

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MERCK SHARP & DOHME LLC,
Petitioner

v.

HALOZYME, INC.,
Patent Owner

Case PGR2025-00017
U.S. Patent No. 12,110,520

PATENT OWNER DISCRETIONARY DENIAL BRIEF

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PATENT OWNER’S UPDATED EXHIBIT LIST

Exhibit No.	Description
2001	Declaration of Barbara Triggs-Raine, Ph.D. in support of Patent Owner Preliminary Response
2002	<i>Curriculum Vitae</i> of Barbara Triggs-Raine, Ph.D.
2003	Disclaimer in a Patent under 37 C.F.R. § 1.321(a), filed in U.S. Patent Application No. 18/068,418, May 7, 2025
2004	“Halozyme Therapeutics to Present Data on PEGPH20 at the Upcoming 2011 EORTC-NCIASCO Annual Meeting,” Halozyme Therapeutics, Inc. Press Release, October 24, 2011
2005	LinkedIn profiles of Michael Shepard, Robert Connor, Ge (Gina) Wei, and Qiping Zhao
2006	Sequence listing of U.S. Patent Application No. 18/068,418
2007-2017	<i>Intentionally Left Blank</i>
2018	Duterme, C., <i>et al.</i> , “Two Novel Functions of Hyaluronidase-2 (Hyal2) Are Formation of the Glycocalyx and Control of CD44-ERM Interactions,” <i>The Journal of Biological Chemistry</i> , 284(48):33495-33508 (November 27, 2009)
2019	Atmuri, V., <i>et al.</i> , “Hyaluronidase 3 (<i>HYAL3</i>) knockout mice do not display evidence of hyaluronan accumulation,” <i>Matrix Biology</i> 27:653-660 (2008)
2020	Hemming, R., <i>et al.</i> , “Mouse Hyal3 encodes a 45- to 56-kDa glycoprotein whose overexpression increases hyaluronidase 1 activity in cultured cells,” <i>Glycobiology</i> 18(4):280-289 (2008)
2021	Miller, A., “Hyaluronidase 2 and its intriguing role as a cell-entry receptor for oncogenic sheep retroviruses,” <i>Seminars in Cancer Biology</i> 18:296-301 (2008)

Exhibit No.	Description
2022	Kaneiwa, T. <i>et al.</i> , “Identification of human hyaluronidase-4 as a novel chondroitin sulfate hydrolase that preferentially cleaves the galactosaminidic linkage in the trisulfated tetrasaccharide sequence,” <i>Glycobiology</i> 20(3):300-309 (March 2010)
2023	Petition for Post-Grant Review, <i>Merck Sharp & Dohme LLC v. Halozyme Inc.</i> , Case No. PGR2025-00004 (P.T.A.B.), November 26, 2024
2024	Petition for Post-Grant Review, <i>Merck Sharp & Dohme LLC v. Halozyme Inc.</i> , Case No. PGR2025-00003 (P.T.A.B.), November 12, 2024
2025	Petition for Post-Grant Review, <i>Merck Sharp & Dohme LLC v. Halozyme Inc.</i> , Case No. PGR2025-00009 (P.T.A.B.), December 27, 2024
2026	Petition for Post-Grant Review, <i>Merck Sharp & Dohme LLC v. Halozyme Inc.</i> , Case No. PGR2025-00006 (P.T.A.B.), December 10, 2024
2027	Petition for Post-Grant Review, <i>Merck Sharp & Dohme LLC v. Halozyme Inc.</i> , Case No. PGR2025-00030 (P.T.A.B.), February 4, 2025
2028	Petition for Post-Grant Review, <i>Merck Sharp & Dohme LLC v. Halozyme Inc.</i> , Case No. PGR2025-00024 (P.T.A.B.), February 21, 2025
2029	Declaration of Michael Hecht, Ph.D. (Exhibit 1003), <i>Merck Sharp & Dohme LLC v. Halozyme Inc.</i> , Case No. PGR2025-00004 (P.T.A.B.), November 26, 2024
2030	Declaration of Michael Hecht, Ph.D. (Exhibit 1003), <i>Merck Sharp & Dohme LLC v. Halozyme Inc.</i> , Case No. PGR2025-00003 (P.T.A.B.), November 12, 2024

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2031	Declaration of Michael Hecht, Ph.D. (Exhibit 1003), <i>Merck Sharp & Dohme LLC v. Halozyme Inc.</i> , Case No. PGR2025-00009 (P.T.A.B.), December 27, 2024
2032	Declaration of Michael Hecht, Ph.D. (Exhibit 1003), <i>Merck Sharp & Dohme LLC v. Halozyme Inc.</i> , Case No. PGR2025-00006 (P.T.A.B.), December 10, 2024
2033	Declaration of Michael Hecht, Ph.D. (Exhibit 1003), <i>Merck Sharp & Dohme LLC v. Halozyme Inc.</i> , Case No. PGR2025-00030 (P.T.A.B.), February 4, 2025
2034	Declaration of Michael Hecht, Ph.D. (Exhibit 1003), <i>Merck Sharp & Dohme LLC v. Halozyme Inc.</i> , Case No. PGR2025-00024 (P.T.A.B.), February 21, 2025
2035	Lokeshwar, V., <i>et al.</i> , "Regulation of Hyaluronidase Activity by Alternative mRNA Splicing," <i>The Journal of Biological Chemistry</i> 277(37):33654-33663 (2002)
2036	Declaration of Michael Hecht, Ph.D. (Exhibit 1003), <i>Merck Sharp & Dohme LLC v. Halozyme Inc.</i> , Case No. PGR2025-00033 (P.T.A.B.), March 7, 2025
2037	Petition for Post-Grant Review, <i>Merck Sharp & Dohme LLC v. Halozyme Inc.</i> , Case No. PGR2025-00033 (P.T.A.B.), March 7, 2025
2038	Declaration of Michael Hecht, Ph.D. (Exhibit 1003), <i>Merck Sharp & Dohme LLC v. Halozyme Inc.</i> , Case No. PGR2025-00039 (P.T.A.B.), March 28, 2025
2039	Petition for Post-Grant Review, <i>Merck Sharp & Dohme LLC v. Halozyme Inc.</i> , Case No. PGR2025-00039 (P.T.A.B.), March 28, 2025
2040-2045	<i>Intentionally Left Blank</i>

Exhibit No.	Description
2046	“2023 Pharma 50: The 50 largest pharma companies in the world,” drugdiscoverytrends.com, accessible at https://www.drugdiscoverytrends.com/2023-pharma-50-largest-companies/ (last accessed April 28, 2025)
2047	“Merck Announces Fourth-Quarter and Full-Year 2024 Financial Results,” Merck Press Release, February 4, 2025
2048	“Products list,” Merck.com, accessible at https://www.merck.com/products/ (last accessed April 28, 2025)
2049	<i>Intentionally Left Blank</i>
2050	“Merck & Company, Inc. Common Stock (new) (MRK),” Nasdaq.com, accessible at https://www.nasdaq.com/market-activity/stocks/mrk (last accessed April 28, 2025)
2051	“Halozyme Therapeutics, Inc. Common Stock (HALO),” Nasdaq.com, accessible at https://www.nasdaq.com/market-activity/stocks/halo (last accessed April 28, 2025)
2052	“Halozyme reports full year 2024 record revenue of \$1.015 billion and Exceeds its Financial Guidance for Royalty Revenue, Adjusted EBITDA and Non-GAAP Diluted EPS,” Halozyme.com, accessible at https://ir.halozyme.com/news/news-details/2025/HALOZYME-REPORTS-FULL-YEAR-2024-RECORD-REVENUE-OF-1.015-BILLION-AND-EXCEEDS-ITS-FINANCIAL-GUIDANCE-FOR-ROYALTY-REVENUE-ADJUSTED-EBITDA-AND-NON-GAAP-DILUTED-EPS/default.aspx (last accessed April 28, 2025)
2053	“Commercial Products,” Halozyme.com, accessible at https://halozyme.com/commercial-products/ (last accessed April 28, 2025)
2054	“About Us,” Halozyme.com, accessible at https://halozyme.com/about-us/#our-focus (last accessed April 28, 2025)

Exhibit No.	Description
2055	<i>Intentionally Left Blank</i>
2056	Petition for Post-Grant Review, <i>Merck Sharp & Dohme LLC v. Halozyme Inc.</i> , Case No. PGR2025-00042 (P.T.A.B.), April 15, 2025
2057	Declaration of Michael Hecht, Ph.D. (Exhibit 1003), <i>Merck Sharp & Dohme LLC v. Halozyme Inc.</i> , Case No. PGR2025-00042 (P.T.A.B.), April 15, 2025
2058	Complaint for Patent Infringement and Declaratory Judgment of Patent Infringement, <i>Halozyme, Inc. v. Merck Sharp & Dohme Corp.</i> , Civil Action No. 2:25-cv-03179-ES (D.N.J.), filed April 24, 2025
2059	“Alteogen announces amendment to license agreement with MSD,” Alteogen Press Release, February 22, 2025, accessible at https://www.alteogen.com/en/ir_1/?uid=2223&mod=document&pageid=1 (last accessed April 28, 2025)
2060	Petition for Post-Grant Review, <i>Merck Sharp & Dohme LLC v. Halozyme Inc.</i> , Case No. PGR2025-00046 (P.T.A.B.), April 29, 2025
2061	Declaration of Michael Hecht, Ph.D. (Exhibit 1003), <i>Merck Sharp & Dohme LLC v. Halozyme Inc.</i> , Case No. PGR2025-00046 (P.T.A.B.), April 29, 2025
2062	Petition for Post-Grant Review, <i>Merck Sharp & Dohme LLC v. Halozyme Inc.</i> , Case No. PGR2025-00050 (P.T.A.B.), May 7, 2025
2063	Declaration of Michael Hecht, Ph.D. (Exhibit 1003), <i>Merck Sharp & Dohme LLC v. Halozyme Inc.</i> , Case No. PGR2025-00050 (P.T.A.B.), May 7, 2025

TABLE OF AUTHORITIES

Cases

AbbVie v. Jansen,
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Adapt v. Teva,
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Advanced Bionics v. MED-EL Elektromedizinische Geräte,
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Pursuant to the March 26, 2025 “Interim Processes Memo,” discretionary denial here is warranted here. Interim Processes Memo, 2. This brief is supported by a declaration from Dr. Triggs-Raine, an expert in hyaluronidases. EX2001; EX2002.

I. INTRODUCTION

First, trial should be denied because Merck failed to establish that the ’520 patent is PGR-eligible¹. PGR-eligibility is a dispositive threshold jurisdictional matter: if the patent is not shown to be PGR-eligible, then the Board lacks jurisdiction to proceed. *Gillette v. Sphere USA*, PGR2022-00030, Paper 31 at 39-40, 54-55 (P.T.A.B. Sept. 19, 2023) (terminating for lack of jurisdiction after determining the patent was PGR-ineligible). Here, Merck needed to prove that the pre-AIA ’731 priority Application failed to provide §112 support as of its December 28, 2012 filing date. Instead, Merck and its declarants, Hecht and Park, never assessed the ’731 Application as of its December 2012 filing date and provided their opinions using the wrong date (and only the wrong date)—a whole year before the application’s filing date. *Reiffin v. Microsoft*, 214 F.3d 1342, 1346 (Fed. Cir. 2000) (“the sufficiency of [a disclosure] under § 112, first paragraph

¹ See Pet., 4-6.

must be judged as of its filing date.”)²; *Ariad v. Eli Lilly*, 598 F.3d 1336, 1355 (Fed. Cir. 2010) (“[A] written description analysis occurs ‘as of the filing date sought.’”). Merck made the same mistake with its §112 grounds. In fact, Merck never assessed the sufficiency of any application in the ’520 patent family as of that application’s filing date, including Application No. 18/068,418, which matured into the challenged ’520 patent. Accordingly, Merck’s written-description and enablement challenges fail. For the sake of improving efficiency, the Director needs no other reason to deny trial because Merck has not met its threshold burden of establishing that the ’520 patent is PGR-eligible.

Second, Merck, one of the largest multinational pharmaceutical companies which has a market capitalization nearly 30 times larger than that of Halozyme—an American company employing approximately 500 people—has now filed *twelve* Petitions for Post-Grant Review seeking to invalidate *twelve* patents covering Halozyme’s proprietary hyaluronidase enzyme technology for drug delivery. In doing so, Merck is attempting to invalidate Halozyme’s extensive portfolio of patents critical to Halozyme’s business.

Halozyme’s patent portfolio, which includes the ’520 patent, safeguards Halozyme’s extensive research into modifications to a human hyaluronidase

² Emphasis is added throughout, except where otherwise indicated.

enzyme, known as PH20. Among its uses, PH20 allows for rapid subcutaneous administration of therapeutic drugs. Halozyme's inventors identified modifications to PH20's amino acid sequence that resulted in novel modified PH20 structures. Merck's new drug product, SC KEYTRUDA® (pembrolizumab), utilizes a modified PH20 that makes rapid subcutaneous administration of KEYTRUDA® possible. After discussions with Merck, Halozyme expected Merck to obtain a commercial license for the intellectual property it is using in SC KEYTRUDA®. However, Merck has failed to do so and instead plans to forge ahead and launch SC KEYTRUDA® notwithstanding Halozyme's patents, including the '520 patent. Indeed, on April 24, 2025, Halozyme was left with no choice but to sue Merck for infringement of, *inter alia*, ten of the twelve patents that Merck is challenging at the PTAB, including the '520 patent. EX2058. Discretionary denial here would protect American innovation and prevent Big Pharma from trampling on the business of a home-grown American company.

Third, Merck's unpatentability challenges are substantively weak, misapply relevant law, and violate Federal Circuit precedent. Claim 1 of the '520 patent recites modified PH20 (a type of hyaluronidase) polypeptides that must contain one amino acid replacement at *position 324* (from amino acid E to any of A, D, H, M, N, R, and S), and retains at least 91% sequence identity to amino acid sequences selected from SEQ ID NO: 3, 7, and 32-66. EX1001, claim 1; EX2006.

The term “modified PH20 polypeptide” as claimed is defined in a purely structural manner, and encompasses modified PH20 polypeptides having hyaluronidase activity as well as modified PH20 polypeptides lacking such activity³. EX1001, 48:38-43; EX2001, ¶67. Although Merck offers no actual claim construction, it improperly imports into the claims⁴ a *functional* requirement, *viz.* hyaluronidase activity. Pet. 22 (“The claims are restricted to one of two alternative embodiments in the patents: ‘Active Mutants.’”). This improper backdoor attempt to import a functional requirement is central to Merck’s §112 Grounds and is merely an attempt to shoehorn the facts here into the law Merck cites, all of which relates to claims containing a functional requirement.

Notably, Merck never performs a claim construction analysis of any claim term and offered *no expert testimony* on claim construction⁵. Merck’s declarants, Hecht and Park, do not even reference any claim construction principles—let alone

³ The specification discloses that the claimed polypeptides are useful as contraceptives irrespective of whether they exhibit hyaluronidase activity. EX1001, 75:58-60, 188:8-27.

⁴ Claims 3-5, 16, and 31-35 of the ’520 patent have been statutorily disclaimed, leaving only claims 1-2, 6-15, and 17-30. EX2003.

⁵ *See* Pet., 17.

apply them—yet they parrot the petition’s incorrect conclusion that the claims require hyaluronidase activity. Merck’s failure to provide focused expert testimony supporting its (incorrect) claim interpretation further weighs against institution.

For its obviousness ground, Merck extensively relies on hindsight-driven, conclusory declarant testimony. To support its obviousness arguments, Merck relies on Park’s testimony, but used hindsight-based *attorney instruction* to lead Park to the claimed modification at position 324. Park concedes he was “asked by counsel to report [his] conclusions with respect to position 324” and neither Hecht nor Park provide any reason to select position 324 except for counsel’s instruction. EX1004, ¶103. Such “conclusory and unsupported” declaration testimony “is entitled to little weight,” particularly in light of each declarant’s utter lack of hyaluronidase experience. *Xerox v. Bytemark*, IPR2022-00624, Paper 9 at 15 (P.T.A.B. Aug. 24, 2022); 37 C.F.R. § 42.65(a). As explained below, neither of Merck’s declarants, Hecht and Park, have the requisite hyaluronidase experience to interpret the claims or analyze the literature, including the cited references Merck relied on for obviousness. Merck’s reliance on conclusory testimony from declarants without the relevant experience further justifies discretionary denial here.

Fourth, Merck’s art and arguments are the same or substantially the same as those the Examiner considered. Merck alleged that the claims would have been

obvious in view of the '429 patent and Chao, but the Examiner considered the '429 patent. And other references the Examiner considered are cumulative to the Chao reference Merck applied in its obviousness Ground. These Examiner-considered references, Stern (EX1008), Zhang (EX1010), and Arming (EX1011), disclose the same basic teachings upon which Merck relied. Indeed, Stern is by itself cumulative to Chao or at the very least cumulative to Chao in combination with Zhang and Arming. Merck did not even attempt to show any Examiner error⁶.

Finally, the precedential decision of *Apple Inc. v. Fintiv, Inc.*, IPR2020-00019, Paper 11 (P.T.A.B. Mar. 20, 2020) (precedential) further justifies utilizing the Director's discretionary power to deny institution. It would be much more efficient to resolve the issues of validity in a single district-court proceeding than *multiple separate PGR proceedings* before the Office. Indeed, the district-court proceeding involves additional patents that are either not PGR-eligible and/or have not yet been challenged in a PGR or IPR. EX2058. As such, the district court proceeding will continue no matter the result in these 12 separate PGR proceedings. Moreover, the identity in parties, the overlap of the issues between

⁶ Merck filed its Petition before the Interim Process Memo issued and therefore should have sufficiently addressed whether §325(d) applied, including any allegations of material error during prosecution.

the district court proceeding and this PGR, and the absence of a *Sotera* stipulation strongly favor discretionary denial. The principles of efficiency, conservation of resources, and fairness would best be served by denying institution. *Fintiv*, IPR2020-00019, Paper 11 at 6.

II. MERCK FAILED TO MEET ITS THRESHOLD BURDEN OF ESTABLISHING PGR ELIGIBILITY.

Merck's Petition failed to demonstrate that the '520 patent was PGR-eligible. Because PGR-eligibility is a dispositive threshold matter that determines whether the Board has jurisdiction to proceed, this failure alone warrants discretionarily denying Merck's Petition. *Gillette*, PGR2022-00030, Paper 31 at 39-40, 54-55 (terminating for lack of jurisdiction after determining the patent was PGR-ineligible). The '520 patent claims priority to a series of applications, including provisionals filed December 30, 2011; and November 1, 2012; and a nonprovisional ("the '731 Application") (EX1026) filed December 28, 2012, before the PGR-eligibility cutoff of March 16, 2013. To show PGR eligibility, Merck bore the burden of proving that the '520 patent or an application to which it claims priority contains or at any time contained a claim that has an effective filing date on or after March 16, 2013. AIA §3(n)(1).

Here, Merck's Petition needed to demonstrate that the claims are not entitled to the benefit of the filing date of the '731 Application—filed on December 28, 2012, but Merck failed to carry out the analysis required by law. EX1026; *Reiffin*,

214 F.3d at 1346 (“the sufficiency of [a disclosure] under § 112, first paragraph *must be judged as of its filing date.*”); *Ariad*, 598 F.3d at 1355 (“[A] written description analysis occurs ‘as of the filing date sought.’”); *Chiron v. Genentech*, 363 F.3d 1247, 1254 (Fed. Cir. 2004) (“Whether the earlier applications enable the claims of the ’561 patent is determined *as of the filing date of each application*”); *Union Carbide v. Shell*, 308 F.3d 1167, 1185 (Fed. Cir. 2002) (“Enablement is determined as of the filing date . . .”).

Instead of assessing the ’731 application as of its 2012 filing date, Merck’s analysis *only* applied a 2011 date, while fatally ignoring the ’731 Application’s December 28, 2012 filing date. Pet., 11-15, 27, 40, 56, 73-78, 82, 88-90, 93-96, 102-103, 107-109. Indeed, Merck’s declarants, Hecht and Park, only ever considered a 2011 date in their analyses. EX1003, ¶¶11-14 (Hecht stating “I understand that my analysis and opinions are to be provided...in the timeframe *before December 29, 2011*”); EX1004, ¶¶10-14 (Park stating “I understand that my analysis and opinions are to be provided...in the *December 2011* time frame”). Merck cites no law holding that the sufficiency of an application under §112 should be assessed one year *before* the application’s filing date because there is none. Merck’s attempt to mix-and-match applications and dates—assessing the ’731 Application in view of the state of the art at the time of a different application—cannot be squared with binding precedents, and is illogical to boot.

Indeed, after receiving Halozyme’s Preliminary Responses and Sur-replies bringing this same error to light in the two earliest-filed related PGRs (PGR2025-00003 and -00004), Merck apparently recognizes its error. In its three most recently-filed PGRs (PGR2025-00042, PGR2025-00046, PGR2025-00050), Merck added language that alleges that none of the provisional applications and the ’731 application “*when each was filed* supported the claims as required by § 112(a).” EX2056, 15-16; EX2060, 15; EX2062, 19. The revised language used in Merck’s three most recently filed Petitions only further highlight Merck’s failure in *this* Petition to assess *any* application in ’520 patent family—including the pre-AIA ’731 application—as of the date the application was filed.

The Board has long denied institution when the Petitioner fails to address the relevant date when assessing a priority application’s compliance with Section 112 to establish PGR-eligibility. *Sandoz v. Biogen*, PGR2022-00054, Paper 16 at 25-28 (P.T.A.B. Feb. 2, 2023) (denying institution where Petitioner failed to “demonstrate that the priority applications’ respective written descriptions were insufficient *in view of the state of the art as of the filing date of each of [the] three pre-AIA applications*”); *Merck v. Wyeth*, PGR2017-00016, Paper 9 at 14 (P.T.A.B. Oct. 20, 2017) (“Petitioner’s failure to address *each relevant date* bolsters our holding that Petitioner fails to show sufficiently that the ’060 patent is post grant review eligible.”). The Director should not make an exception here. *Ariad*, 598

F.3d at 1355 (“[A] written description analysis occurs ‘as of the filing date sought.’”); *Chiron*, 363 F.3d at 1254; *Union Carbide*, 308 F.3d at 1185.

Furthermore, the Examiner assigned the ’520 patent pre-AIA status during prosecution, which is a factor supporting a finding that the ’520 patent is *ineligible* for post-grant review. EX1002, 480 (“The present application is being examined under the pre-AIA first to invent provisions.”); *Aradigm v. Insmmed*, PGR2017-00021, Paper 10 at 20 (P.T.A.B. Nov. 15, 2017) (Examiner’s acknowledgement during prosecution that a patent application is entitled to a pre-AIA priority date may be a factor supporting a finding of PGR-ineligibility).

Because Merck failed to meet its burden of assessing the sufficiency of the ’731 application under §112 as of its December 2012 date, Merck has failed to establish PGR eligibility. Merck should be held to the incorrect 2011 date it used to assess the ’731 application because as the Petitioner, Merck is the “master of its own petition.” *Qualcomm v. Apple*, Nos. 2023-1208, 2023-1209, slip op. at *22 (Fed. Cir. Apr. 23, 2025). This reason alone is sufficient to deny institution and preserve the finite resources of the Office.

III. DENYING TRIAL WOULD PROTECT AMERICAN INNOVATION AGAINST MERCK’S HARASSMENT CAMPAIGN TO WIPE OUT HALOZYME’S PATENTS AND ITS BUSINESS.

Merck is one of the largest multinational pharmaceutical companies in the world. EX2046, 2. In 2024 alone, Merck generated sales of nearly \$64 billion, with

sales from Merck's KEYTRUDA® drug product earning Merck roughly \$30 billion. EX2047, 1. On its website, Merck has listed 48 different drug products that it manufactures, markets, and/or distributes around the world. EX2048.

In contrast, Halozyme is an innovative American biopharmaceutical company based in San Diego, California with a market capitalization 1/30th the size of Merck's with approximately 500 employees spread across America⁷. EX2050, 1; EX2051, 1. In 2024, Halozyme generated over 60 times less revenue than Merck. EX2052, 1. After dedicating over two decades to research and development in an industry where small companies often fail, Halozyme now has two FDA-approved products featuring its proprietary delivery technologies utilizing hyaluronidase enzymes. EX2053, 1. Notably, through licenses granted to leading pharmaceutical companies like Pfizer, Eli Lilly, Roche, Bristol-Myers Squibb, and others, Halozyme has been able to improve the treatment outcomes of over a million patients. EX2052, 1.

Halozyme has over 25 years of experience innovating and conducting pioneering research and development in the field of hyaluronidases for use with subcutaneous injectables. EX2054, 1. Halozyme's innovations are protected by a

⁷ Halozyme is headquartered in San Diego, CA and has offices in Ewing, NJ and Minnetonka, MN. Minnetonka is also the site of its operations facility.

patent portfolio, which includes the '520 patent, that Halozyme filed to safeguard its groundbreaking subcutaneous delivery technology. Moreover, Halozyme's pioneering hyaluronidase technology has culminated in collaborations and licensing agreements that include commercial partner products for the subcutaneous delivery of important medications using its technology. EX2052, 1-3.

Now, Halozyme is fighting to survive *twelve* PGR Petitions Merck has filed back-to-back within the last six months. This patent portfolio is of significant value to Halozyme and is the rightful result of Halozyme's innovation. Were the Board to institute trial here, multinational Merck would be one step closer to wiping out Halozyme's patent portfolio to a technology that can improve outcomes in patients undergoing treatment for debilitating and life-threatening conditions. Founded in 1998 with the intention of developing a recombinant human hyaluronidase for therapeutic uses, Halozyme represents a real American success story, and denying institution here is one way to help protect Halozyme's continued ability to innovate on behalf of patients.

Denying trial here is warranted because it is in the best interests of protecting American innovation by a home-grown biopharmaceutical company under attack from Big Pharma. Given the 12 successive PGRs Merck has filed, and in view of the overlap with the district court proceeding, it would not be an

efficient use of the PTAB's limited resources to institute trial rather than allow validity issues to be resolved in a single district court proceeding. Interim Processes Memo, 2-3.

Furthermore, Merck's harassment campaign (twelve PGR Petitions and counting) shows its plans to disrespect Halozyme's duly issued patents instead of obtaining a commercial license like so many other large pharmaceutical companies have. Indeed, Merck intends to market its new drug product, SC KEYTRUDA®, which allows for rapid subcutaneous administration of KEYTRUDA®. Notably, Merck's Chairman and CEO, Robert M. Davis, explained for SC KEYTRUDA® that "it was crucial to get approval and launch as soon as possible" in order to "launch well ahead of the LOE [loss of patent exclusivity for KEYTRUDA®], so a meaningful portion of patients are already transitioned to the subcutaneous version." EX2058, ¶9. Merck's intentions are plain to see. And now, Merck is using a hyaluronidase from the South Korean company Alteogen to make its SC KEYTRUDA® product. EX2059, 2. This is a compelling economic consideration that warrants the Director's attention.

Additionally, by filing these multiple similarly flawed Petitions, Merck is calling into question the specialized technical expertise of *five* separate Examiners who have properly assessed the patentability of the family of patents, including the '520 patent. EX1002, 425; PGR2025-00003 EX1002, 421; PGR2025-00004

EX1002, 436; PGR2025-00009 EX1002, 448; PGR2025-00017 EX1002, 462;
PGR2025-00030 EX1002, 458; PGR2025-00024 EX1002, 818; PGR2025-00033
EX1002, 1174; PGR2025-00039 EX1002, 427; PGR2025-00042 EX1002, 901;
PGR2025-00046 EX1002, 487; PGR2025-00050 EX1002, 504. Granting
institution would amount to accepting that five different Examiners repeatedly
erred in their assessment of these similar patents. As explained in this brief, Merck
has failed to meet its burden of establishing that the '520 patent claims are
unpatentable. Merck's efforts to eliminate Halozyme's justly awarded patent
portfolio warrants discretionary denial here.

**IV. MERCK'S PETITION MISAPPLIES THE LAW AND RELIES ON
HINDSIGHT-BASED, CONCLUSORY DECLARANT TESTIMONY.**

Considerations identified in the Interim Processes Memo justify
discretionary denial of Merck's Petition. The "strength of the unpatentability
challenge," "[t]he extent of the petition's reliance on expert testimony," and
"changes in the law or new judicial precedent" all counsel for denial.

**A. Neither of Merck's Declarants Possess the Requisite Hyaluronidase
Experience to Properly Assess the Patentability of the Claims, nor
Does Merck's POSA Even Apply the Correct Date.**

Each of Merck's unpatentability Grounds (Ground I written description,
Ground II enablement, Ground III obviousness) must be analyzed from the
viewpoint of a POSA. *See KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 420 (2007)
(the question for obviousness is "whether the combination was obvious to a person

with ordinary skill in the art”); *Falko-Gunter Falkner v. Inglis*, 448 F.3d 1357, 1363 (Fed. Cir. 2006) (written description is “judged from the perspective of one of ordinary skill in the art”); *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988) (“[p]atents ... are written to enable those skilled in the art to practice the invention”). Yet, Merck and its declarants, Hecht and Park, use an incorrect lens through which a POSA considers each ground, materially affecting their conclusions and showing that the “strength of [its] unpatentability challenge[s]” is weak. Interim Processes Memo, 2; *Innovation Toys, LLC v. MGA Ent., Inc.*, 637 F.3d 1314, 1323 (Fed. Cir. 2011) (rejecting validity findings where use of wrong POSA lens “affects the ultimate conclusion”).

The Federal Circuit has long considered factors such as the “(1) the educational level of the inventor; (2) type of problems encountered in the art; (3) prior art solutions to those problems; (4) rapidity with which innovations are made; (5) sophistication of the technology; and (6) the educational level of workers active in the field” as a guide in determining the level of ordinary skill in the art. *Env'tl. Designs v. Union Oil Co. of Cal.*, 713 F.2d 693, 696–97 (Fed. Cir. 1983); *Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001) (the prior art may reflect the appropriate skill level of a POSA). The Federal Circuit has also held that “[t]he patent’s purpose” and the prior art may reflect the appropriate skill level of a POSA. *Best Med. Int’l, Inc. v. Elekta Inc.*, 46 F.4th 1346, 1353 (Fed. Cir. 2022);

Okajima, 261 F.3d at 1355.

Here, the '520 patent is directed to modified PH20 polypeptides. EX2001, ¶65; EX1001, claim 1. In particular, the '520 patent specification discloses that “active mutant” PH20 polypeptides are useful because they possess hyaluronidase activity and can be used, e.g., “for treating a hyaluronan-associated disease or condition” or to “increas[e] delivery of a therapeutic agent to a subject.” EX1001, 4:30-50, 39:5-15, 39:25-26, 52:13-15. The specification further discloses that the claimed polypeptides are useful as “antigens in contraception vaccines,” irrespective of whether they exhibit hyaluronidase activity. EX1001, 75:58-60, 188:8-27, *id.*, 72:48-73:51; EX1011, 814; EX2001, ¶75. Merck cannot deny that the prior art it uses for alleging obviousness is likewise directed to hyaluronidases: the '429 patent relates to soluble neutral active hyaluronidases, and Chao discusses the structure of human hyaluronidase-1. EX2001, ¶29; EX1005; EX1006.

In view of the patented invention's and the cited prior art's overall focus on hyaluronidases described above, a POSA would, critically, have *at least two years of practical experience with hyaluronidases*. EX2001, ¶32; EX2004; EX2005.

Without this significant practical experience, the POSA would not have the requisite skill to be able to properly interpret the claims, analyze the literature, and draw conclusions from aligning hyaluronidase sequences, and evaluate the contraceptive use of PH20 polypeptides described in both the patent specification

and in the prior art. EX2001, ¶¶32-46.

Merck's POSA definition, which does not require *any* experience with hyaluronidases, does not account for the requisite level of skill needed to view the prior art and the claimed invention. Pet., 15-16; EX1003, ¶13; *Okajima*, 261 F.3d at 1355 (the level of skill in the art is "a prism or lens" through which to view the prior art and the claimed invention). Indeed, for obviousness, Merck's declarant performed an alignment of 88 different hyaluronidase proteins and determined that a POSA allegedly would have had a reason to substitute glutamic acid (E) with aspartic acid (D), asparagine (N), and arginine (R) at the claimed position 324 because aspartic acid (D) was the most prevalent amino acid found at position 324 and asparagine (N) and arginine (R) appeared in many of the 88 different hyaluronidases. Pet., 95-98. But Merck's declarant aligned the amino acid sequences of *vastly* different hyaluronidases, and then jumped to conclusions without considering the various enzymes' diverse biological activities and different substrates, something a POSA having hyaluronidase experience would not ignore. Pet., 95-98; EX2001, ¶¶107-113; EX2018-EX2022. And as discussed below, Merck's use of a POSA lens that does not take into account this requisite practical experience materially affects its conclusions, rendering the Grounds flawed and weak.

Indeed, nothing in Hecht's or Park's CVs or even their own discussion of

their “Qualifications” indicates that either declarant has any experience with hyaluronidases, and there is no evidence that they consulted with anyone who had it before rendering their opinions. EX1003, App’x B; EX1004, App’x B. Their combined lack of hyaluronidase experience undermines the reliability of their testimony regarding, e.g., how POSAs would have interpreted the claims, reasons to modify the art, and conclusions drawn from aligning hyaluronidase sequences, and contraceptive use of PH20 polypeptides. EX2001, ¶46. “[A]n expert must at a minimum possess ordinary skill in the art.” *Osseo v. Planmeca*, 116 F.4th 1335, 1340 (Fed. Cir. 2024); *Kyocera v. ITC*, 22 F.4th 1369, 1376–77 (Fed. Cir. 2022); *Avail v. Teladoc*, IPR2022-00444, Paper 10 at 24-28 (P.T.A.B. July 21, 2022) (“it would be inappropriate for us to consider any testimony by [the inexperienced expert] on any issue that is analyzed through the lens of [a POSA]”). A person of ordinary skill *in this art*, or a member of that POSA’s multidisciplinary team, would have practical experience with hyaluronidases. Because both Hecht and Park lack this experience, Merck’s reliance on their testimony further demonstrates the Petition’s weaknesses.

B. Merck’s Patentability Challenges Fail Because Merck Failed to Construe the Claims and Improperly Defines the Claims as Functional.

1. Merck Failed to Construe the Claims as Required under 37 C.F.R. §42.204(b)(3).

By failing to comply with the requirement under 37 C.F.R. §42.204(b)(3) to

identify how the claims should be construed or provide sufficient evidence supporting its claim interpretation, the Director should deny trial. Instead of construing *any* claim term, Merck merely offers the bare statement that: “[t]he claim terms are either expressly defined in the common disclosure or are used with their common and ordinary meaning.” Pet., 17. However, under 37 C.F.R. §42.204(b)(3), Merck carries an “affirmative burden” to identify how the claims are to be construed. *Orthopediatrics v. K2M*, IPR2018-01548, Paper 9 at 10 (P.T.A.B. Mar. 1, 2019) (“our rules place an affirmative burden on [P]etitioners to ‘set forth: ... [h]ow the challenged claim is to be construed.’”). Petitioners must also explain “[h]ow the construed claim is unpatentable” under §42.204(b)(4). *Id.* By failing to identify—and provide sufficient support for—how the challenged claim is to be construed (e.g., identify which terms are given their plain and ordinary meaning and provide that meaning, or identify and apply an express definition), Merck failed to meet its burden to show that it is more likely than not that at least one construed claim is unpatentable. Pet., 17; 37 C.F.R. §§42.204(b)(3)-(4); *Samsung v. Cobblestone Wireless*, IPR2024-00319, Paper 16 at 20-21 (P.T.A.B. June 24, 2024); *Volkswagen Group of America v. Michigan Motor Techs.*, IPR2020-00229, Paper 13 at 9-10 (P.T.A.B. Jul. 6, 2020).

Neither Merck nor its declarants undertakes any claim construction analysis. Merck’s Park never states he even reviewed the patent or its claims. And his

declaration reflects no understanding of the concept of claim construction.

EX1004. Likewise, Merck's Hecht does not mention claim construction principles or how to apply them, revealing his lack of understanding of claim construction.

EX1003, ¶¶23-32. Moreover, his declaration does not even purport to engage in claim construction under *Phillips. Id.* Indeed, neither Merck nor its declarants undertake the requisite *Phillips* claim construction inquiry: they do not evaluate the language of the claims, the specification, or the file history to construe the claims. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1313, 1317 (Fed. Cir. 2005).

Nonetheless, Hecht states, “[a] skilled artisan would have understood the claims to necessarily *cover* modified PH20 polypeptides that are active mutants, *and would not view them as including inactive mutants.*” EX1003, ¶134; EX2001, ¶63. With no appreciation for claim-construction principles, Hecht essentially repeats the Petition's arguments improperly importing a requirement for hyaluronidase activity. Pet., 22-26; EX1003, ¶¶126-135; EX2001, ¶63; *Xerox*, IPR2022-00624, Paper 12 at 4-5 (P.T.A.B. Feb. 10, 2023) (Vidal, Dir.) (giving “little weight” to the expert testimony that “merely offer[s] conclusory assertions without underlying factual support and repeated, verbatim, [Xerox's] conclusory arguments.”); *Deeper v. Vexilar*, IPR2018-01310, Paper 7 at 26-27 (P.T.A.B. Jan. 24, 2019) (“This conclusory analysis set forth in the Petition . . . , by itself, renders Petitioner's showing insufficient. But even if we were to go beyond the Petition

and also consider the cited [expert] testimony ..., Petitioner’s showing would still be insufficient because that cited testimony is itself conclusory”). In fact, Hecht wrongly assumes what the claims *cover* in lieu of performing claim *construction*. *In re Entresto*, 125 F.4th 1090, 1098 (Fed. Cir. 2025) (determining what a claim covers is not claim construction).

Despite citing the express definition of “modified PH20 polypeptide,” Hecht overlooks that the definition does not require hyaluronidase activity. EX1003, ¶129; EX1001, 48:38-43. Thus, Merck failed to offer evidence as to how the claims would be construed by a POSA since Merck’s declarants evince no understanding of claim construction principles and neither declarant performed an analysis under *Phillips. Head Sport v. Vermont Safety Developments*, IPR2024-01099, Paper 15 at 39 (P.T.A.B. Jan. 15, 2025) (denied institution in part because Petitioner failed to provide evidence of how a term “would be understood by a [POSA].”).

To the extent Merck’s claim interpretation relies on Hecht or Park, their testimony does not constitute competent, factual evidence, because neither declarant evinced any understanding of claim construction principles nor applied them. EX1003; EX1004. Merck’s claim interpretation is founded *only* on attorney argument. *Invitrogen v. Clontech*, 429 F.3d 1052, 1068 (Fed. Cir. 2005) (“Unsubstantiated attorney argument regarding the meaning of technical evidence

is no substitute for competent, substantiated expert testimony.”); *In re Payne*, 606 F.2d 303, 315 (C.C.P.A. 1979).

Because Merck and its declarants rely on importing a functional requirement into the claims as a predicate to all of its unpatentability arguments—i.e., requiring the patent describe and enable what is *not* required by the claims—this failure to construe the claims alone renders Merck’s Petition fundamentally flawed and weak. *In re Entresto*, 125 F.4th at 1097-1100 (finding that a patent need only describe and enable what the claim *requires* as ascertained via claim construction, and *not* what the claim simply *covers*); *see also LG Display Co. v. Delaware Display Grp. LLC*, IPR2014-01359, Paper 12 at 5-7 (P.T.A.B. Mar. 2, 2015) (denying institution and finding that petitioner failed to meet the requirements of 37 C.F.R. §42.204(b)(3)-(4) for failure to properly construe key claim terms); *Head Sport*, Paper 15 at 34. Accordingly, Merck failed to meet its burden under 37 C.F.R. §42.204(b)(3), and the Director should deny institution.

2. Merck Improperly Imports a Functional Requirement Into the Claims.

Merck’s petition treats the claims as though they require hyaluronidase activity despite never identifying any claim term(s) that imposes such a functional requirement. Merck’s flawed interpretation of the claims infects the entire petition because the petition contains no arguments applying the correct construction and its §112 grounds rely on importing a functional requirement (*viz.*, hyaluronidase

activity) into the claims. Merck's inappropriate interpretation of the claims throughout the Petition, particularly in its §112 Grounds, further proves the weakness of its unpatentability challenges and justifies discretionary denial here.

The challenged claims recite a “modified PH20 polypeptide,” which is defined as a PH20 polypeptide that contains at least one amino acid modification, such as at least one amino acid replacement as described herein, in its sequence of amino acids compared to a reference unmodified PH20 polypeptide. EX1001, 48:38-43. As is clear from this definition, the “modified PH20 polypeptide” is solely defined by its structure, i.e., its sequence of amino acids, and not by function. EX2001, ¶68. Merck discusses this definition outside its claim-construction section⁸, but does not otherwise sufficiently construe the term in view of that definition. Pet., 17-18. The Board has held that where “the specification of the challenged patent provides an express construction of an important claim term, Petitioner’s failure to recognize and address the express construction, coupled with Petitioner’s failure to otherwise sufficiently address the meaning of the term, is insufficient to satisfy the requirements of 37 C.F.R. §42.104(b)(3).” *Volkswagen*,

⁸ To the extent Merck acknowledges the express definition of “modified PH20 polypeptide,” it underscores the impropriety of requiring hyaluronidase activity because this definition makes no mention of hyaluronidase activity.

IPR2020-00229, Paper 13 at 9-10.

Although Merck argues that no term requires an express construction, Merck's §112 attacks are predicated on importing a functional requirement that does not appear in the claims, *viz.* hyaluronidase activity. Merck's claim interpretation directly contradicts the specification's express definition of "modified PH20 polypeptide." EX1001, 48:38-43; Pet., 17-18; *Jack Guttman v. Kpykake Enterprises*, 302 F.3d 1352, 1361 (Fed. Cir. 2002) ("[w]here, as here, the patentee has clearly defined a claim term, that definition usually is dispositive; it is the single best guide to the meaning of a disputed term." (cleaned up)). For this reason, the Director should deny trial.

Despite the plain *structural* language used to describe the modified PH20 polypeptide, Merck's written description, enablement, and obviousness unpatentability Grounds hinge on interpreting the claims as *defined* by the PH20 polypeptide's functionality, *i.e.*, hyaluronidase activity. Specifically, Merck argues the claims are limited to only active mutants. Pet., 22-26. But again, neither Merck nor its declarants *undertake any claim construction analysis* justifying that the claims are, in fact, defined in a functional way, as is required to meet their burden to show that it is more likely than not that at least one construed claim is unpatentable. 37 C.F.R. §§42.204(b)(3)-(4); *Samsung*, IPR2024-00319, Paper 16 at 20-21 ("Where a *petitioner specifically relies on a particular construction of a*

claim term ... particularly a construction different from the ordinary meaning, that claim construction is part of the unpatentability analysis, and the *petitioner must provide a sufficient basis to support that construction*"); see also *Orthopediatrics*, IPR2018-01548, Paper 9 at 10.

Moreover, the Federal Circuit has long held that claim terms should not be interpreted "in a way that excludes embodiments disclosed in the specification." *Oatey v. IPS*, 514 F.3d 1271, 1276 (Fed. Cir. 2008). Merck does just that in stating, "the specification describes two mutually exclusive categories of 'modified PH20 polypeptides' (i.e., 'active mutants' vs. 'inactive mutants') but the claims are limited to one (i.e., 'active mutants')." Pet., 22; EX2001, ¶¶83-84. Merck did not—and could not—identify any claim language limiting the claims to just active mutants. EX1003, ¶¶126-135; Pet., 25-26; EX2001, ¶¶85-86. And, the specification indisputably uses the term "modified PH20 polypeptide" to refer to both active and inactive mutants. EX1001, 115:41-58, 251:1-6; EX2001, ¶75.

Merck further states that "active mutants" are "therapeutically useful because they possess hyaluronidase activity," but alleges "inactive mutants" allegedly have "implausible" utility despite the specification identifying their utility "as antigens in contraception vaccines." Pet., 24. Merck's attempt to discredit the utility of "inactive mutants" to justify importing a hyaluronidase-activity limitation into the claims is improper: claims must be read "in light of the

specification,” not in spite of the specification. *Phillips*, 415 F.3d at 1315 (“Claims must always be read in light of the specification.”). Although claim terms are interpreted in the context of the entire patent, it is improper to import limitations from the specification into the claims. *Head Sport*, Paper 15 at 27 (citing *Phillips*, 415 F.3d at 1323).

Merck also relies on the specification’s disclosure that modifications *can be* in any PH20 polypeptide “so long as the resulting modified PH20 polypeptide exhibits hyaluronidase activity.” Pet., 26; EX1001, 48:38-53. Again, the specification merely states that modifications *can be made to* create active “modified PH20 polypeptides;” it does not state that all claimed “modified PH20 polypeptides” must exhibit hyaluronidase activity. The identified statements—divorced from the express definition of “modified PH20 polypeptide” and uses of the term elsewhere—do not indicate that Patent Owner “clearly express[ed] an intent to redefine” “modified PH20 polypeptide” to require enzymatic activity. EX1001, 115:41-58, 251:1-6; EX2001, ¶87; *Bradium Techs. v. Iancu*, 923 F.3d 1032, 1044 (Fed. Cir. 2019).

Merck wrongly argues that the claims are limited to “active mutants” because they require each “modified PH20 polypeptide” to have one of seven replacements at position 324 that yielded an “active mutant.” Pet., 25; EX1003, ¶¶126-128; EX2001, ¶¶86-88. Not so. Claim 1 is not limited to “active mutants.”

Merck ignores that dependent claims 18-19 further require glycosylation⁹, which the patent states is critical for hyaluronidase activity. Pet., 12; EX2001, ¶86; EX1001, 70:60-71:4. Merck’s claim interpretation disregards the doctrine of claim differentiation. *Seachange Int’l v. C-Cor*, 413 F.3d 1361, 1368–69 (Fed. Cir. 2005); *United Services Automobile v. PNC Bank*, IPR2021-01248, Paper 27 at 18, 23 (P.T.A.B. Jan. 3, 2023). Merck’s claim interpretation contradicts the express definition of “modified PH20 polypeptide,” is inconsistent with the plain language of the claims, and contradicts the specification—each violations of black letter claim construction law.

Because Merck improperly imports into the claims a requirement for hyaluronidase activity and relies on this interpretation for all grounds, the Petition’s unpatentability Grounds are weak, justifying discretionary denial here. *Head Sport*, IPR2024-01099, Paper 15 at 50 (denying institution because Petitioner relied on an incorrect claim construction); *Samsung*, IPR2024-00319, Paper 16 at 16–23 (holding that because Petitioner’s obviousness showing was based on an incorrect claim construction, Petitioner did not demonstrate a reasonable likelihood that a claim limitation was disclosed by, or would have been obvious over, the

⁹ Hecht states, “PH20 enzymes must be glycosylated to exhibit their catalytic activity.” EX1003, ¶197; EX2001, ¶72.

cited reference); *Intellectual Ventures I LLC v. Motorola Mobility LLC*, 870 F.3d 1320, 1325–26 (Fed. Cir. 2017) (rejecting §112 challenge predicated on an incorrect claim construction). Given the Board’s resource constraints and the stated goal of improving PTAB efficiency, the Director should deny trial here. Interim Processes Memo, 3.

C. Merck’s Written Description and Enablement Grounds Fail Under Multiple Additional Discretionary Factors.

1. Merck’s Petition Failed to Properly Assess Written Description or Enablement.

As discussed above, Merck does not provide sufficient evidence or argument to sustain its written-description and enablement challenges. *Reiffin*, 214 F.3d at 1345 (“the sufficiency [of a disclosure] under § 112, first paragraph must be judged *as of its filing date*.”). In fact, Merck never assesses the sufficiency of any application in the ’520 patent family as of that application’s filing date; thus, Merck’s written-description and enablement challenges fail. For example, Merck never assessed the sufficiency of Application No. 18/068,418, which matured into the challenged ’520 patent, as of the ’418 application’s December 19, 2022 filing date.¹⁰ Likewise, as discussed in Section II, Merck wrongly assesses the

¹⁰ For both §112 grounds, Merck relies on the “common disclosure” between the patent and the ’731 Application, which Merck admits has a substantively

sufficiency of the '731 priority application as of 2011, rather than the '731 application's December 28, 2012 filing date. EX1003, ¶¶11-14; EX1004, ¶¶10-14 (Hecht and Park applied the December 2011 timeframe). And similarly, Merck failed to assess Halozyme's Provisional Application No. 61/796,208 as of its November 1, 2012 filing date. Indeed, Hecht and Park never even considered either of Halozyme's provisional applications. EX1051-1052; EX1003, 146-147; EX1004, App'x A.

2. Merck's Written Description and Enablement Challenges Violate *In re Entresto* and Rely on Inapplicable Law Regarding Functionally Defined Claims.

After the '520 patent issued, the Federal Circuit issued its January 10, 2025, decision in *In re Entresto*, 125 F.4th 1090 (Fed. Cir. 2025). In that case, the Federal Circuit expressly stated that a patent need only describe and enable what the claim *requires* as ascertained via claim construction, and *not* what the claim simply *covers*. *Id.* at 1097-1100 (finding that, although the claims covered certain subject matter, they did not require it, and so the specification did not need to describe and enable the covered but not required subject matter). Yet Merck's written description and enablement grounds wrongly focus entirely on whether the

identical specification to the '520 patent. Pet., 6, 17, 23, 27, 32, 34-37, 41-86, 108, 115.

'520 patent describes and enables claim features that are *not* actually required by the claims, i.e., hyaluronidase activity.

Merck asserts that because the claims are *limited* to enzymatically active modified PH20 polypeptides, the '520 patent must (but did not) adequately describe and enable the PH20 polypeptides within the claimed genus. Pet., 2-3, 28-85. Yet, as discussed above in Section IV.B, the claims are *not* defined functionally; nor are they defined or required to exhibit hyaluronidase activity. Indeed, the specification confirms that claimed “modified PH20 polypeptides” are defined by their *structure*, i.e., its sequence of amino acids. EX1001, 48:38-43. Furthermore, the specification discloses that “modified PH20 polypeptide” also refers to polypeptides that do not exhibit hyaluronidase activity. EX1001, 115:41-58; *id.*, 251:1-6, 75:49-60; EX2001, ¶¶75-76. Thus, Merck’s written description and enablement analysis inappropriately evaluates whether the specification describes and enables what the claim simply *covers* but does not require, and so violates recent, binding Federal Circuit law. *See In re Entresto*, 125 F.4th at 1097-1100. Because Merck’s written description and enablement grounds violate this “new judicial precedent,” the “strength of its unpatentability challenge” is likewise weak, warranting discretionary denial. *See Interim Processes Memo*, 2.

Additionally, because Merck inappropriately cabins the claims to only active mutants for its written description and enablement grounds, it relies solely on

inapposite law to support its arguments. This further undermines Merck's arguments and shows the weakness of its patentability challenges. Indeed, for written description, Merck's three allegedly "especially probative" cases (*AbbVie*, *Idenix*, and *Boehringer I*) are inapposite because they are directed to claims reciting *functionally defined* genera, which are not germane to the challenged patent's purely structural modified PH20 polypeptide claims. Pet., 30-32. Because Merck failed to identify any authority supporting its written-description challenge of *structural*, not functional, claims, Merck's arguments fall short.

Merck first relies on *AbbVie*, but in that case, the Federal Circuit found that claims directed to an antibody "that *binds to human IL-12 and dissociates from human IL-12 with a k_{off} rate constant of 1×10^{-2} s⁻¹ or less*" lacked written description support. *AbbVie v. Jansen*, 759 F.3d 1285, 1292 (Fed. Cir. 2014). The Court held, "[w]hen a patent claims a *genus using functional language* to define a desired result, 'the specification must demonstrate that the applicant has made a generic invention that *achieves the claimed result . . . by showing . . . species sufficient to support a claim to the functionally-defined genus.*'" *Id.* at 1299. Likewise, in *Idenix*, claims to a "*method for the treatment [of HCV]*" lacked written description because the specification "fail[ed] to provide sufficient blaze marks to direct a POSA to the specific subset of 2'-methyl-up nucleosides that are *effective in treating HCV.*" *Idenix v. Gilead*, 941 F.3d 1149, 1164 (Fed. Cir. 2019).

Merck also cites *Boehringer v. Kansas State*, PGR2020-00076, Paper 42 at 6 (P.T.A.B. Jan. 31, 2022) (“*Boehringer I*”). There, the Board found credible Petitioner’s expert’s testimony that “the ’351 Patent does not disclose which of the thousands of different claimed homologous sequences, if any, the inventor possessed, much less had discovered *to be antigenic.*” *Boehringer I*, PGR2020-00076, Paper 42 at 34. In other words, the Board held that the claims required functional activity (*see block quote below*).

In a subsequent decision involving the same parties and a related patent, the Board reiterated that the claims in *Boehringer I* “used functional language to define a composition.”¹¹ *Boehringer v. Kansas State*, PGR2022-00021, Paper 9 at 19 (P.T.A.B. July 15, 2022) (“*Boehringer II*”); *Boehringer II*, Paper 11 at 5-6 (P.T.A.B. Feb. 24, 2023).

In contrast to *Boehringer I*, the Board in *Boehringer II* found that claims reciting “at least 90% sequence homology” to specific recited sequences were structural and adequately supported by the specification, stating:

[I]n contrast to the claims set forth in [*Boehringer I*], *this is not the case where the claims use functional language to define a composition. See*

¹¹ The ’274 Patent in *Boehringer II* is a divisional of the ’351 patent in *Boehringer I*, both claiming priority to the same provisional. *Boehringer II*, PGR2022-00021, Paper 9 at 5-6.

PGR2020-00076. Specifically, the challenged claims are not directed to a subset of species with certain antigenic properties. *The recited sequences share at least 90% of the structure of disclosed sequences while limiting the amount of variation to 10% sequence homology or sequence identity. ... Thus, unlike the claims [in Boehringer I], the products claimed in the '274 patent recite structural limitations—there is no requirement that the protein be capable of inducing an immunological response, for example. Id.*

PGR2022-00021, Paper 13 at 20 (P.T.A.B. Mar. 22, 2023).

Notably, upon Director Review of *Boehringer II*, Director Vidal agreed that the claims in *Boehringer II* did not use functional language, stating “The Board was correct to focus on whether the claims themselves were enabled and *to find inapposite Petitioner’s arguments as to whether functional language — appearing only in the specification — was enabled.*” *Id.*, Paper 11 at 5 (P.T.A.B. Feb. 24, 2023). Like the claims in *Boehringer II*, the challenged claims here are not functional and recite at least 91% sequence identity.

It is surprising that Merck references *Boehringer I* but never acknowledges the existence of, and similarity of the present case to, *Boehringer II*. Pet., 31-32. This is particularly surprising because Merck was named a real-party-in-interest (RPI) in both *Boehringer* cases. *Boehringer II*, PGR2022-00021, Paper 4 at 1 (P.T.A.B. Jan. 11, 2022); *Boehringer I*, PGR2020-00076, Paper 6 at 1 (P.T.A.B. Sept. 28, 2020).

In sum, all of the cases Merck cites to support its written description ground involve functional claims, with the holdings all turning on that specific fact.

Meanwhile, Merck conveniently ignores cases finding written-description support of purely structural claims. *GlaxoSmithKline v. Banner Pharmcaps*, 744 F.3d 725, 731 (Fed. Cir. 2014); *Boehringer II*, PGR2022-00021, Paper 9 at 19; *Ex parte Friedberg, et al.*, No. 2004-2314 at 4-6 (B.P.A.I. Nov. 17, 2004). It is no wonder Merck improperly imports a functional requirement into the claims to support its arguments that the claims lack written description. *In re Entresto*, 125 F.4th at 1098 (an improper construction of the claims, conflating claim *coverage* with claim *construction*, “led [the district court] astray in evaluating written description”); *ParkerVision*, 88 F.4th at 977. No law supports Merck’s written-description arguments and Merck’s reliance on irrelevant law demonstrates the weakness of its patentability challenge.

For enablement in Ground II, Merck repackages its written-description arguments to argue lack of enablement. Merck again improperly imports a functional requirement (hyaluronidase activity) in an effort to align its arguments with the cited cases (*Amgen*, *Idenix*, *Wyeth*, and *Baxalta*). But all cited cases involved claims having functional, not structural, limitations. Pet., 67-68.

Amgen’s claims to antibodies that “bind to” PCSK9 and “block PCSK9 from binding to [receptors]” recited functional, not structural, language and therefore

lacked enablement. *Amgen v. Sanofi*, 598 U.S. 594, 614 (2023) (“Amgen seeks to monopolize an entire class of things defined by their *function*.”). *Idenix* also involved functionally defined claims (method of treating HCV infection), and the patent lacked enablement. *Idenix*, 941 F.3d at 1162.

Likewise, *Wyeth* and *Baxalta* involved functional claims and are similarly inapposite. *Pet.*, 67; *Wyeth v. Abbott*, 720 F.3d 1380 (Fed. Cir. 2013) (method of treating restenosis); *Baxalta v. Genentech*, 81 F.4th 1362 (Fed. Cir. 2023) (antibodies that bind Factors IX or IXa and increase procoagulant activity). In sum, the cases Merck extensively cites and relies upon for its written description and enablement arguments involve functionally defined claims, with the holdings all turning on that fact. That is not the case here. Merck’s heavy reliance on factually inapposite law further shows the weakness of its written description and enablement challenges.

D. Merck’s Obviousness Ground III Fails Under Multiple Discretionary Factors.

As detailed below, “[t]he strength of the unpatentability challenge” set forth in Merck’s obviousness ground is weak, and further extensively “reli[es] on expert testimony” that is hindsight-driven, conclusory, and misapplies the law, further justifying discretionary denial. *See Interim Processes Memo*, 2.

1. Merck Failed to Identify Where the Specific Elements of the Claims Are Found in Cited References for Ground III.

Under 37 C.F.R. §42.204, Merck was required to indicate “where each element of the claim is found in the prior art” for prior-art grounds. However, for Ground III, Merck failed to identify where the specific elements of the claims are found within the applied references. EX2001, ¶¶21, 89-97. *Lenovo v. LiTL*, IPR2021-00800, Paper 7 at 18-19 (P.T.A.B. Nov. 2, 2021) (Petitioner must “specify where each element of the claim is found in the prior art [] relied upon” and to both “identify[] specific portions of the evidence that support the challenge” and explain “the relevance of [that] evidence to the challenge raised.” 37 C.F.R. §§42.104(b)(4)–(5); 37 C.F.R. §42.22(a)(2). Merck cannot deny that a modified PH20 polypeptide with an amino acid modification at position 324 is not mentioned in the ’429 patent or Chao, much less the specific A, D, H, M, N, R, and S replacements claimed for position 324. The elements of the claims are *absent* from the asserted prior art. EX2001, ¶¶96-97.

Unsurprisingly, neither Merck nor its declarants provides a claim chart identifying where each claim limitation is found in the art, because they cannot. EX2001, ¶¶96-97; *PAR Pharmaceutical v. TWi Pharmaceuticals*, 773 F.3d 1186, 1196 (Fed. Cir. 2014) (a proper analysis under §103 requires “determining that claimed elements are present in the prior art.”). Not only does the prior art not teach E324D, E324N, or E324R substitutions in PH20, Merck has not identified

any other reason why POSAs would have made these modifications. EX2001, ¶¶98-100. For example, Merck has not asserted nor shown that common sense might supply this limitation. *Arendi v. Apple*, 832 F.3d 1355, 1361-1362 (Fed. Cir. 2018) (common sense can fill a missing limitation when the “limitation in question was unusually simple and the technology particularly straightforward” and “*cannot be used as a wholesale substitute for reasoned analysis and evidentiary support, especially when dealing with a limitation missing from the prior art references specified.*”).

Even if Merck had argued that common sense supplied this missing limitation, Merck’s petition still failed to provide a reasoned analysis with evidentiary support to show that E324D, E324N, or E324R modifications were “unusually simple” or “particularly straightforward.” Nor has Merck provided a reasoned explanation supported by evidence that POSAs would have had a reason to make the claimed modifications at position 324 in the first place. EX2001, ¶97. Indeed, Park’s analysis focuses on position 324 *at the request of Merck’s counsel*, and Hecht does not provide any reason to pick position 324 beyond referring to Park’s analysis. EX2001, ¶100; EX1003, ¶215; EX1004, ¶¶32, 103 (Park conceding he was “asked by counsel to report [his] conclusions with respect to position 324”). Merck also alleges that POSAs would have had to engage in approximately *30 steps* to arrive at the E324D, E324N, or E324R modifications

and *an additional ~50 steps* to expect that the claimed substitutions would yield an active PH20 protein. Had Merck alleged that “common sense” bridged this missing limitation from the cited art, Merck still failed to explain away the caveats to such an argument established in *Arendi* and provide a reasoned analysis with evidentiary support.

In addition, Merck has failed to establish that “ordinary creativity” could serve as a gap-filler for the modification at position 324. *DSS v. Apple*, 885 F.3d 1367, 1374-1375 (Fed. Cir. 2018) (“the Board’s invocation of ‘ordinary creativity’ is no different from the reference to ‘common sense’” and requires the same “searching” inquiry for a reasoned basis for resorting to ordinary creativity to supply a missing limitation).

Merck also failed to demonstrate that common knowledge supplied this missing limitation. As discussed below, Merck failed to provide a reasoned explanation supported by evidence that POSAs would have had a reason to combine the ’429 patent and Chao to arrive at the claimed invention with a reasonable expectation of success. *In re Google*, 56 F.4th 1363, 1368 (Fed. Cir. 2023) (“while common knowledge can be invoked, even potentially to supply a limitation missing from the prior art, it must still be supported by evidence and a reasoned explanation.”).

Merck’s failure to identify where each element is found in the prior art

references relied upon in its obviousness ground shows the weakness of Ground

III.

2. Merck Failed to Establish a Reason to Combine the '429 Patent and Chao to Arrive at the Claimed Invention.

a. Merck Failed to Show that a POSA Would Have Been Motivated to Make an Amino Acid Substitution in Non-Essential Regions of PH20 and Identify Position 324.

The Federal Circuit has long held, “obviousness concerns whether a skilled artisan *not only could have made*” any particular modification, “*but would have been motivated to make the combinations or modifications of prior art* to arrive at the claimed invention.” *Belden v. Berk-Tek*, 805 F.3d 1064, 1073 (Fed. Cir. 2015). Here, Merck failed to provide a reason why a POSA would have been motivated to make single amino acid substitutions in non-essential regions of PH20, or make the claimed amino acid modification at position 324 in view of the '429 patent and Chao. EX2001, ¶¶101-106. This further demonstrates the weakness of Merck’s obviousness arguments in Ground III.

Merck failed to establish that the '429 patent “motivates a skilled artisan to make single amino acid substitutions in non-essential regions of PH20₁₋₄₄₇.” Pet., 87-89. The '429 patent merely states, “[s]uitable conservative substitutions of amino acids are known to those of skill in this art and *can be* made generally without altering the biological activity...” and “in general, single amino acid

substitutions in non-essential regions of a polypeptide do not substantially alter biological activity....” EX1005, 16:14-22; EX2001, ¶103. This disclosure—that substitutions *can be* made—would not have provided a POSA a *reason* to make such substitutions, let alone the claimed amino acid modification. EX1005, 16:14-22; EX2001, ¶103.

Merck’s Petition provides no *reason* why a POSA would have been motivated to make an amino acid substitution(s) in non-essential regions of PH20, let alone identify position 324 as one such position, particularly given that the ’429 patent does *not* identify any non-essential residues. Merck, Hecht, and Park do not explain why a POSA would have been motivated to expend resources to make an amino acid substitution in non-essential regions of PH20 when Merck’s cited art suggests that doing so would be pointless (“without altering the biological activity” and “have the same utility [and] therapeutic applications”). Pet., 87-89; EX2001, ¶103.

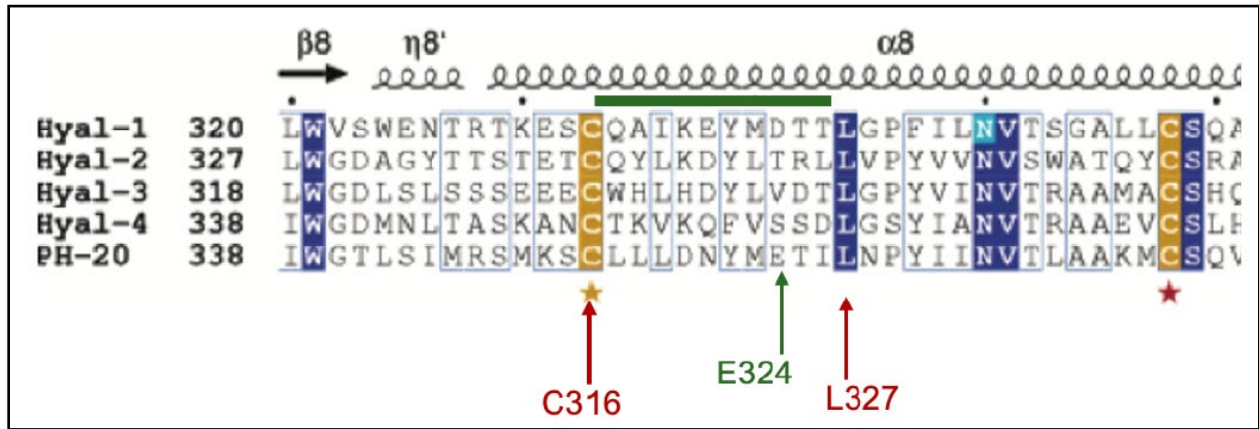
Merck alleges a POSA “[g]uided by her familiarity with rational protein design and the teachings of the ’429 patent and Chao...would have readily identified single amino acid substitutions in non-essential regions of PH20₁₋₄₄₇ that would have been tolerated (*i.e.*, a PH20₁₋₄₄₇ with that single substitution would retain its enzymatic activity).” Pet., 86. But, such an argument is simply a restatement that such mutations *can be* made, and Merck never provides a *reason*

why a POSA would have been motivated to combine the two references (or any of the dozen or so references Merck also cites) to make the claimed amino acid substitution in PH20. *Metalcraft of Mayville v. Toro*, 848 F.3d 1358, 1366 (Fed. Cir. 2017) (“it is insufficient to simply conclude the combination would have been obvious without identifying any reason *why* a person of skill in the art would have made the combination”); *Stara v. AGCO*, IPR2024-01459, Paper 12 at 38-39 (P.T.A.B. Mar. 25, 2025) (“What Petitioner must show is *why* and *how* those skilled in the art would modify [the prior art] to arrive at the claimed invention without using the claimed invention as a guide to get there”).

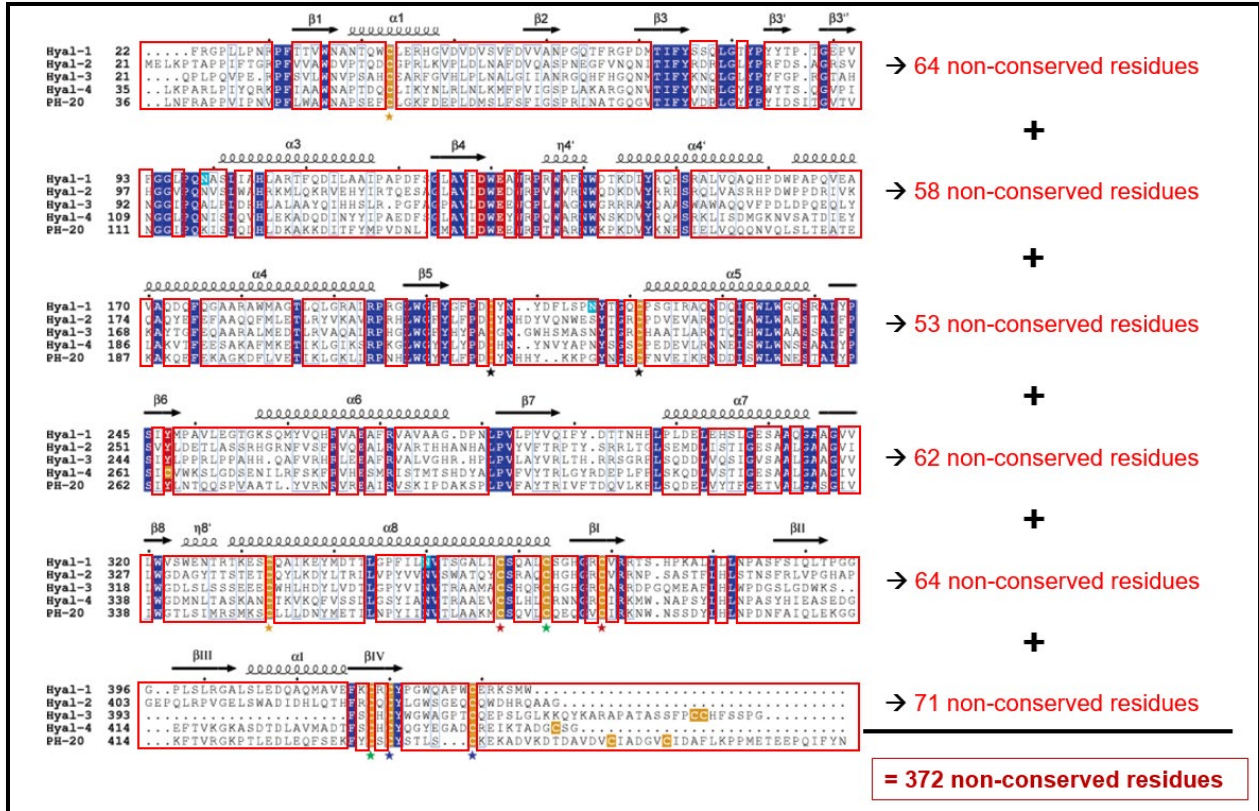
For example, Merck never argues that making a modification in non-essential regions of PH20 would have improved or increased hyaluronidase enzymatic activity. Rather, Merck states that such a modification would have the “same utility [and] therapeutic applications” as wild-type PH20. Pet., 89; EX2001, ¶92. Thus, Merck failed to offer a reason why a POSA would have been motivated to modify PH20 at a non-essential region that would merely “exhibit comparable hyaluronidase activity to unmodified PH20₁₋₄₄₇” and not alter existing enzymatic activity. Pet., 108-109; *Virtek v. Assembly*, 97 F.4th 882, 886-87 (Fed. Cir. 2024) (Petitioner did not articulate a “reason why a skilled artisan” would make the claimed invention).

Merck alleges that the claimed position 324 is “within a non-essential region

of PH20₁₋₄₄₇” flanked by the bounding essential residues highlighted in yellow and blue at positions 316 and 327, respectively. Pet., 95. To illustrate the point, Merck annotates and crops Chao’s Figure 3 below to visualize position 324 relative to its bounding essential residues at positions 316 and 327:



Pet., 95; EX1003, ¶217; EX2001, ¶114. Merck, however, fails to grapple with the fact that there are nearly 90 bounding essential residues in Chao’s Figure 3 (highlighted in yellow, blue, and red), and 372 non-conserved residues that fall within these 90 bounding residues. EX2001, ¶115. In the annotated Figure 3 below, there are a total of 372 non-conserved residues boxed in red.



EX2001, ¶115; EX1006, FIG. 3 (annotated).

Merck offers no reason to make the claimed modification at position 324 out of the 371 other non-conserved residues disclosed in Chao’s Figure 3. EX2001, ¶116.

b. Merck Extensively Relies on Hindsight and Declarant Testimony to Explain Why a POSA Would Allegedly Have Been Motivated to Make the Claimed E324D, E324N, and E324R Modifications.

In view of the Interim Process Memo’s enumerated consideration regarding the “extent of the petition’s reliance on expert testimony,” the Director should deny institution here because of Merck’s egregious use of hindsight. Interim Process

Memo, 2.

In fact, to allegedly demonstrate that a POSA would have been motivated to replace glutamic acid (E) at position 324 with aspartic acid (D), asparagine (N), or arginine (R), Merck utilizes hindsight and relies almost exclusively on the counsel-directed testimony of both Hecht and Park instead of the asserted prior art. Pet., 95-99. *First*, Merck uses hindsight to lead Park to the claimed modifications at position 324. In fact, Park concedes he was “*asked by counsel* to report [his] conclusions with respect to position 324.” EX1004, ¶103; EX2001, ¶100. Park never provides a reason why POSAs would have focused on position 324 among the 300 or so non-conserved residues. EX1004, ¶32. Instead, Park simply states that he believes that “position 324, align[s] with what I consider to be the ‘non-essential regions’ referred to by the ’429 Patent.” EX1004, ¶32. Likewise, Hecht relies on Park and does not provide any reason to select position 324. Instead, Hecht broadly alleges that POSAs “would have performed in 2011” the analysis that Park performed. EX1003, ¶215; EX2001, ¶99. But Park’s analysis focuses on position 324 only because counsel directed him to that position. EX1004, ¶103. Neither of Merck’s declarants provide a concrete reason to identify position 324 apart from Merck’s counsel instructing Park to analyze position 324 and then Hecht simply relying on Park’s attorney-directed analysis. Triggs-Raine confirms that, even in combination, the ’429 patent and Chao do not provide any reason to

select position 324 as an amino acid to modify. EX2001, ¶¶93-117.

Only hindsight—provided by counsel instructions—led Park and Hecht to position 324. *In re Stepan*, 868 F.3d 1342, 1346 n.1 (Fed. Cir. 2017) (when “selecting from large lists of elements in a single reference, there must be a motivation to make the combination and a reasonable expectation [of success], otherwise a skilled artisan would not arrive at the claimed combination.”). Merck’s hindsight analysis is even more pronounced now that Merck has filed *ten other* PGRs alleging that Halozyme’s patents claiming other modifications are invalid as obvious. EX2001, ¶¶133-136. In these ten other petitions where Merck alleges obviousness, Hecht and Park use the same art and reasoning to argue obviousness of modifying positions 307, 309, 312, 313, 317, and 320.

PGR	Patent	Position Modified
PGR2025-00003	11,952,600	320
PGR2025-00004	12,018,298	313
PGR2025-00006	12,152,262	317
PGR2025-00009	12,123,035	312
PGR2025-00024	12,060,590	307
PGR2025-00030	12,054,758	317
PGR2025-00033	12,049,652	320
PGR2025-00039	12,104,185	320
PGR2025-00042	12,037,618	309
PGR2025-00046	12,091,692	313

EX2023, 91-107; EX2024, 85-111; EX2025, 92-108; EX2026, 86-113; EX2027, 84-113; EX2028, 84-113; EX2029-EX2034; EX2036; EX2037, 85-109; EX2038, EX2039, 89-110; EX2001, ¶¶133-136; EX2056-EX2057; EX2060, 90-110;

EX2061¹².

The Board has clarified that “the failure to provide focused expert testimony may weigh against institution.”¹³ Here, Merck has proffered deeply flawed testimony from two declarants, suggesting that any questions are better resolved in an Article III court. Indeed, to the extent Merck offers any focused testimony with respect to identifying position 324, such testimony was directed by counsel and strictly hindsight-based with no reason articulated for arriving at position 324 other than the hindsight-based counsel-instruction. Given Merck’s overt hindsight, Merck’s arguments relying on such testimony are flawed and weak, warranting discretionary denial here.

Second, Merck relies exclusively on declarant testimony from both Hecht and Park to argue that a POSA allegedly would have had a reason to make the E324D, E324N, and E324R modifications. To do so, a POSA would have had to

¹² In Merck’s latest filed Petition, PGR2025-00050, Merck does not allege obviousness of the challenged claims. EX2062-EX2063.

¹³ FAQs for Interim Processes for PTAB Workload Management can be found here: https://www.uspto.gov/patents/ptab/faqs/interim-processes-workload-management?utm_campaign=subscriptioncenter&utm_content=&utm_medium=email&utm_name=&utm_source=govdelivery&utm_term=.

perform nearly *thirty* different steps—beyond the disclosures in the '429 patent and Chao—to make these modifications. Pet., 93-99; EX1003, ¶¶21, 83, 195, 214-218, 220-221; EX1004, ¶¶21, 26, 28-32, 41-43, 88-91, 97-98, 156-160, Appendix D-1, and Appendix D-2. EX2001, ¶¶118-119; *Adapt v. Teva*, 25 F.4th 1354, 1365 (Fed. Cir. 2022) (obviousness requires “identify[ing] a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does.”); *TQ Delta v. Cisco*, 942 F.3d 1352, 1359 (Fed. Cir. 2019) (“a conclusory assertion with no explanation is inadequate to support a finding that there would have been a motivation to combine.”).

These approximately *thirty* steps include, *inter alia*, *15 discrete steps* for performing sequence searches, extracting sequence information, using high-level computer programming language to determine the accession history of each sequence, removing duplicate sequences, *four steps* for generating a multiple sequence alignment, and *eleven steps* for identifying “non-essential” residues, identifying frequencies of amino acids that occur in homologous PH20 sequences, and determining the variability of amino acids at position 324, just to arrive at the alleged conclusion that it was obvious to substitute aspartic acid, asparagine, or arginine with glutamic acid at position 324 of PH20. Pet., 93-99; EX2001, ¶119. No combination of the '429 patent and Chao discloses these steps, and Merck has not established that these steps would have been merely a matter of exercising

“ordinary creativity” or common sense. EX2001, ¶¶120-122; *KSR*, 550 U.S. at 421.

Nor does Merck provide a sufficient reason why a POSA would have performed *any* of these steps based on the combination of the '429 patent and Chao, especially to only arrive at a modified PH20 polypeptide that worked equivalently to wildtype PH20. Merck's failure to provide “focused expert testimony” here further justifies discretionary denial.

3. Merck Likewise Relies Exclusively on Declarant Testimony to Allege Reasonable Expectation of Success.

Merck's argument that a POSA would have reasonably expected the E324D, E324N, and E324R substitutions in PH20₁₋₄₄₇ “would yield an enzyme with substantially the same activity as unmodified PH20₁₋₄₄₇” depends solely on declarant testimony from Hecht and Park. Pet., 100-109. Indeed, to show that a POSA allegedly would have reasonably expected success, Merck cites to Hecht and Park's declarations where Park undertook over about *fifty* additional steps, not disclosed in the '429 patent or Chao, to supposedly demonstrate that a POSA would expect that the claimed substitution would yield an active PH20 protein. *Id.*; EX1004, ¶¶33-36, 39-40, 44-103, 105, 107-110, 113-153, 162-165, 167, 177-178; EX2001, ¶¶125-128. However, Merck again failed to provide evidence demonstrating that a POSA would have been motivated to perform each of these steps. This failure to provide focused testimony further shows that Merck's unpatentability challenge is weak.

Furthermore, Merck fails to establish that the '429 patent combined with Chao provides the requisite reasonable expectation of success that the E324D, E324N, and E324R substitutions in PH20 would not only be tolerated, but would result in a protein that exhibits at least comparable hyaluronidase activity to unmodified PH20₁₋₄₄₇, particularly when Merck merely offers the “general approach” that “[s]uitable conservative substitutions of amino acids” can be “made generally without altering the biological activity, for example enzymatic activity, of the resulting molecule.” Pet., 87-89; EX1005, 16:14-22; *Medichem v. Rolabo*, 437 F.3d 1157, 1165-66 (Fed. Cir. 2006) (prior art fails to provide reasonable expectation of success where “the prior art gave only *general guidance* as to the particular form of the claimed invention or how to achieve it.”).

Here, the '429 patent provides only *general guidance* that amino acid substitutions in non-essential regions of a polypeptide “do not *substantially* alter biological activity,” and POSAs would not have reasonably expected the E324D, E324N, and E324R substitutions to yield a protein that exhibits at least comparable hyaluronidase activity to unmodified PH20₁₋₄₄₇ based on this general guidance. EX1005, 9:47-50; EX2001, ¶¶130-132.

The Federal Circuit has established that “to have a reasonable expectation of success, one must be motivated to do more than merely to *vary all parameters or try each of numerous possible choices until one possibly arrived at a successful*

result,” where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful.” *In re Stepan*, 868 F.3d at 1347.

Furthermore, Merck has not established that any alleged reasonable expectation of success was “founded in the prior art,” including the ’429 patent and Chao. *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991) (“the reasonable expectation of success must be founded in the prior art, not in the applicant’s disclosure.”).

Because Merck failed to provide the requisite reason to combine the ’429 patent and Chao to arrive at the claimed invention with a reasonable expectation of success, Merck’s obviousness challenge is weak and warrants discretionary denial. *Eli Lilly v. Teva*, 8 F.4th 1331, 1348-49 (Fed. Cir. 2021) (it is, “at all times, [Petitioner]’s burden to show that the claims would have been obvious, including that a skilled artisan would have had a reasonable expectation of success in achieving the claimed invention.”).

V. THE PETITION RELIES ON THE SAME OR SUBSTANTIALLY THE SAME ART AND ARGUMENTS CONSIDERED DURING PROSECUTION.

The Interim Processes Memo expressly states that its discretionary considerations—including “[w]hether the PTAB or another forum has already adjudicated the validity or patentability of the challenged patent claims—are “consistent” with the *Advanced Bionics* framework for discretionary denial under

§325(d). Interim Processes Memo, 2. Here, Merck’s petition presents “the same or substantially the same prior art or arguments previously ... presented to the Office” and failed to identify any material error committed by the Office affecting the patentability of the challenged claims. 35 U.S.C. §325(d); *Advanced Bionics v. MED-EL Elektromedizinische Geräte*, IPR2019-01469, Paper 6 at 7–11 (P.T.A.B. Feb. 13, 2020). Because Merck does not meaningfully address *Advanced Bionics*’ two-part framework and relies entirely on unsupported attorney argument, its Petition fails. Pet., 115-116.

A. Part 1: Merck Advances the Same or Substantially the Same Art and/or Arguments Previously Considered

Merck alleges in Ground III that the ’520 patent claims “would have been obvious from the ’429 patent in view of Chao and the knowledge of a skilled artisan.” Pet., 85. However, the Examiner considered art the same as or cumulative to the ’429 patent and Chao. Under the first part of the *Advanced Bionics* framework, the Board may consider the relevant *Becton, Dickinson* factors: (a) the similarities of the asserted art and the art previously considered; (b) the cumulative nature of the asserted art and the art previously considered; and (c) the extent to which the asserted art was evaluated during examination, including whether the prior art was the basis for rejection. *Advanced Bionics*, IPR2019-01469, Paper 6 at 9-10 (citing *Becton, Dickinson and Co. v. B. Braun Melsungen*, IPR2017-01586, Paper 8 at 17–18 (P.T.A.B. Dec. 15, 2017) (informative)). As such, the Board

should consider whether the cited art is used in the same manner as previously considered by the Office, in determining whether the prior art is “substantially the same.” *Monolithic Power Systems v. Volterra Semiconductor*, IPR2020-01348, Paper 19 at 10-14 (P.T.A.B. Mar. 4, 2021). Each of these *Becton, Dickinson* factors apply here, and the Director should discretionarily deny institution.

Merck’s Cited Reference	Prior Consideration by Examiner
’429 patent	Included in IDS and considered by the Examiner (initialed IDS reference CK)
Chao	Substantially the same art as Stern, Zhang, and Arming that were each considered by the Examiner (initialed IDS references HE, OB, and PK)

1. The Examiner Considered the ’429 Patent

The ’429 patent was cited to and considered by the Examiner, and it was discussed in the specification. EX2001, ¶¶138-140; EX1002, 500 (initialed IDS, reference CK); EX1001, 70:10, 71:47-48, 73:49-50, 74:18, 128:49-50, 175:11, 184:61, 188:48. This satisfies *Advanced Bionics* part one and *Becton, Dickinson* factor (c). *Becton, Dickinson*, IPR2017-01586, Paper 8 at 17–18; *Keysight v. Centripetal Networks*, IPR2022-01421, Paper 14 at 5 (P.T.A.B. Aug. 24, 2023); *Ecto World v. RAI*, IPR2024-01280, Paper 10 at 9-11 (P.T.A.B. Mar. 6, 2025); *Agrinomix v. Mitchell Ellis Prods.*, IPR2017-00525, Paper 8 at 10-11 (P.T.A.B.

June 14, 2017).

2. The Examiner Considered Several References with Teachings Cumulative to Those Relied-Upon From Chao.

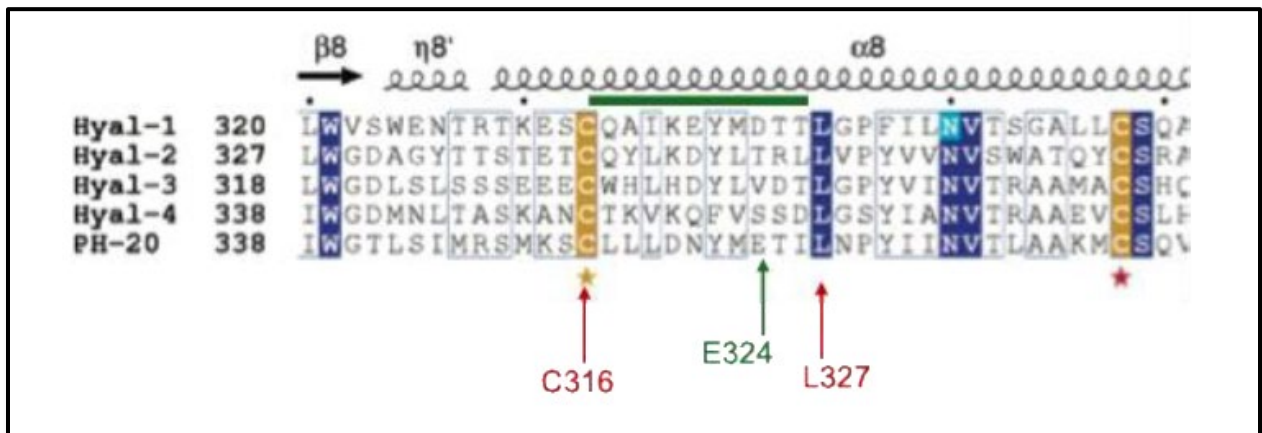
The Examiner considered Stern (EX1008), Zhang (EX1010), and Arming (EX1011). *Becton, Dickinson*, IPR2017-01586, Paper 8 at 17–18. Stern alone includes teachings substantially similar and cumulative to the relevant teachings in Chao. EX2001, ¶¶142-156. Zhang and Arming provide teachings that, considered in combination with Stern, further confirm the cumulative nature of Chao. EX2001, ¶¶157-165. Thus, *Becton, Dickinson* factors (a)-(c) apply here.

Merck asserts Chao provides “insights into the structure of human hyaluronidase enzymes,” such as PH20. Pet., 90. Dr. Park relies upon structural data for PH20 that he states was reported in Chao, Zhang, Stern, and Arming. EX1004, ¶¶88-101; EX2001, ¶153. In particular, Park alleges that Chao “reported an experimentally-determined structure of the human HYAL1 protein and used it to characterize the HA binding site and other regions important to activity.” EX1004, ¶89; EX2001, ¶¶153-155. Park then relies on Chao’s “multiple sequence alignment of the 5 human hyaluronidase enzymes,” which “shows 90 positions in PH20 that are 100% conserved among the five human hyaluronidases.” EX1004, ¶¶90-92; EX2001, ¶147. Park states that Zhang, like Chao “identified residues expected to be important in HYAL1’s active site” and described the Hyal-EGF domain, which Park states is “a unique domain found in mammalian

hyaluronidases.” EX1004, ¶¶94, 97; EX2001, ¶¶158-159. Park further states that Stern, like Chao, “identified residues involved in the active site of PH20,” while Arming recognized “four conserved cysteine residues that form disulfide bonds” in PH20. EX1004, ¶¶100-101; EX2001, ¶163. Except for Chao, the Examiner considered each reference. EX1002, 504 (reference HE), 513 (reference OB), 514 (reference PK). EX2001, ¶¶139-140.

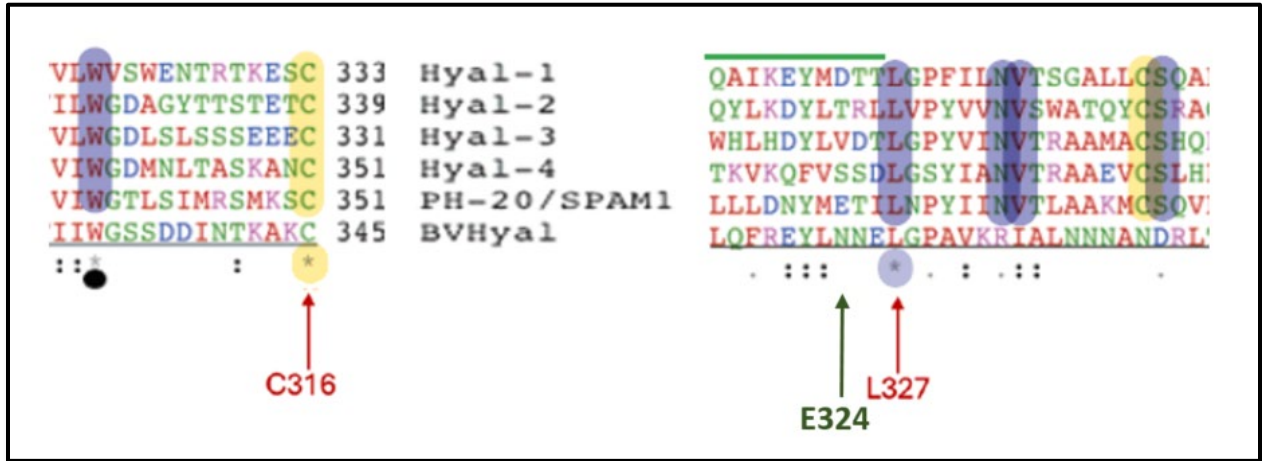
Chao adds nothing materially new to what the Examiner considered, because these references include the same teachings regarding PH20’s structure that are relevant to Merck’s obviousness challenge. EX2001, ¶¶142-165.

First, Merck relies on Chao’s disclosure of an alignment of hyaluronidases to identify conserved residues, pointing to the below excerpt from Chao’s Figure 3 (EX1006, 6916), contending it suggests residue 324 is in a non-essential region. Pet., 93, 96.



EX1006, FIG. 3 (annotated by Merck, Pet., 94).

But this alignment and (allegedly) “non-essential” region (green line annotation) were disclosed in Stern. EX2001, ¶148.



EX1008, 826, FIG. 3 (excerpted and annotated with green line, purple and yellow highlighting, and arrows identifying residues C316, E324, L327¹⁴); EX2001, ¶148.

Stern expressly recognized the *same conserved residues* at C316 and L327 Merck identifies in Chao. EX1008, 826 (FIG. 3 legend, “The conserved residues are marked as follows: * = identical in entire column”). And Stern, like Chao,

¹⁴ Triggs-Raine explains that the residue numbers in Stern’s and Chao’s sequences differ because Stern’s sequences discloses more of the N and C-termini than in Chao and Chao does not include a line for bee venom hyaluronidase (bvHyal). EX2055, ¶149.

discloses a threonine (T) at residue 312 in Hyal-1¹⁵. Accordingly, Stern includes substantially the same teachings as Chao regarding the relied-upon alignments, including conserved residues. EX1004, ¶100 (Park admits Stern “identified residues involved in the active site of PH20.”); EX2001, ¶149.

Second, Merck relies on Chao’s alignment to identify predicted secondary structures. Pet., 89-92, 94. But, Stern likewise includes an alignment of five human hyaluronidases with bee venom hyaluronidase (“bvHyal”), which had “an established 3D structure,” and secondary structures are identified in Stern’s Figure 3. EX1008, 824, 826; EX2001, ¶¶148-154.

Stern also provides other relied-upon teachings of Chao:

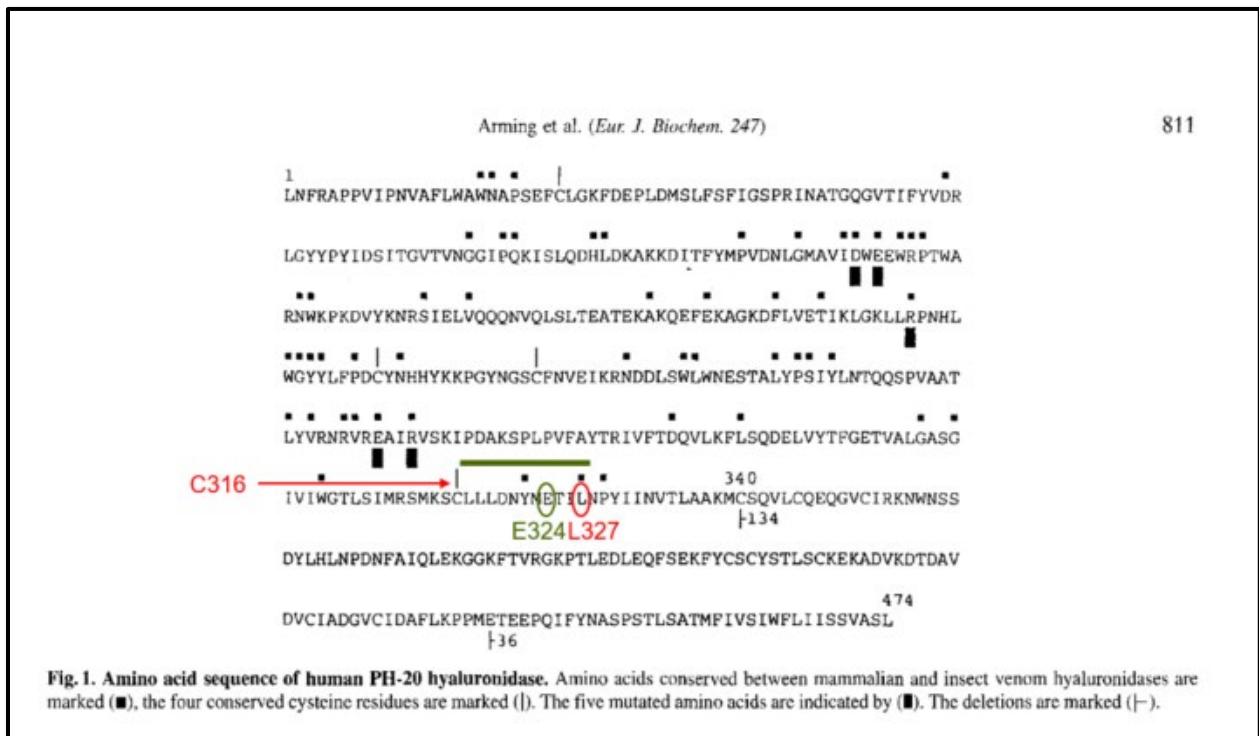
Merck’s Relied-Upon Teaching of Chao	Same Teaching in Stern (considered by the Examiner)
“There are five homologous hyaluronidases encoded in the human genome: hHyal-1 through -4 and the sperm adhesion molecule 1 (termed PH-	“All models of human Hyal-1—4 as well as for HPH-20 are of high quality and are essentially identical to one another in the structure of their main

¹⁵ Stern and Chao’s alignments are so similar that both HYAL3 sequences contain the same incorrect C-terminus sequence. EX2001, ¶151; EX2035, 33660, FIG. 8.

<p>Merck's Relied-Upon Teaching of Chao</p>	<p>Same Teaching in Stern (considered by the Examiner)</p>
<p>20)." EX1006, 6911; Pet., 11, 12-13.</p>	<p>domain (Figures 4 and 5). These five models, therefore, represent reliable structural models for all five human Hyal enzymes." EX1008, 828.</p>
<div data-bbox="233 716 743 1045"> </div> <p>“(A) Stereoscopic representation of the active site region of hHyal-1 (gray ribbon) superimposed on that of bvHyal (yellow ribbon; (22)). Selected amino acids are colored in the atomic color scheme: red, oxygen; blue, nitrogen; gray (hHyal-1) and yellow (bvHyal), carbon.” EX1006, 6917, FIG. 4; Pet., 91.</p>	<div data-bbox="846 726 1273 1199"> </div> <p>“(B) Comparison of the 3D structures of Hyal-1 and BVHyl enzymes. ... The positions of the catalytic Glu and carbonyl positioning residues are essentially identical in the two structures (data not shown). The BVHyal does not have a C-terminal</p>

Merck's Relied-Upon Teaching of Chao	Same Teaching in Stern (considered by the Examiner)
	domain.” EX1008, 830.

Further confirming the Examiner considered conserved residues in hyaluronidase structure, Arming, like Chao, also recognized conserved cysteines (including C316) and conserved residues such as L327. EX1011, 811-813; EX1004, ¶¶88, 101; EX2001, ¶164.



EX1011, 811 (annotated with green line and arrows/circles identifying residues C316, E324, L327); EX2001, ¶164.

Finally, Merck points to Chao’s disclosure of a HyalEGF-like domain at positions 337-409, but Merck failed to establish its relevance to Merck’s

obviousness theory. Pet., 12-13, 38-39, 92-93; EX2001, ¶153. Residue E324 is not within this domain. Pet., 38; EX1004, ¶98; EX2001, ¶153. And, Chao neither resolved the tertiary structure of *PH20* nor identified a HyalEGF-like domain in *PH20*. EX2001, ¶¶153-155. Park admits, “the structure of human PH20 was not solved [in December 2011].” EX1004, ¶36. At most, Chao speculates that mammalian hyaluronidases contain a HyalEGF-like domain, but Chao then concedes there are differences in the C-terminal domain of PH20. EX1006, 6916; EX2001, ¶¶152-153. Ultimately, Chao states, “What then is the role of this domain? ... The exact role of the EGF domains is yet to be determined in many cases.” EX1006, 6916; EX2001, ¶¶153-154.

Regardless, Park admits the HyalEGF-like domain was already described in Zhang, which the Examiner considered. EX1004, ¶¶96-97, 99 (acknowledging Zhang “found a mutation at Asn350 in the ‘c-terminal EGF-like domain’”); EX1010, 9438 (noting residue Asn 350 “was located in the C-terminal EGF-like domain.”); EX2001, ¶¶159-160.

Because Stern, Zhang, and Arming were previously considered and are cumulative to the relied-upon teachings of Chao, part one of *Advanced Bionics* is met for Chao. *Siemens Mobility v. Metrom Rail*, IPR2024-00947, Paper 12 at 12-17 (P.T.A.B. Nov. 19, 2024). EX2001, ¶¶138-165.

* * *

Merck alleges “the present obviousness grounds also rely on Chao (EX1006), which was not cited or considered during examination.” Pet., 115. But Merck ignores that the ’429 patent, Stern, Zhang, and Arming were all considered by the Examiner, and Chao is cumulative to these references. *Becton, Dickinson*, IPR2017-01586, Paper 8 at 17–18. Merck should have been aware of this art’s relevance to the §325(d) inquiry, as Park expressly relied on Stern, Zhang, and Arming with Chao, but Merck did not address it. EX1004, ¶¶88-101. Part 1 is satisfied for the Petition’s Ground III.

B. Part 2: Merck Does Not Even Attempt to Show Material Error Under *Advanced Bionics* Part 2.

Discretionary denial is further warranted under the second step of the *Advanced Bionics* framework because Merck has failed to sufficiently point out “how the Examiner erred in its evaluation of the asserted prior art.” *Becton, Dickinson*, IPR2017-01586, Paper 8 at 17-18. Indeed, Merck does not allege any material error as to the asserted obviousness ground during prosecution. Pet., 115-116. Accordingly, Ground III lacks merit. *Advanced Bionics*, IPR2019-01469, Paper 6 at 8–9; *Ecto World*, IPR2024-01280, Paper 10 at 11 (denying institution; Petitioner makes no allegation of material error).

The Board has previously denied institution when the Petitioner “is silent on material error” or does not even “try to flesh out any material error the Examiner made.” *Vital Connect v. Bardy Diagnostics*, IPR2023-00381, Paper 7 at 19-20

(P.T.A.B. July 11, 2023) (“[P]etitioner is silent on material error, even though its relied-upon references (or their substantially identical disclosures), were before the Office during examination of the application leading to the ’743 patent”); *Siemens Mobility*, IPR2024-00947, Paper 12 at 17-19 (“the Petition does not try to flesh out any material error the Examiner made when he allowed claim 1 over the substantially similar combination of Knott and Soderi”); *Boehringer II*, PGR2022-00021, Paper 13 at 21-26 (denying grounds on §325(d) and other grounds on the merits).

Here, Merck has failed to meet its burden of overcoming “the deference that is due to a qualified government agency [like the Patent Office] that is *presumed* to have properly done its job” with respect to assessing the patentability of the ’520 patent. *PowerOasis v. T-Mobile*, 522 F.3d 1299, 1304 (Fed. Cir. 2008); *Advanced Bionics*, IPR2019-01469, Paper 6 at 9 (“At bottom, this framework reflects a commitment to defer to previous Office evaluations of the evidence of record unless material error is shown.”); M.P.E.P. §1302.01 (Applications ready for allowance “should be reviewed [] to make certain that...the language of the claims is enabled by, and finds adequate descriptive support in, the application disclosure as originally filed.”); M.P.E.P. §2173.06 (“the examiner should review each claim *for compliance with every statutory requirement for patentability in the initial review of the application and identify all of the applicable grounds of rejection in*

the first Office action to avoid unnecessary delays in the prosecution of the application”); 37 C.F.R. §1.104(a)(1) (“the examiner shall make a thorough study thereof and shall make a *thorough investigation of the available prior art relating to the subject matter of the claimed invention.*”).

By allowing the ’520 patent claims, the Examiner here reviewed the application for compliance with *every* statutory requirement for patentability. *See* M.P.E.P. §2173.06. Indeed, the Examiner considered art cited in the specification (the ’429 patent) and art cumulative to Merck’s cited art (Stern, Arming, and Zhang). Furthermore, *five* separate Examiners with specialized technical expertise properly assessed the patentability of Halozyme’s family of patents, including the ’520 patent. *See supra* Section III. Merck has failed to overcome the deference due to the Examiner by showing material error. Accordingly, it would be an inefficient use of the Board’s resources to revisit patentability of the ’520 patent. The Director should deny institution.

VI. DISCRETIONARY DENIAL IS PROPER UNDER *FINTIV*.

On April 24, 2025, Halozyme sued Merck for infringement of, *inter alia*, the ’520 patent in *Halozyme v. Merck*, Case No: 2:25-cv-03179 (D.N.J.) (“the District Court Proceeding”). The Board weighs the following *Fintiv* factors when assessing whether the same issues will be resolved between the same parties in the parallel District Court proceeding:

1. whether the court granted a stay or evidence exists that one may be granted if a proceeding is instituted;
2. proximity of the court's trial date to the Board's projected statutory deadline for a final written decision;
3. investment in the parallel proceeding by the court and the parties;
4. overlap between issues raised in the petition and in the parallel proceeding;
5. whether the petitioner and the defendant in the parallel proceeding are the same party; and
6. other circumstances that impact the Board's exercise of discretion, including the merits.

Fintiv, IPR2020-00019, Paper 11 at 5-6. These six factors, when considered as a whole, support *denying* institution. Factors 2 and 3 are neutral, Factors 4-6 strongly weigh in favor of denial, Factor 1 either favors denial or is neutral, and no factor weighs against exercising the Director's discretion to deny institution.

As discussed below, the Director should exercise discretion to deny the Petition under *Fintiv* because the same issues will be resolved between the same parties in the parallel District Court proceeding. Thus, *Fintiv* provides an independent basis to deny institution of the Petition.

A. Merck Has Not Sought a Stay, Favoring Denial (Factor 1)

This factor favors discretionary denial because Merck has not sought a stay

in the District Court proceeding. To the extent it is unclear whether a stay would be granted if requested by Merck, any evidence on this factor is neutral. *Fintiv*, IPR2020-00019, Paper 15 at 12 (P.T.A.B. May 13, 2020) (informative) (holding the Board should “decline to infer ... how the District Court would rule should a stay be requested by the parties.”).

B. Proximity of the District Court Proceeding’s Trial Date is Neutral (Factor 2)

Trial has yet to be scheduled in the District Court proceeding. However, as *Fintiv* outlines, “if the court’s trial date is at or around the same time as the projected statutory deadline...or even significantly after the projected statutory deadline, the decision whether to institute will likely implicate other factors.” *Fintiv*, IPR2020-00019, Paper 15 at 9 (informative). Therefore, this factor is neutral.

C. The Investment in the Parallel Proceeding is Neutral (Factor 3)

The parties and the Court will have expended resources in litigating this case by the time the Board issues a Decision on Institution (DI) in this PGR, expected by July 14, 2025. For this factor, the Board considers “the amount and type of work already completed in the parallel litigation by the court and the parties at the time of the institution decision.” *Fintiv*, IPR2020-00019, Paper 11 at 9. By July, Merck will have responded to Halozyme’s Complaint and a Scheduling Conference will most likely have taken place. Thus, this factor is neutral.

D. The Overlap in Claims Favors Denial (Factor 4)

There is overlap between the claims that are being litigated in the parallel district court proceeding and the claims being challenged in this Petition. Indeed, Merck's Petition challenges *all* claims of the '520 patent and Halozyme's filed Complaint alleges that Merck has infringed one or more claims of the '520 patent. Pet., 1; EX2058, ¶¶227-239. Merck will presumably challenge the validity of all asserted claims of the '520 patent in district court. Should co-pending validity challenges be raised in the district court, there is a high likelihood of inefficiencies and concerns regarding the potential for conflicting decisions should the PTAB proceed to institution here. The Board looks at the overlap between the issues raised in the Petition and in the parallel proceeding in order to evaluate "concerns of inefficiency and the possibility of conflicting decisions." *Fintiv*, IPR2020-00019, Paper 11 at 12.

Furthermore, Merck has not filed a *Sotera*-type stipulation, and thus Merck has not committed to adjudicating the merits of the '520 patent only before the Board. This factor favors discretionary denial.

E. The Same Parties Are in the Parallel District Court Proceeding, Favoring Denial (Factor 5)

Because Merck is the defendant in the parallel district court litigation, this factor further favors discretionary denial. *Sotera v. Masimo*, IPR2020-01019, Paper 12 at 19 (P.T.A.B. Dec. 1, 2020). Thus, "proceeding in parallel with the district

court litigation is an inefficient use of [the Board's] time and resources." *NHK Spring v. Intri-plex Techs.*, IPR2018-00752, Paper 8 at 11 (P.T.A.B. Sept. 12, 2018) (precedential). Under *Sotera*, when the parties are the same, this factor supports denying institution. *Sotera*, IPR2020-01019, Paper 12 at 19.

F. The Additional Factors Outlined Above Further Warrant Denial (Factor 6)

Under the sixth *Fintiv* factor, the Board may consider other circumstances that impact the Board's exercise of discretion, including the merits. *Fintiv*, IPR2020-00019, Paper 11 at 14-15. As explained above, Merck's Petition suffers from multiple fundamental flaws that warrant discretionary denial. The Petition failed to establish PGR-eligibility, failed to put forth a strong unpatentability challenge, and failed to show material error in the Office's previous consideration of the same or substantially the same art or arguments. Moreover, Merck's onslaught of twelve successive PGR Petitions (and counting) challenging twelve patents protecting Halozyme's proprietary drug-delivery technology further justifies discretionary denial so as to preserve the Board's finite resources. Indeed, the Board previously found that a Petitioner filing *eleven* IPRs over several months weighed in favor of denying trial. *Nokia v. Pegasus*, IPR2025-00037, Paper 14 at 14-15 (P.T.A.B. Apr. 25, 2025). For the sake of efficiency, the Director should deny trial here for the same reasons.

Additional relevant considerations addressed above (including the extent of

the petition's reliance on conclusory, hindsight-driven expert testimony and the clarification in the law in *Entresto*) also support discretionary denial under *Fintiv*. On balance, as Factors 4, 5, and 6 favor denial, Factors 2 and 3 are neutral, and Factor 1 either favors denial or is neutral, the *Fintiv* analysis favors discretionary denial. Even if Factors 2 and/or 3 are found to not favor exercising the Director's discretion to deny the Petition, the balance of the factors still strongly favor denial.

Accordingly, the *Fintiv* factors in combination with additional considerations outlined above, including Merck's failure to establish PGR-eligibility, compelling economic factors that warrant protecting American innovation, and the multiple weaknesses in the Petition, strongly favor discretionary denial here.

VII. CONCLUSION

Halozyme respectfully requests that the Director exercise her discretion to deny institution based on the totality of circumstances presented in this case.

Respectfully submitted,

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CERTIFICATE OF WORD COUNT (37 C.F.R. § 42.24(d))

1. This Discretionary Denial Brief complies with the type-volume limitation of 14,000 words, comprising 13,997 words, excluding the parts exempted by 37 C.F.R. § 42.24(a)(1).
2. This Brief complies with the general format requirements of 37 C.F.R. § 42.6(a) and has been prepared using Microsoft® Word 2016 in 14-point Times New Roman font.

Respectfully submitted,

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CERTIFICATE OF SERVICE (37 C.F.R. § 42.6(e))

I certify that the above-captioned **PATENT OWNER DISCRETIONARY DENIAL BRIEF** and associated Exhibits 2001-2006, 2018-2039, 2046-2054, and 2056-2063 were served in their entireties on May 12, 2025, upon the following parties via electronic mail:

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