, that's correct.

1 Q. And some of those compounds actually have a
2 better EC50 -- strike that, let me say it a different
3 way.

4 Some of the compounds have a lower EC50
5 than Orforglipron; is that right?

6 A. My memory is that that is right.

7 Q. Okay. And despite that, your opinion is a
8 skilled artisan would identify Orforglipron as the
9 lead compound in this patent, right?

10 A. Correct.

11 Q. And you say -- I'm looking at paragraph 72
12 of your declaration. You say that -- in the second
13 sentence there, "It's identical to the compound
14 studied in Kawai and is the only compound advanced to
15 pharmacokinetic studies in Yoshino."

16 Do you see that?

17 A. Right.

18 Q. Okay. And sorry, then after that, you say,
19 "As such, it can be identified as a lead compound due
20 to its demonstrated potential for further
21 development," correct?

22 A. Right.

23 Q. Okay. So why does the fact that it's
24 identical to the compound studied in Kawai make you
25 think that it's a lead compound for further

1 development?

2 A. Well, Kawai does do further development
3 beyond pharmacokinetics, and Kawai chooses
4 Orforglipron to determine the structure because that
5 is the compound that they are taking into clinical
6 study.

7 So, I mean, you don't take your -- your
8 crummy compounds and go to the trouble to determine
9 their structures, you take your drug compound that
10 you're trying to develop and determine its structure
11 with its target.

12 And those -- those are the features that
13 identify Orforglipron as a lead compound.

14 Q. Okay. But why is it important that it was
15 the only compound advanced to pharmacokinetic
16 studies? Why does that indicate that it could be
17 identified as a lead compound?

18 A. Well, there's a process of development that
19 requires more work, and if you -- if you don't do
20 that work, you can't advance it. So if you've chosen
21 this one to advance and you do structural biology on
22 it and you do other studies on it, that indicates the
23 view of the inventors this is our, you know -- the
24 compound we're taking forward. It's a really good
25 compound.

1 Q. Okay.

2 A. And I might point out, the Yoshino has
3 2014, which is only that compound, right. That is a
4 further indication that that is the compound that
5 they are really interested in that's going to be
6 their drug.

7 Q. Okay. In paragraph 73, you opine that
8 Yoshino discloses modifying Orforglipron -- or
9 discloses a compound that's similar to Orforglipron,
10 but with a tetrahydrofuran ring in place of the
11 methyl on the indazole moiety, correct?

12 A. Indeed, yes.

13 Q. Okay. In your opinion, would a person
14 skilled in the art consider a cyclopropyl ring and
15 tetrahydrofuran ring to be similar?

16 MR. CHEN: Objection. Form.

17 THE WITNESS: So the teaching that the
18 tetrahydrofuran ring offers in Yoshino is -- is not related
19 to, like, are these two rings similar, it is that ring
20 compounds, as well as simple alkyl groups, as in
21 Orforglipron, are well-tolerated in the interaction of the
22 drug with the receptor.

23 And ring compounds are appealing to a person of
24 ordinary skill in the art because of some of their intrinsic
25 chemical properties.

1 BY MR. BIEGLER:

2 Q. Okay. You'd agree that tetrahydrofuran
3 ring is a heterocycle, right?

4 A. A tetrahydrofuran is a heterocycle.

5 Q. And a tetrahydrofuran has polar properties,
6 correct?

7 A. It is an ether, which is moderately polar.

8 Q. And cyclopropyls and cyclobutyls -- let's
9 say cycloalkyls. Let me back up.

10 Cyclopropyls and cyclobutyls are part of a
11 class known as cycloalkyls, right?

12 A. That's right.

13 Q. And those are non-polar rings, correct?

14 A. So depending on the size of the ring,
15 different cycloalkyls can have different physical
16 properties.

17 Q. Okay. Let's stick with the ones at issue
18 here.

19 So you'd agree that a cyclopropyl is a
20 non-polar ring, correct?

21 A. Cyclopropyl is a non-polar ring, but as
22 compared to other cycloalkyls actually has some
23 polarizability to it.

24 Q. A cyclobutyl is a non-polar ring, correct?

25 A. Cyclobutyl is a non-polar ring like other

1 cycloalkyls, but also because of its intrinsic strain
2 energy has some polarizability to it.

3 Q. And in your opinion, you say that Compounds
4 40 and 67 -- so, let me back up.

5 Compound 67 in Yoshino is Orforglipron,
6 correct?

7 A. It is.

8 Q. Okay. And Compound 40 in Yoshino has the
9 tetrahydrofuran ring in place of the methyl group in
10 Orforglipron?

11 A. It does.

12 Q. Okay. And in your opinion, Compound 40 and
13 Compound 67 exhibit a similar level of activity; is
14 that right?

15 A. Yes.

16 Q. And Yoshino discloses for Orforglipron an
17 EC50 of 1.2 nanomolar?

18 A. 1.2 nanomolar is correct.

19 Q. And for Compound 40, Yoshino discloses an
20 EC50 of 2.2 nanomolars, correct?

21 A. Correct.

22 Q. So Compound 40 has a 1.8-fold lower potency
23 than Orforglipron; is that right?

24 A. That's right.

25 MR. CHEN: Objection. Form.

1 BY MR. BIEGLER:

2 Q. And by your own measure from our discussion
3 in Meng, that's a significant difference in potency,
4 correct?

5 A. We discussed that amount, yes, a
6 significant difference.

7 Q. In paragraph 74, you state that Compound
8 54, compared to Orforglipron, shows a loss of
9 activity when removing the dimethyl group, correct?

10 A. That's not correct.

11 Q. I'm sorry, I got that wrong. Let me try
12 that again.

13 So in paragraph 74, you first show
14 Orforglipron, correct, Compound 67?

15 A. Compound 67, yes.

16 Q. And then you show Compound 54, which has
17 multiple changes from Orforglipron, correct?

18 A. That's correct.

19 Q. One of those changes is the removal of the
20 dimethyl group from the tetrahydropyran moiety,
21 correct?

22 A. Correct.

23 Q. And that compound has an over 3-fold
24 decrease in EC50, right, Compound 54?

25 A. Yes, that's right.

1 Q. Okay. And then your opinion is that by
2 replacing the methyl on the indazole moiety in
3 Compound 54, you get Compound 8, and that restores
4 some of the activity, correct?

5 A. That's -- that's correct.

6 Q. Okay. But Compound 8, the EC50 provided by
7 Yoshino is 2.4 nanomolar, correct?

8 A. Correct.

9 Q. And that's a -- I got a 2.08 fold
10 difference in activity relative to Orforglipron; does
11 that sound right?

12 A. Yeah, that's close.

13 Q. Okay. So that's still a significantly less
14 active compound than Orforglipron, correct?

15 A. It is different, though compounds with
16 potency in the low nanomolar are still very viable as
17 drug candidates.

18 Q. Sure.

19 But you said before that a 1.6 fold
20 difference for the compounds in Meng, that was a
21 significant --

22 A. Sure.

23 Q. -- difference in the EC50, right?

24 MR. CHEN: Objection. Form.

25 THE WITNESS: Yeah.

1 BY MR. BIEGLER:

2 Q. The only difference between Compound 8 and
3 claimed Compound 19 is the replacement of the
4 cyclopropyl for the THF ring, correct, on the
5 indazole moiety?

6 A. Incorrect.

7 Q. Okay. I'm going to move on from that.

8 In paragraph -- let's go to 169 of your
9 declaration.

10 Okay. So in paragraph 169, you say, "Of
11 the 80 compounds listed in Table 3 of Yoshino with
12 reported biological activity, more than 30
13 incorporate a non-substituted achiral tetrahydropyran
14 ring," correct?

15 A. Yes.

16 Q. And that's the removal of the dimethyl
17 group from the tetrahydropyran, correct?

18 A. Right.

19 Q. Okay. So Yoshino took 30 of those
20 compounds to EC50 testing; is that correct?

21 A. Yes.

22 Q. None of the compounds with the dimethyl
23 group removed from the tetrahydropyran moiety was
24 advanced to pK studies, correct?

25 MR. CHEN: Objection. Form.

1 THE WITNESS: The one compound in Yoshino that was
2 advanced was Orforglipron. These are not Orforglipron, so
3 these were not advanced.

4 BY MR. BIEGLER:

5 Q. Right.

6 So there was no compound with the dimethyl
7 group removed from the tetrahydrofuran moiety that
8 made it to pK studies, correct?

9 A. Correct.

10 Q. There was also no compound with a THF
11 moiety in place of the methyl on the indazole moiety
12 that made it to pK studies, correct?

13 A. No compound that was structurally variant
14 from Orforglipron was advanced to pK studies, so --

15 Q. And despite -- despite having 30 compounds
16 without the dimethyl group that went forward to EC50
17 testing, Yoshino does not disclose a compound that is
18 identical to Orforglipron but with the dimethyl group
19 removed, correct?

20 MR. CHEN: Objection. Form.

21 THE WITNESS: I'm not sure.

22 BY MR. BIEGLER:

23 Q. Okay. If we go to paragraph 162 of your
24 declaration. I apologize, I got the compound numbers
25 wrong before.

1 So if we look at Compound 22, which is the
2 end of paragraph 162, Compound 22, that compound is
3 the same as Compound 19 that's claimed in the patent
4 at issue here but with a tetrahydrofuran ring in
5 place of the cyclopropyl on the indazole, correct?

6 A. Yes, that's correct. Sorry, it's not
7 correct.

8 Q. What's not -- what else is different?

9 A. The indazole here does not have a fluorine.

10 Q. Okay. So those are the only two
11 differences, correct?

12 A. Correct.

13 Q. And for that compound, Yoshino reports an
14 EC50 of 2.3 nanomolars?

15 A. For Compound 22, that's right.

16 Q. And that's a 1.9-fold worse potency than
17 Orforglipron, correct?

18 A. Orforglipron is 1.2 to 2.3, yeah, that's
19 probably 1.9.

20 Q. Okay.

21 MR. BIEGLER: Do we want to take a break?

22 MR. CHEN: Sure.

23 MR. BIEGLER: Take a five-minute break, ten-minute
24 break?

25 THE WITNESS: That's fine.

1 (A brief recess was taken.)

2 MR. BIEGLER: Okay. Welcome back.

3 BY MR. BIEGLER:

4 Q. I want to talk now about Su and your
5 discussion of that, just to orient you, starts at
6 paragraph 60 of your declaration.

7 A. Okay.

8 Q. And you agree that Su discloses 218 working
9 examples, correct?

10 A. Yeah, I state that at the bottom of
11 page 30, yeah.

12 Q. And your focus for your obviousness
13 opinions are on two of those compounds, 44 and 175,
14 correct?

15 A. That's right.

16 Q. And to be fair, for 175, you looked at the
17 deuterated and non-deuterated versions, one of which
18 is 175 and one is 176, correct?

19 A. Compound 176 is deuterated. Compound 175
20 is the parent that is not deuterated.

21 Q. Okay. And in paragraph 63 and 64 -- let's
22 look at 63. You say that "Compounds 176, 44," and
23 then another one," "35, share a common scaffold ring
24 structure."

25 Do you see that?

1 A. Yes.

2 Q. And then the next paragraph, you say that
3 they have the "same scaffold ring structure as
4 Orforglipron," correct?

5 A. Correct.

6 Q. Okay. And what exactly did you mean by a
7 "common scaffold ring structure"?

8 A. So the ring structure that I'm referring to
9 there, it is the indazole, and then there's a ring
10 called imidazolone, and then there is a two-ring
11 system that's called a pyrrolo pyrazole, and then
12 there is a ring that is an indole, and then there is
13 a ring that is the tetrahydropyran.

14 Okay. So all those rings along the
15 structure of Orforglipron constitute that scaffold.

16 Q. Okay. So you're looking at Compound 176,
17 right?

18 A. At the moment, I am.

19 Q. Okay. It seems to me like you called out
20 every ring structure in that compound except for the
21 cyclopropyl that's attached to the indazole, correct?

22 A. Well, I didn't mention the cyclopropane
23 ring and the fancy heterocycle that's on the nitrogen
24 of the indole, but that also is a constant structure
25 of all of these -- of all of these compounds, or the

1 dimethyl fluorophenyl ring.

2 I mean, there's a great deal of structural
3 conservation of these molecules, but you're right,
4 the cyclopropyl was not something that I called out
5 as part of the core of Orforglipron because
6 Orforglipron does have a cyclopropyl.

7 Q. Okay. But so when you're referring to the
8 common scaffold ring structure, you are referring to
9 sort of -- not sort of, to all of the rings in
10 Compound 176 except for the cyclopropyl; is that
11 right?

12 A. That's fair.

13 Q. And you're also referring to those rings
14 having the same atoms, right? In other words,
15 there's no swapping of nitrogens or oxygens for
16 carbons or vice versa; is that right?

17 MR. CHEN: Objection. Form.

18 THE WITNESS: Well, there is one obvious difference
19 in Compound 176 and Compound 44 in that Compound 176 has
20 methyl groups on the tetrahydropyran, and the other does not,
21 but the tetrahydropyran part is in common.

22 BY MR. BIEGLER:

23 Q. Yeah, I guess what I'm asking when you talk
24 about the common scaffold ring structure of
25 Orforglipron, do you mean of all the rings that we

1 just talked about with the same atoms in the rings
2 too?

3 MR. CHEN: Objection. Form.

4 THE WITNESS: I mean I really do identify the
5 common structural elements of these compounds compared with
6 Orforglipron, and I can identify, you know, on -- on all of
7 the basis of that the -- you know, a common structural core,
8 and with the only differences being the ring on the indazole
9 and the tetrahydropyran ring.

10 BY MR. BIEGLER:

11 Q. Right. And so if one of those compounds
12 had -- let's just take an example.

13 If the tetrahydrofuran ring didn't have an
14 oxygen and became a benzene --

15 A. Okay.

16 Q. -- you wouldn't consider that to be the
17 same common scaffold ring structure, right? Do I
18 have that right?

19 A. That's fair. There are compounds of that
20 structure included in Yoshino that actually have a
21 pyridine ring instead of a tetrahydropyran ring, for
22 example.

23 Q. Okay. Going back to the 218 exemplary
24 compounds.

25 There's no EC50 -- first of all, there's no

1 activity data provided for any of the 218 compounds;
2 is that right?

3 A. There's no activity on the GLP-1 receptor
4 provided for the compounds in Su.

5 Q. So we have no EC50 for Compound 44,
6 correct?

7 A. We don't have EC50 data, but we have the
8 knowledge that that these compounds were chosen to be
9 deuterated, and the fact that they were chosen to be
10 deuterated is an important indicator of the interest
11 of these compounds and their potential.

12 And so in a certain sense, that's -- that
13 is -- it allows us to draw the same conclusion as if
14 we had other data.

15 Q. So is the EC50 of Compound 44 better,
16 worse, or the same for Orforglipron based on Su?

17 MR. CHEN: Objection. Form. Calls for
18 speculation.

19 THE WITNESS: So, yes. Since the data is not
20 presented, there's no reasonable way to answer. The key
21 element is that this compound was prepared in deuterated
22 form, and that indicates that it has potential for
23 development and -- in the view of these inventors, and that's
24 all I need to know to identify it as a lead compound.

25 BY MR. BIEGLER:

1 Q. I understand that's your opinion. That's
2 not my question, though.

3 My question is simply, there's no way to
4 tell from Su whether Compound 44 has an EC50 that's
5 better, worse, or the same than Orforglipron,
6 correct?

7 MR. CHEN: Objection. Form.

8 THE WITNESS: So, I mean, that's not strictly true
9 because I have a great deal of knowledge about
10 structure-activity relationships in this art, and I -- I have
11 other information from Yoshino that removal of the methyl
12 groups from the tetrahydropyran ring -- you know, some have
13 slightly different activity, but those compounds are still
14 good compounds that have significant potential.

15 BY MR. BIEGLER:

16 Q. Okay.

17 A. So the main difference with Compound 44 is
18 that there are not methyl groups in the
19 tetrahydropyran ring, but my knowledge of the art, as
20 a whole, suggests that this compound would have some
21 good activity against the GLP-1 receptor, and I know
22 it's been deuterated, therefore, it has potential for
23 development.

24 Q. There's no EC50 data in Super Compound 44,
25 correct?

1 MR. CHEN: Objection. Form. Calls for
2 speculation.

3 THE WITNESS: Yeah, I answered the question. And I
4 would answer it again the same way. This compound has good
5 reason for further development.

6 BY MR. BIEGLER:

7 Q. Not my question. Not my question.

8 There's no EC50 data in Su for Compound 44.
9 It's pretty straightforward.

10 A. So there's no EC50 data in Su.

11 Q. There's no EC50 data in Su for Compound
12 175, correct?

13 A. There's no EC50 data in Su.

14 Q. So we don't know if Compound 175 has better
15 potency, worse potency, or the same potency, as
16 opposed to -- or as compared to Orforglipron,
17 correct?

18 MR. CHEN: Objection to form.

19 THE WITNESS: We do have a basis of assessing the
20 activity of Compounds 176 and 44 based on what we know about
21 structure activity relationships that comes from other art
22 like Yoshino, and we have good indication that these are good
23 compounds with development potential because they were
24 deuterated.

25 BY MR. BIEGLER:

1 Q. There's no pK data for Compounds 44 and 175
2 in Su, correct?

3 A. I'm not aware of any.

4 Q. There's no way to know, based on Su,
5 whether the pK of compounds -- excuse me, strike
6 that.

7 There's no way to know, based on Su, if the
8 pK of Compounds 44 and 175 were better, worse, or the
9 same as Orforglipron, correct?

10 MR. CHEN: Objection. Form.

11 THE WITNESS: Su does not report pK data for 176,
12 but no data is required in a patent to receive a patent, and
13 the fact that these compounds were prepared in deuterated
14 form, one of the main reasons to do that is to determine the
15 pK. And these inventors prepared this compound in the
16 deuterated form, and that indicates their value as
17 candidates.

18 BY MR. BIEGLER:

19 Q. Now, there are five compounds in Su that
20 are advanced to pK testing, correct?

21 MR. CHEN: Objection. Form.

22 BY MR. BIEGLER:

23 Q. If it's helpful --

24 A. So there is -- do I have Su?

25 Q. I didn't give you Su yet.

1 A. I don't have Su.

2 Q. Let me give it to you. Sorry. I'm going
3 to hand you what's been marked already as
4 Exhibit 1007.

5 (Exhibit 1007 identified.)

6 BY MR. BIEGLER:

7 Q. And do you recognize Exhibit 1007 as the
8 English translation of I think what we refer to as Su
9 2 in the papers?

10 A. Right. Right. Yes, that's it. It's my
11 Exhibit 7, 1007.

12 Q. Correct.

13 So I'll point you to pages 294 and 295 of
14 Exhibit 1007.

15 A. Right.

16 Q. And so the question was, there are five
17 compounds in Su that are advanced to pK testing,
18 correct?

19 A. That's right.

20 Q. You don't mention those compounds in your
21 declaration, do you?

22 A. I'm not sure.

23 Q. Are you aware that none of those five
24 compounds advanced to pK testing in Su maintain the
25 core structure of Orforglipron?

1 A. Yes, that is correct, that those compounds
2 don't have the Orforglipron structure core.

3 Q. And none of the compounds that were
4 advanced to pK testing in Su have the substitutions
5 that are made in the compounds claimed in the patent
6 in this case, right?

7 MR. CHEN: Objection. Form.

8 BY MR. BIEGLER:

9 Q. I can ask that individually, if it's
10 easier.

11 A. Yeah, that question is confusing.

12 Q. Okay.

13 None of the compounds advanced to pK
14 testing in Su have cyclopropyl in place of the methyl
15 on the indazole moiety, correct?

16 A. That's correct.

17 Q. And none of the compounds advanced to pK
18 testing in Su remove the dimethyl group on the
19 tetrahydropyran moiety, correct?

20 A. So really, what is represented in the data
21 in Su is not meaningful because it's not incumbent on
22 investors to provide the data for all compounds that
23 they have. Data is not a requirement for the patent.

24 They happened to choose to include this
25 data on these compounds, and whether they did or did

1 not include data on compounds with methyl groups
2 removed from the tetrahydropyran ring or cyclopropyl
3 groups added to the indazole ring is irrelevant.

4 MR. BIEGLER: Objection. Move to strike.
5 Nonresponsive.

6 BY MR. BIEGLER:

7 Q. None of the compounds advanced to pK
8 testing in Su remove the dimethyl group on the
9 tetrahydropyran moiety, correct?

10 A. That's incorrect. None of the compounds
11 whose pK is reported in Su contain methyl groups from
12 the cyclopropane, but that does not mean that no
13 compounds with dimethyl groups removed were studies
14 for pK. And the fact that Compound 44 was prepared
15 is an indicator that it would be subject to pK study.

16 Q. But Su doesn't give us that information,
17 correct?

18 MR. CHEN: Objection. Form.

19 THE WITNESS: Su gives us the information that
20 Compound 44 was prepared in deuterated form, and the -- and a
21 purpose for that is to pK study.

22 BY MR. BIEGLER:

23 Q. You'd agree that the fact that these five
24 compounds were the only compounds advanced to
25 pharmacokinetic studies in Su is indicative of their

1 lead compound status, correct?

2 MR. CHEN: Objection. Form.

3 THE WITNESS: I disagree.

4 BY MR. BIEGLER:

5 Q. Okay. So you told me before that the fact
6 that Orforglipron was advanced to pharmacokinetic
7 studies in Yoshino indicated lead compound status,
8 but when it comes to Su, you have a different
9 approach?

10 A. Mischaracterizes my testimony.

11 Q. Well, we can read it. Let's go to
12 paragraph 72 of your declaration.

13 You say in the second sentence, "It is also
14 referred to as Orforglipron is identical to the
15 compound studied in Kawai and is the only compound
16 advanced to pharmacokinetic studies in Yoshino. As
17 such, it can be identified as a lead compound due to
18 its demonstrated potential for further development."

19 So you consider the fact that Orforglipron
20 was advanced to pharmacokinetic studies in Yoshino to
21 be at least one factor that indicated it was a lead
22 compound, correct?

23 A. It was absolutely one factor indicating it
24 is a lead compound, and as -- as the sum of this art
25 shows, there are many other factors as well.

1 Q. And so you would agree that in Su, in
2 Exhibit 1007, the fact that the five compounds on
3 page 291 were advanced to pharmacokinetic studies is
4 at least one factor that indicates they might be lead
5 compounds, correct?

6 A. They absolutely could be lead compounds,
7 but it's a matter of prioritization, and other
8 factors are more persuasive for Compounds 175 or 176
9 and 44 to be lead compounds in Su.

10 Q. You didn't choose these compounds because
11 they don't have the features that are in the claims,
12 correct?

13 MR. CHEN: Objection. Form.

14 THE WITNESS: I don't understand your question.

15 BY MR. BIEGLER:

16 Q. You didn't focus on the compounds that
17 actually advanced to pK studies in Su because they
18 don't have the features in the patent you're trying
19 to say is obvious?

20 A. I did not choose the compound -- I don't
21 choose as lead compounds those compounds given in
22 Table 3 on page 291 of the Su patent because these
23 compounds do not have the same core ring structure as
24 does Orforglipron. That is the key feature that
25 gives those a lower priority, in my view, than those

1 compounds for which pharmacokinetics happened to be
2 reported.

3 Q. You say that -- I'm looking now at
4 paragraph 61, 62, you say in your declaration a
5 skilled person -- you've talked about a little bit
6 today -- would look to Compounds 44 and 176 because
7 they're deuterated, correct?

8 A. Right.

9 Q. Su doesn't disclose the reason that those
10 compounds were deuterated, does it?

11 MR. CHEN: Objection. Form.

12 THE WITNESS: Su does not make statements about the
13 reason for the deuteration of those compounds, but a person
14 of ordinary skill in the art would understand the main
15 functions of making deuterated drug candidates as being
16 determination of pharmacokinetics, as well as suppression of
17 metabolism.

18 BY MR. BIEGLER:

19 Q. Right.

20 You say in paragraph 62, "Deuteration is
21 often examined to enhance metabolic traits of drug
22 candidates," right?

23 A. Right.

24 Q. And when you say, "enhance metabolic
25 traits," what do you mean by that?

1 A. So drugs -- when drugs are administered,
2 they're -- there are four processes that they
3 undergo: Absorption, distribution, metabolism, and
4 excretion, and those often go by the acronym ADME,
5 A-D-M-E, and that is often used interchangeably with
6 the term pharmacokinetics or pK, as we have
7 discussed.

8 And so the M of ADME, metabolism, is what's
9 referred to here. Deuteration is examined to enhance
10 metabolic traits of drug candidates. Deuteration, at
11 a particular site of metabolism, can change the
12 metabolism of a drug and affect its efficacy.

13 Q. Got it.

14 And so Su doesn't disclose any -- I think
15 we've been over this, but just to make sure that it's
16 clear -- Su doesn't disclose any metabolic data for
17 the deuterated compounds that you point to, right?

18 A. Su doesn't disclose metabolic data for any
19 compounds. The fact of the deuteration is an
20 indicator that this is a matter of concern to these
21 inventors, and that would be an indicator for a
22 person of ordinary skill in the art that these are
23 compounds of high interest.

24 Q. And because we don't have any metabolic or
25 pK data for the compounds that were deuterated, we

1 have no way to tell from Su if the deuteration worked
2 or didn't work, correct?

3 MR. CHEN: Objection. Form.

4 THE WITNESS: We -- the disclosure of the
5 deuterated compounds indicates that deuteration of the drug
6 was successful, and the isotopic labeling of the drug
7 candidate would be intrinsically useful in determining
8 pharmacokinetics and those ADME properties.

9 And that's -- that's more than sufficient as an
10 indicator of high interest in these -- in these drug
11 candidates, even if there was no involvement in metabolism at
12 the sites of deuteration.

13 So I would say that these were -- these compounds
14 were successful because they could be -- they could be made,
15 and they could be used for pK studies.

16 BY MR. BIEGLER:

17 Q. But that wasn't might question.

18 So my question is, if the purpose of the
19 deuteration for the compounds you focused on was to
20 enhance metabolic traits, Su doesn't provide any data
21 to tell you if that was successful, if metabolic
22 traits were enhanced or not, correct?

23 MR. CHEN: Objection. Form.

24 THE WITNESS: Yes. There's no evidence that there
25 are metabolic traits that are being enhanced here, but at

1 this stage of drug development, that's not typical, that's
2 not intrinsic. So a person of ordinary skill in the art is
3 going to look to those special compounds, a few special
4 compounds that are identified among the larger group, and
5 this is the way to do that.

6 BY MR. BIEGLER:

7 Q. In paragraph 154 of your declaration --
8 sorry to jump around a little bit here.

9 So I'm really focused on the table that is
10 at the end of that section, page 98.

11 A. Okay.

12 Q. And here, you're comparing Orforglipron to
13 Compound 44, correct?

14 A. Right.

15 Q. And first, you show Compound 44, which has
16 two deuterions in place of the methyl groups on the
17 tetrahydropyran ring?

18 A. Right.

19 Q. And then below that, you show the
20 non-deuterated counterpart of Compound 44, correct?

21 A. That is there, yes.

22 Q. And I just want to be clear, that structure
23 does not appear in Su, correct? You put that in?

24 MR. CHEN: Objection. Form.

25 THE WITNESS: So Su does not draw the structure of

1 the non-deuterated version of Compound 44.

2 BY MR. BIEGLER:

3 Q. And it doesn't even indicate that it was
4 made, correct?

5 A. So this compound, 44, was made, and it
6 would be intrinsic to the compound being made with
7 deuterium to have had, and studied, the
8 non-deuterated compound that is depicted here.

9 Q. You say it's intrinsic, but there's no
10 indication in Su itself that Su made or studied the
11 non-deuterated version of Compound 44?

12 A. A person of ordinary skill in the art in
13 reading this disclosure would believe that the basis
14 of synthesizing Compound 44 with deuterium there for
15 studies like pharmacokinetics and metabolism is based
16 on the properties of the non-deuterated counterpart,
17 as shown in this table.

18 Q. Okay. So your opinion, if I understand it
19 correctly, is that a person of skill looking at Su
20 would be motivated to combine Compound 44 with
21 Compound 175; is that right?

22 A. That's right.

23 Q. And you say that both Compound 44 and 175
24 were important compounds in Su because they were --
25 they had deuterated -- they were deuterated or had

1 deuterated counterparts, correct?

2 MR. CHEN: Objection. Form.

3 THE WITNESS: So it's -- it's much more than just
4 the fact that they were deuterated. They were deuterated.
5 They fit into the important core, backbone structure of
6 Orforglipron, and our understanding of SAR from Yoshino
7 teaches that these should be good GLP-1 receptor items.

8 BY MR. BIEGLER:

9 Q. So let's take away the deuteration part.

10 Your opinion is that Compounds 44 and 175
11 were important to the Yoshino inventors; is that
12 right?

13 A. The --

14 MR. CHEN: Objection. Form.

15 THE WITNESS: Yeah, that's not correct.

16 BY MR. BIEGLER:

17 Q. You don't think Compounds 44 and 175 were
18 important?

19 MR. CHEN: Objection. Form.

20 THE WITNESS: So Compounds 44 and 175 are shown to
21 be important compounds for development in Su.

22 BY MR. BIEGLER:

23 Q. Uh-huh. I think we're saying the same
24 thing.

25 You think that Compounds 44 and 175 were

1 shown to be important compounds for development in
2 Su, correct?

3 A. Correct.

4 Q. Okay. Su itself does not disclose the
5 combination of Compound 44 and 175; is that right?

6 MR. CHEN: Objection. Form.

7 THE WITNESS: So I'm not aware of the -- of a
8 compound that specifically does what you're describing to get
9 to Compound 19, right, to put cyclopropyl on and take the
10 methyl groups off.

11 BY MR. BIEGLER:

12 Q. Exactly.

13 So we have no indication from Su that the
14 scientists who were actually working with Compounds
15 44 and 175 thought to make both of those
16 modifications in one compound, true?

17 MR. CHEN: Objection. Form.

18 THE WITNESS: Well, my sense of that -- another way
19 of saying this is that the Su inventors did not synthesize
20 Compound 19 first, and that's a true statement, but we
21 have -- we have art that we have -- that combines two -- two
22 pieces of information that does lead to Compound 19.

23 BY MR. BIEGLER:

24 Q. But, again, we have nothing to suggest that
25 the Su inventors actually working with compounds

1 144 -- excuse me, let me start again.

2 We have no indication that the scientists
3 in Su actually working with Compounds 44 and 175
4 thought to make the modifications in each of those in
5 one compound, right?

6 MR. CHEN: Objection. Form.

7 THE WITNESS: The Su inventors didn't synthesize
8 that Compound 19, and that's all we know about that.

9 BY MR. BIEGLER:

10 Q. Okay. If you can turn to paragraph 67 of
11 your declaration.

12 So there are -- there are multiple
13 compounds in Su that are deuterated. You then focus
14 down on Compounds 176, 44 --

15 A. So this is paragraph 67? Sorry, I went to
16 the wrong page.

17 Q. Oh, yeah, yeah, yeah.

18 A. Okay.

19 Q. So let me back up a little bit.

20 63, paragraph 63. There are 7 deuterated
21 stereoisomerically pure compounds in Su, correct?

22 A. Yes.

23 Q. And then from there, you focus down on
24 Compounds 176, 44, and 35 because they share the
25 common scaffold ring structure we discussed earlier?

1 A. Yes.

2 Q. You then -- you focus from those three
3 compounds on 44 and 176 because you say compound 35
4 has a change in electronic character compared to the
5 other compounds; is that right?

6 MR. CHEN: Objection. Form.

7 THE WITNESS: So in -- in paragraph 67, I say that
8 "Deuterated Compound 35 replaces an" --

9 THE REPORTER: I'm sorry, slow down, please.

10 THE WITNESS: Sure, sure.

11 "Although sharing the same scaffold ring structure,
12 deuterated Compound 35 replaces an electron-withdrawing
13 fluorine atom present in Orforglipron with an
14 electron-donating amino group."

15 BY MR. BIEGLER:

16 Q. And what data did you rely on to reach that
17 conclusion?

18 A. This statement is simply about chemical
19 structure, so I can look at the chemical structure
20 and make that statement.

21 Q. Okay. So there was no data that formed the
22 basis of that opinion?

23 MR. CHEN: Objection. Form.

24 THE WITNESS: So data is not needed to affirm the
25 statement I made. I can look at the structures. I can look

1 at the chemical structures and make that statement.

2 BY MR. BIEGLER:

3 Q. And your opinion is that, based on the
4 structure, you can make the statement that the
5 "modification constitute a more" -- "constitutes a
6 more pronounced, yet less favorable, change in
7 electronic character compared to the other
8 compounds"?

9 A. There is a great deal of structural
10 relationship about Orforglipron analogs in this art,
11 and one particular part of these compounds that is
12 relatively conserved is the dimethyl fluorophenyl
13 ring, and some slight changes are made there, but
14 they are typically what I would call conservative
15 changes, not changing electronic character, not
16 changing size in appreciable ways, and that what is I
17 refer to here.

18 An amino group is a wholly different -- of
19 wholly different electronic character compared to a
20 fluorine group, and that is the reason that Compound
21 35 was of lower priority as a lead compound because
22 it does not conserve the character of that ring that
23 is found in Orforglipron.

24 Q. But you have no way of knowing if the -- if
25 the change is more favorable or less favorable

1 without looking at data on it, correct?

2 MR. CHEN: Objection. Form.

3 THE WITNESS: A person of ordinary skill in the art
4 is going to be focused on preserving the parts of
5 Orforglipron that they can and make guided changes to the
6 parts that they can, and that particular change in that
7 particular ring was, therefore, of lower priority.

8 BY MR. BIEGLER:

9 Q. But that wasn't my question.

10 There's no way to know whether the change
11 results in a less favorable or more favorable
12 compound without some data, right?

13 MR. CHEN: Objection. Form.

14 THE WITNESS: A person of ordinary skill in the art
15 considering this compound isn't operating in a vacuum. They
16 have understanding of this field and the structures that are
17 good GLP-1 receptor agonists. And because that compound,
18 even though it is deuterated, does not share the same sort of
19 electronic structure in that particular ring, it would be of
20 lower priority irrespective of whether you give me data on it
21 or not.

22 BY MR. BIEGLER:

23 Q. Okay. Let's see. Let's turn to -- let's
24 turn to Talele briefly, or how do you pronounce it?

25 A. We've been calling it Talele.

1 Q. Okay, I've been calling it Talele, so I
2 don't know who's right, but I'll call it Talele.
3 Let's go to Talele. Let's see, where is that? You
4 discuss that starting in paragraph 80 of your
5 declaration.

6 A. Okay.

7 Q. And you agree with me that Talele, or
8 Talele, does not discuss Orforglipron at all, right?

9 A. So Talele is an article that covers a wide
10 range of medicinal chemistry, active structures, and
11 different kinds of targets, and it is a broad and
12 general teaching that pre-dates lots of research on a
13 GLP-1 receptor.

14 So it's understandable that it wouldn't
15 cover specific things concerning the cyclopropyl
16 group, which is its focus, in context of the GLP-1
17 receptor.

18 Q. Let me hand you Exhibit 1009.

19 (Exhibit 1009 identified.)

20 BY MR. BIEGLER:

21 Q. And do you recognize Exhibit 1009 as
22 Talele?

23 A. Yes, this is the Talele publication.

24 Q. Okay. And you'd agree that Talele
25 discloses examples where the cyclopropyl group has

1 the opposite effect of what was expected or hoped
2 for, correct?

3 MR. CHEN: Objection. Form.

4 THE WITNESS: So if there's a specific teaching in
5 Talele that you believe states that, I'd appreciate being
6 directed to that part of the paper.

7 BY MR. BIEGLER:

8 Q. Sure, let's go to page 20 of Talele. And
9 in the right-hand column, in the discussion of the
10 BACE1 inhibitor, the last three sentences state that
11 "It is interesting to note that the cyclopropyl ring
12 has played a role in achieving selectivity in many of
13 the examples described previously; however, a
14 spirocyclopropyl substitution at the benzylic
15 position at 105 led to the loss of selectivity. The
16 reason for the loss of selectivity of 105 is not
17 known at this time. Therefore, one design strategy
18 does not work for all cases and is
19 context-dependent."

20 Do you see that?

21 A. Okay. Yes, I read that.

22 Q. And do you agree with that statement, one
23 design strategy does not work for all cases and is
24 context-dependent?

25 MR. CHEN: Objection. Form.

1 THE WITNESS: So read in the full context of this
2 statement, the important thing to note is that it is the
3 so-called spirocyclopropyl substitution in this case that has
4 not worked for all cases, and cyclopropyl substitution, as
5 stated here, has played a role in achieving selectivity at
6 this time.

7 So it is a spirocyclopropyl group specifically that
8 Talele is teaching might not always lead to the desired
9 effect.

10 Even beyond that, this paper exists because of the
11 wide number of examples in medicinal chemistry, where
12 cyclopropyl substitution has been effective. And it teaches
13 that -- and that would be known to a person of ordinary skill
14 in the art.

15 So not every strategy works 100 percent of the
16 time. Here is an example specifically identified as
17 spirocyclopropyl substitution that was not effective.

18 In the Compound 19, we don't have a
19 spirocyclopropyl substitution, so there's no basis for
20 disfavoring that based on this comment in Talele.

21 BY MR. BIEGLER:

22 Q. So you agree that Talele does not teach
23 that substituting a cyclopropyl into a compound
24 improves its properties in every instance, right?

25 A. Factually, there are examples where

1 introducing a cyclopropane is not -- is not
2 beneficial as any structural change that is part of
3 the toolbox of the medicinal chemist does not work in
4 every single example. But these are all the
5 strategies that a person of ordinary skill in the art
6 would apply and emphasize when they're trying to make
7 modifications to lead compounds.

8 Q. And you don't need Talele to tell you that,
9 right, you know as a medicinal chemist that there's
10 no design strategy that's going to work in every
11 case, right?

12 MR. CHEN: Objection. Form.

13 THE WITNESS: The most important thing about not
14 needing Talele is that putting a cyclopropane into a compound
15 to increase properties to -- to benefit drug properties and
16 to suppress metabolism and so forth is part of the training
17 that a person of ordinary skill in the art would have in
18 medicinal chemistry and would know.

19 And the fact that this is a review article that
20 compiles in one place large numbers of examples where this
21 strategy is successful, it just codifies my belief
22 that addition of a cyclopropane ring is a very well-known
23 strategy that would be known to and applied by a person of
24 ordinary skill in the art to lead optimization.

25 BY MR. BIEGLER:

1 Q. Sure. It's one of many possible
2 strategies, correct?

3 MR. CHEN: Objection. Form.

4 THE WITNESS: There are other -- there are other
5 strategies, of course, for lead optimization.

6 BY MR. BIEGLER:

7 Q. Let's go to page 24.

8 And do you see the discussion of the
9 Histamine H3 Receptor Agonist 123?

10 A. Yeah, that's in the left-hand column.

11 Q. So it starts in the left-hand column, and I
12 think it continues to the right.

13 A. Okay.

14 Q. And in the right column, it says,
15 "Specifically, introduction of a cyclopropyl ring
16 reduced the pKa of the piperazine ring compared to
17 the isopropyl substitution, thereby increasing plasma
18 clearance and reducing half-life. It may be noted
19 that unlike other examples" -- and it provides some
20 examples -- "where a cyclopropyl ring led to an
21 increased half-life, in the case of 123, the
22 cyclopropyl ring produced decreased half-life.
23 Therefore, pK can be modulated with a cyclopropyl
24 group; however, it is context-dependent, and one
25 strategy does not work in all cases."

1 Do you see that?

2 A. Right. That's correctly read from the
3 paper.

4 Q. And you agree with that statement?

5 MR. CHEN: Objection. Form.

6 THE WITNESS: Well, I mean, that's the teaching in
7 Talele, and so I accept that as written.

8 BY MR. BIEGLER:

9 Q. And that's an example where a cyclopropyl
10 substitution resulted in worse properties, correct?

11 A. So it is not required that any particular
12 strategy is guaranteed to give a particular outcome.
13 It's only necessary that a person of ordinary skill
14 in the art applying this particular strategy for lead
15 optimization would have a reasonable expectation of
16 success.

17 Q. So that wasn't my question at all.

18 This is an example where a cyclopropyl
19 substitution resulted in worse properties, right?

20 MR. CHEN: Objection. Form.

21 THE WITNESS: This is an example of that, and
22 because it is -- it is not the common observation, as
23 reflected in the voluminous literature that's cited in this
24 review article, it is reasonable for a person of ordinary
25 skill in the art to try this modification with an expectation

1 of success.

2 BY MR. BIEGLER:

3 Q. And the only way that a person of skill
4 would know if they had succeeded in improving the
5 property of a compound by adding a cyclopropyl group
6 is to make it and test it, correct?

7 MR. CHEN: Objection. Form.

8 THE WITNESS: I mean, that's the ultimate test
9 that's going to be applied to all drug, you know -- drug
10 compounds that one would design is to make them and test
11 them. That's what -- that's what medicinal chemists do for a
12 living.

13 MR. CHEN: Counsel, do you want to take a lunch
14 break, or do you have a pending question?

15 MR. BIEGLER: I think we're at a good place for a
16 break --

17 MR. CHEN: Okay.

18 MR. BIEGLER: -- I will say, though, I think I have
19 maybe one session, at tops, left.

20 THE WITNESS: Okay.

21 MR. BIEGLER: So I don't know if you want to take a
22 full lunch or if you want to power through --

23 THE WITNESS: I would prefer to take a break.

24 MR. BIEGLER: That's totally fine. No problem.

25 (Lunch recess.)

1 MR. BIEGLER: Welcome back.

2 BY MR. BIEGLER:

3 Q. Let's turn to paragraph 91 in your
4 declaration, and I want to just talk about Ren for a
5 little bit.

6 A. Okay.

7 MR. BIEGLER: So can you actually give me Ren, too.

8 BY MR. BIEGLER:

9 Q. I'm going to hand you also what has been
10 marked as Exhibit 1030.

11 (Exhibit 1030 identified.)

12 BY MR. BIEGLER:

13 Q. So you rely in Ren on Compounds 76 and 90,
14 correct?

15 A. Right. 90 is the primary one.

16 Q. Okay. And that's one of over 100 exemplary
17 compounds in Ren?

18 MR. CHEN: Objection. Form.

19 THE WITNESS: I'm not sure. I didn't count the
20 compounds in Ren.

21 BY MR. BIEGLER:

22 Q. If you look at page 230, do you see
23 Table 29?

24 A. Okay.

25 Q. And my only question there is that table

1 has results for compounds that go up to No. 103,
2 right?

3 A. Yes, it does.

4 Q. Okay. Do you have any reason to think
5 there's not over 100 compounds disclosed in Ren
6 specifically?

7 A. There must be more than 100 compounds in
8 Ren since they give data for a lot of them.

9 Q. Okay. And if we go -- stay sort of
10 there -- on the next page, so it's page 231 of Ren.

11 Do you see Table 30?

12 A. I do.

13 Q. Okay. And Table 30 has some pK data for
14 certain of the Ren compounds, right?

15 A. Correct.

16 Q. And you rely on some of that data in your
17 declaration?

18 A. Right. In paragraph 93.

19 Q. Okay. And that Table 30 has
20 pharmacokinetic data on Reference Compound 1, which
21 is Orforglipron, right?

22 A. Oh, I see. The table was split across the
23 columns. Can you point me to the information about
24 Reference Compound 1 being Orforglipron?

25 Q. Probably, give me one second.

1 Let me -- while we're looking for that in a
2 different -- in addition to Reference Compound 1,
3 Table 30 has pharmacokinetic data for Compound 19 of
4 Ren, Compound 73 of Ren, Compound 76 of Ren, Compound
5 90 of Ren, and Compound 91 of Ren, correct?

6 A. Yes. 1973, 76, 90, and 91.

7 Q. Okay. And in your -- and it has -- the
8 table has Cmax, AUC, and F, which, I believe, is
9 bioavailability data; is that right?

10 A. F percent is -- my reading of that is
11 that so-called free fraction.

12 Q. Okay.

13 A. Which reflects the amount of compound
14 that's bound to serum proteins. Actually,
15 bioavailability is defined right there in my
16 declaration there in paragraph 93, so that is
17 bioavailability, sorry.

18 Q. Okay. So Table 30 has Cmax, AUC, and
19 bioavailability data for the compounds?

20 A. Right. Right.

21 Q. And in your -- in your declaration, you
22 focus only on the bioavailability data; is that
23 right?

24 MR. CHEN: Objection. Form.

25 THE WITNESS: So the only parameter of this pK data

1 that's discussed in the declaration is, indeed, the
2 bioavailability.

3 BY MR. BIEGLER:

4 Q. Okay. And I guess I should have seen this
5 earlier, but right below the Table 30, it shows the
6 structure of Reference Compound 1, right?

7 A. Ah, it does.

8 Q. And that's Orforglipron, correct?

9 A. It is Orforglipron.

10 Q. Okay.

11 A. There we go.

12 Q. So you don't discuss the AUC specifically
13 in your declaration from Table 30, right?

14 A. That's right, I'm focusing on
15 bioavailability, which is more a -- it's like the
16 terminal question about an orally active drug.

17 Q. You'd agree, though, that the AUC for
18 Compound 90, which you rely on, is lower than the AUC
19 for Orforglipron, based on the data here, correct?

20 A. Let's see.

21 MR. CHEN: Objection. Form.

22 THE WITNESS: So the AUC for Orforglipron given
23 here is 4528, and the AUC for 90 is 3338.

24 BY MR. BIEGLER:

25 Q. Okay. You can put that to the side, I

1 think.

2 If you can turn in your declaration to --
3 it's going to be around page 13 -- page 14, paragraph
4 24.

5 A. Okay.

6 Q. In 24, you provide your understanding of
7 the legal standard for anticipation; is that right?

8 A. Uh-huh.

9 Q. But you don't have any opinion in this case
10 that any of the claimed compounds are anticipated,
11 right? Your opinions are all based on obviousness?

12 A. Right. Yes. This is -- this declaration
13 is relying on obvious arguments.

14 Q. Okay. And then the rest of this section,
15 25 -- paragraph 25 through 29 discuss your
16 understanding of the legal standards for obviousness,
17 right?

18 A. Uh-huh.

19 Q. And I don't see in here any mention of the
20 use of hindsight; is that right?

21 A. I don't discuss that here.

22 Q. And did you know that you're not allowed to
23 use hindsight in assessing whether a claim is obvious
24 or not?

25 MR. CHEN: Objection. Form.

1 THE WITNESS: So I am aware of concerns about the
2 use of hindsight in doing obviousness analysis, yes.

3 BY MR. BIEGLER:

4 Q. Why didn't you mention that in your legal
5 standards?

6 A. It didn't occur to me that I needed to do
7 so. I would just say an oversight. And also, I
8 mean, I'm certainly sensitized to issues of
9 hindsight, and since it never occurred to me that the
10 processes that we engaged in involved hindsight, it
11 didn't occur to me to include statements about that.

12 Q. If you can turn to paragraph 44.

13 A. Okay.

14 Q. So in this section, you're talking about
15 small-molecule GLP-1 receptor agonists, right?

16 A. Uh-huh.

17 Q. And you walk through a few examples of
18 drugs that people were pursuing, right?

19 A. Right.

20 Q. And one of them is -- at least one drug or
21 more that were being pursued by Pfizer in this space?

22 A. Yes.

23 Q. And you're aware that Pfizer discontinued
24 that program, correct?

25 MR. CHEN: Objection. Form.

1 THE WITNESS: I have aimed to be aware of
2 happenings in this space, and while I -- I believe that
3 Pfizer compound has been -- its clinical work on it for some
4 indications has been discontinued, it may still be currently
5 pursued for other indications. But, of course, what matters
6 is what the state of the art was at the time the patents were
7 filed, and at that time, Pfizer was pursuing clinical work on
8 its GLP-1 receptor agonists.

9 BY MR. BIEGLER:

10 Q. But that candidate has since failed for --
11 at least for treating obesity, correct?

12 MR. CHEN: Objection. Form.

13 THE WITNESS: I'm not sure.

14 BY MR. BIEGLER:

15 Q. Okay. I think you mentioned before you had
16 been deposed a handful times previously; is that
17 right?

18 A. I've been deposed multiple times before.

19 Q. Sorry, what was the ballpark of how many
20 times?

21 A. Probably a dozen.

22 Q. Okay. And how many of those depositions
23 have involved patent disputes?

24 A. Almost all of them.

25 Q. Have any of them involved GLP-1 receptor

1 agonists?

2 A. No.

3 Q. And have any of them involved claims to --
4 to novel small-molecule compounds?

5 MR. CHEN: Objection. Form.

6 THE WITNESS: I want to revise my statement
7 earlier. I think I said almost all were involved in -- oh.
8 So when I said almost all were involved in patent disputes,
9 that's still a correct statement.

10 BY MR. BIEGLER:

11 Q. Okay.

12 A. And I had a fair amount of experience in
13 patent disputes in the area of DNA diagnostics and so
14 forth where I also have research activity. But in
15 terms of the patent disputes that are -- well, patent
16 disputes involving small-molecule drugs such as
17 Hatch-Waxman cases, I've done several of those. So a
18 significant number of those are involved in
19 invalidating patents, yes.

20 Q. Okay. And some of those cases have
21 involved claims to new small-molecule compounds
22 themselves?

23 A. That's right.

24 Q. To your recollection, what were -- well,
25 were those representations, did they all become

1 public?

2 A. I'm not sure.

3 Q. Okay. Have you testified in court in any
4 of those Hatch-Waxman cases?

5 A. I have.

6 Q. Okay. And where was that?

7 A. That was in the federal district in
8 Delaware.

9 Q. Was that one case or more than one case?

10 A. That was one case --

11 Q. Okay.

12 A. -- with a lot -- with multiple generics and
13 the patentholder of the branded.

14 Q. And you were on the side of one of the
15 generics?

16 A. I worked -- we had a joint team, and I
17 worked for all the generics.

18 Q. Okay. And what was the drug at issue, the
19 brand drug in that case?

20 A. Dustasteride.

21 MR. CHEN: Caution the witness, only disclose the
22 public information.

23 THE WITNESS: Right.

24 MR. BIEGLER: He just said he testified in court.

25 BY MR. BIEGLER:

1 Q. Is that the only court testimony that
2 you've given? Let's just limit it to small
3 molecules.

4 A. Yes, that's it, that's the only court
5 appearance I've done.

6 Q. Okay. In preparing your declaration or
7 preparing for the deposition, did you speak to anyone
8 besides -- besides counsel at Fox Rothschild?

9 A. I did not.

10 Q. You didn't speak to any individuals at
11 Conjupro, for instance?

12 A. I did not.

13 Q. Or CSCP?

14 A. I don't know what CSCP is --

15 Q. Okay.

16 A. -- therefore, I couldn't have spoken to
17 someone there.

18 Q. Okay. Fair enough.

19 And your rate for this case is 450 an hour;
20 is that right?

21 MR. CHEN: Objection. Form.

22 THE WITNESS: I'll direct you to my declaration,
23 which does state my billing rate.

24 BY MR. BIEGLER:

25 Q. Did I get it wrong?

1 A. No, no, no, you're correct. I just want
2 you to know --

3 Q. Okay.

4 A. -- that that's in my declaration.

5 Q. Okay. And approximately how many hours
6 have you billed to this matter thus far?

7 A. I'm not sure. I have not counted it up.

8 Q. Okay. Do you have a ballpark idea of how
9 many hours you've billed?

10 A. The preparation -- the preparation of the
11 declaration last year, probably upwards of 50 hours,
12 and then the preparation for this deposition this
13 month, probably upward of 30 hours, but I haven't
14 counted it.

15 Q. And is that universe of time sort of -- let
16 me ask a clearer question.

17 Is that roughly 80 hours, not holding you
18 to the exact amount, is that the full amount of time
19 you've spent on this matter to date?

20 MR. CHEN: Objection. Form.

21 THE WITNESS: I mean, yes, that's the amount of
22 time I've spent working with Fox attorneys, and I was told
23 about the -- about the area of art, and I probably reviewed
24 some review articles and stuff like that --

25 BY MR. BIEGLER:

1 Q. Yeah.

2 A. -- before I became engaged --

3 Q. Okay.

4 A. -- and therefore, I was not compensated for
5 that early work. But in terms of working on this
6 case, that's -- I think that's a fair assessment of
7 the amount of time I've spent on this.

8 Q. Have you worked with Conjupro prior to this
9 case?

10 A. Never.

11 Q. Okay. And have you worked with Fox
12 Rothschild before this case?

13 A. Never.

14 Q. Have you received any compensation from
15 Conjupro before this case?

16 A. Never.

17 MR. BIEGLER: Okay. I think that's all the
18 questions that I have. Thank you.

19 MR. CHEN: Give us five minutes. We may need to
20 redirect.

21 THE WITNESS: Okay.

22 (A brief recess was taken.)

23 MR. CHEN: So, Dr. Pirrung, I have one question.

24 EXAMINATION

25 BY MR. CHEN:

1 Q. What do you consider as a potent GLP-1
2 receptor agonist?

3 A. So drug potency in the GLP-1 receptor world
4 is going to be similar to what most of the medicinal
5 chemistry role is like. If you can get compounds
6 into single-digit nanomolar potency, that's perfectly
7 good. You've got compounds that will be worthy of
8 further development, so lots of the -- of the
9 compounds that we've seen here qualify in that
10 regard.

11 MR. CHEN: Okay, that's all we have.

12 MR. BIEGLER: I don't have anything further.

13 MR. CHEN: Okay.

14 (Deposition Concluded at 1:32 p.m.)
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C E R T I F I C A T I O N

I, MICHAEL C. PIRRUNG, Ph.D., say I have read or had interpreted to me the foregoing deposition and declare under penalty of perjury that my answers as indicated are true and correct.

(Date)

(Signature)

Certificate of Reporter

-000-

I, the undersigned, a Certified Shorthand Reporter,
Licensed by the State of California, being empowered to
administer oaths and affirmations pursuant to Section
30(f)(1) of the Federal Rules of Civil Procedure, do hereby
certify:

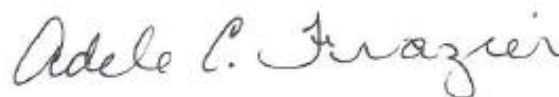
That the foregoing proceedings were taken before me
at the time and place herein set forth; that any witness in
the foregoing proceedings, prior to testifying, were placed
under oath; that a verbatim record of the proceedings was
made by me using machine shorthand which was thereafter
transcribed by me under my direction; further, that the
foregoing is an accurate transcription thereof.

I further certify that I am neither financially
interested in the action nor a relative or employee of any
attorney or any of the parties.

Further, that if the foregoing pertains to the
original transcript of a deposition in a Federal Case, before
completion of the proceedings, review of the transcript was
requested.

IN WITNESS WHEREOF, I have this date subscribed my
name.

DATED: March 2, 2026



Adele C. Freeman, CSR 9690

1 Reference No.: 14306701

2

3 Case: Conjupro Biotherapeutics vs Ascleitis Pharma China Co.

4

5 **DECLARATION UNDER PENALTY OF PERJURY**

6

7 I declare under penalty of perjury that
8 I have read the entire transcript of my Depo-
9 sition taken in the captioned matter or the
10 same has been read to me, and the same is
11 true and accurate, save and except for
12 changes and/or corrections, if any, as indi-
13 cated by me on the DEPOSITION ERRATA SHEET
14 hereof, with the understanding that I offer
15 these changes as if still under oath.

16

17

18 _____
19 Michael C Pirrung Ph.D.

20

21

22 **NOTARIZATION OF CHANGES**

23

24 (If Required)

25

26

27 Subscribed and sworn to on the _____ day of

28

29

30 _____, 20____ before me,

31

32

33 (Notary Sign)_____

34

35

36 (Print Name) _____ Notary Public,

37

38

39 in and for the State of _____

40

1 Reference No.: 14306701
2 Case: Conjupro Biotherapeutics vs Ascletis Pharma China Co.

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Michael C Pirrung Ph.D.

1 Reference No.: 14306701
2 Case: Conjupro Biotherapeutics vs Ascleitis Pharma China Co.

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25 SIGNATURE: _____ DATE: _____
Michael C Pirrung Ph.D.