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Paper No. 46

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

FORESIGHT DIAGNOSTICS INC.,
Petitioner,

v.

PERSONALIS, INC.,
Patent Owner.

IPR2023-00224 (Patent 11,384,394 B2)
IPR2023-00317 (Patent 11,408,033 B2)

Record of Oral Hearing
Held: March 19, 2024

Before: ULRIKE W. JENKS, ROBERT A. POLLOCK, and TIMOTHY G. MAJORS, *Administrative Patent Judges*.

APPEARANCES:

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The above-entitled matter came on for hearing on March 19, 2024, commencing at 1:00 p.m., via video teleconference.

1 P R O C E E D I N G S
2 - - - - -
3 JUDGE POLLOCK: Good morning. I am Judge Pollock.
4 With me are Judges Jenks and Majors. This is the final hearing in IPR2023-
5 00224 and IPR2023-00317 which relate to U.S. patent numbers 11,384,394
6 and 11,408,033, respectively. This hearing is open to the public. Petitioner
7 is Foresight Diagnostics Incorporated, Patent Owner is Personalis
8 Incorporated. Counsel for Petitioner Foresight, would you kindly identify
9 yourself and your colleagues?
10 MR. KRAUSE: Yes. Good morning, Your Honors. You have
11 Andrew Krause from Irell & Manella. And with me and also presenting
12 today will be Alan Heinrich from Irell & Manella. And also on the line is
13 our co-counsel, Amir Naini, from Naini, P.C.
14 JUDGE POLLOCK: Good afternoon. Counsel for Patent
15 Owner Personalis, would you kindly identify yourself and your colleagues?
16 Mr. Luman, you're on mute right now.
17 MR. LUMAN: Thank you. All right. My name is Nate
18 Luman. I'm from the law firm of Knobbe Martens. And joined with me
19 today is lead counsel, Derek Walter. And through the public webcast link,
20 we're going to be joined by Stephen Moore, who's Vice President, General
21 Counsel, and Corporate Secretary for Patent Owner Personalis.
22 JUDGE POLLOCK: Well, good afternoon.
23 MR. LUMAN: Thank you.
24 JUDGE POLLOCK: As set forth in our order of February
25 23rd, the Petitioner will have 45 minutes to present its argument, and Patent

1 Owner will offer a total of 45 minutes to respond. Petitioner will open the
2 hearing by presenting its case regarding the challenge claims for which the
3 Board instituted trial. Thereafter, Patent Owner will respond to Petitioner's
4 argument. Counsel for Petitioner, would you like to reserve any time for
5 rebuttal?
6 MR. KRAUSE: Yes, Your Honor. We would like reserve 15
7 minutes for rebuttable.
8 JUDGE POLLOCK: All right. Mr. Luman, you may have the
9 last words. Would you'd like reserve any time?
10 MR. LUMAN: Yes. I'd like to reserve five minutes, please.
11 JUDGE POLLOCK: Okay. A few matters of housekeeping
12 before we begin. First, the panel will attempt to keep an accurate account of
13 the time, but we suggest the parties do the same. For the courtesy of all
14 parties, and to minimize technical interference, please mute your
15 microphone when not speaking. For the clarity of the record, please identify
16 yourself each time you speak and refer to each demonstrative by page
17 number. We have digital access to the full record, but to the extent you refer
18 to something other than a demonstrative, please give us some time to locate
19 a copy as we may not be able to clearly read the text or the context of what
20 you post to video. To the extent there are objections to today's
21 demonstratives, we will take them under advisement, address them in our
22 final written decision to the extent necessary.
23 Should counsel raise any additional objections, please wait until
24 the conclusion of any portion of opposing counsel's presentation before you
25 do so. We will likewise take them under advisement. Petitioner will go first

1 as it bears the burden of showing unpatentability of the challenge claims.
2 Mr. Krause or Mr. Heinrich, you may begin.
3 MR. KRAUSE: Thank you, Your Honors, and may it please
4 the Board. May I have permission to share our screen so I could show the
5 demonstratives?
6 JUDGE POLLOCK: You're welcome to. I do remind you that
7 they're a little small on our screen, but we're following along on other
8 screens.
9 MR. KRAUSE: Thank you. One second, we're having a slight
10 technical issue.
11 JUDGE POLLOCK: Take your time. We'll start the clock
12 when you begin speaking. How's that?
13 MR. KRAUSE: Thank You, Your Honor. I believe it is now
14 up and running. So thank you, Your Honors. May it please the Board. We'll
15 begin with slide 3, which is an overview of the grounds at issue in these IPR
16 proceedings involving the '394 patent and the '033 patent. We're going to
17 focus primarily today on Ground 1 of each, but we'll also talk about the
18 secondary grounds in each. But the main issues governing this proceeding, I
19 think, are fairly addressed to a large extent in Ground 1 of each proceeding.
20 The record in this trial, if you go to slide 2, has largely
21 confirmed the Board's analysis in the institution decisions. And in each
22 proceeding, a key issue is the construction of the claim term capture probes,
23 and the trial record is established that the Board was correct in determining
24 that that term encompasses PCR primers such as those used in Leary and
25 Forshew.

1 For the '394 proceeding, the other key issue is the question of
2 whether Leary uses or renders obvious whole-genome sequencing, which the
3 record confirms it does. In the '033 proceeding, the other main issue is
4 Personalis's attempt to swear behind Forshew, which we believe it has failed
5 to prove. And we'll address some of the subsidiary arguments along the
6 way. But those also do not imbue these claims of patentability.
7 So if we turn first to the global issue of the construction of
8 capture probes. It's slide 8 is the -- bodies. Slide 7 is the construction from
9 the institution decision, which confirmed that in the context of these patents,
10 the term capture probe encompasses at a minimum PCR primers and
11 solution-based hybridization capture probes. This has been confirmed at
12 trial. The intrinsic record sets forth a fairly expansive view of what's
13 encompassed by capture probes. It sets forth a few structural requirements,
14 each of which are satisfied by the PCR primers of Leary and Forshew. And
15 that is that the capture probe has one or more nucleotides that hybridized to
16 one of more nucleic acids. That has been confirmed. Throughout the trial, it
17 has also been confirmed that PCR primers can satisfy the functional
18 requirements of capturing DNA.
19 Slide 10 shows testimony from Dr. Quackenbush's initial
20 declaration where he fleshed this out, that PCR primers are used to capture
21 sequences of interest for subsequent sequencing. The references of record
22 also confirm this. Forshew describes PCR as a technique for capturing
23 template molecules. In reply, further evidence from the head of the
24 Cambridge Laboratory identifying both PCR and oligo probes as capture
25 mechanisms that are used for sequencing technologies. Similarly, right side

1 of the Mamanova Exhibit, when it describes targeted enrichment techniques
2 that include PCR, molecular inversion probes, and hybrid capture
3 techniques, describes each of these techniques as techniques for selectively
4 capturing DNA for subsequent sequencing.
5 And further still, at deposition, the inventor, Mr. West,
6 confirmed this function of PCR primers. He was asked, question, did you
7 ever try to use PCR primer to capture DNA for sequencing? Answer, yes.
8 So I certainly had done that. So this record, I think, establishes that PCR
9 primers meet the structural and functional requirements that could be
10 imbued in capture probes. And we'll address next some of Personalis's
11 arguments throughout the proceedings.
12 If we go to slide 14, we've seen a little bit of inconsistency in
13 Personalis's papers in terms of what's included in the scope of capture
14 probes. In the POR, they set forth in one -- one vein of argument was that a
15 capture probe is synonymous with a pulldown probe, and we'll address that
16 in more detail in a minute. But in addition to that, in response to some of the
17 questions raised by the institution decision, they also said that a capture
18 probe could include a single guanine, a ligase detection reaction, PCR zip
19 code array, and a southern blot probe in additional to array based hybrid
20 capture and solution-based hybrid capture. Essentially, right, they're trying
21 to establish a negative limitation that excludes only PCR. And in sur-reply,
22 they took a little bit different tack and really focused on saying now capture
23 probes are just synonymous with hybridization capture. These other
24 techniques that Dr. Furneaux said were capture probes fell by the wayside to
25 a degree. And on kind of the other end of the spectrum, the inventor at

1 deposition testified that really what he was focused on was just the idea of
2 Agilent's sure select solution phase hybridization capture probes.
3 Now, all this goes to show that it's not really clear what exactly
4 Patent Owner is describing a capture probe to be. But the intrinsic record, as
5 we spoke through earlier, suggests that it includes PCR primers and there's
6 no support for the exclusion that Patent Owner has advanced. There's two
7 key pieces of the intrinsic record that further support this argument. One is
8 the dependent claims to barcoded capture probes and we'll go to slide 18.
9 And in each patent, the '394 Claim 13, and the '033 Claim 10, there is a
10 dependent claim that recites, quote, capture probes further comprise
11 barcodes, or said capture probes, further comprised bar codes. And now
12 there's really no dispute that PCR primers are barcoded and those barcodes
13 are incorporated into the DNA molecules for sequencing, and that barcode
14 can then be used.
15 There's no dispute about that. There is also no evidence in the
16 record of an example of a barcoded pulldown probe or the sort of
17 biotinylated oligonucleotide used for hybridization capture and solution.
18 That's not there. And further, the Personalis inventor contradicted his
19 declaration at deposition in support of the swear behind, and again this is in
20 the context where he testified that he was specifically working with the
21 solution phase baits. He said that using capture probes that further comprise
22 barcodes as part of an accuracy program, but at deposition he testified that
23 actually the bar codes are not part of the capture probes.
24 So that's, again, consistent with the position that if there is a bar
25 coded capture probe, the structure that can meet that function is the PCR

1 primer and not the pulldown probe that they focus on.

2 JUDGE POLLOCK: Counsel, --

3 MR. KRAUSE: Yes, Your Honor.

4 JUDGE POLLOCK: Let's first address capture probes further
5 comprising barcodes. Where would you say that the zip code PCR/ligase
6 micro detection arrays taught by Gerry would fit in here?

7 MR. KRAUSE: So the testimony from Dr. Quackenbush is that
8 those are more similar to a PCR primer. Certainly, there's no evidence that
9 those are a pulldown probe. The Gerry array involves, you know, ligating
10 an initial probe and then hybridizing further to the array. It's not clear that
11 the capture probe is barcoded. There's very little testimony from Dr.
12 Furneaux on that subject, but certainly this isn't right now that their position
13 is capture probe is a hybridization capture probe. There's no evidence that
14 the Gerry array is a hybridization capture probe in the sense that it's using
15 the other literature of record.

16 If we can turn to the pulldown probe issue. This is another
17 example of the intrinsic record supporting the construction that includes
18 PCR primers within the scope of capture probes.

19 JUDGE POLLOCK: I'm sorry to interrupt counsel, but as a
20 matter of housekeeping, would you kindly tell us which slide you're on so
21 we can follow the record later?

22 MR. KRAUSE: My apologies, Your Honor. This is slide 20.
23 And so the institution decision posed the question of whether a capture
24 probe and a pulldown probe are synonymous, and the answer to that is no.
25 Certainly, pulldown probes are a subset of capture probes, but the two are

1 not co-extensive. The testimony from Mr. West and the evidence of record
2 from Dr. Quackenbush is that a pulldown probe is almost always in this
3 record and typically is a biotinylated oligonucleotide. The biotin is attached
4 to the nucleic acid and it can interact with another molecule such as
5 streptavidin to be quote unquote pulled down. And this is in the
6 specification and identified as something that is an optional feature. Biotin
7 and/or streptavidin are identified as linkers and labels, and the specification
8 is plain that such linkers and labels are optional features.
9 So therefore, as Dr. Quackenbush testified, the specification, it
10 sets forth in the definition of capture probes, capture probes that do not
11 include linkers and labels, and the example of that is the PCR primers
12 identified in Leary and Forshew.
13 I will pause there for any questions, but otherwise turn it to Mr.
14 Heinrich to address some of the other global issues.
15 JUDGE POLLOCK: All right. Thank you.
16 MR. KRAUSE: Thank You.
17 MR. HEINRICH: Good morning, Your Honors, or good
18 afternoon. Alan Heinrich for Petitioner Foresight.
19 I'm going to start addressing the attempt to swear behind --
20 Patent Owner's attempt to swear behind Forshew and Chan. I want to start
21 with a couple examples of why Patent Owner's conception story is just not
22 credible, and then address the lack of corroboration for their conception and
23 their lack of establishing reduction to practice.
24 So on credibility, their conception story that the claims have a
25 conception date no later than May 8th, 2012 is fundamentally inconsistent

1 with their own inventorship. So there are two inventors at issue here, Dr.
2 Luo and Dr. Bartha, and their conception story is inconsistent with both.
3 Now, Mr. West testified at deposition that actually the last piece of the
4 invention for the '394 and '033 patents actually came together in March of
5 2012. The May 8th is there is sort of a no later than date. But Dr. Bartha
6 didn't start work at Personalis until May 1st, and Dr. Luo didn't start work at
7 Personalis until June 18th, well past the May 8th no later than date.
8 JUDGE POLLOCK: Mr. Heinrich, what is this alleged last
9 piece of the invention that Mr. West was talking about? I haven't read the
10 transcript.
11 MR. HEINRICH: So this is in reference to a paper published
12 by Dr. Snyder's group at Stanford. And Personalis is relying on that paper
13 for the elements of the claims that require serial monitoring and serial
14 sequencing of additional samples over time, which is not something that
15 there's any evidence of anyone at Personalis doing in this time period. So
16 they're relying on the Snyder paper in March of 2012 for that piece of the
17 claimed inventions.
18 JUDGE POLLOCK: Thank you.
19 MR. HEINRICH: So the main piece of evidence that
20 Personalis is relying is the May 8th, 2012 CEO overview. Of course, that
21 was drafted before the May 8th presentation date. Dr. -- Mr. West refers to
22 some meetings in May 3rd and May 4th where the inventions were allegedly
23 being discussed. But Dr. Bartha is not listed as an attendee at those
24 meetings, and there's simply no evidence that he had any role in anything
25 that was conceived by May 8th, and certainly he wasn't even around in

1 March of 2012, contrary to Mr. West's testimony that that's when the last
2 piece came together.
3 And then it's also undisputed that Dr. Luo didn't even join
4 Personalis until June 18th, which is completely inconsistent with Mr. West's
5 testimony on conception. So this is slide 32. Of course, conception is the
6 touchstone of inventorship. A person must contribute to the conception of
7 the claimed invention to qualify as a joint inventor. Simply participating in
8 reduction to practice is not enough. So, and we cited some cases in our reply
9 that the earliest date of conception has to be the date, you know, at least the
10 date the last of the joint inventors began working on creating the invention.
11 So that's past the May 8th date and past Forshew and Chan.
12 The next issue on credibility is that it's important to take a step
13 back here and see exactly what Patent Owner is claiming. They're claiming
14 that Claims 1 of both patents not only cover their next personal minimum
15 residual disease or MRD test for detecting residual cancer in cancer patients
16 who have undergone treatment, Personalis has explicitly taken the position
17 that those claims, claim 1 of both patents, is co-extensive with the next
18 personal test. They're saying this in the context of trying to obtain a
19 presumption of nexus.
20 But what that means under the case law is that they're saying
21 that the next personal MRD test is the invention claimed in these patents.
22 Well, there's absolutely no evidence that they were working on any MRD
23 test in 2012. The evidence that they're relying on for conception relates to
24 what they call their accuracy program. It was a program to make sequencing
25 more accurate. It wasn't an MRD test. So this is another issue that goes to

1 the overall credibility of the story.

2 But putting that aside, on corroboration, we have unrebutted
3 expert testimony that a person of skill reviewing the materials that they've
4 started to establish conception would not have seen this as enabling the
5 inventions claimed in these patents. Personalis argues that this is
6 immaterial. It's immaterial what a POSA would have understood by
7 reviewing these materials, but that's not the law. And so the law is
8 conception must be proven by evidence showing what the inventor has
9 disclosed to others and what that disclosure means to one of ordinary skill in
10 the art.

11 So, Personalis relies heavily on slide 5 of Exhibit 2112. This
12 is -- the title is an overview of Personalis's accuracy program. It's really just
13 a jumble of conventional techniques. Our expert, Dr. Quackenbush, has
14 unrebutted testimony that a POSA would have found here at most an
15 incipient research project for improving the accuracy of sequencing
16 technology that would involve the use of an undefined combination of
17 various conventional techniques. It does not corroborate any of the claims
18 of the patents at issue here. They have a failure of proof on conception.

19 So, in the interest of time, I'm going to move on to Ground 1 of
20 the '394. Let's see. So this is slide 64. Ground 1 on the '394 focuses on
21 Leary. We're highlighting here the main -- well the disputed elements at
22 issue. Mr. Krause has already addressed the capture probe issue. I'm going
23 to focus here, given the time, on the whole-genome sequencing issue. We
24 believe that the trial record establishes quite clearly, that Leary's first step in
25 the serial biomarker detection and monitoring assay disclosed is a whole-

1 genome sequencing step, as really everyone in the field acknowledged.
2 So in the institution decision, the Board's preliminary
3 construction for whole-genome sequencing was a non-targeted approach to
4 sequencing all or almost all of a genome. But we would submit that the
5 record here shows that actually an express construction is not needed. It's
6 not needed to resolve the issue here. And the reason is because the intrinsic
7 record and the extrinsic evidence both show that Leary is, in fact, a full
8 genome sequencing.
9 So in terms of the intrinsic record, the specification draws a
10 distinction between targeted and non-targeted sequencing. Targeted
11 sequencing would be, say, whole exome sequencing versus non targeted
12 genome wide or whole-genome sequencing. There's nothing in the
13 specification that says whole-genome sequencing has to be almost all of the
14 genome, much less all. It was known at the time that there were gaps in the
15 sequence, and of the 3.2 billion base pairs in the human genome there were
16 only about 2 -- 1 -- so it's 3.2 billion based pairs in human genome, only
17 2.86 were in reference genome at that time. The rest were gap areas. And
18 nothing in the specification indicates that there's some cut off, some
19 percentage that is sort of the cut off for what constitutes whole-genome
20 sequencing.
21 JUDGE POLLOCK: Well, Mr. Heinrich, if I understand
22 correctly, your position would be that whole-genome sequence -- whole-
23 genome sequencing is non-targeted sequencing of some portion of the entire
24 genome, which is distinguishing it from targeting exons, for example.
25 (INDISCERNIBLE).

1 MR. HEINRICH: I think that's fair. So, it would be non-
2 targeted sequencing where the sequence reads are mapped back on to a
3 reference genome.
4 JUDGE POLLOCK: What is this map back? Explain that for
5 me, please.
6 MR. HEINRICH: Well, so after you get your sequence reads,
7 if you're doing whole-genome sequencing, even low coverage whole-
8 genome sequencing, the reads are matched to the reference genome. And
9 that's providing genome-wide information. And you are getting genome
10 wide information even if you're doing as little as 10 percent coverage of the
11 genome, and we'll see some evidence in the record on that issue. But the
12 key is that you're looking genome-wide, you are doing non-targeted
13 sequencing, and you're mapping your sequence reads onto the reference
14 genome.
15 So, let's see. We'll go to slides --
16 JUDGE POLLOCK: You have seven minutes of your time
17 before you cut into your reserve time, sir.
18 MR. HEINRICH: Thank you. So, the Board noted that
19 Forshew, a contemporary of Leary, described Leary's initial step, the mate-
20 pair step, as a whole-genome sequencing step. And that is consistent with
21 everything in the record. Patent Owner said that Foresight's founders
22 excluded Leary from their list of whole-genome sequencing, but that's not
23 correct. We have Exhibit 1112. It's a patent filing from Foresight's founders
24 listing Leary as a whole-genome sequencing reference. We have Forshew
25 listing Leary as whole-genome sequence. We have the Meyerson reference,

1 Exhibit 1031, that identifies Campbell as a whole-genome sequencing
2 reference. Campbell is a shallow paired end whole-genome sequencing
3 assay. It's using the same mate-paired approach as McBride and Leary, and
4 their expert, Dr. Furneaux, recognized this in his own declaration.
5 Then let me go forward to slide -- let's see -- 91. So Dr.
6 Furneaux does some calculations. He has various numbers associated with
7 how much of the genome Leary sequenced. His lowest number is 60
8 percent, but 60 percent is well within what a person of skill recognized as
9 constituting whole-genome sequencing, including patents from Personalis in
10 the same time period. We have evidence in the record. This is slide 88, that
11 Personalis's contemporaneous patents identify whole-genome sequencing as
12 going down to at least 50 percent, and in fact, included low coverage
13 sequencing that would go down even to 10 percent, as I mentioned a
14 moment ago. This slide 90 with various references that we've cited in our
15 reply.
16 JUDGE POLLOCK: So, Mr. Heinrich, can I jump off into
17 another question here? We have five minutes left.
18 MR. HEINRICH: Yes, Your Honor.
19 JUDGE POLLOCK: Claim 1 of the '394 patent indicates that
20 the plurality of capture probes hybridized to one or more polymorphisms.
21 How -- how does a PCR reaction hybridized to one or more polymorphisms,
22 as opposed to a polymorphism being between two flanking PCR primers?
23 Well, what in the record addresses that?
24 MR. HEINRICH: Sure. Can I turn that to Mr. Krause who's
25 handling the capture probe issue?

1 JUDGE POLLOCK: Yes.

2 MR. KRAUSE: So thank you, Your Honor. I think the clearest
3 example that the PCR primer is flanking a polymorphism hybridized to the
4 polymorphism is the dependent claims that recite that the claimed
5 polymorphisms include deletions. And Dr. Quackenbush addresses that in
6 his declaration. I can pull the site before our rebuttal, but he explains that.
7 So the polymorphism is the polymorphic sequence is the area including the
8 deletion. It's not simply the base pairs at which the mutation exists. And
9 that is how under the way the claims are drafted, this sort of direct
10 hybridization is not required, because otherwise you wouldn't hybridize to a
11 deletion where no nucleic acids exist.

12 JUDGE POLLOCK: All right. If you could find me those
13 citations sometime today, that would be great.

14 MR. KRAUSE: Will do.

15 JUDGE POLLOCK: And Dr. Quackenbush's reports.

16 MR. KRAUSE: Say a few words. Yeah, thank you, Your
17 Honor. And we'll say a few words quickly on Ground 3 of the '394. So this
18 is -- so obviously Ground 1 is based on Leary on its own, under the correct
19 construction of the institution decision that the PCR primers of Leary
20 constitute capture probes. And we go to slide 107, the addition of Chan to
21 Leary further renders obvious the use of a solution phase hybridization
22 capture dates to hybridize to the polymorphisms, and Chan motivates doing
23 this for large numbers of single nucleotide variants, whereas Leary focused
24 on translocations, which are a combination of a deletion and a structural
25 variant. And Chan points to success that they already had in doing so in the

1 analogous situation in prenatal monitoring.

2 To touch on the other issue in Ground 1 of the '033 patent, I'll
3 turn to slide 111 briefly and really on the anticipation by force issue, other
4 than the capture probe argument, the main argument Personalis makes is this
5 idea that sequencing an amplicon does not constitute sequencing nucleic
6 acids generated from the sample. The Board correctly rejected this
7 argument in institution, intermediate steps like generating these amplicons is
8 entirely consistent with the claim, which is a comprising claim that allows
9 additional steps.

10 And I'll address briefly the secondary considerations arguments.
11 Mr. Heinrich already addressed the sort of implausibility of their nexus
12 argument based on co-extensiveness, and the Federal Circuit cite for that is
13 Fox Factory v. SRAM, 944 F.3d, 1366 at 1376. But I think the other key
14 point on nexus is the failure of proof on whether these claims are actually
15 practiced. And so all that Dr. Furneaux did was essentially parrot the chart
16 that Personalis presented in the POPR, and that's not really even discussed in
17 the POR. So that evidence should not be credited.

18 And I think the other key point on secondary considerations is,
19 you know, the '033 patent, there's anticipation by Forshew, so obviously, the
20 secondary considerations are not relevant. And, in addition, given the strong
21 obviousness case in the other grounds, this sort of tangential evidence of
22 secondary considerations, if it's given any weight, should not outweigh and
23 save these claims.

24 So if there's not any further questions, we will reserve the rest
25 of our time.

1 JUDGE POLLOCK: Judge Majors, Judge Jenks, do you have
2 questions right now? I do not. Thank you.
3 JUDGE MAJORS: I do not. Thank you.
4 MR. KRAUSE: Thank you, Your Honors.
5 JUDGE POLLOCK: All right. Mr. Luman, would you like to
6 begin?
7 MR. LUMAN: Just a moment, Your Honor. I want to make
8 sure my slides are visible. Are you able to see my slide?
9 JUDGE POLLOCK: Yes. And again, please list the number of
10 the slide as you speak about it. That helps us greatly later on.
11 MR. LUMAN: Thank You, Your Honor. May I proceed?
12 JUDGE POLLOCK: Please.
13 MR. LUMAN: So, Your Honor, you did hear many things
14 from Petitioner's counsel just now, and I'll need to correct many of the things
15 that he said. And I think we should begin with capture probes. So if you
16 will turn with me to slide number 5. Capture probes, they are required by
17 Claim 1 of both patents, and that's highlighted in yellow on the screen. So
18 I'd like to look at the parties' constructions of this term. If you'll turn with
19 me to slide 6. A central dispute is the construction of capture probes, and it's
20 Patent Owner's construction that reflects the plain meaning of capture probes
21 to the person of skill in the art. And if we look at Petitioner's construction,
22 that can't be correct because it recites PCR primer capture probes. And that
23 is a term that they made up for this proceeding.
24 It has no basis in this specification or in the literature. So let's
25 start with what the specification says about capture probes. And if you'll

1 turn with me to slide 7. You heard Petitioner talk about what the
2 specification says about capture probes, and it's true that the specification
3 does describe several features of capture probes. But it doesn't describe all
4 aspects of capture probes. If a Patent Owner had to fully describe or define
5 every term that already had a plain meaning, the specification would be full
6 of definitions and thousands of pages long. Here, the specifications does not
7 define capture probes. Patent Owner did not act as a lexicographer, but
8 Petitioner is trying to treat the specification as if it did contain a definition.
9 But I mean, according to Patent Owner, the only requirement for a capture
10 probe is to be one or more nucleotides long and to have a nucleic acid
11 binding site.
12 JUDGE JENKS: Mr. Luman?
13 MR. LUMAN: Yes.
14 JUDGE JENKS: Sorry, I was trying to cut in here. So, in your
15 specification, you do in my opinion, define capture probes. You spend
16 approximately 700 words on your section defining capture probes. Your
17 section says a capture probe comprises a nucleic acid binding site, and then
18 it says it may further comprise linkers and may further comprise labels but
19 capture probes do not require these. These are optional parts of a capture
20 probe. This was on, and I'm quoting from the '033 patent, column 31.
21 Now I go to how you define primers, which is in column 40,
22 about midway through, and you say primers. Primers are a string of nucleic
23 acid sequences. So the question I have is, capture probes and primers
24 appear to be just strings of a nucleic acid sequences. Can you please explain
25 to me the difference between a capture probe, how as you define it in your

1 specification versus a primer, how you define those in your specification?
2 MR. LUMAN: Yes.
3 JUDGE JENKS: I understand you don't have to explain
4 everything, but all of a sudden you define capture probes as basically just
5 being nucleic acids, and now you want us to limit capture to something very
6 specific that I don't find support in your specification for. So, please explain
7 to me how these nucleic acids are different so I can understand your
8 argument with respect to capture probes.
9 MR. LUMAN: Yes, and thank you, Your Honor. We -- the
10 Patent Owner did not act as a lexicographer by saying herein described
11 defined our capture probe which are. Now, we do have a lot in our
12 specification that provides some description of capture probes. But
13 importantly, the specification is written to the person of skill in the art. And
14 they would understand what capture probes are and what PCR primers are,
15 and they would understand that they are different. Yes, they're both
16 nucleotides. Yes, they both can hybridize to other nucleotides, but they
17 have important differences that a person skill in the art would have known
18 about. And because the specification is written to the person of skill on the
19 art, the persons here would have understand that.
20 Let's start with PCR primers, for example. If you'll turn with
21 me to slide 8. In order to perform a polymerase chain reaction, PCR, you're
22 going to need two PCR primers, an upstream primer, and a downstream
23 primer. You're also going need a polymerase enzyme and lots of nucleotides
24 and several cycles of reaction to generate copies of DNA. PCR primers
25 copy DNA, and that's what a person of skill in the art would have

1 understood in light of our specification, and the knowledge of the person of
2 ordinary skill in the art that they bring when they read the specification.
3 And if you'll turn with me to slide 9, capture probes are
4 different. This figure is taken from the Petition. Capture probes hybridize to
5 target DNA so that the target DNA can be physically isolated and removed
6 from non-targets. The capture probes can only capture the DNA that's
7 already present in solution. It doesn't make copies of DNA, so there's only
8 one capture probe that is required to physically pulldown the target DNA
9 strand, and in contrast, PCR can make only copies of a DNA. That is what a
10 person of skill in the art would have understood. And our specification
11 provides enough written description support to fill out some descriptions of
12 what capture probe is and what PCR primers are without defining the term.
13 JUDGE JENKS: I'm sorry. So shall we go to your
14 specification? Again, I am looking at capture probes on this patent '033,
15 column 31, capture probe says, the nucleic acid binding site and the capture
16 probe may further comprise linkers or comprise labels. So let's go look at
17 labels, because a capture probe, as you are describing it, requires a bead and
18 something to pull it out. But you also have labels just here that are just like
19 photoaffinity label.
20 A photo affinity label is not going to pull something down. So
21 you're describing capture probes as being all kinds of different ways of
22 capturing a nucleic acid, yet not all of them are going pull it down as you say
23 one of ordinary skill in the art would understand this to be. Again, your
24 specification is much broader on the term capture probe than you're trying us
25 to, you know, adopt right now. So I don't understand the difference between

1 your capture probes and your primers, what the differences are when I don't
2 need to actually pull anything down.
3 MR. LUMAN: Yes. Thank you, Your Honor. From our
4 perspective, the specification is written to the person of ordinary skill in the
5 art. And that person brings to, when they read the description in the
6 specification, they are bringing that background knowledge to the
7 specification. And our specification is not laying down a specific definition.
8 The specific understanding of what a capture probe comes from the
9 literature. And the person who's coming out brings that to their knowledge.
10 And if you'll look, for example, at slide 11, we have Foresight's
11 Mamanova exhibit that has a section entitled Hybrid Capture, and it includes
12 on-array capture and in-solution capture. And it involves direct selection of
13 target DNA. And the term capture probes is used exclusively with hybrid
14 capture. There's a whole different section of Mamanova that describes PCR
15 primers, and that section it avoids using the terms capture probes. And
16 Foresight didn't --
17 JUDGE JENKS: But here again, you created the specification.
18 You told me that the capture probe do not include these beads and these
19 ways to capture it to an array. All I need to do is have a nucleic acid
20 sequence and maybe a label on it. All I need to, you know, I need the
21 chromophore on my label, and that's my capture pro.
22 MR. LUMAN: Those are the descriptions in the specification,
23 Your Honor. However, a person of skill would understand that is not
24 enough to just be a capture probe because of what the person of skill in the
25 art understands about capture probes. And the description in the literature is

1 what a person of skill in the art would understand about capture probe.
2 That's our position. And if --
3 JUDGE JENKS: So you're basically saying ignore what I said
4 in my specification as to what I'm claiming capture probes is, and only view
5 what maybe somebody of skill in the art would understand at the time. So
6 why include all of this in the specification if you didn't mean capture probe
7 to be something more than a string of nucleic acids on a bead or on an array?
8 MR. LUMAN: Because the specification contains a description
9 enough to support written description, enough to tell the reader some
10 parameters about capture probe, but not saying that we are using capture
11 probes in an unusual way or in a way that's not consistent with what the
12 persons skill in the art would have understood about it.
13 JUDGE POLLOCK: Mr. Luman?
14 MR. LUMAN: Yes?
15 JUDGE POLLOCK: If I can interject. Say we agree with you
16 that a capture probe must provide a function of rendering a target DNA
17 amenable to physical capture or isolation. What is your evidence that the
18 capture probe must exclude the function of replication?
19 MR. LUMAN: Thank you, Your Honor. For example, a
20 person of skill in the art would understand that those are quite different
21 things. And so, Foresight's Mertes exhibit, for example, it teaches that
22 hybrid capture and PCR amplification are two different enrichment
23 techniques. They have different core reaction principles. Hybrid capture
24 involves hybridizing capture probes to target regions of interest so that one
25 can physically capture and isolate the sequence of interest. The core

1 reaction principle of PCR primers is amplification that is making copies of
2 DNA, and they're not the same.
3 Mertes explains that given the operational characteristics of
4 these different targeted enrichment methods, they naturally vary in their
5 suitability for different fields of application. And so Petitioner argues that
6 there's no distinction specification between capture probes and PCR primers.
7 But the specification is written to the person of skill in the art, and the
8 person of skill in the art knows that they have different functions and
9 different core reaction principles.
10 If you'll turn with me to slide 14, we talked to Dr. Quackenbush
11 about Mamanova and Mertes, and they are representative examples, and
12 they provide complementary sources of information about the background
13 on capture technology. And its Patent Owner's construction that stays true
14 to the plain meaning of capture probes known to the skilled artisan. And if
15 you'll turn with me to slide 19, please. We had Petitioner's slides 10 and 11,
16 and they had a title of PCR Primers Captured DNA Through Hybridization.
17 But that's not right. Capture probes do capture itself does not occur simply
18 by hybridization.
19 For example, Dr. Quackenbush said, it would be hard for me to
20 think of any technology where capture would simply occur the moment
21 hybridization occurred. PCR primers don't become capture probes simply
22 because they contain a nucleic acid binding site. And if you'll turn with me
23 to slide --
24 JUDGE POLLOCK: How is this different from your
25 biotinylated probes where the first step is hybridization and the later step is,

1 say, pulling them down with magnetic beads or what have you? Not sure if I
2 follow the relevance of your argument.
3 MR. LUMAN: So, the difference is that when you are isolating
4 PCR amplicons, you're isolating only the copies of DNA. You're not
5 actually isolating the original target DNA that was in solution. And that is
6 the key difference between PCR primers and capture probes.
7 JUDGE POLLOCK: So you're not considering DNA to be
8 information. You're considering it to be a unique molecule, one molecule?
9 MR. LUMAN: That's correct.
10 JUDGE POLLOCK: That seems like pretty thin soup, sir. I'm
11 sorry, go ahead, yeah. I'm sorry to interject.
12 MR. LUMAN: Another thing that came up that you heard
13 Petitioner say was that our claims don't require physical isolation, only
14 contacting DNA of capture probes. And I want to make sure that Patent
15 Owner is clear on this point that the claims do require physical isolations.
16 And that's for two reasons, because the definition of capture probes requires
17 that one can physically capture target DNA. And second, limitation 1(d)
18 requires conduct, it requires conducting a second sequencing assay on the
19 subset of nucleic acid molecules contacted with the capture approach from
20 limitation 1(c). And so the physical isolation by pullout is implicitly
21 required to do the sequencing of limitation 1(d). And the same is true for the
22 '033 patent limitations 1(b) and 1(c) that work together in the same manner.
23 And I --
24 JUDGE POLLOCK: Mr. Luman, I'm looking through Claim 1,
25 you have it up on the screen on slide 20. Would you explain to me where

1 you find a requirement to pull down a unique target molecule, as opposed to
2 say a PCR replicated molecule? I'm not seeing this in here, but maybe it is,
3 please.
4 MR. LUMAN: Yeah, of course. Thank you, Your Honor. The
5 briefing explains that the capture probes are used to catch target DNA to be
6 physically pulled down or fished out. And that's the '394 Patent Owner
7 response at pages 19 to 20. And the patent --
8 JUDGE POLLOCK: Is there something in the claim steps that
9 tells me that, or is that all coming in through your interpretation of the term
10 capture probe?
11 MR. LUMAN: It is coming in through the definition of capture
12 probe and that in order to do the sequencing required by step 1(d), the
13 physical pullout is implicitly required to do this sequencing. And if you'll
14 turn with me to slide 17, I'll further elaborate on that. Dr. Quackenbush
15 explained that using capture probes for sequencing involves pulling down or
16 fishing out the captured target DNA. And he says the process involves
17 selective recovery and subsequent sequencing. So the physical isolation is
18 implicitly required to do the claim sequencing steps on the subset of
19 nucleotides generated by contact with the capture probes.
20 JUDGE POLLOCK: What he's talking about in that paragraph
21 regarding on-array capture probes. Isn't that a specific subset of capture
22 probes?
23 MR. LUMAN: We believe that the proper construction of
24 capture probes would be in solution for an on-array capture probes that
25 function to physically pulldown or isolate the target DNA. And that comes

1 from the person's knowledge and skill in the art based on the representative
2 examples of the literature provided in Mertes and Mamanova.
3 JUDGE POLLOCK: How do you address Petitioner's
4 argument that you have successively narrowed down your definition of what
5 is a capture probe?
6 MR. LUMAN: So because the specification is written to the
7 person of skill in the art, they bring that understanding with them and
8 understand that our definition -- our specification does not provide a
9 definition. It provides some description, but not a complete description.
10 With that, I'd like to move on to Antedation. Would that be
11 okay?
12 JUDGE POLLOCK: Please.
13 MR. LUMAN: Antedation, the invention here, I'm on slide
14 number 28. The invention was conceived by May 8, 2012, and it was
15 diligent and reduced to practice between May and January of 2013. And this
16 means that Forshew and Chan are not prior art. And this is a dispositive
17 issue for all three grounds of the '033 patent and ground three of '394 patent.
18 The evidence of antedation is extensive, it includes a declaration by Mr.
19 West, the founding Chief Executive Officer of Personalis, and co -inventor
20 of the '394 and '033 patents. And his testimony is corroborated by Dr.
21 MacQuitty, who was the Chairman of Personalis's Board of Directors, and is
22 the prominent figure in the life science industry. Mr. Zeman confirms that
23 supporting exhibits were made and maintained in the regular course of
24 business. And this evidence includes over 80 supporting and corroborating
25 exhibits. And Petitioner does not seek to exclude any of this evidence. So

1 let's discuss what they do dispute. If you'll turn with me to slide --
2 JUDGE POLLOCK: Mr. Luman, it sounds to me that
3 Petitioner is saying that for Ms. Luo, it's a physical impossibility for Ms.
4 Luo to have contributed to conception because she didn't start until after
5 your claimed conception date. How do you address that one?
6 MR. LUMAN: Thank you, Your Honor. Let's talk about Ms.
7 Luo. So Ms. Luo, she joined -- she join Personalis on June 18th. And then
8 in August of 2012, she improved the variable length tandem repeat aspect of
9 Claim 3 of the '394 patent, and also Claim 4 of the '033 patent by identifying
10 a DNA sequencing chemistry that provided enough reads for certain difficult
11 variable length tandem repeats.
12 JUDGE POLLOCK: Is that a claim element? How is that
13 claimed?
14 MR. LUMAN: That is claimed in Claim 3 of the '394 patent
15 and Claim 4 of the '033 patent. And so Claim 3 was conceived by the other
16 inventors in May 8th and then further improved in August of 2012. So we
17 believe that Ms. Luo's improvement in August makes her a joint inventor of
18 the '394 patent under the Ethicon v. U.S. Surgical case cited in the briefing.
19 And importantly, we're obligated to list all inventors on the
20 patent, even if they contribute to only one claim or one aspect of the claim,
21 which is why she's listed on patent. And Petitioner is trying to make Ms.
22 Luo's inventorship an issue that applies to all claims of both patents. But it
23 really only applies to one dependent claim in each patent. And if the Board
24 were to agree with Petitioner, that would mean that conception of dependent
25 Claim 3 occurred in August instead of May. But it doesn't change that the

1 rest of the claims have priority back to May 8, 2012, and that Forshew and
2 Chan are not prior art to the claim. If there's any other questions on
3 antedation, I'd be happy to answer them. Otherwise I could move on to
4 whole-genome sequencing.
5 JUDGE POLLOCK: Please.
6 MR. LUMAN: Please turn with me to slide 38. Claim 1 of the
7 '394 patent recites whole-genome sequencing. And so let's take a look at the
8 constructions of whole-genome sequencing if you'll turn with to me slide 40.
9 Patent Owner agrees with the Board's construction of whole-genome
10 sequencing, and you heard Petitioner say that the specification doesn't
11 support the almost all aspect of the Board's construction. But that's not true
12 because the specification explains that whole-genome sequencing can have
13 zero mean coverage regions, and the almost all aspect of the Board's
14 construction correctly accounts for this.
15 Petitioner's construction, that's not supported by the record, and
16 it doesn't give any significance to the meaning of word whole in whole-
17 genome sequencing. And it also gives difficulty with figuring out what
18 mapping back to the reference means. And so, Petitioner doesn't seriously
19 defend its construction.
20 With respect to the Board's construction, you've heard
21 Petitioner argue that almost in whole-genome sequencing can be just 50
22 percent or even lower based on various extrinsic references and patent
23 specifications.
24 JUDGE POLLOCK: Well, Mr. Luman, I'm very concerned
25 about Petitioners pointing to Personalis's own '058 and '405 patents that

1 expressly state that whole-genome sequencing can cover sequences of the
2 whole-genome of about or at least about 50 percent. So, I'm reading from
3 the '405 patent, Exhibit 1214, column 13, line 31 to 44. Why isn't that an
4 appropriate baseline here? I note that the '405 patent has a provisional filing
5 date in 2013, which seems fairly contemporaneous with the 2012 priority
6 date you're asserting here.
7 MR. LUMAN: Yes, Your Honor. That is a different patent
8 with a different specification and different claims. And I think we need to
9 figure out what the bottom line is on whole-genomes.
10 JUDGE POLLOCK: There's virtually nothing in the instant
11 patents about the meets and bounds of whole-genome sequencing. Why
12 shouldn't we look to another patent by the same company and see what
13 they're saying there when they get into more details?
14 MR. LUMAN: So, as far as that goes, we feel like the Board's
15 construction is very well grounded in the intrinsic evidence of this specific
16 specification, which talks about zero mean coverage, which covers the
17 almost all aspect, and it distinguishes whole-genome sequencing from
18 exome sequencing. And that is the intrinsic evidence that was cited in the
19 institution decision. And there are other references, including Patent
20 Owner's own specification and other patents that describe whole-genome
21 sequencing differently. But that is exactly why we need a construction here.
22 And if you'll turn with me to slide 41.
23 JUDGE POLLOCK: First, Mr. Luman, if you look at Claim 1
24 of the '394 patent, steps A and B entail whole-genome sequencing of first set
25 of nucleic acids. And then steps 1C through 1G relate to the use of capture

1 probes to identify the presence or absence of polymorphisms in a second and
2 third set of nucleic acids and the ultimate generation of a report. But I see
3 nothing in the claim language linking the whole-genome sequencing of steps
4 1A and 1B with anything that follows. So can you explain that to me? I'm
5 quite confused about how to read this claim.
6 MR. LUMAN: Yes, Your Honor. So the whole-genome
7 sequencing is recited in an operand limitation. And a person of skill in the
8 art would understand that the claimed invention is a series of method steps
9 one after another. And these steps will have to be conducted in order based
10 on the way that the method is written. And so a person of skill in the art
11 would understand that the whole-genome sequencing from the limitation 1A
12 does have a cascading effect on other claim limitations.
13 And as far as whole-genome sequencing goes, we know that
14 that term has taken on many different flavors of meaning, which is exactly
15 why we need a construction here. And we think the Board reached the right
16 construction based on the intrinsic evidence of the patents in suit.
17 Specifically that whole-genome sequencing is different from exome
18 sequencing, and the language of the claim itself, which uses the word whole
19 to modify genome, and that indicates that the entirety, and not a subset of the
20 genome, must be sequenced. And a person of skill in the art would
21 understand that that carries through to the other claim limitations.
22 JUDGE POLLOCK: Was the entire -- was it possible to
23 sequence the entirety of genome at the time this application was filed?
24 MR. LUMAN: It was not -- Your Honor, it was not possible to
25 sequence every single base. There were some regions of the genome that

1 were inaccessible at the time. And that is why the Board's construction of
2 almost all is appropriate because it takes into account the person of skill in
3 the art's understanding that at that time every last base couldn't be sequenced
4 because there were some difficult to reach areas.
5 JUDGE POLLOCK: And a year after your filing date,
6 Personalis's own patent suggests that the whole-genome sequencing could be
7 accomplished with something more than 50 percent of the whole-genome
8 being sequenced. And it seems to say that almost all of that time was very
9 broad indeed.
10 MR. LUMAN: It could be. In some instances, there were
11 instances of whole-genome sequencing being used in different manners.
12 And that's why it's important to get the construction right here based on the
13 intrinsic evidence of this specification, because there weren't any.
14 JUDGE POLLOCK: The intrinsic record? The intrinsic
15 reference merely states whole-genome sequencing. It doesn't give us any
16 more information about it as far as I can see.
17 MR. LUMAN: Yes, Your Honor. And so the specification
18 does distinguish between whole-genome sequencing and exome sequencing,
19 and that would be targeted versus untargeted. And it does say that there are
20 specific genome regions that can be selected, and that those can comprise
21 either the entire genome or portion thereof. So --
22 JUDGE POLLOCK: So perhaps the best construction of
23 whole-genome sequencing in this context is untargeted sequencing of the
24 genome. Full stop.
25 MR. LUMAN: But we think of the whole-genome because the

1 language does include whole and whole genes.

2 JUDGE POLLOCK: Whole. Yes, meaning untargeted.

3 MR. LUMAN: Yes, untargeted, and then it becomes an issue
4 of what would be the threshold amount of sequencing that needs to be done
5 to reach whole-genome sequencing. And that's why we think the Board's
6 construction of almost all is appropriate. And because that almost all
7 accounts for the known issue that not every base could be sequenced.

8 JUDGE POLLOCK: And why is something more than 50
9 percent not appropriate here?

10 MR. LUMAN: Because the way the specification is written, it
11 includes whole-genome sequencing and we think the plain meaning of
12 whole would be at least as close as possible to all of the genome that could
13 be sequenced. And there were many different definitions of whole-genome
14 sequencing floating around in the prior art, which is why it's important to get
15 it right for this specification.

16 JUDGE POLLOCK: But the specification defines no threshold
17 for the amount of sequencing required under your definition for whole-
18 genome sequencing, correct?

19 MR. LUMAN: So it does not have a cutoff for that. And but
20 we do think that it's fair to say at the time it was accepted that 90 percent
21 would be the appropriate cutoff for whole-genome sequencing. That
22 comes --

23 JUDGE POLLOCK: Based on what?

24 MR. LUMAN: That is based on --

25 JUDGE POLLOCK: Not based on your later patents, which

1 lists something down to 50 percent and above.

2 MR. LUMAN: And that's correct, Your Honor, that the
3 specifications and other patents do say a lower percentage could qualify as
4 whole-genome sequencing. And I think regardless of what the definition of
5 whole-genome sequencing comes to, we have to consider whether or not a
6 person of skill in the art would have considered Leary's approach to be
7 whole-genome sequencing. And if you'll turn to slide 42, I would say a
8 person of skill in the art would not have understood Leary's 2010 sequencing
9 to be whole-genome sequencing. It describes a mate pair approach and a
10 solid sequencing by ligation approach.

11 It wasn't until two years later that the Leary authors published
12 their first article describing a whole-genome sequencing method. And to
13 achieve whole-genome sequencing, Leary 2012 did something different.
14 They used Luminara's sequencing by synthesis with a paired end approach,
15 which is different than the 2010 solid sequencing bio ligation mate-pair
16 approach. And so even the Leary 2010 authors did not characterize their
17 approach as whole-genome sequencing. It wasn't until two years later that
18 they did that.

19 JUDGE POLLOCK: But why does it matter how you get there
20 if you have sequence information over the selected genome?

21 MR. LUMAN: It does matter because Leary's PARE approach,
22 PARE, it didn't sequence all or almost all of the genome. They intentionally
23 sequenced only the 25 mate pair end tags of the original fragments. They
24 left out the 1,400 bases in the middle of fragments, which are shown in black
25 in this figure on slide 44. Those were intentionally discarded, that only three

1 to four percent of each sheared DNA strand was sequenced. And that leaves
2 96 to 97 percent of each strand unsequenced, and if --
3 JUDGE POLLOCK: I fail to see the relevance, sir. They're
4 sequencing lots of small bits and putting them together. How does it matter
5 whether they take those small bits individually or from the ends of a loop?
6 MR. LUMAN: Ah, thank you, Your Honor. On slide 45, we
7 asked Dr. Quackenbush, what would happen if you did have to shear Leary's
8 DNA strands down to the 50 bases so that every single base would be
9 sequenced. And he explained that that would require 28 times more
10 sequencing. And that would assume that none of the main pairs overlapped
11 with each other. but Leary's mate pairs, they were overlapping. And so if
12 you'll turn me to slide 46, Dr. Quackenbush did concur that Leary's mate
13 pairs overlapped with each other. But Leary's mate pairs, they were
14 overlapping. And so if you'll turn with me to slide 46, Dr. Quackenbush did
15 concur that Leary's mate pairs overlapped.
16 And if you'll turn with me to the slide 47, Dr. Quackenbush said
17 he didn't know how much the mate pairs overlap because he hadn't done the
18 calculation. And if you'll turn with me to slide 48, it was Dr. Furneaux who
19 performed the calculation, which shows that the Leary's mate pair tags did
20 overlap by a factor of 1.7. And if you'll turn with me to slide 49, accepting
21 Dr. Furneaux's calculation, that leads at best to Leary sequencing 53 to 60
22 percent of the genome. And that's not whole-genome sequencing, that half
23 genome sequence using the word whole in whole-genome sequencing. And
24 that has to be given meaning to what whole means in whole-gene
25 sequencing.

1 JUDGE POLLOCK: And yet that is well within what
2 Personalis's later patents called whole-genome sequencing. More than 50
3 percent.
4 MR. LUMAN: In that specification, that's correct, Your Honor,
5 but not in this specification. Those statements were not made in this
6 specification.
7 JUDGE POLLOCK: No, I'm not sure why the definition of
8 whole-genome sequencing jumps around from one specification to another
9 at Personalis.
10 MR. LUMAN: It does. Your honor, it was clear from Dr.
11 Quackenbush's testimony that whole-genome sequencing has taken on many
12 different flavors in many different contexts. And so getting the correct
13 construction in this specific context is important.
14 What I would like to do, Your Honor, is move to slide --
15 JUDGE JENKS: In regards to whole-genome sequencing, can
16 we not just use what a person of ordinary skill in the art would understand
17 whole-genome sequencing to be at the time you put together your
18 specification, which may include less than 50 percent, or 50 percent, 60
19 percent, somewhere in there?
20 MR. LUMAN: Your Honor, we do think that this specification,
21 because it doesn't contain those unusual descriptions of down to 50 percent
22 being whole-genome sequencing, a person of skill in the art would not think
23 that the specification here would use whole-genome sequencing in an
24 unusual manner to get down to 50 percent sequencing. And in particular, I
25 think we need to look -- the question here is whether Leary qualifies as

1 whole-genome sequencing, and Leary's pair approach doesn't come close to
2 sequencing all or almost all of the genome.
3 If it would be all right, I would like to make a few comments
4 about limitation 1(f) and Claim 19. We are on slide 61, and the Petition fails
5 to prove obviousness of the '394 patent limitation 1(f) in Claim 19.
6 Limitation 1(f) requires a third sequencing assay and Claim 19 requires
7 repeating a third sequencing assay one or more times. And the prior art does
8 not teach these limitations, which is an independent reason for upholding the
9 patentability of Claim 1 of the '394 patent and Claim 19. And if you'll turn
10 with me to slide 62, I can explain why.
11 Leary used verification sequencing of PCR products to confirm
12 that the assay worked. And afterwards, Leary used digital PCR of plasma
13 samples to monitor the tumor throughout the course of treatment, and no
14 sequencing was done while monitoring treatment. And Leary does not
15 disclose conducting an additional re-verification sequencing step during the
16 monitoring of treatment. Leary already had the complete and accurate
17 sequence of PCR products from the verification sequencing, and it's that
18 verification sequencing that Foresight relies on to meet limitation 1(d).
19 And so a person of skill in the art would not have done a re-
20 verification sequence of Leary's digital PCR products to arrive at limitation
21 1(f). And they wouldn't do a re, re-verification sequence to arrive at Claim
22 19. And that is especially true given that Foresight's Forshew exhibit
23 criticizes Leary's existing workflow as being difficult to implement on a
24 routine basis, that's Exhibit 1030 at page 10, and not widely adopted, that is
25 at page 8. So adding more sequencing steps would only make the process

1 more difficult to implement and less adopted. And this is an independent
2 reason why Petitioner did not prove obviousness of the '394 patent.
3 I'd like to make a few comments about the '033 patent. If you'll
4 turn with me to slide 63. Limitation 1(d) of the '033 patent requires
5 repeating steps (b) to (c) on a subsequently obtained biological sample. And
6 if you'll turn with me to slide 64. Foresight, they admit that Wagle does not
7 repeat steps of (b) to (c) because the sample type, and because it was an
8 interrogation of tumor tissue that did not require repeating. So, there's no
9 motivation to repeat Wagle's approach on a subsequently obtained tumor
10 sample or on the plasma samples that included cell-free tumor DNA. And if
11 you'll turn with me to slide 65, I'll elaborate.
12 First, obtaining another tumor sample that would require an
13 invasive procedure. Forshew explains that biopsies are invasive and costly.
14 And Foresight's founders admit that tumors cannot be repeatedly sampled
15 without invasive procedures. And Wagle further explains that the cost
16 remained a limiting barrier of his approach. That's exhibit 1033 at page 90.
17 And that they're --
18 JUDGE POLLOCK: I'm sorry, Mr. Luman. The claims don't
19 require resampling tumors, right? They talk about multiple samples from
20 the same individual. Am I correct?
21 MR. LUMAN: Yes, Your Honor.
22 JUDGE POLLOCK: What does it matter if you're sampling a
23 tumor versus later sampling plasma from that individual?
24 MR. LUMAN: Thank you, Your Honor. So I'm back on slide
25 64, and the two reasons that Petitioner offered for why somebody would

1 sequence, why they would repeat steps (b) to (c) with Wagle's assay are that
2 there would be either a subsequently obtained tumor sample or on plasma
3 samples that included cell-free tumor DNA. And so we are addressing those
4 two supposed motivations that Petitioner is putting forward. And as far as
5 their theory that a person of skill in the art would go on and do a repeat assay
6 on subsequently obtain tumors samples, on slide 65 you can see that there
7 are real reasons why someone would not do that. Biopsies are invasive and
8 costly, and they can't be repeated without invasive procedures.
9 And if you'll turn with me to slide 67, we can address their
10 second theory that a person of skill in the art would have just done sampling
11 on a cell-free tumor DNA in a plasma. But Forshew explains that cell free
12 tumor DNA is present in only a few two amplifiable copies per milliliter of
13 blood. And that's not enough for the microgram quantities of DNA required
14 for Wagle's capture probes. We talked, Wagle's --
15 JUDGE POLLOCK: Can you point me to where your expert
16 has said this is not enough? At the end of your talk is fine.
17 MR. LUMAN: Sure, of course. Our expert addressed that in
18 discussing Wagle. And so this is the Patent Owner response for the '033
19 case at page 71. And Wagle's capture probes, they need 3,600 nanograms or
20 36 micrograms of DNA. And Foresight's Mamanova exhibit also teaches
21 that you need about three micrograms to use capture probe. So that's
22 Mamanova at Table 1. And that is at least 100 times more, or in many cases,
23 3,000 times more than the nanogram amounts of DNA and force used
24 plasma DNA. And you can find the briefing on that at the '033 Patent
25 Owner Response at page 71, and in the '033 sur-reply at pages 20 to 21.

1 JUDGE POLLOCK: Thank you. Oh, you're cutting into your
2 rebuttal time now if you'd like to wrap up.
3 MR. LUMAN: I will stop now unless you have any additional
4 questions. Thank you, Your Honor.
5 JUDGE POLLOCK: Judge Jenks?
6 JUDGE JENKS: I do not have any questions.
7 JUDGE POLLOCK: Judge Majors? Okay. Thank you very
8 much.
9 MR. HEINRICH: All right. So I'm going to address a few of
10 the points on whole-genome sequencing and the other Ground 1 issue
11 counsel raised. Let's see, share our screen now, okay. Okay, so going back
12 to some arguments that counsel made on whole-genome sequencing, I have
13 here slide 89 from our presentation. And we have a call out from
14 Personalis's '968 patent that refers to untargeted sequencing data. For
15 example, a low coverage whole-genome sequencing data. So clearly, their
16 own patent is saying that full doesn't mean all or almost all because you can
17 have low coverage whole-genome sequencing.
18 The '968 patent actually incorporates Pasaniuc by reference,
19 Pasaniuc is, I believe, 1223 of record in this proceeding, and Pasaniuc refers
20 to ultra-low coverage sequencing down to 10 percent as still constituting
21 whole-genome sequencing. Counsel says, well, it's a different patent,
22 different specification, so whole-genome sequencing needs something
23 different there. But we've actually filed a petition against the '968 patent.
24 And in Personalis's POPR, they insist that the Board should apply the same
25 construction for whole-genome sequencing in that proceeding as the Board

1 indicated in its preliminary construction here. So they're only saying the
2 definition of whole-genome sequencing flip-flops around when it pleases
3 them.
4 JUDGE POLLOCK: Mr. Heinrich, would you address Mr.
5 Luman's discussion of whether Leary is not whole-genome sequencing
6 because of its methodology, not because of the amount?
7 MR. HEINRICH: Yes.
8 JUDGE POLLOCK: No, rather, separately from the amount.
9 MR. HEINRICH: Sure. So, Leary uses this mate-pair end
10 approach where there are 25 base pairs on either end of the fragment that are
11 sequenced. The fragment has a 1.4 kilobase insert. Leary shows that this
12 methodology actually provides 18-fold physical coverage of the genome.
13 You're getting genome-wide information from that sequencing approach.
14 And going to slide 83, this is again another one of Personalis's
15 contemporaneous patents. This is the '058 patent that has a 2013 priority
16 date. And Personalis itself, again, refers to this specific methodology, a
17 mate pair approach, mate pair read approach including a mate pair read
18 approach that has an insert size of 1.4 kilobases. In fact, --
19 JUDGE POLLOCK: Thank you.
20 MR. HEINRICH: -- and the same patent actually gives an
21 example of, again, whole-genome sequencing, untargeted sequencing that
22 you can achieve using the solid system by Applied Biosystems that Leary, in
23 fact uses. So this particular methodology, Personalis, also
24 contemporaneously refers to as whole-genome sequencing. So what we
25 really have here is that all of the intrinsic record here recognizes that Leary

1 and Leary's approach, and the extent of Leary's coverage constitutes whole-
2 genome sequencing, and it's really just Personalis's expert in this proceeding
3 that says otherwise.
4 One -- so I'm going to move on briefly to the re-sequencing
5 issue counsel raised. I just want to make clear that after Leary's initial
6 whole-genome sequencing step, Leary discloses re-sequencing in a targeted
7 fashion on multiple occasions. So Leary uses a second sample, so a second
8 set of nucleic acids from the tumor and sequences by in targeted fashion the
9 PCR products that result from applying her PCR primers to that second
10 sample, that's at the bottom of page 3 of Exhibit 1002. And then Leary
11 discloses sequencing the PCR products from the plasma sample using
12 Sanger sequencing. Again, doing the sequencing of the products from the
13 capture probes in the broad sense that Personalis uses it, and confirms that
14 she's found the rearrangements that she was targeting through her capture
15 technique.
16 And she discloses furthermore multiple plasma samples
17 monitoring the patient's cancer over time, and a person of skill in the art, it
18 would be the height of obviousness to repeat that confirmatory sequencing
19 that Leary expressly discloses for those subsequent plasma samples as well.
20 So we think that, again, just looking to the four corners of Leary, it renders
21 obvious Claim 1 of each patent, and then Claim 19 that counsel called out as
22 well. So I'm going to turn things over now to Mr. Krause to address some
23 additional capture probe issues.
24 MR. KRAUSE: Thank you, Your Honors. And you had
25 requested a cite for Dr. Quackenbush's testimony about the PCR primer

1 hybridizing to a polymorphism, and that's in the '394 proceeding, Exhibit
2 1020 at paragraph 133.
3 I'd like to turn back on the capture probe issue to the
4 specification. And one of the arguments that counsel made was that this
5 language simply omits what's well known to a person of skill in the art. And
6 that argument seems to be a little bit unusual because it seems weird that a
7 POSA would need to have called out to them that a capture probe could
8 include a nucleotide, but no other of the parameters. This is, I think, a
9 specification that was drafted to encompass as much as possible, not
10 something that was omitting allegedly well-known features that are
11 mentioned nowhere in here.
12 On the overall discussion of Mamanova, Exhibit 1007, when it
13 describes these various target enrichment techniques, it describes them all as
14 performing the function of capturing DNA for sequencing. So the
15 distinction that somehow PCR does not capture is inconsistent with the
16 record. Also like to go briefly to slide number 23 and just address the
17 argument about the use of the term PCR primer capture probe as a way of
18 mapping the claim elements.
19 This is testimony from Dr. Furneaux establishing that in the
20 context of this patent, structures can constitute a capture probe even if
21 they're not expressly referred to. And the record here establishes that on the
22 whole, the term capture probe is inclusive and includes many techniques.
23 The term PCR primer capture probes in the Petition avoids exactly the sort
24 of confusion that Personalis tries to sow. For example, in the sur-reply, they
25 have these entire sections that refer to capture probes basically presupposing

1 their construction that it's limited to solution phase hybridization capture
2 baits. This is slide 22. But of course, under the correct construction of this
3 claim term, capture probes includes far more.
4 Turn briefly to slide 24, there was some arguments about
5 capture probes in the claims requiring the physical isolation and that is not
6 the case. These claims require contacting a nucleic acid sample with capture
7 probes. It does not require physical isolation as Personalis has argued. It's
8 contacting to create a subset and the specification defines that, at least one
9 way of identifying a subset is just based on whether or not capture probes
10 are hybridized. The idea of physical separation that they're trying to import
11 into the claims is described as something else in the specifications, which is
12 performing the elution reaction. That's not claimed here, as Your Honors
13 have observed.
14 I'll turn to slide 113 to briefly address the argument regarding
15 the DNA quantities in for in the combination of Forshew and Wagle. And
16 so one of the arguments counsel for Personalis has made is that use of
17 Wagle's capture probes or hybrid capture probes would not be compatible
18 with Forshew based on Table Two, which shows subdivided plasma samples
19 from Forshew. So they say, oh, well, there's not enough DNA present in
20 these small samples to use Wagle's hybridization capture probes. But
21 Forshew has heavily subdivided the samples, and it's clear from the
22 reference that much more plasma is drawn. And further, as Dr.
23 Quackenbush explains, Wagle itself describes first PCR amplifying its DNA
24 before the hybrid capture baits are used. So we think that argument does not
25 negate the obviousness of the '033 patent in the combination of Forshew and

1 Wagle.

2 I'm going to turn it back to Mr. Heinrich to address the swear

3 behind.

4 MR. HEINRICH: Right. Just one last couple of points. I do

5 want to just very briefly address counsel's arguments with regard to Dr. Luo.

6 I want just to emphasize that the issue isn't whether she was properly named

7 as an inventor. The issue is whether, amongst all the other issues, bedeviling

8 Personalis's swear-behind arguments, this is a yet further indication of the

9 lack of credibility of their credibility story. And we say, of course it is. So

10 this is slide 34.

11 Counsel pointed to Claim 3 that refers to -- well, it's a

12 dependent claim from Claim 1, and it just simply says that the one or more

13 polymorphisms claimed in Claim 1 can include, among others, a variable

14 length tandem repeat. There's nothing in here about any kind of specific

15 DNA sequencing chemistry required for Claim 3. And this is not a basis for

16 claiming a May 8th conception date if she contributed to that, where she

17 didn't join the company until June 18th. They cite the Ethicon District Court

18 case that refers to a modified invention, but there's no modification here.

19 There's just a complete disconnect between their inventorship, which again,

20 we're not disputing, but it just makes their conception story all the more

21 lacking in credibility.

22 So with that, I think that is all we have. Thank you very much,

23 Your Honors.

24 JUDGE POLLOCK: Thank You. All right, Mr. Luman, you

25 have five minutes, I believe.

1 MR. LUMAN: Thank you, Your Honor. I'd like to talk about
2 antedation for a minute, because this is a dispositive issue for all three
3 grounds of the '033 patent and Ground 3 of '394 patent. And the evidence of
4 antedation is extensive, and the only real serious dispute is Ms. Luo's
5 contribution. And Petitioner tries to make Ms. Luo's inventorship an issue
6 that applies to all claims of both patents. Now we believe she was an
7 appropriate inventor because we are obligated to list all inventors, even
8 those who contribute to only one claim or only one aspect of the claim, and
9 they have to be listed on the patent. But even if the Board were to agree
10 with Petitioner, that would mean that conception of dependent Claim 3
11 would be in August instead of May. It doesn't change that the rest of the
12 claims have priority back to May 8th of 2012, and that Forshew and Chan
13 are not prior art to those claims.
14 I'd like to touch briefly on claim limitation 1(f) from the '394
15 patent. And so what I will do is take us to slide number 61. And here we
16 have limitation, 1(f) and Claim 19. These are the third sequencing assays
17 and the third sequencing assay being repeated on one or more samples. And
18 Petitioner has not shown that Leary suggests doing this because the Leary is
19 the reference they rely upon. And so I'm on slide 62, and Leary did not
20 disclose that any of the monitoring of the treatment should be verified with
21 any type of sequencing.
22 And a person of skill in the art would not have been motivated
23 to do that because Leary's assay was already difficult to implement on a
24 routine basis. That's Forshew, Exhibit 1030 at page 10, and not widely
25 adopted, that's Forshew at Page 8. So adding even more sequencing steps

1 would just make Leary's process more difficult to implement and less
2 adopted. And this is an independent reason why Petitioner has not proven
3 obviousness of the '394 patent.
4 And I'd like to make a few comments now on slide 63 about
5 limitation 1(d) of the '033 patent. The repeating steps 1(b) and 1(c) in
6 subsequently obtained biological sample. And if you'll turn with me to slide
7 64, there are only two reasons that Petitioner proffers for repeating these
8 using Wagle's approach. One is the subsequently obtained tumor samples,
9 which would be invasive and costly. And the second one is plasma samples
10 that included cell-free tumor DNA.
11 And what I would like to do is look at slides 23 and 24. So I'm
12 taking us to slide 23. On slide 23, we can see that Forshew, the assay there
13 involves minute amounts of DNA ranging from just 0.9 to 19.7 nanograms.
14 And that's shown, for example, in Table Two. And that amount of the DNA
15 is too small to use with Wagle's capture probes. That's confirmed by Wagle
16 and Mamanova. As you'll see, if we turn to slide 24, Wagle's capture probes
17 require 3,600 nanograms. That's 3.6 micrograms. And the Petitioner says,
18 well, you could just take more blood draws from the Forshew patient. But
19 that's not what Forshew was designed to do. Forshew was designed to
20 operate on minute amounts of DNA.
21 And so increasing the amount of blood drawn is not something
22 that a person of skill in the art would have been motivated to do. And even
23 if they did draw enough -- draw more blood, there still in many instances
24 would not be enough DNA to use. And that is found in the sur-reply brief.
25 And I believe that's found at page 20 to 21 in the sur-reply brief.

1 Now, I would like to make one comment on capture probes.
2 And if you will turn with me to slide 20. Slide 20, we are looking at
3 limitation 1(c). And importantly, limitation 1(c) requires that the capture
4 probes hybridize to polymorphisms. And so a person of skill in the art
5 would have understood that the appropriate length for a capture probe to
6 hybridized to polymorphisms would be something on the order of 60 to 100
7 bases long. And that's found in the briefing at the '394 Patent Owner
8 Response at pages 23 to 24, because Mertes and Mamanova teach that a
9 person of skill in the art would understand that that length is required in
10 order for limitation 1(c) to have capture probes that hybridize to
11 polymorphisms. And PCR primers, as Your Honor pointed out earlier
12 today, those do not hybridize to polymorphism.
13 And with that, I'll take any questions if you have them.
14 JUDGE POLLOCK: Judge Jenks, any questions?
15 JUDGE JENKS: I do not have any questions.
16 JUDGE POLLOCK: Judge Majors?
17 JUDGE MAJORS: Nor do I. Thank you.
18 JUDGE POLLOCK: Thank you very much counsel. This has
19 been very helpful and well argued. The matter is submitted to the panel for
20 determination and preparation of the final written decision. And we are now
21 adjourned.
22 (Whereupon, the above-entitled matter went off the record at 2:37
23 p.m.)

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