

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

FUJIREBIO DIAGNOSTICS, INC.,
Petitioner,

v.

QUANTERIX CORP.,
Patent Owner.

IPR2025-01060
Patent 11,275,092

Title: METHODS OF DETERMINING A TREATMENT PROTOCOL FOR AND/OR A
PROGNOSIS OF A PATIENT'S RECOVERY FROM BRAIN INJURY

PATENT OWNER'S BRIEF IN SUPPORT OF DISCRETIONARY DENIAL

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EXHIBIT LIST

Exhibit No.	Description
2001	U.S. Patent Application No. 15/269,142, Office Action Rejection dated January 29, 2015
2002	U.S. Patent Application No. 15/269,142, Office Action Rejection dated December 31, 2018

I. INTRODUCTION

Patent Owner respectfully requests that the Director exercise discretion to deny institution of IPR2025-01060. Discretionary denial is warranted under 35 U.S.C. § 325(d) because the Petition raises art that was already considered or cumulative of art already submitted, and presents arguments substantially similar to those already presented during prosecution of challenged U.S. Patent No. 11,275,092 (the “’092 patent”).

During prosecution, the Examiner carefully considered, and allowed the claims over, prior art disclosing Patent Owner’s ultra-sensitive, single-molecule protein assay (coined Simoa®) together with art suggesting a need to detect a protein in blood—tau—that is associated with brain injuries and other neurological conditions including Alzheimer’s Disease. Both concepts—existence of the assay, and general suggestions to search for tau in blood—appear in prior art references that the Examiner cited as a basis for claim rejections. Although the Examiner allowed the claims over these disclosures, the Petitioner now asks the Patent Office to address the same arguments already presented and overcome during prosecution. The Director should reject Petitioner’s request to reconsider its findings of patentability over the same or highly similar prior art and arguments and deny the

Petition under § 325(d). The Petitioner has not met (and cannot meet) its burden to show that the Office erred in a manner material to its finding of patentability.

Discretionary denial is further justified by the Petitioner's decision not to file a stipulation that would eliminate the risks of duplicative efforts or conflicting decisions between this proceeding and parallel district court litigation.

II. BACKGROUND

A. Petitioner Filed an IPR Petition and Declaratory Judgment Action and Patent Owner Counterclaimed for Infringement

On May 28, 2025, Petitioner filed its Petition, along with a lawsuit in the U.S. District Court for the District of Delaware, requesting a declaratory judgment of non-infringement of the '092 patent. (*Fujirebio Diagnostics, Inc. v. Quanterix Corp.*, No. 1:25-cv-00659 (D. Del.), Dkt. No. 1.) Patent Owner filed a counterclaim alleging infringement of the '092 patent on June 23, 2025. (*Id.*, Dkt. No. 12.)

B. The '092 Patent Issued Over Art that Disclosed Ultrasensitive Assay Methods and that Identified Tau Protein as a Potential Blood-Based Biomarker Target

The '092 patent claims methods of producing bodily fluid samples for quantification of tau protein that is present in exceedingly low concentrations in a patient's blood sample. (*See, e.g.*, '092 patent, claim 1; Petition at 1; *see also* Ex. 1002 at 555.) The '092 patent issued after the Examiner and Patent Owner

resolved obviousness rejections raised in the only office action made during prosecution.

1. The Examiner's Obviousness Rejections Relied on Patent Owner's Prior Art Assay Method and a Suggestion to Apply Such Methods to Detect Tau Protein in Blood

The Examiner relied on the combination of “Duffy” (Ex. 1015), and “Quanterix 2010a” (Ex. 1033), as the primary basis of rejection for pending claims 11, 20-24, and 92-102. (Ex. 1002 at 496.) Both Duffy and Quanterix 2010a originate from and describe or relate to Patent Owner's ultra-sensitive protein assay, and Duffy is cited in the '092 patent specification among a long list of Patent Owner's disclosures related to that assay. (Ex. 1001, '092 patent, 16:48-53.) The Examiner also rejected these same claims in further view of either “Wunderlich” (Ex. 1017) or “Mortberg” (Ex. 1018), and rejected pending claim 103 based on Duffy in view of Quanterix 2010a and Wunderlich. (Ex. 1002 at 500-02.)

In the rejection, the Examiner asserted that Duffy teaches an ultra-sensitive assay for measuring proteins in blood, which alone discloses each claim limitation except that “the protein being detected is tau” and obtaining a sample “from a patient recovering from brain injury.” (Ex. 1002 at 496-97.) Even then, the Examiner concluded that “[n]evertheless, one of ordinary skill in the art at the time of the

invention would have found it obvious that the method of Duffy could be used to” detect and quantify tau as recited by the claims “in a blood/serum/plasma sample of a patient recovering from a brain injury,” as required by then-pending independent claim 92. (Ex. 1002 at 497.) The Examiner reasoned that a skilled artisan would have anticipated success in applying the Duffy assay in the same way to quantify tau. (*Id.* (discussing *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 420-21 (2007)).)

The Examiner further asserted that even if Duffy alone did not render obvious the claim limitations that “the protein being detected is tau” and obtaining a sample “from a patient recovering from brain injury,” the combination of Duffy and Quanterix 2010a did so. (Ex. 1002 at 497.) According to the Examiner, Quanterix 2010a teaches not only “the same assay as Duffy,” but also “explicitly teaches the assay can detect tau in a blood sample and suggests doing so in a subject recovering from a brain injury.” (Ex. 1002 at 498.)

The Examiner also rejected pending claims 11, 20-24, and 92-102 based on the combination of Duffy and Quanterix 2010a in further view of either Wunderlich or Mortberg. (Ex. 1002 at 500-01 (in further view of Wunderlich), 501-02 (in further view of Mortberg).) The Examiner found both Wunderlich and Mortberg teach quantifying tau following brain injury (including injuries resulting from the specific

events recited in the pending claims, e.g., hypoxic and ischemic events), and therefore fill that potential gap in Quanterix 2010a. (*E.g.*, Ex. 1002 at 501 (“Wunderlich teaches that approximately 30 pg/mL of tau are detected in blood . . . after a stroke”); *id.* (“Mortberg teaches measuring tau in plasma after cardiac arrest”).)

The Examiner additionally rejected pending claim 103, which recited collecting the patient sample within 12 hours of a brain injury, based on the combination of Duffy, Quanterix 2010a, and Mortberg. (Ex. 1002 at 501.) The Examiner observed that Quanterix 2010a provided “the teachings to make obvious measuring tau in the blood of a subject with a brain injury[,] . . . Wunderlich provides a reasonable expectation of detecting tau in said blood within 12 hours of a brain injury.” (*Id.*)

2. The Examiner Withdrew the Obviousness Rejections and Allowed the Claims After Considering Patent Owner’s Rebuttal Evidence

The Examiner allowed the ’092 patent claims after holding an interview with Patent Owner’s representatives and reviewing Patent Owner’s rebuttal evidence and claim amendments.

The Examiner and Patent Owner’s representatives discussed the obviousness rejection over Duffy and Quanterix 2010a during an interview attended by David Duffy—the named inventor on Duffy and the presenter of the Quanterix 2010a slides, who then served as Patent Owner’s Chief Technology Officer. (Ex. 1002 at 554.) Among other issues, Mr. Duffy explained why a skilled artisan would not have been motivated to pursue the claimed tau protein assay method in light of the conventional wisdom in the art, and how it was only after the underlying patent application published that the field experienced a “sea-change” in the approach to measuring tau in blood samples. (*Id.* at 555, 627.) This was evidenced by an article—Ding, Ex. 1019—that catalogued a dramatic, post-publication uptick in the use of Patent Owner’s ultra-sensitive assay (Simoa® assays), and other sensitive assays, to detect tau in blood. (*Id.* at 556, 627.)

Patent Owner also addressed the obviousness rejections in written remarks, emphasizing the lack of a reasonable expectation of success in reliably producing an analytically quantified sample from blood containing tau at the levels claimed and using the level of sensitivity claimed. (*Id.* at 555, 558.) More specifically, Patent Owner explained that at the time of the invention, there was no clear impetus in the field to use ultra-sensitive assay methods to detect tau, and that conventional assay

methods had been used and generally accepted. (*Id.* at 555-56.) Patent Owner pointed out that those conventional techniques were used by Mortberg and Wunderlich, among others. (*Id.* at 555-57, 559.) And Patent Owner explained that Quanterix 2010a reported tau measurements using conventional techniques—not Patent Owner’s ultra-sensitive assay—and only in hindsight was it recognized that those results lacked reliability and overestimated tau concentration. (*Id.* at 557, 559.) Patent Owner then reiterated that it was only after publication of the underlying application that the field adopted a reasonable expectation of success detecting tau in blood and moved away from the gold-standard method of quantifying tau in cerebrospinal fluid. (*Id.* at 559-61.) That adoption was accompanied by praise for—and the commercial success of—Patent Owner’s ultra-sensitive tau assay. (*Id.* at 561-62.)

After considering Patent Owner’s arguments, the Examiner allowed the claims. In particular, the Examiner acknowledged that the alleged *prima facie* case presented in the non-final office action could not stand given that no group had used Patent Owner’s ultra-sensitive Simoa® assay to detect tau until after the effective filing date. (*Id.* at 659.) As succinctly put by the Examiner:

In this case, no group prior to the effective filing date had done more than perhaps suggest using Simoa to detect tau (see Quanterix document previously discussed), while dozens of groups utilized Simoa to detect tau after the date of Applicant’s contribution. It is on this fact that the Examiner finds the argument persuasive and concludes that the rebuttal evidence is sufficient to overcome the obviousness rejection.

(*Id.* at 660.)

C. The Petition’s Obviousness Grounds Mirror Those Raised and Overcome During Prosecution

The Petitioner presents two Grounds of obviousness, both of which use the same base reference, Rissin (Ex. 1005):

Ground	Basis	Claims	Reference(s)
1	§ 103	1, 6-21	Rissin in view of Todd
2	§ 103	1, 6-21	Rissin in view of Voorheis

According to Petitioner, Rissin “teaches performing a SMA [single molecule assay] (digital ELISA) to measure low concentrations of protein biomarkers in blood and blood serum” by “us[ing] single arrays of femtoliter-sized reaction chambers’ that ‘can isolate and detect single enzyme molecules.’” (Petition at 28.) According to Petitioner, Rissin discloses all elements of the challenged claims except targeting tau. (*See, e.g., id.* at 38, 61-62.)

According to Petitioner, Todd “describes the use of a SMA technology . . . that could be used to detect tau biomarker in the blood plasma of patients for early detection of [Alzheimer’s Disease].” (Petition at 31.) The Petitioner also relies on Todd as identifying Alzheimer’s Disease as an area where ultra-sensitive assay techniques might be used, and pointing to tau as a known biomarker candidate for clinical diagnosis of Alzheimer’s Disease. (*Id.* at 33-34.)

According to Petitioner, Voorheis “is directed to methods and kits for diagnosing [Alzheimer’s Disease] and other neurological disorders by screening for tau in the blood of a patient.” (Petition at 56.) Petitioner also describes Voorheis as “recogniz[ing] the need for early detection and diagnosis of [Alzheimer’s Disease],” and as having “developed a blood-based diagnostic assay using tau as a method for doing so” that involves diluting a blood sample and performing an immunoassay. (*Id.* at 57.)

For Ground 1 combining Rissin and Todd, Petitioner asserts that “[a] POSA would have been motivated to use the SMA procedure of Rissin to quantify endogenous tau in the blood of patients suspected of having a neurological disorder as taught by Todd to arrive at the inventions claimed by the Challenged Claims for several reasons,” including a shared field of endeavor and their common disclosure

of use of SMAs to quantify ultra-low concentration of analytes in blood. (Petition at 34.) In other words, Petitioner argues that a skilled artisan would have been motivated to apply the ultra-sensitive assay technique of Rissin to detect tau protein as suggested by Todd, which itself suggests use of ultrasensitive assays for detection of biomarkers relevant to diagnosis of Alzheimer’s disease. (*Id.* at 38-44.)

For Ground 2 combining Rissin and Voorheis, Petitioner asserts that “[a] POSA would have been motivated to combine the teachings of Rissin with the teachings of Voorheis in order to quantify endogenous tau in the blood of patients suspected of having a neurological disorder as claimed by the ’092 patent,” because a POSA would know an ultra-sensitive technique to detect trace amounts of analyte in blood, like in Rissin, would be beneficial for early Alzheimer’s Disease diagnosis, and in particular tau, as described in Voorheis. (Petition at 58-60.)

D. The Petition’s Primary Reference—Rissin—Has Long Served as an Obviousness Reference in Prosecution of Related Applications Involving the Same Examiner

The Petitioner’s resort to Rissin as a primary reference, rather than the Duffy reference cited by the Examiner, is a distinction without a difference. The contents of Rissin and Duffy are very similar, which is no surprise. The authors of Rissin worked for Patent Owner Quanterix and Rissin’s author list includes every one of

the named inventors of the Duffy reference (i.e., David Duffy, Evan Ferrell, Jeff Randall, David Rissin, and David Walt). (*Compare* Ex. 1005, *with* Ex. 1015.) Furthermore, and of greater significance to the question of discretionary denial, the same Examiner that evaluated and allowed the '092 patent's claims had long considered and relied on Rissin during examination of '092 parent applications.

To illustrate, during prosecution of the earliest patent application in the '092 patent's family, U.S. Patent Application No. 14/111,326¹, the same Examiner rejected the pending claims over the combination of Rissin, which describes Patent Owner's "assay which detects serum proteins at subfemtomolar concentrations (title)," with Hulstaert (WO 2000/14546), which claimed "a method for early detection or quantification of CNS damage in an individual by determining (i.e., detecting) the level of tau in said individual and comparing it to the level of tau in control healthy individuals (claim 1)." (Ex. 2001 at 15.) The Examiner's obviousness rationale was that a skilled artisan "would have been motivated to use the technique of Rissin in the method of Hulstaert," to arrive at the claimed invention

¹ The '092 patent is a continuation of, and claims priority to, the '326 application.

because of the motivation to measure tau, per Hulstaert, “with the greatest sensitivity available as this is the general nature of scientific experimentation.” (*Id.* at 15.) In other words, the Examiner’s argument was that it would have been obvious to apply Patent Owner’s ultra-sensitive assay to tau because tau was a known biomarker for brain injury.

During prosecution of the next-filed application in the family, U.S. Patent Application No. 15/269,142², the same Examiner rejected the then-pending claims under § 101, referencing Rissin as describing a known sensitive assay to detect proteins, along with Quanterix 2010a, which the Examiner characterized as teaching the use of Patent Owner’s assay to detect tau. (Ex. 2002 at 6-8.)

Thus, whether as described in Duffy or Rissin, the same Examiner was intimately aware of the prior art status of Patent Owner Quanterix’s ultra-sensitive assay methods for measuring proteins in blood, and had cited Rissin and Duffy interchangeably for essentially the same teachings throughout his examination of applications in the ’092 patent family.

² The ’092 patent is a continuation of, and claims priority to, the ’142 application.

III. ARGUMENT

A. Discretionary Denial Is Warranted Because the Petition Raises the Same or Substantially the Same Prior Art and Arguments the Examiner Previously Considered

1. Legal Standard for Discretionary Denial Under § 325(d)

The Board applies a two-part framework to analyze discretionary denial under § 325(d): “(1) whether the same or substantially the same art previously was presented to the Office or whether the same or substantially the same arguments previously were presented to the Office; and (2) if either condition of [the] first part of the framework is satisfied, whether the petitioner has demonstrated that the Office erred in a manner material to the patentability of challenged claims.” *Advanced Bionics, LLC v. MED-EL Elektromedizinische Geräte GmbH*, IPR2019-01469, Paper 6 at 8 (PTAB Feb. 13, 2020) (“*Advanced Bionics*”) (precedential).

“If a condition in the first part of the framework is satisfied and the petitioner fails to make a showing of material error, the Director generally will exercise discretion not to institute *inter partes* review.” *Id.* at 8–9. “[T]his framework reflects a commitment to defer to previous Office evaluations of the evidence of record unless material error is shown.” *Id.* at 9.

In the first step of the *Advanced Bionics* framework, the Board may consider *Becton, Dickinson* factors (a), (b) and (d), which are:

- a) the similarities and material differences between the asserted art and the prior art involved during examination;
- b) the cumulative nature of the asserted art and the prior art evaluated during examination; and
- d) the extent of the overlap between the arguments made during examination and the manner in which Petitioner relies on the prior art or Patent Owner distinguishes the prior art.

Advanced Bionics, Paper 6 at 10; see also *Becton, Dickinson & Co. v. B. Braun Melsungen AG*, IPR2017-01586, Paper 8 at 17-18 (PTAB Dec. 15, 2017) (“*Becton, Dickinson*”) (precedential). “Previously presented art includes art made of record by the Examiner, and art provided to the Office by an applicant, such as on an Information Disclosure Statement (IDS), in the prosecution history of the challenged patent.” *Advanced Bionics*, Paper 6 at 7–8.

In the second step of the *Advanced Bionics* framework, the Board may consider *Becton, Dickinson* factors (c), (e), and (f), which are:

- c) the extent to which the asserted art was evaluated during examination, including whether the prior art was the basis for rejection;
- e) whether Petitioner has pointed out sufficiently how the Examiner erred in its evaluation of the asserted prior art; and
- f) the extent to which additional evidence and facts presented in the Petition warrant reconsideration of the prior art or arguments.

Id. at 10.

2. *Advanced Bionics* Step 1 Is Met Because the Petition Raises the Same or Similar Prior Art and Arguments

The Petition raises art already considered (Rissin and Voorheis), that is cumulative of art already considered, and presents substantially the same obviousness arguments as those that were already overcome during prosecution. Step 1 of the *Advanced Bionics* framework is thus met.

a. The Examiner Considered Rissin and Voorheis

Two of the three references that the Petition raises, Rissin and Voorheis, were submitted by the Patent Owner on an IDS that the Examiner electronically signed. The Examiner signed the individual IDS pages where Rissin and Voorheis appear, noting “ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /AMW/,” without crossing off Rissin or Voorheis. (Ex. 1002 at 512, 534.)

Because a reference presented to the Patent Office in an IDS citation alone is deemed previously presented to and considered by the Office, *Advanced Bionics* step 1 is met as to Rissin and Voorheis. *Ecto World, LLC & SV3 LLC v. RAI Strategic Holdings, Inc.*, IPR2024-01280, Paper 13 at 4 (PTAB May 19, 2025) (“*Ecto World*”)

(precedential) (Acting Director Stewart) (“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.” (citations omitted)); *Advanced Bionics*, Paper 6 at 7-8 (stating that previously presented art includes art cited in an IDS); *see also Google LLC v. Valtrus Innovations Ltd.*, IPR2022-01197, Paper 18 at 15 (PTAB June 13, 2023) (“[P]roviding a document to the Office in an Information Disclosure Statement is sufficient to satisfy prong one of the *Advanced Bionics* analysis.”); *Microsoft Corp. v. Koninklijke Philips N.V.*, IPR2018-00279, Paper 11 at 12, 14-15 (PTAB June 8, 2018) (“The bottom of each page of the signed Information Disclosure Statement reads, ‘ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH....’ Willey is not lined through. Thus, we find that Willey was previously presented to, and considered by, the Office.” (citations omitted)).

In addition, the same Examiner repeatedly cited Rissin in claim rejections during prosecution of parent patent applications, underscoring that the Examiner was fully aware of Rissin’s teachings during examination of the ’092 patent. (Ex. 2001 at 15; Ex. 2002 at 6-8.)

b. Rissin Is Cumulative of and Immaterially Different from Duffy

Petitioner's primary obviousness reference, Rissin, is cumulative of Duffy, the primary obviousness reference raised in prosecution. Both describe Patent Owner Quanterix's ultra-sensitive assay for detection and measurement of proteins.

Rissin describes Patent Owner Quanterix's "single-molecule enzyme-linked immunosorbent assay (digital ELISA)" and discloses the method's ability to measure certain proteins in serum at subfemtomolar concentrations. (Ex. 1005 at 1; Petition at 28.) Rissin describes this digital assay as using "arrays of femtoliter-sized reaction chambers" "that can isolate and detect single enzyme molecules." (Ex. 1005 at 1, 6; Petition at 28.) The assay operates by forming a sandwich antibody complex on microscopic beads, after which bound antibodies are labeled with enzymes. The sample is then introduced to the labeled complex, whereby the labeled antibodies capture the target proteins of interest. (Ex. 1005 at 1, 6; Petition at 30.) These complexes are then put into femtoliter-volume wells for isolation and detection of single molecules. (Ex. 1005 at 1, 2, 6.) Rissin's Figure 1 depicts this set up. (Ex. 1005 at 2; Petition at 28.) Rissin discloses assay results for detecting two proteins, PSA and TNF- α , and generally states a belief that the "digital ELISA

has the potential to facilitate earlier diagnosis and treatment of disease.” (Ex. 1005 at 3, 5; *see also* Petition at 37.)

Duffy, titled “Ultra-Sensitive Detection of Molecules on Single Molecule Arrays,” also describes Patent Owner Quanterix’s ultra-sensitive assay technology for detecting analyte molecules or particles in a fluid sample like blood, and determining their concentration, including in subfemtomolar ranges. (Ex. 1015 at 1, 29, 43, 51, 57 (tbl. 1).) Like Rissin, Duffy describes capturing the target molecule in a complex that can include beads associated with capture antibodies and a detectable label. (*See, e.g.*, Ex. 1015 at 57 (Example 11).) Duffy also makes use of arrays comprising a plurality of reaction vessels to isolate and detect the analyte molecule. (*See id.*) Duffy also describes application of the ultra-sensitive assay to the detection of PSA and TNF- α , just like Rissin. (Ex. 1015 at 57-58 (Examples 11-12).)

As is evident from the above, Rissin is cumulative of and not materially different from Duffy, and Rissin’s content largely mirrors Duffy’s teachings of Examples 11 and 12, which use Patent Owner’s ultra-sensitive assay to detect TNF- α and PSA, respectively. And what is more, just as the Examiner asserted Duffy disclosed all limitations of pending independent claim 92 but tau protein, (Ex. 1002

at 496-74; Petition at 8), Petitioner asserts Rissin discloses that same exact scope for that same claim, which issued as claim 1, (Petition at 37-44, 61-65 (identifying Rissin for all limitations of claim 1 except tau)), and the same Examiner took essentially the same position while examining the '092 patent's parent applications, (Ex. 2001 at 15; Ex. 2002 at 6-8). Simply put, Rissin and Duffy are substantially similar, and Rissin is cumulative of Duffy.

**c. Todd and Voorheis Are Cumulative of the Multiple
“Tau References” the Examiner Considered**

Todd and Voorheis serve a singular purpose in the Petition: addressing the claim limitations that require detection of tau in a blood sample, which Rissin does not disclose. (*See, e.g.*, Petition at 34, 38, 42-43, 58, 61-62, 63-65.) As demonstrated below, Todd and Voorheis are duplicative of multiple references already considered by the Examiner, including Quanterix 2010a, Mortberg, and Wunderlich, that disclosed attempts to detect and quantify tau in blood samples.

Todd describes a “biomarker movement” in drug discovery and disease diagnosis, and the need to develop advanced protein detection systems. (Ex. 1006 at 1-2; Petition at 32.) Among other applications, Todd asserts that protein biomarker programs in Alzheimer's disease might benefit from immunoassay

technologies with ultra-sensitive detection, and identifies “beta-amyloid and tau proteins” as potentially “hopeful candidates” as clinical markers for Alzheimer’s diagnoses. (Ex. 1006 at 3; Petition at 33-34.) Todd further reports on “next generation immunoassay systems,” including “Single Molecule counting (SMC)-based systems” by Singulex that are capable of “quantifying biomarkers at the sub-picogram level.” (Ex. 1006 at 3; Petition at 31.)

Voorheis discloses that fragments of tau protein can be detected outside the brain and describes the use of conventional immunoassay techniques to detect tau protein fragments in patient blood samples for purposes of diagnosing Alzheimer’s Disease. (Ex. 1007 at 1, 6, 10.)

Todd’s identification of tau protein as a hopeful candidate for an Alzheimer’s Disease biomarker coupled with the disclosure of ultra-sensitive assay techniques, and Voorheis’s disclosure that the presence of tau protein fragments in blood could be exploited to diagnose Alzheimer’s Disease, offer the same information that Quanterix 2010a, Mortberg, and Wunderlich provided during prosecution of the ’092 patent. The Examiner relied on those three references for motivation to detect tau protein in blood, as each suggested or reported doing so, at least with

conventional assay techniques. (Ex. 1002 at 498, 501, 502.) Todd and Voorheis are thus cumulative of and substantially similar to those three references.

d. The Petition's Grounds Are Based on Cumulative Art and Duplicative Arguments the Examiner Already Considered

Petitioner's arguments based on Rissin together with Todd or Voorheis are cumulative of, and overlap with, the Examiner's reliance on Duffy and Quanterix 2010a alone or in further view of Wunderlich or Mortberg.

Both of Petitioner's proposed Grounds rely on combining the single molecule assay taught by Rissin, which omits quantifying tau, with references (Todd and Voorheis) that identify tau as a target analyte. (*See, e.g.*, Petition at 34-38, 58-62.) In each instance, Petitioner argues that a POSA would have "been motivated to modify the teachings Rissin [sic] with the teachings of [Todd/Voorheis] in order to quantify protein concentration in blood for clinical diagnosis of neurological disease for the reasons discussed in the Motivation to Combine Section." (*Id.* at 38, 62.)

Petitioner's proposed Grounds are duplicative of those the Examiner previously considered. Indeed, as the Petition acknowledged, "[t]he Examiner found that Duffy taught a [single-molecule assay] that met the limitations of [then-pending claim 1], except measuring tau as the specific analyte of interest, and the sample

being obtained from a patient ‘recovering from a brain injury’”; however, the Examiner found “[t]hose limitations . . . disclosed in [Quanterix 2010a].” (Petition at 8; *see also* Ex. 1002 at 497 (“Duffy teaches . . . [q]uantifying through the use of an analytical protein concentration measurement assay a concentration of protein . . . ”); *id.* at 498 (Quanterix 2010a “explicitly teaches the assay can detect tau in a blood sample.”).) The Examiner also explicitly considered the state of the art and a skilled artisan’s anticipated success based on Duffy alone and in combination with Quanterix 2010a. (*E.g.*, Ex. 1002 at 497-98.) The Petition follows the Examiner’s rejections like a roadmap.

Moreover, the Petition emphasizes that Rissin cites two articles discussing tau protein as a blood biomarker for Alzheimer’s Disease, further exposing the cumulative nature of Petitioner’s arguments, since the Examiner decidedly knew of Rissin, having used it as a basis of rejection in examining two parent applications. (Petition at 35-36; Ex. 2001 at 15; Ex. 2002 at 6-8.)

Petitioner’s other arguments fare no better and are similarly cumulative over the arguments that the Examiner considered. For example, dependent claim 16 recites collecting a patient sample within 12 hours of a brain injury. Petitioner argues that this would have been obvious based on Rissin in view of the “State of the Art”

and either Voorheis, which generally teaches diagnostic testing, or Todd, which teaches that tau can be detected at 3-, 6-, and 12-hour intervals after a stroke. (Petition at 55, 71-72.) But these arguments are cumulative of the Examiner's assertion that Wunderlich "teaches that . . . tau [is] detected in blood at 3, 6, and 12 hours after a stroke." (Ex. 1002 at 501.) The Examiner asserted that "Quanterix 2010a provides the teachings to make obvious measuring tau in the blood of a subject with a brain injury while Wunderlich provides a reasonable expectation of detecting tau in said blood within 12 hours of a brain injury, making such a method of 'producing a body fluid sample' obvious." (*Id.*) This is the exact argument Petitioner advances.

Similarly, Petitioner argues dependent claims 17-21, which recite collecting a patient sample following different types of brain injuries, are obvious over Rissin in view of the "State of the Art" and either Voorheis or Todd, based on general knowledge regarding quantifying tau protein for diagnosis of neurological disease. (Petition at 38, 52-55, 61-62, 71.) But again, these arguments are cumulative of those considered by the Examiner, who considered collecting patient samples following the different types of brain injuries recited by these claims to be obvious over (1) Duffy in combination with Quanterix 2010a based on a skilled artisan's

“reasonable expectation of success,” and (2) Duffy in combination with Quanterix 2010a and Wunderlich or Mortberg, which taught detecting tau following the types of brain injuries recited by the claims. (Ex. 1002 at 498, 501-02.) Thus, all of Petitioner’s Grounds and arguments are cumulative of and substantially similar to those already considered by the Examiner.

For all the above reasons, *Advanced Bionics* step 1 is met as to the entirety of the Petitioner’s asserted art and Grounds.³

3. *Advanced Bionics* Step 2 Is Met Because the Petition Fails to Show Examiner Error

Where, as here, *Advanced Bionics* step 1 is met, “the Director generally will exercise discretion not to institute *inter partes* review” unless the petitioner makes a showing of material error. *Advanced Bionics*, Paper 6 at 8-9. Petitioner has not

³ Given that the Petitioner’s Grounds advance arguments essentially copied from prosecution that are supported by cumulative art and fail to refute the factual findings that were the basis for allowance, denial under 35 U.S.C. § 314(a) is alternatively warranted because the “strength of the patentability challenge” is exceedingly weak.

met—and cannot make—the required showing, so the Director should exercise discretion not to institute *inter partes* review.

4. The Examiner Did Not Err in a Manner Material to Patentability

Under *Advanced Bionics* step 2, “if the Examiner applied the asserted prior art or substantially the same prior art during examination, then a petitioner must demonstrate that, for example, the previously presented art teaches the limitations of the challenged claims, and that no reasonable examiner could have found otherwise.” *Ecto World*, Paper 13 at 5-6.

As the analysis above applying *Advanced Bionics* step 1 illustrates, Rissin and Voorheis were considered by the Examiner, and both of Petitioner’s proposed Grounds are cumulative of the prior art cited by the Examiner. Accordingly, Petitioner must demonstrate that no reasonable examiner could have allowed the claims of the ’092 patent, or else its Petition should be denied institution. *Id.* (reciting standard and clarifying that “a petitioner must provide an analysis [under part two of *Advanced Bionics*] even when the asserted prior art is on an IDS, but the Examiner did not apply the reference”).

Neither the Petition nor its accompanying expert declaration directly

addresses whether the Examiner materially erred, or attempts to explain why no reasonable examiner could have concluded that the Patent Owner's rebuttal evidence overcame the Examiner's obviousness rejections.

The gist of Petitioner's criticism of the Examiner is that he accepted the Patent Owner's evidence of non-obviousness without considering other evidence that might have contributed to the uptick in usage of highly sensitive assays to measure tau in blood, apart from the publication of the underlying application. (Petition at 9-10.) The Petitioner's argument falls far short of meeting its burden of proof, and all of the evidence Petitioner cites is cumulative of the information the Examiner considered. The Petition cites three Exhibits (Exs. 1039, 1040, 1041) relating to Patent Owner Quanterix's Simoa® technology and patents which are expressly cited on the face of the '092 patent. (*See* Ex. 1001 at 2 (listing Ex. 1040 (U.S. Pat. No. 8,236,574)); *id.* (listing three patents related to Patent Owner's Simoa® technology issued during 2013, one of which was assigned to Patent Owner (U.S. Pat. No. 8,415,171) and others assigned to Tufts University (U.S. Pat. Nos. 8,460,878, 8,460,879, and 8,492,098), which are described in Ex. 1041); *id.* at 4 (listing Ex. 1039).) The remaining two exhibits that Petitioner relies upon reflect nothing more than what the Examiner already knew from the Ding reference—i.e., that Patent

Owner's Simoa® assay, including as described in Rissin,⁴ was marketed and used to detect tau in blood after the '092 patent's priority date. (See Ex. 1034 (Patent Owner's website page from 2013 describing its Simoa® technology and tau assay kit); Ex. 1042 (Journal article published in 2017 describing blood-based detection of tau using Patent Owner's Simoa® platform).) *Advanced Bionics* step 2 is met because the Petitioner cannot show material error by merely pointing to the same evidence that the Examiner already considered, and then second-guessing the result.

Petitioner also halfheartedly attacks the Ding article. (Petition at 9-10.) But those arguments are cumulative too, because the Examiner expressly considered Ding, including Ding's list of publications concerning the use of highly sensitive assays to detect tau in blood. (See Ex. 1002 at 556 (summary of 6/20/2021 Examiner interview during which Ding was discussed); *id.* at 567, 575-88 (6/29/2021 email from Patent Owner to Examiner attaching Ding); *id.* at 659 (notice of allowance discussing Ding).) There is no evidence to support Petitioner's insinuation that the

⁴ Ding cites Rissin as describing the Simoa technology that had been used to detect tau in the studies included in its meta-analysis. (See Ex. 1019 at 1-2 & n.13.)

articles analyzed by Ding were published for any purpose other than to report the results of notable scientific studies, and Petitioner's observation that 17 publications out of 66 listed an author with some connection to Patent Owner Quanterix does nothing to undermine the correctness of the Examiner's conclusions. In summary, the Petition offers no evidence or argument to refute the Examiner's conclusion of non-obviousness based on Ding's findings that no group had used highly sensitive assays to detect tau in blood before the effective filing date of the '092 patent, and at least 42 groups did so afterwards. (*See* Ex. 1002 at 659.)

The only other quibble offered by the Petitioner with respect to the Examiner's allowance of the '092 patent is that he incorrectly wrote in his Reasons for Allowance that "Ding table 1 lists Applicant's claimed assay (tau Simoa) used by at least forty-two groups after the effective filing date of 4/12/11," and that, "in reality," the correct term was "studies (publications), not groups." (Ex. 1003, ¶ 47 (emphasis added); *see also* Petition at 10.) Petitioner's picayune word choice critique is not evidence of an error, much less a "material" error. *Robert Bosch Tool Corp. v. SD3, LLC*, IPR2016-01754, Paper 15 at 19-20 (PTAB March 22, 2017) (denying institution under § 325(d) after giving "little probative weight" to expert declaration that "provide[d] insufficient probative facts and evidence beyond what was already

considered by the Examiner during prosecution”).

The Board has consistently exercised its discretion to deny institution in cases with similar facts, where a Petitioner’s argument is essentially that the evidence submitted to the Examiner is incorrect and the Petitioner has submitted an expert declaration to controvert the evidence that the Examiner relied on in allowing the claims. *See Boragen, Inc. v. Syngenta Participations AG*, IPR2020-00124, Paper 16 at 29-30 (PTAB May 5, 2020) (finding no material error by the Examiner in crediting applicants’ arguments that there was no reasonable expectation of success based on the cited evidence); *ADVA Optical Networking, Inc. v. RAD Data Commc’ns Ltd.*, IPR2016-01848, Paper 6 at 19-20 (PTAB Mar. 9, 2017) (denying institution and finding that Petitioner’s arguments were substantially the same as the art and arguments which were considered by the Examiner); *Skechers U.S.A., Inc. v. Nike, Inc.*, IPR2025-00141, Paper 20 at 20-21 (PTAB June 3, 2025) (“For example, even if we were to disagree with the Examiner’s findings, that does not necessarily mean that those findings are unreasonable.”); *Eyenovia, Inc. v. Sydnexis*, IPR2022-00963, Paper 7 at 21 (PTAB Nov. 8, 2022) (finding no material error where Examiner accepted “Patent Owner’s argument that a POSA would not have had sufficient motivation” to use compound in claimed way).

At best, Petitioner asks the Board to second-guess a reasonable judgment made by the Examiner during the prosecution of the '092 patent. Petitioner's arguments and evidence thus fall far short of its burden of proving that no reasonable examiner could have allowed the claims of the '092 patent to issue. Accordingly, the Petition should be denied under § 325(d).

B. Discretionary Denial Is Warranted to Avoid Duplicative Efforts and the Risk of Conflicting Decisions in Parallel Litigation

Petitioner simultaneously filed its Petition and a lawsuit seeking a declaratory judgment of non-infringement in the District of Delaware. (*Fujirebio Diagnostics*, No. 1:25-cv-00659, Dkt. No. 1.) Patent Owner responded with counterclaims of infringement. (*Id.*, Dkt. No. 12.) Petitioner has not offered a stipulation to address concerns of duplicative efforts and potentially conflicting decisions.⁵ Petitioner's

⁵ According to the Interim Director Discretionary Process webpage, "If a petitioner chooses to file a stipulation, such as a *Sotera* stipulation, they should file it as soon as practicable, so that the patent owner may address the impact of the stipulation in its discretionary denial brief." (*See* Section I.(D)., Interim Director Discretionary

decision not to offer a stipulation weighs in favor of discretionary denial, even though no trial date has been set in the district court action. *See DataDome S.A. v. Arkose Labs Holdings, Inc.*, IPR2025-00693, Paper 13 at 3 (PTAB Aug. 14, 2025) (denying institution where trial date in parallel litigation had not yet been set and Petitioner had not filed a *Sotera* stipulation).

IV. CONCLUSION

For these reasons, the Director should exercise discretion and deny institution of the Petition.

Dated: August 20, 2025

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Process (Mar. 26, 2025), <https://www.uspto.gov/patents/ptab/interim-director-discretionary-process>.)

CERTIFICATE OF COMPLIANCE WITH WORD COUNT

Pursuant to 37 C.F.R. § 42.24(d), I certify that this Patent Owner's Brief in Support of Discretionary Denial complies with the type-volume limits of 37 C.F.R. § 42.24(b)(3) and the PTAB's March 26, 2025 Memorandum re Interim Processes for PTAB Workload Management because it contains 6,224 words, according to the word-processing system used to prepare this Brief, excluding the parts of this Brief that are exempted by 37 C.F.R. § 42.24(a) (including the table of contents, a table of authorities, mandatory notices, a certificate of service or this certificate word count, appendix of exhibits, and claim listings).

DATED: August 20, 2025

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CERTIFICATE OF SERVICE

Pursuant to 37 C.F.R. §§ 42.6(e) and 42.105(b), the undersigned certifies that a true and correct copy of the foregoing **PATENT OWNER'S BRIEF IN SUPPORT OF DISCRETIONARY DENIAL AND EXHIBITS 2001 AND 2002** were served on August 20, 2025, via email to counsel for Petitioners at the following:

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