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

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SAMSUNG BIOEPIS CO, LTD.,
Petitioner,
vs.
REGENERON PHARMACEUTICALS, INC.,
Patent Owner.

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Case IPR2023-008844

U.S. Patent No. 11,253,572

VIDEO-RECORDED
DEPOSITION OF: MICHAEL STEWART, MD

DATE: May 30, 2024

TIME: COMMENCED: 8:49 a.m.
CONCLUDED: 2:03 p.m.

TAKEN BY: Petitioner

PLACE: Hampton Inn Jacksonville/Ponte Vedra Beach
1220 Marsh Landing Parkway
Jacksonville Beach, Florida 32250

REPORTED BY: Mae Fisher, RMR, CRR





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I N D E X

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S T I P U L A T I O N S

It is hereby stipulated and agreed by and between counsel present for the respective parties, and the deponent, that the reading and signing of the deposition are hereby RESERVED.



P R O C E E D I N G S

THE VIDEOGRAPHER: Good morning. My name is Joseph Mackin, the videographer, and we are now on live video record. 08:49:25 08:49:40 08:49:44

Please be aware that microphones are sensitive and can pick up whispering, private conversations and cellular interference. Please silence all cell phones or place them away from the microphones, as they can interfere with the deposition's audio. Audio and video recording will continue to take place unless all parties agree to go off the record. 08:49:45 08:49:49 08:49:51 08:49:54 08:49:56 08:50:00

We are here recording live at 1220 Marsh Landing Parkway in Jacksonville Beach, Florida 32250, for the video deposition of Michael W. Stewart. The time is 8:50. The date is Thursday, May 30, 2024. 08:50:02 08:50:05 08:50:08 08:50:12

Would all counsel please state their appearance for the record and the witness will be sworn in. 08:50:18 08:50:21

MR. NIMROD: Ray Nimrod from Quinn Emanuel for petitioner. 08:50:22 08:50:25

MR. BRAUSA: Adam Brausa from Morrison & Foerster on behalf of patent owner and joined by my colleague, Rebecca Weires. And I believe on the remote realtime is Eileen Woo from Regeneron. 08:50:25 08:50:30 08:50:33 08:50:38

THE COURT REPORTER: Can you raise your right hand, please. 08:50:47





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Do you solemnly swear or affirm that the testimony you are about to give in this cause will be the truth, the whole truth, and nothing but the truth?
THE WITNESS: I do. 08:50:48
MICHAEL STEWART, MD, 08:50:48
a witness herein, having been first duly sworn, was examined, and testified as follows: 08:50:49
DIRECT EXAMINATION 08:50:49
BY MR. NIMROD: 08:50:49
Q. Good morning, Dr. Stewart. 08:50:50
A. Good morning, Mr. Nimrod. 08:50:51
MR. NIMROD: I'd like to mark as Stewart 08:50:55
Exhibit 1 a copy of the 572 patent. 08:50:56
(Exhibit No. 1 was marked for identification.) 08:51:08
MR. NIMROD: I'd also like to mark as Stewart 08:51:22
Exhibit 2 a copy of Dr. Stewart's declaration. 08:51:23
(Exhibit No. 2 was marked for identification.) 08:51:34
BY MR. NIMROD: 08:51:34
Q. Here you go. 08:51:36
A. Thank you. 08:51:37
MR. BRAUSA: Thank you. 08:51:37
BY MR. NIMROD:
Q. Dr. Stewart, if you could turn in your 08:51:42
declaration to paragraph 65, please -- 64. 08:51:44
A. Okay. 08:51:56



Q. You state in paragraph 64: It is my opinion 08:51:56
based on the claims and specification of the 572 patent 08:52:00
that a POSA would understand that challenged claims, 08:52:04
specifically claim 15 and thereby claim 25, be limited 08:52:08
to a predetermined fixed dosing schedules. 08:52:14
Do you see that? 08:52:16
A. Yes, I do. 08:52:17
Q. And then on paragraph 74, you state -- seems more 08:52:18
broadly, in the last sentence of paragraph 74. Are you 08:52:26
with me? 08:52:29
A. I see it. 08:52:30
Q. It says: In my opinion -- it is my opinion that 08:52:30
a POSA would see this as further evidence that the 572 08:52:33
patent claims are drawn to predetermined fixed interval 08:52:37
dosing regimens. 08:52:41
Do you see that? 08:52:42
A. I see it. 08:52:42
Q. Is it your opinion that all the claims of the 572 08:52:43
patent are directed to predetermined fixed interval 08:52:47
dosing regimens? 08:52:52
A. Yes, it is, it's my opinion. 08:52:56
Q. So if we could turn to Exhibit 1, which is the 08:52:58
patent, the 572 patent. And go to claim 27, claims near 08:53:02
the end. You're already there. Good. 08:53:13
Claim 27 depends from claim 26. And it requires 08:53:16



in the dependent claim only two secondary doses are 08:53:24
administered to the patient. 08:53:28
Do you see that? 08:53:29
A. Yes, I do. 08:53:29
Q. So what is the predetermined fixed dosing regimen 08:53:31
required by claim 27? 08:53:35
MR. BRAUSA: Objection; form. 08:53:39
THE WITNESS: So since 27 depends on 26, my 08:53:41
understanding is that this is a method of treating 08:53:48
age-related macular degeneration and the patient need 08:53:53
thereof, comprising sequential administration of a 08:53:56
single dose of 2 milligrams of Aflibercept. 08:54:00
And then 27 says: Wherein, only two secondary 08:54:03
doses are administered to the patient and then 08:54:07
followed by one or more tertiary doses of 2 milligrams 08:54:14
of Aflibercept. 08:54:19
And then you have the qualifier: And those 08:54:20
doses, the tertiary doses, are given at eight weeks 08:54:24
intervals. Each secondary dose is four weeks 08:54:27
following immediate preceding dose. 08:54:30
And then you have a qualifier for a visual 08:54:32
result at the end. 08:54:35
BY MR. NIMROD: 08:54:36
Q. Okay. So for claim 27, the fixed regimen 08:54:36
requires three initial doses that are a month apart and 08:54:42



then followed by dosing every eight weeks till the end 08:54:44
of treatment; is that right? 08:54:48
MR. BRAUSA: Objection; form. 08:54:50
THE WITNESS: So 27 when combined with 26 08:54:51
requires three initial doses, a primary, two 08:54:56
secondaries, and then followed by tertiary doses at 08:54:59
eight-week intervals. 08:55:03
BY MR. NIMROD: 08:55:04
Q. And to be within the scope of claim 27, I think 08:55:05
we talked about this last time, it's your opinion that 08:55:13
if by happenstance or by treatment by PRN, a physician 08:55:16
does not have a predetermined regimen but simply through 08:55:21
observation of the patient decides on an ongoing basis 08:55:26
to do first dose, two secondary doses and then have 08:55:30
eight-week dosing after that, that would not fall within 08:55:35
the scope of the claims; is that right? 08:55:37
MR. BRAUSA: Objection; form. 08:55:39
THE WITNESS: Would you repeat the question, 08:55:40
please? You combined a couple of different factors 08:55:43
there. 08:55:46
BY MR. NIMROD: 08:55:46
Q. Right. So if a physician does not have a 08:55:47
predetermined dosing regimen, does that mean that the 08:55:48
treatment does not fall within the scope of claim 27? 08:55:52
MR. BRAUSA: Objection; form. 08:55:56





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THE WITNESS: So my opinion, 27 requires a predetermined dosing regimen. 08:55:57 08:56:03

BY MR. NIMROD: 08:56:08

Q. If you could then turn to page 30 and 31 and just read paragraph 65 to yourself, please -- I'm sorry -- of your declaration. 08:56:08 08:56:12 08:56:16

A. Okay. Paragraph 65? 08:56:17

Q. Yes, please. 08:56:21

A. Okay. 08:57:17

Q. All right. On page 31, you -- sorry, go back to 30. You say: Fixed regimens are those where doses are administered on a predetermined schedule regardless of observed outcomes at any given visit. 08:57:18 08:57:23 08:57:28 08:57:31

Do you see that? 08:57:33

A. Yes, I see that. 08:57:34

Q. Okay. And then you go on and say that fixed regimens include monthly doses, as well as regimens involving a set number of loading doses all by dosing at longer fixed interval as described in the EYLEA label. 08:57:36 08:57:39 08:57:42 08:57:46

Do you see that as well? 08:57:50

A. Yes, I do. 08:57:51

Q. And then you go on the next sentence and you say that: Sometimes adherence to the predetermined schedules in perfect regimens are still considered fixed when the intended dosing interval is based on a schedule 08:57:52 08:57:55 08:58:00 08:58:01



rather than patient outcomes. 08:58:05

Do you see that? 08:58:06

A. Yes, I do. 08:58:07

Q. What do you mean by rather than patient outcomes? 08:58:09

MR. BRAUSA: Objection; form. 08:58:13

THE WITNESS: By that, we mean that we adhere to the predetermined schedule and whether the patient has significant success, marginal success, we stick to the schedule, regardless of that and we do not use patient-determined data at the visit to modify the dosing. 08:58:14 08:58:19 08:58:23 08:58:30 08:58:34 08:58:38

BY MR. NIMROD: 08:58:40

Q. So then does that mean that if -- strike that. 08:58:41

When you -- strike that again. 08:58:45

If a physician decides to use a predetermined dosing regimen, as called for by claim 27 in the 572 patent, does the physician know -- can the physician predict in advance whether an individual patient will have a specific outcome? 08:58:49 08:58:51 08:58:55 08:59:00 08:59:02

MR. BRAUSA: Objection; form. 08:59:05

THE WITNESS: You're speaking of treating with Aflibercept? 08:59:07 08:59:10

BY MR. NIMROD: 08:59:10

Q. Yes, I am. 08:59:10

A. And according to claim 27, which, of course, 08:59:11



follows 26, my answer is no, in advance, you cannot predict the outcome of a given patient. 08:59:16 08:59:20

Q. So does that mean that for claim 27, where you have a predetermined fixed schedule, that is not based on patient outcomes, as you're going along with the treatment, one would simply measure the outcome at 52 weeks to see if a patient achieved the required gain or not; is that right? 08:59:24 08:59:28 08:59:34 08:59:37 08:59:42 08:59:47

MR. BRAUSA: Objection; form. 08:59:48

THE WITNESS: In order to meet -- in order to meet claim 26, then you would measure the outcome at week 52 to see if the claim were followed. In clinical practice, obviously that's not something you would consider. 08:59:51 08:59:56 09:00:02 09:00:06 09:00:09

BY MR. NIMROD: 09:00:11

Q. You wouldn't consider whether or not -- what the outcome was at 52 weeks in particular? Is that what you mean? 09:00:11 09:00:13 09:00:16

A. You wouldn't -- 09:00:17

MR. BRAUSA: Objection; form. 09:00:17

THE WITNESS: You would not compare it to the claim. 09:00:17 09:00:22

BY MR. NIMROD:

Q. You would not compare it to -- how do you pronounce that again -- Ranibizumab? 09:00:24 09:00:28



A. Ranibizumab. 09:00:30

Q. Got it. Okay. So in actual clinical practice, you would not compare your patient's results to what the patient would have achieved with Ranibizumab -- 09:00:31 09:00:36 09:00:40

MR. BRAUSA: Objection. 09:00:43

BY MR. NIMROD: 09:00:43

Q. -- for an individual patient? 09:00:44

MR. BRAUSA: Objection; form. 09:00:45

THE WITNESS: So in clinical practice, we have no way to know what that patient would have achieved had they received Ranibizumab instead of Aflibercept. 09:00:46 09:00:50 09:00:54

BY MR. NIMROD:

Q. So for claim 26, how would a physician know whether or not the -- let me strike that again. 09:01:01 09:01:09

How would a -- for claim 26, how would a skilled artisan know whether they were practicing claim 26 and specifically know whether or not they had achieved a gain in visual acuity as compared to Ranibizumab? 09:01:14 09:01:18 09:01:24 09:01:26

MR. BRAUSA: Objection; form. 09:01:32

THE WITNESS: Well, if you look at the writing of 26, and you are concerned about meeting the claim, then you would compare it to the comparator, which is Ranibizumab, if you were worried about meeting the claim. 09:01:33 09:01:38 09:01:43 09:01:47 09:01:51

BY MR. NIMROD: 09:01:52





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Q. But the claim 26 and, therefore, claim 27 refer to treating a patient. Do you see that? 09:01:52 09:01:58

A. Yes. 09:02:00

Q. So for a patient, how would you determine, as a skilled artisan, whether you were practicing the method -- let me start over again, okay? 09:02:00 09:02:04 09:02:08

All right. So let's say a physician decides to practice the dosing regimen that's required by claim 27, which is an initial dose, two secondary doses and then one month apart, and then tertiary doses that are eight weeks apart, do you follow me? 09:02:10 09:02:15 09:02:20 09:02:24 09:02:28

A. Yes. 09:02:31

Q. Okay. So a skilled person is then treating a patient following that regimen, that's required by claim 27, how does the skilled person know whether the patient that they're treating meets the limitation -- limitation of wherein is as effective in achieving a gain in visual acuity as monthly administration of 0.5 milligrams of Ranibizumab by intravitreal injection in human subjects with age-related macular degeneration at 52 weeks following the initial dose? 09:02:31 09:02:35 09:02:39 09:02:44 09:02:49 09:02:53 09:02:58 09:03:03 09:03:09

MR. BRAUSA: Objection; form. 09:03:11

THE WITNESS: So let me answer that two ways. So one, the physician would not know what might have happened if Ranibizumab had been used instead of 09:03:12 09:03:19 09:03:22



Aflibercept. So you get the results that you get. 09:03:27

Secondly, if you're looking to know, does it meet the claim, then you look at the data -- you look at the monthly -- the expected visual acuity results at 52 weeks with monthly Ranibizumab. 09:03:33 09:03:35 09:03:42 09:03:46

BY MR. NIMROD:

Q. And what is the expected visual acuity results at 52 weeks for monthly Ranibizumab? 09:03:50 09:03:56

A. So my understanding is that comes from the specifications. And that comes -- and that comes from table 1 in the specifications. And in table 1, there are two numbers. Column 15. 09:03:59 09:04:03 09:04:09 09:04:16

Q. I'm there. Yeah. 09:04:22

A. Yeah. So 8.1 and 9.4. Those are derived from two parallel similarly structured studies. 09:04:24 09:04:28

Q. So is it your opinion that in order for a method to fall within the scope of claim 27, there has to be a mean improvement in visual acuity of 8.1 or 9.4? 09:04:31 09:04:38 09:04:44

MR. BRAUSA: Objection; form. 09:04:51

THE WITNESS: So if treating with Aflibercept according to the specifications in 26 and 27, then my understanding is it has to meet those numbers. Now, we can argue is it 8.1, is it 9.4, but that's the comparator for Ranibizumab that's specified in the claim. 09:04:51 09:04:55 09:04:59 09:05:03 09:05:09 09:05:13



BY MR. NIMROD: 09:05:14

Q. So in order to meet the method of claim 27, the patient would have to achieve at least 8.1 in terms of improved visual acuity? 09:05:14 09:05:17 09:05:23

MR. BRAUSA: Objection. 09:05:25

BY MR. NIMROD: 09:05:25

Q. Is that right? 09:05:26

MR. BRAUSA: Objection; form. 09:05:26

THE WITNESS: So treated, according to 26 and 27, with Aflibercept, patient would -- at 52 weeks, would have to meet eight letters. We don't measure at point 1. 09:05:28 09:05:30 09:05:35 09:05:41

BY MR. NIMROD: 09:05:43

Q. You also said in your answer, you get the results that you get. What -- let me start over again. 09:05:44 09:05:53

In your answer, you said you get the results that you get at 52 weeks. What did you mean by that? 09:05:57 09:05:59

A. Sort of a colloquial way of saying it. You treat according to your regimen. And the results you end up with are what you end -- are what you have for that patient. You have no way of comparing to a different regimen that could have been used or a different drug that could have been used. 09:06:03 09:06:08 09:06:11 09:06:14 09:06:19 09:06:21

Q. And when you say you get what you get, if you're practicing the method of claim 27, that means that you 09:06:24 09:06:26



don't have a way of predicting whether or not you're going to be above or below the baseline for Ranibizumab of eight letter gains; is that right? 09:06:29 09:06:31 09:06:34

A. So you're saying -- 09:06:36

MR. BRAUSA: Objection; form. 09:06:39

THE WITNESS: That if you treat according to the specifications in claims 26 and 27, that there's no way in advance to know if your 52-week visual acuity result is going to be above or below the comparator, which is Ranibizumab result. 09:06:43 09:06:44 09:06:47 09:06:52 09:06:54

BY MR. NIMROD: 09:06:58

Q. And you agree with that? 09:06:58

A. As I stated it, yeah. Well, as I stated it, yes. 09:07:00

Q. You stated it better. Let me just repeat that, then. 09:07:05 09:07:12

A. Okay.

Q. It's your opinion that if you treat according to the dosing regimen of claims 27, I'll say, there's no way to know in advance if you're going to meet the 52-week visual acuity result that is going to be above or below the comparator, which is Ranibizumab; is that right? 09:07:12 09:07:16 09:07:18 09:07:22 09:07:27 09:07:30

A. Treating with Aflibercept, yes. That's correct. 09:07:30

Q. And when I say claim 27, that -- of course, that always requires Aflibercept, just -- 09:07:34 09:07:38





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