

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

TEMPUS AI, INC.,
Petitioner,

v.

GUARDANT HEALTH INC.,
Patent Owner.

Case No. IPR2025-01435
Patent No. 10,793,916

**PATENT OWNER'S BRIEF IN SUPPORT OF
DISCRETIONARY DENIAL**

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I. INTRODUCTION

Pursuant to the Memorandum on Interim Processes for PTAB Workload Management, Patent Owner Guardant Health, Inc. (“Guardant”) requests the Director exercise discretion to deny institution of *inter partes* review of U.S. Pat. No. 10,793,916 (“the ’916 patent”).

The ’916 patent issued more than five years ago in view of the same art at issue in this case. There is no fresh art or argument to consider—it is just the same tired attack based on the same Schmitt et al. (“Schmitt”) reference the Office has rejected countless times, including in a recent FWD. Petitioner identifies no error with the Office’s prior considerations of Schmitt nor could it. To show material error would require demonstrating that multiple Examiners and the Board got it wrong when they rejected Schmitt. Asking the Board to take yet another look at the same failed prior art is an inefficient use of resources. Taken as a whole, the circumstances here counsel for discretionary denial.

II. THE DIRECTOR SHOULD EXERCISE DISCRETION TO DENY THE PETITION

Guardant is a leading precision oncology company that provides to patients a suite of blood-based (“liquid biopsy”) tests including the FDA-approved Guardant360® tests (e.g., CDx, Response, Liquid). EX2016, 1-3; EX2017, 1-3; EX2018, 1-2. Guardant360® tests rapidly (e.g., 7-10 days) identify genetic alterations associated with cancer, which allows doctors to tailor treatment plans

for individual cancer patients. EX2016, 2. As the FDA explained in 2020 when it approved Guardant360® CDx “In addition to benefitting from less invasive testing, patients are provided with a simultaneous mapping of multiple biomarkers of genomic alterations, . . . , which can translate to decreased wait times for starting treatment and provide insight into possible resistance mechanisms.” EX2018, 1.

The Guardant360® tests have been well-received in the industry, resulting in improved outcomes for patients. For example, a study published in 2024 demonstrated Guardant360® CDx test allows patients to “receive targeted treatment tailored to them based on comprehensive genomic profiling results.” EX2019, 2. The study further demonstrated that “patients who received targeted treatment guided by liquid biopsy results lived approximately twice as long as those who did not.” *Id.* The benefits Guardant360® tests provide to patients has resulted in widespread adoption and, to date, over 500,000 tests have been performed by Guardant. EX2020, 2; *Belden Inc. v. Commscope, Inc.*, IPR2025-00833, Paper 13 at 2 (finding commercialization of the invention supports settled expectations). For its innovations, the Office has awarded Guardant a portfolio of over 120 patents, including the ’916 patent that embodies Guardant’s highly successful Guardant360® tests.

Unfortunately, competitors took notice of Guardant’s success and improperly copied Guardant’s technology. In 2017, Guardant filed a complaint

against Foundation Medicine, Inc. (“FMI”) (Case No.: 1:17-cv-01616) for infringement of multiple patents. FMI filed six IPR petitions challenging four patents—most were denied institution and the FWD against U.S. Pat. No. 9,834,822 (“the ’822 patent”) was vacated by the Federal Circuit. That litigation settled with FMI taking a license to Guardant’s ’916 patent among others. EX2021, 1. Guardant patents were also subject to litigation with Illumina, Inc. in Case No.: 1:22-cv-00334.

In 2022, Guardant asserted several patents in Case No.: 1:21-cv-01126 against Twinstrand Biosciences, Inc., (“Twinstrand”) which controls the Schmitt reference asserted here. Twinstrand filed six IPR challenges against Guardant patents, all of which asserted the PCT version of Schmitt, and all of which failed completely. Of these six Schmitt-based IPRs, five of them were denied at the institution stage. Only one IPR was instituted for review—the IPR2022-01400 (“the 1400IPR”) addressing U.S. Pat. No. 11,149,306 (“the ’306 patent”). That case too eventually failed. The ’306 patent was challenged with the same art asserted here and the claims upheld by the Board at FWD.

Several years later, in 2024, Guardant asserted the ’306 patent (among others) in Case No.: 1:24-cv-00687 against the present petitioner. *See* EX2022.

A. Prior Adjudication in the 1400IPR Favors Discretionary Denial

Petitioner cites an old and vacated Board decision but never discusses the recent and more pertinent decision in the 1400IPR distinguishing the same relied-upon prior art from the claims of the '306 patent. Various unrebutted findings in the 1400IPR undermine the current petition challenge but are ignored here.¹

For example, the Board in the 1400IPR determined that claims reciting “attaching” molecular barcodes to cfDNA molecules—just like the currently challenged claims—do not encompass Schmitt’s hybrid embodiment relied on here. Specifically, the Board found that the plain language of claim 1 of the '306 patent “distinguishes the duplex tags [comprising molecular barcodes] from the ends of the cfDNA molecule to which they are attached.” EX1027, 21. “That is, the duplex tag is not part of the cfDNA molecule itself, but rather is ‘attached to both the ends’ of that molecule by ‘tagging’ it as recited in element 1(b).” *Id.* The Board further found that such claims “do[] not encompass Schmitt’s hybrid embodiment” because the SMI (molecular barcode) includes sequences within the DNA molecule itself (“end of the target DNA”). *Id.*, 21-22. That is, Schmitt’s

¹ Petitioner is challenging the '306 patent in the co-pending IPR2025-01434.

hybrid molecular barcode includes part of the DNA molecule itself rather than being “attached” to the DNA molecule.

Claims 13 and 30 of the '916 patent similarly recite “ligating” or “attached” molecular barcodes that are distinguished from the cfDNA molecule itself. The plain language of claim 13 specifies the “molecular barcodes” are *ligated* to the “cell-free nucleic acid molecules.” Claim 30 specifies the “molecular barcodes” are *attached* to the “cfDNA molecules.” That is, unlike the relied-upon Schmitt method, the claimed molecular barcode is not part of the original cfDNA molecule.

Despite this distinction confirmed previously, Petitioner here relies on the same Schmitt hybrid embodiment rejected by the Board in the 1400IPR. With respect to step **a** of claim 13, Petitioner points to the hybrid method as satisfying the claim limitation. *See* Pet. 36 (citing EX1005, 9:9-13) (“Schmitt also discloses a DCS ‘hybrid method’ ...”). Petitioner relies on this same disclosure for step **a** of claim 30. Pet. 56 (“see 13[a]”), 62 (pointing to Ground 1). Petitioner’s assertion of Schmitt’s hybrid embodiment for the “ligating”/“attached” step of independent claims 13 and 30 fails for the same reason as it did in the 1400IPR.

Moreover, the relied-upon “hybrid embodiment” was exposed as a half-baked and essentially one sentence hypothetical in Schmitt, whereas un rebutted evidence in the 1400IPR seriously called into question its operability, let alone

suitability for mutation detection in cfDNA.² The Board, for example, credited scientific literature publications and Schmitt owner's (Petitioner in the 1400IPR) own admissions confirming Schmitt's methods were plagued with problematic corruption/error, as well as gross sample and data loss. EX1027, 29 ("Patent Owner cites evidence, as well as Petitioner's own argument, to show that 'this problem was widely recognized in the scientific literature...'", 33 (crediting evidence of "sequencing errors" and "data loss"); *see also* EX2006, 24, 27-29; EX2007, 29:20-30:9 ("No, Your Honor, Petitioner did not dispute Dr. Quackenbush's calculations"). The current petition ignores such countervailing evidence and findings by the Board.

The 1400IPR also revealed a follow-up publication by the same Schmitt inventors reporting their methods essentially inoperable where the SMI tag (e.g., alleged molecular barcode) was less than 12 nucleotides in length. EX2006, 33-34; EX2008, 18 citing Kennedy et al. ("a tag length of <12 is incompatible with the Illumina sequencer...and should be avoided."). Remarkably, the present petition ignores this (Kennedy et al. is uncited) and proposes a combination the Schmitt

² Petitioner here proposes modifying Schmitt's disclosure for application to scarcely available and degraded cfDNA from blood.

inventors themselves instructed should be “avoided” as non-functional. Pet. 36 (“4-mer tags”), 7-9, 48 (discussing Illumina sequencing).

Rehashing the same asserted art and argument already adjudicated and correctly found deficient is both improper and a poor use of Board resources. Petitioner provides no reason for a different outcome here. *See SynQor, Inc. v. Vicor Corp.*, 988 F.3d 1341, 1351 (Fed. Cir. 2021) (“Factual determinations made by the expert agency entrusted by Congress to make those determinations—and to make them finally—need not be endlessly reexamined.”); *Azurity Pharma., Inc. v. Exelixis Inc.*, IPR2025-00427, Paper 13 at 2 (granting discretionary denial where the petitioner’s challenges were “substantially similar to those raised against a related patent—containing substantially similar claim language” and the Board rejected the prior challenges); *see also* Prior Adjudication Memo.

B. The Same Art and Argument Has Been Considered Repeatedly

As outlined in the memorandum providing for interim processes for PTAB workload management, “all relevant considerations” will be evaluated in determining whether to exercise discretionary denial consistent with existing Board precedent. *See* Memorandum, Interim Processes for PTAB Workload Management, 2 (Mar. 26, 2025). *Advanced Bionics, LLC v. Med-El Elektromedizinische Geräte GMBH*, IPR2019-01469, Paper 6 at 8-9 (precedential); *see also TankLogix, LLC v. SitePro, Inc.*, Paper 10 at 2-3 (discretionary denial

avored where “the same prior art was previously presented to the Office” and Petitioner failed to demonstrate Office error). The Office previously considered the art presented in the petition and Petitioner fails to demonstrate material error. The petition should be denied accordingly.

1. *Advanced Bionics* favors denial

The petition advances grounds based solely on art that was already considered and rejected by the Office. *See Advanced Bionics*, Paper 6 at 9-10 & n.10 (listing *Becton, Dickenson* factors).

The petition challenges the claims with the Schmitt, Forshew, Porreca, and Sacko references. Each of these references was before the Office during prosecution of the ’916 patent. *E.g.*, EX1002, 139, 412, 170, 317, 146, 419, 359-362, 364, 473-474, 861, 864, 969. These facts are sufficient to satisfy Step 1 of *Advanced Bionics. Ecto World, LLC v. Rai Strategic Holdings, Inc.*, IPR2024-01280, Paper 13 at 4 (precedential) (“Challenging the claims using the same prior art that was previously presented on an IDS is sufficient to satisfy the first part of the *Advanced Bionics* framework.”).

The Office has previously considered the art both individually and in combination. As Petitioner acknowledges (*e.g.*, pp. 14-15), the Office was made aware, on multiple occasions, of an IPR concerning the ’822 patent. Petitioner also acknowledges (p. 11) that the ’822 and the ’916 patent share a common parent

application. The '822 patent was challenged with an obviousness combination including Schmitt and Forshew. Guardant submitted the petition and institution decision (among other filings) and even withdrew the claims from issuance to apprise the Examiner of the FWD in the IPR. EX1002, 185, 448, 1282, 1381-1448, 1455-56, 1460. Guardant further submitted invalidity contentions in which disclosure in Schmitt and Forshew were mapped to the claims of the '822 patent. EX1002, 275, 303; EX2001; EX2002. With respect to Sacko, it was applied by the Examiner in an Office action. EX1002, 359-362, 364, 473-474, 861, 864, 969.

To the extent the IDSs, IPR papers, and the invalidity contentions were not enough to repeatedly apprise the Office of the asserted combinations, Guardant also submitted Office actions from co-pending cases including U.S. Appl. Nos. 15/669779, 16/601168, 16/672267. EX1002, 196, 396, 483, 1243. In the Office action for the '779 application, the Examiner expressly considered claims in view of a combination including Schmitt and Forshew. EX2003, 4-14. In the Office actions for the '168 and '267 applications, the Examiner analyzed claims in view of a combination including Schmitt and Sacko. EX2004, 6-7; EX2005, 6-7. The Examiner that issued two of the cited Office actions was the same Examiner in the instant case. EX1002, 1458; EX2004, 1; EX2005, 1.

There is also no question Porreca was considered by the Office. In fact, in a parent case (Appl. No. 15/828099), the same Examiner rejected the claims in view

of Porreca and Schmitt. EX2009, 20. This rejection was overcome when Guardant demonstrated that neither reference supports detecting somatic genetic variants in cfDNA. EX2009, 12-13; *see also id.*, 5 (“free of the prior art”). In view of the foregoing, Petitioner’s false statements about “buried” references or “[t]here is no suggestion that the Examiner substantively considered” the same art and argument is a head-scratching mischaracterization of the prosecution history. Pet. 25.

Petitioner even admits as much elsewhere in the petition. *E.g.*, Pet. 3 n. 3 (“Guardant submitted the 822FWD via IDS”), 14 (“the applicant filed a Notice of Concurrent Proceedings ...”), 15 (“applicant filed a petition to withdraw application from issue ...”), 22 (“The Board relied on Forsheew”).

The Office was well-aware of Schmitt, Forsheew, Sacko and Porreca individually and in combination when it allowed the claims. Step 1 is satisfied, and Petitioner was obligated to demonstrate material error under Step 2. Of course, Step 2 of the *Advanced Bionics* framework is satisfied because the petition does not mention any error, much less demonstrate any in the Office’s prior consideration of the asserted art. *See Advanced Bionics*, Paper 6 at 10-11. Discretionary denial is warranted. *See, e.g., TankLogix*, Paper 10 at 2-3.

2. The Office has never accepted Schmitt as applicable to microsatellite changes in cfDNA

The Office has repeatedly considered Schmitt—not just in this case—but across Guardant’s portfolio and recognized the deficiencies in the prior art regarding detection of somatic variants (e.g., in microsatellite regions) in cfDNA. Detection of somatic variants in cfDNA derived from cancer patients requires methods that are highly sensitive for variants present at very low frequency (e.g., <1%) in cfDNA. *E.g.*, EX1001, 61:35-65 (Table 1), 7:47-50. Schmitt, however, lacks the requisite sensitivity, as the Office has found numerous times. Non-limiting examples are provided below.

As discussed above, the Office considered Schmitt in the 1400IPR where its lack of applicability to detection of somatic variants in cfDNA was laid bare. As the Board observed, multiple literature references and admissions by Schmitt’s owner confirmed that the method is so plagued with error and data corruption that all but *2 molecules out of every billion DNA fragments* are lost. EX2006, 29-30, 33. Somatic mutations present in <1% of molecules cannot be detected when >99% sample molecules are never analyzed. *Id.*; EX2007, 29:20-30:9 (“do you dispute his calculation of the magnitude of that reduction in molecules? ... “No, Your Honor, Petitioner did not dispute Dr. Quackenbush’s calculations”). On this basis, the Board questioned Schmitt’s applicability to cfDNA. EX2007, 31:1-4 (“But

isn't there a point where one filters out too much data such that Schmitt's DCS method might not be the best choice of sequencing methods in a scenario where you have a more limited supply of input DNA, such as might be the case with cfDNA?").

The Office considered Schmitt in Appl. No. 15/828,099—a parent of the '916 patent—and agreed that Schmitt does not teach detecting the presence or absence of somatic genetic variants in cfDNA. EX2009, 5, 12-13. The Office also considered Schmitt in Appl. No. 16/593,633—a child of the '916 patent—and agreed that Schmitt does not teach detection of rare variants in cfDNA. EX2010, 6, 14-20, 22-30. The Office considered Schmitt yet again in Appl. No. 16/277,724—which shares a common parent with the '916 patent—in relation to claims requiring detection of somatic genetic variants in cfDNA. The Examiner found that Schmitt was likely “not enabled” for such an application. EX2011, 18.

Petitioner Tempus itself argued during prosecution of its own patents that existing prior art (which would include Schmitt) did not teach microsatellite instability (“MSI”) detection in cfDNA. For example, Petitioner has its own application (US2021/0098078, EX2012) with claims directed to MSI detection in cfDNA with an earliest claimed filing date of August 1, 2019. Petitioner bemoaned the difficulty of MSI detection in cfDNA from cancer patients (“liquid biopsy”) as

“unconventional,” “significantly challenging and problematic,” and distinguished from solid tissue analysis (like Schmitt).

[T]he mere use of a liquid biopsy assay for determining the MSI status of a cancer in a patient was unconventional at the time the present application was filed. This is evidenced by paragraphs [0008] and [0024] ..., which state that at the time the present application was filed, determining the MSI status of a cancer was conventionally performed by evaluating DNA from a solid tumor biopsy sample:

EX2013, 50.

As can be seen, claim 1 is directed to determining the MSI status of a test subject using a plurality of mapped cell-free nucleotide sequences from a liquid biopsy sample of the test subject despite the fact that detecting and/or validating cancer-specific genomic alterations of a liquid biopsy sample is significantly challenging and problematic.

Id., 147. Petitioner’s statements to the Office regarding the state of the art in 2019 are consistent with the Office’s prior considerations of Schmitt but wholly ***inconsistent*** with arguments in the petition (p. 30) describing the asserted combination as a “predictable use of known techniques to address a recognized problem using conventional tools.”

C. The Board’s Vacated Decision in the 652IPR Does Not Help Petitioner

In addition to improperly ignoring its own inconsistent argument and more pertinent guidance by the Office, Petitioner’s reliance on the vacated Board’s

decision in IPR2019-00652 (“the 652IPR”) concerning the ’822 patent is misplaced for several reasons.

As an initial matter, the 652IPR decision could not control because it was vacated by the Federal Circuit. *Guardant Health, Inc. v. Vidal*, No. 2021-1104, 2023 U.S. App. LEXIS 11037 (Fed. Cir. 2023). A “judgment’s vacatur on appeal renders it a legal nullity.” *Statewide Reapportionment Advisory Comm. v. Beasley*, 99 F.3d 134, 136 (4th Cir. 1996) (quoting *S-1 by & Through P-1 v. State Bd. of Educ.*, 6 F.3d 160, 171 (4th Cir. 1993)); *see also Durning v. Citibank, N.A.*, 950 F.2d 1419, 1424 n.2 (9th Cir. 1991) (“[A] decision that has been vacated has no precedential authority whatsoever.” (citing *O’Connor v. Donaldson*, 422 U.S. 563, 578 n.12 (1975))). Contrary to Petitioner’s argument (pp. 2, 63), the ’822 claims have not been invalidated nor have they been partially canceled.

Even if the vacated 652IPR FWD is considered it can be of no impact here because ’822 patent claims are materially different than those of the ’916 patent. For example, claim 1 of the ’916 patent is directed to detecting “genetic variation in one or more microsatellite regions” and further recites determining “a quantitative measure of polymorphic forms comprising microsatellite changes in one or more microsatellite regions.” Such language is not recited in the ’822 patent claims, which do not mention “microsatellite” changes or regions. In fact, claim 1 of the ’822 patent does not require detection of somatic variants in cfDNA nor do

they mention cancer patients, the petition does not assert otherwise. Given Petitioner's statements to the Office, there does not appear to be any dispute that detecting microsatellite changes in cfDNA was a materially different and "significantly challenging" problem not solved by prior art methods. *E.g.*, EX2013, 50, 147.

In addition, the '822 patent claims recite "converting the population of cfDNA molecules into a population of non-uniquely tagged parent polynucleotides"—language not found in the '916 patent claims. In contrast, the '916 patent claims recite "ligating molecular barcodes" (claim 13) and specify "molecular barcodes [] attached to both ends" of the cfDNA molecule (claim 30). As discussed above (see §II.A), the Board already determined the more specific "ligating"/"attached" language as recited in the '916 claims distinguishes from the Schmitt's hybrid method now relied upon in the present petition.

To the extent Petitioner argues the difference in claim scope is not material, that only makes matters worse for them. Guardant presented evidence during the 652IPR the Guardant360® test has been commercially successful and satisfied a long-felt need, thereby providing objective indicia of nonobviousness. The Federal Circuit vacated the 652IPR FWD for improperly ignoring this evidence. Petitioner here cites to the vacated decision but ignores the Federal Circuit's most salient holding to commit the same error. Indeed, "objective indicia of nonobviousness

must be considered in every case where present.” *Apple Inc. v. Samsung Elecs. Co.*, 839 F.3d 1034, 1048 (Fed. Cir. 2016)). Indeed, the petition materials make no attempt to address the known evidence of objective indicia of nonobviousness from the very vacated case it cites. *See* EX1003, ¶253 (“there are no secondary considerations supporting non-obviousness”).³ Failure to address known objective evidence of nonobviousness also means Petitioner’s present challenge is incurably deficient. *Gilead Sciences, Inc. v. United States*, IPR2019-01456, Paper 17 at 52-53 (“Petitioner’s failure to persuasively address the [unexpected] results in its Petition means Petitioner falls short of its burden to establish a reasonable likelihood of success in prevailing on its challenge.”); *Coalition for Affordable Drugs V LLC, v. Hoffman La-Roche Inc.*, IPR2015-01792, Paper 14 at 17-18 (denying institution where petitioner did not address known objective indicia of nonobviousness).

III. PETITIONER’S IMPROPER AND INCONSISTENT CLAIM CONSTRUCTION ARGUMENTS FAVOR DISCRETIONARY DENIAL

The petition (p. 17) acknowledges Petitioner’s burden to explain “[h]ow the challenged claim is to be construed” and, under Petitioner’s constructions, “[h]ow

³ The Guardant360® test detects microsatellite instability. EX2014.

the construed claim is unpatentable.” Petitioner then argues it “does not believe any terms require construction.” Indeed, its expert does not purport to have any difficulty understanding the challenged claims under their plain and ordinary meaning. EX1003, ¶37 (“claim terms are presumed to take on the ordinary and customary meaning”).

At district court, however, Petitioner asserts that the scope of the claims of the '916 are indeterminable and unpatentably indefinite based on multiple recited terms. For other terms, Petitioner has argued narrow interpretations to avoid infringement. None of these district court claim construction arguments or positions are disclosed in the petition materials, let alone accounted for in the prior art mapping allegations of the petition.

Petitioner’s district court positions regarding claim terms recited in independent claims 13 and 30 are reproduced below. *See* EX2015, 2-3. Petitioner also alleges at district court that the term “unique sequence read” recited in claim 30 is indefinite.

“the amplified progeny polynucleotides” (’306 claims 1 and 17) / “the amplified tagged progeny polynucleotides” (’916 claims 1, 13, 30)	the polynucleotides generated by amplification of the tagged parent polynucleotides
“sequence information of the molecular barcodes” (’916 claims 1, 13, 30)	Indefinite

“a quantitative measure of polymorphic forms comprising microsatellite changes” (’916 claim 13)	Indefinite
“amplifying the tagged parent polynucleotides” (’916 claim 30)	amplifying every one of the tagged parent polynucleotides

Where Petitioner has proposed constructions at district court, those constructions are not presented in the petition materials and, in some instances, are irreconcilable with the claim mapping presented in the petition. For example, at district court Petitioner argues the “amplifying” step of claim 30 requires amplifying “every one” of the tagged polynucleotides. Yet, the petition maps this claim element to an amplification step that produces only “a set” of amplified molecules (i.e., less than “every one”). Pet. 56 (“See 13[b] (Section IX.C.1.c.)”), 37 (citing EX1005, 3:10–20); EX1003, ¶¶158-160, 227. Petitioner makes similar arguments (but inconsistent with its district court argument) in the concurrently filed IPR2025-01434 against a different Guardant patent. In that 1434IPR petition, Petitioner argues that prior art amplification is “not perfect” such that it is typical that not “every one” of the tagged parent polynucleotides gets amplified. 1434IPR Pet. 35 (“amplifications are not perfect, so every strand of every original template molecule is not recovered”). The present petition does not explain this inconsistency—or address Petitioner’s different district court constructions and arguments at all—burdening Patent Owner and the Board with resolving the conflicting argument.

Asking the Board to sort through different constructions in a petition compared to those being advocated for at district court infringement purposes is not only improper, but a poor use of Office resources. Indeed, the Federal Circuit has explained that “claims must be interpreted and given the same meaning for purposes of both validity and infringement analyses.” *Amazon.com, Inc. v. Barnesandnoble.com, Inc.*, 239 F.3d 1343, 1351 (Fed. Cir. 2001). Petitioner’s inconsistent arguments and theories are best resolved at district court to better ensure the district court can properly address validity and infringement under the same construction. *Sun Pharms. Indust., Inc. v. Nivagen Pharms., Inc.*, IPR2025-00893, Paper 18 at 2-3 (granting discretionary denial where “Petitioner has taken different claim construction positions in this proceeding and the parallel district court proceeding”).

Regarding the various district court allegations of indefiniteness, the petition correctly concedes “the Board may not cancel claims for indefiniteness in an IPR proceeding.” Pet. 17 (quoting *Samsung Elecs. Am., Inc. v. Prisia Eng’g Corp.*, 948 F.3d 1342, 1350 (Fed. Cir. 2020)). But Petitioner simply cannot meet its burden of proving invalidity as alleged where it expressly “takes no position in this Petition as to whether the claims meet the requirements of Section 35 U.S.C § 112.” *Id.* Indeed, Petitioner did clearly take the position at district court that the same claims are allegedly indefinite and of indeterminable scope. The petition offers no

explanation how it could possibly meet its burden of showing the challenged claims encompass the prior art where it asserts the metes and bounds of those same claims is indeterminable. *Cambridge Mobile Telematics, Inc. v. Sfara, Inc.*, IPR2024-00952, Paper 12 at 8 (“At a minimum, the Petition should have explained...why the inconsistent positions are warranted...”). Instead, the petition offers no explanation at all and ignores entirely its inconsistent district court arguments that the metes and bounds of the challenged claims are unknown. In some instances, Petitioner does not even bother to map allegedly indefinite terms to the prior art—it ignores those too. For example, at district court Petitioner alleges the claim term “unique sequence read”—which is recited only in independent claim 30—is indefinite. For the prior art argument in the present petition, the argument for claim 30 merely refers back to its mapping for claim 13. Pet. 55-56, 62. Claim 13 does not recite the term “unique sequence read,” and the petition never even addresses how this limitation recited in claim 30 is allegedly satisfied by the prior art. Having made its choice to pursue its indefiniteness theory, Petitioner presents improper and incomplete prior art invalidity arguments in its petition that are nothing more than a waste of Board resources.

IV. CONCLUSION

For at least the reasons above, Patent Owner respectfully requests that the Director exercise discretion to deny institution of the petition.

Date: October 20, 2025

Respectfully submitted,

/ Michael T. Rosato /

Michael T. Rosato, Lead Counsel

Reg. No. 52,182

V. APPENDIX

Exhibit No.	Description
2001	FMI Invalidity Chart Exhibit B-1
2002	FMI Invalidity Chart Exhibit D-1
2003	Excerpts from File History of U.S. Patent Application No. 15/669,779
2004	Excerpts from File History of U.S. Patent Application No. 16/601,168
2005	Excerpts from File History of U.S. Patent Application No. 16/672,267
2006	IPR2019-01400 - Patent Owner's Response
2007	IPR2022-01400 - Hearing Transcript
2008	IPR2022-01400 - Patent Owner's Surreply
2009	Excerpts from File History of U.S. Patent Application No. 15/828,099
2010	Excerpts from File History of U.S. Patent Application No. 16/593,633
2011	Excerpts from File History of U.S. Patent Application No. 16/277,724
2012	Patent Application Publication No. US20210098078A1
2013	Excerpts from File History of U.S. Patent Application No. 16/945,588
2014	Guardant360-Liquid-Specification-Sheet
2015	Tempus Proposed Claim Constructions, <i>Guardant Health, Inc., v. Tempus AI, Inc.</i> , Case 1:24-cv-00687

2016	<p>Guardant Health Introduces Major Smart Liquid Biopsy Upgrade to Market – Leading Guardant 360 Test, Further Extending its Best-In-Class Performance.</p> <p>https://investors.guardanthealth.com/press-releases/press-releases/2024/Guardant-Health-Introduces-Major-Smart-Liquid-Biopsy-Upgrade-to-Market-Leading-Guardant360-Test-Further-Extending-Its-Best-in-Class-Performance/default.aspx (last viewed on October 20, 2024)</p>
2017	<p>Guardant Health to Showcase New Data at ESMO 2022 Demonstrating Utility of its Portfolio of Blood Tests for Advanced – Stage Cancer Patients.</p> <p>https://investors.guardanthealth.com/press-releases/press-releases/2022/Guardant-Health-to-showcase-new-data-at-ESMO-2022-demonstrating-utility-of-its-portfolio-of-blood-tests-for-advanced-stage-cancer-patients/default.aspx (last viewed on October 20, 2024)</p>
2018	<p>FDA Approves First Liquid Biopsy Next-Generation Sequencing Companion Diagnostic Test. News Provided by U.S. Food and Drug Administration</p> <p>https://www.prnewswire.com/news-releases/fda-approves-first-liquid-biopsy-next-generation-sequencing-companion-diagnostic-test-301108536.html (last viewed October 20, 2024)</p>
2019	<p>GOZILA Study Published in Nature Medicine Shows Patients with Advanced Cancer Who Receive Liquid Biopsy – Guided Treatment Using Guardant360 CDX Survive Twice as Long.</p> <p>https://investors.guardanthealth.com/press-releases/press-releases/2024/GOZILA-Study-Published-in-Nature-Medicine-Shows-Patients-With-Advanced-Cancer-Who-Receive-Liquid-Biopsy-Guided-Treatment-Using-Guardant360-CDx-Survive-Twice-as-Long/default.aspx (last viewed October 20, 2024)</p>
2020	<p>Guardant Health Named to TIME100 Most Influential Companies. https://investors.guardanthealth.com/press-releases/press-releases/2024/Guardant-Health-Named-to-TIME100-Most-Influential-Companies/default.aspx (last viewed October 20, 2024)</p>

2021	Guardant Health and Foundation Medicine Reach Settlement in Digital Sequencing Technology Litigation. https://investors.guardanthealth.com/press-releases/press-releases/2022/Guardant-Health-and-Foundation-Medicine-Reach-Settlement-in-Digital-Sequencing-Technology-Litigation/default.aspx (last viewed October 20, 2024)
2022	Guardant Health, Inc.'s First Amended Complaint, <i>Guardant Health, Inc., v. Tempus AI, Inc.</i> , Case 1:24-cv-00687

CERTIFICATE OF SERVICE

The undersigned certifies that the foregoing Patent Owner's Brief In Support of Discretionary Denial and accompanying Exhibits 2001-2022 were served on October 20, 2025, on the Petitioner at the electronic correspondence address of the Petitioner as follows:

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