

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MERCK SHARP & DOHME LLC,
Petitioner

v.

HALOZYME, INC.,
Patent Owner

Case PGR2025-00030
U.S. Patent No. 12,054,758

PATENT OWNER DISCRETIONARY DENIAL BRIEF

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PATENT OWNER’S EXHIBIT LIST

Exhibit No.	Description
2001	Declaration of Barbara Triggs-Raine, Ph.D. in support of Patent Owner Discretionary Denial Brief
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. 18/066,960, June 13, 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. 18/066,960
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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)

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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. PGR2025-00017 (P.T.A.B.), January 17, 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. PGR2025-00017 (P.T.A.B.), January 17, 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
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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)
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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)

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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)
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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
2064	Declaration of Michael Hecht, Ph.D. (Exhibit 1003), <i>Merck Sharp & Dohme LLC v. Halozyme Inc.</i> , Case No. PGR2025-00053 (P.T.A.B.), June 6, 2025

Exhibit No.	Description
2065	Petition for Post-Grant Review, <i>Merck Sharp & Dohme LLC v. Halozyme Inc.</i> , Case No. PGR2025-00053 (P.T.A.B.), June 6, 2025

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Pursuant to the “Interim Processes Memo,” discretionary denial is warranted here. This brief is supported by a declaration from Dr. Triggs-Raine, an expert in hyaluronidases. EX2001; EX2002.

I. INTRODUCTION

First, the precedential decision of *Apple Inc. v. Fintiv, Inc.*, IPR2020-00019, Paper 11 (P.T.A.B. Mar. 20, 2020) (precedential) 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 PGR-*ineligible* 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 13 separate PGR proceedings. Moreover, the identity in parties, the overlap of the issues between 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.

Second, trial should be denied because Merck failed to establish that the ’758 patent is PGR-eligible¹. PGR-eligibility is a dispositive threshold

¹ See Pet., 4-6.

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); *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*”)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 '758 patent family as of that application's filing date, including Application No. 18/066,960, which matured into the challenged '758 patent. Accordingly, Merck's written-description and enablement challenges fail. For the sake of improving efficiency, the Director

² Emphasis is added throughout, except where otherwise indicated.

needs no other reason to deny trial because Merck has not met its threshold burden of establishing that the '758 patent is PGR-eligible.

Third, Merck's unpatentability challenges are substantively weak, misapply relevant law, and violate Federal Circuit precedent. Claim 1 of the '758 patent recites modified PH20 (a type of hyaluronidase) polypeptides that must contain one amino acid replacement at *position 317* (from amino acid L to any of A, I, K, M, Q, and R), 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., 21 ("The claims are restricted to one of two alternative embodiments in the patents:

³ The specification discloses that the claimed polypeptides are useful as contraceptives irrespective of whether they exhibit hyaluronidase activity. EX1001, 75:60-63, 187:41-46.

⁴ Claims 3-5 and 31-40 of the '758 patent have been statutorily disclaimed, leaving only claims 1-2, 6-30. EX2003.

‘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 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 testimony. Merck relies on Park’s testimony, but used hindsight-based *attorney instruction* to lead Park to the claimed modification at position 317. Park concedes he was “asked by counsel to report [his] conclusions with respect to position 317” and neither Hecht nor Park provide any reason to select position 317 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*,

⁵ See Pet., 16-17.

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, Merck, one of the largest multinational pharmaceutical companies

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.

which has a market capitalization nearly 30 times larger than that of Halozyme—
an American company employing approximately 500 people—has now filed
thirteen Petitions for Post-Grant Review seeking to invalidate *thirteen* 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 ’758 patent, safeguards
Halozyme’s extensive research into modifications to a human hyaluronidase
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 ’758 patent.
Indeed, on April 24, 2025, Halozyme was left with no choice but to sue Merck for
infringement of, *inter alia*, eleven of the thirteen patents that Merck is challenging
at the PTAB, including the ’758 patent. EX2058. Discretionary denial here would

protect American innovation and prevent Big Pharma from trampling on the business of a home-grown American company.

II. DISCRETIONARY DENIAL IS PROPER UNDER *FINTIV*

A. The *Fintiv* Factors Call for Discretionary Denial

Halozyme, a mid-sized American company, is fighting *thirteen* PGR Petitions that multinational Merck has filed in succession within the last seven months (PGRs 2025-00003, -00004, -00006, -00009, -00017, -00024, -00030, -00033, -00039, -00042, -00046, -00050, -00053). Halozyme sued Merck for patent infringement in the District of New Jersey on April 24, 2025, asserting infringement of 15 patents including eleven of the thirteen patents⁷ for which Merck seeks PGR. EX[Complaint]. The 11 most-recent Petitions are subject to the March 26, 2025 Interim Processes for PTAB Workload Management, and PGR2025-00017 is currently awaiting a Discretionary Denial decision. Halozyme also intends to request Director Review of the decisions instituting trial in PGR2025-00004 and PGR2025-00006.

The six *Fintiv* factors are weighed when assessing whether the same issues

⁷ Each of the 13 Halozyme patents being challenged contain the same disclosure and claim priority to the same parent '731 Application and the same two provisional applications, each with the same filing dates.

will be resolved between the same parties in the parallel District Court proceeding. *Fintiv*, IPR2020-00019, Paper 11 at 5-6. Factor one favors denial of institution. Merck has not sought a stay, nor is there any evidence suggesting the Court would grant one. Indeed, given the presence of PGR-ineligible patents and Merck's failure to file a *Sotera* stipulation, there is no reason to believe the district court would grant a stay because the issues will not be simplified or eliminated by a PGR. Merck will raise the same §112 defenses and claim construction issues regarding at least the three PGR-ineligible patents involved in the litigation—and Merck has not promised to forgo those arguments as to the challenged patents—so the district court will be required to resolve them.

Factor two similarly favors denying institution. *Fintiv* directs consideration of trial date proximity primarily to avoid duplication of effort. In PGR2025-00006 and -00009, the Director found that the district court trial was likely several years off, weighing that factor against discretionary denial. But because, in the present case, there are PGR-ineligible patents at issue in the district court, that trial will nonetheless go forward. Halozyme thus will have trials in two forums, and the district court will have to resolve highly similar issues—along with other issues, such as infringement and damages—regardless of the PGR. That is inefficient, burdensome on Halozyme, and a waste of PTAB resources.

For similar reasons, *Fintiv* factors 3-5 weigh heavily in favor of

discretionary denial. *Fintiv*, IPR2020-00019, Paper 11 at 5-6. There is substantial overlap between the district court proceeding and these PGR proceedings. All fifteen of the patents asserted in the district court litigation, as well as the eleven PGR-challenged patents, are directed to modified PH20 polypeptides with substitutions at certain positions. The claim construction argument central to the institution decision—whether a modified PH20 polypeptide must have hyaluronidase activity—will be resolved by the district court. Likewise, the district court also will undoubtedly address Merck’s § 112 and obviousness arguments, given the lack of a *Sotera* stipulation. Such overlapping issues weigh in favor of denying institution.

Given the inevitability of the district court case proceeding, it would be significantly more efficient to address claim construction and invalidity in the Article III court, instead of having the PTAB address these issues for a subset of the patents-in-suit. If trial is instituted on all thirteen patents, there will be fourteen different proceedings (including the district court litigation) evaluating the same claim construction and validity issues. That is highly inefficient, and Merck should not be allowed to dual-track challenges to Halozyme in the PTAB and district court, generating multiple bites at the apple. *See NHK Spring v. Intri-plex Techs.*, IPR2018-00752, Paper 8 at 11 (P.T.A.B. Sept. 12, 2018) (precedential) (“Thus, “proceeding in parallel with the district court litigation is an inefficient use of [the

Board’s] time and resources.”).

Finally, factor 6 also favors denial. As explained below, Merck presented *zero evidence* as to whether the ’758 patent is entitled to claim priority to the 2012 application; Merck’s experts *only* analyzed the 2011 date. Taken together, the *Fintiv* factors strongly favor denying institution.

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

Merck’s Petition failed to demonstrate that the ’758 patent is 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 ’758 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 ’758 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, 26, 39, 55, 72, 74-75, 77, 81, 86, 88-89, 92, 92-97, 101-105, 107. 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 three 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 recently filed Petitions further highlights Merck’s failure in *this* Petition to assess *any* application in ’758 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 ’758 patent pre-AIA status during prosecution, which is a factor supporting a finding that the ’758 patent is *ineligible* for post-grant review. EX1002, 476 (“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 Inc. v. Apple Inc.*, 134 F.4th 1355, 1367 (Fed. Cir. 2025). This reason alone is sufficient to deny institution and preserve the Office’s finite resources.

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. *Envvtl. 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 ’758 patent is directed to modified PH20 polypeptides. EX2001, ¶65; EX1001, claim 1. In particular, the ’758 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, 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, 75:60-62, 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 leucine (L) with glutamic acid (Q) at the claimed position 317 because glutamic acid (Q) was the most prevalent amino acid found at position 317. 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., 16-17. 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., 21-25; 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.

Claim 1 of the '758 patent is directed to a "*modified PH20 polypeptide*" wherein at least 91% of the residues of the amino acid sequence of the modified PH20 polypeptide is identical to a group of sequences consisting of SEQ ID Nos: 3, 7, and 32-66 and the polypeptide comprises an amino acid modification at a position corresponding to position 317. EX1001, Claim 1. The terms of patent claims "are generally given their ordinary and customary meaning." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (en banc). However, if the patentee "acts as his own lexicographer" then the definition in the specification controls. *Thorner v. Sony Computer Ent. Am. LLC*, 669 F.3d 1362, 1365 (Fed. Cir. 2012). "To act as its own lexicographer, a patentee must 'clearly set forth a

definition of the disputed claim term,” and must “‘clearly express an intent’ to define the term.” *Id.*

The '758 patent clearly defines “modified PH20 polypeptide” and then provides non-limiting examples:

As used herein, “modified PH20 polypeptide” or “variant PH20 polypeptide” refers to 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. A modified PH20 polypeptide can have up to 150 amino acid replacements, so long as the resulting modified PH20 polypeptide exhibits hyaluronidase activity. Typically, a modified PH20 polypeptide contains 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50 amino acid replacements. It is understood that a modified PH20 polypeptide also can include any one or more other modifications, in addition to at least one amino acid replacement as described herein. EX1001, 48:38-53.

The first sentence above constitutes a definition, but the other sentences above are merely non-limiting examples. Alynlam Pharms., Inc. v. Moderna, Inc., 2025 WL 1572001 (Fed. Cir. 2025). A statement is definitional if (1) “the sentence in question appears under the title ‘Definitions’; (2) “the term to be defined . . . is set off in quotation marks”; (3) the sentence “uses the term ‘refer to’...which

generally ‘conveys an intent for that sentence to be definitional’; or (4) “elsewhere in the Definitions section, [the patent used] non-limiting terms that contrast with the ‘refer to’ language at issue here.” *Id.* Applying that same analysis to the facts of the present case leads to the conclusion that the term “modified PH20 polypeptide” is explicitly defined in this first sentence (using the phrases “as used herein” and “refers to”) and the sentences that follow this definition are simply exemplary, non-limiting descriptions of the term. Indeed, “modified PH20 polypeptide” is defined under the “Definitions” section of the patent, set off in quotation marks, and uses “refers to” to convey an intent for that sentence to be definitional.

EX1001, 44:55, 48:38-53; *see also ParkerVision, Inc. v. Vidal*, 88 F.4th 969, 977 (Fed. Cir. 2023); *Kyocera Senco Indus. Tools Inc. v. ITC*, 22 F.4th 1369, 1378 (Fed. Cir. 2022).

Notably, Merck agreed in its Petition that this *single* sentence (EX1001, 48:38-43) constitutes the “definition of ‘modified PH20 polypeptides.’” Pet., 17 (stating that “‘modified PH20 polypeptides,’ which the common disclosure *defines as* ‘a PH20 polypeptide that contains at least one amino acid modification, such as at least one amino acid replacement ... in its sequence of amino acids compared to a reference unmodified PH20 polypeptide.’”). The sentences that follow the single-sentence definition are not part of the definition; they are non-limiting examples of “modified PH20 polypeptides.”

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., 25; EX1001, 48:38-53. This sentence is not part of the definition. The '758 patent used "non-limiting" terms such as "can have" to differentiate this later sentence from the actual definition of "modified PH20 polypeptide." *Alnylam*, slip op. at 10. In short, this sentence in the specification does not limit "modified PH20 polypeptide" to only active molecules. In fact, the paragraph containing the express definition of the "modified PH20 polypeptide" also includes further exemplary, non-limiting descriptions of the term:

A modified PH20 polypeptide *can have* up to 150 amino acid replacements . . . [A] modified PH20 polypeptide also *can include* any one or more other modifications, in addition to at least one amino acid replacement as described herein.

EX1001, 48:38-53. Here, the terms "can have" and "can include" are non-limiting. The '758 patent contains over 100 paragraphs that provide express definitions of various terms in the first sentence, as evidenced by the phrases "*as used herein*" and "*refers to,*" which are then followed by exemplary, non-limiting descriptions of the applicable terms. For example, for the term "soluble PH20," the patent uses the terms "as used herein" and "refers to" to denote the definitional sentence, while the remaining sentences that follow contain phrases such as "for example" and

“can be” to describe non-limiting aspects of “soluble PH20.” *See* EX1001, 46:24-52 (definition of “soluble PH20”).

Moreover, the term “modified PH20 polypeptide” cannot be limited to enzymatically active proteins because the specification repeatedly uses that term to refer to proteins that *do not have* hyaluronidase activity. For example, under the header, “Inactive Mutants,” the ’758 patent specifies that these mutants are “*modified PH20 polypeptides* that contain one or more amino acid replacements in a PH20 polypeptide and that are *inactive, whereby the polypeptides do not exhibit hyaluronidase activity* or exhibit low or diminished hyaluronidase activity.” EX1001, 115:53-58.

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. The Board has held that where “the specification of the challenged patent provides an express construction of an important claim term,

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.

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*, 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; *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., 21-25. 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., 21; EX2001, ¶¶83-84. Merck did not—and could not—identify any claim language limiting the claims to just active mutants. EX1003, ¶¶126-135; Pet., 24; EX2001, ¶¶85-86. And, the specification indisputably uses the term “modified PH20 polypeptide” to refer to both active and inactive mutants. EX1001, 115:53-61; 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., 23. 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 wrongly argues that the claims are limited to “active mutants” because they require each “modified PH20 polypeptide” to have one of six replacements at position 317 that yielded an “active mutant.” Pet., 24; 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

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

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 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 ’758 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. 18/066,960, which matured into the challenged ’758 patent, as of the ’960 application’s December 15, 2022 filing date.¹⁰ Likewise, as discussed in Section II, Merck wrongly assesses the 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.

¹⁰ For both §112 grounds, Merck relies on the “common disclosure” between the patent and the ’731 Application, which Merck admits has a substantively identical specification to the ’758 patent. Pet., 6, 16-17, 22, 26, 31, 33-39, 40-85, 106, 113.

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

After the ’758 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 ’758 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 ’758 patent must (but did not) adequately describe and enable the PH20 polypeptides within the claimed genus. Pet., 2-3, 26-83. 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, 115:53-61; 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.*, 27-31. 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 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

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.

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., 30-31. 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 supports 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.*, 66-67.

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.*, 66-67; *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 317 is not mentioned in the '429 patent or Chao, much less the specific A, I, K, M, Q, and R replacements claimed for position 317. 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 the L317Q substitution 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 the L317Q modification was “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 317 in the first place. EX2001, ¶97. Indeed, Park’s analysis focuses on position 317 *at the request of Merck’s counsel*, and Hecht does not provide any reason to pick position 317 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 317”). Merck also alleges that POSAs would have had to engage in approximately *30 steps* to arrive at the L317Q modification 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.

Additionally, Merck has failed to establish that “ordinary creativity” could serve as a gap-filler for the modification at position 317. *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 art 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 317.**

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).

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., 85-88. 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 317 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., 87-88; EX2001, ¶103.

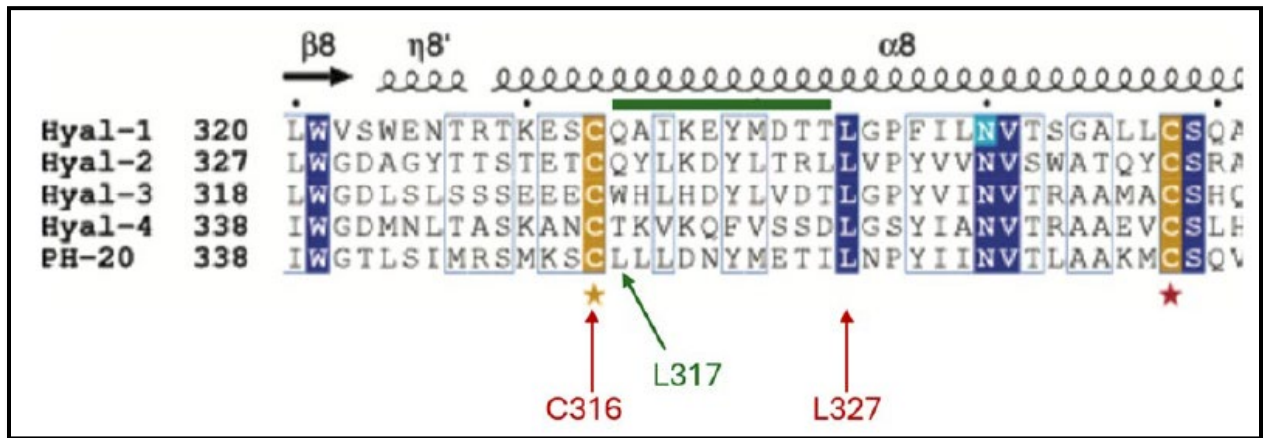
Merck alleges a POSA “[g]uided by her familiarity with rational protein design and the teachings of the ’429 patent and Chao...would have readily identified single amino acid substitutions in non-essential regions of PH20₁₋₄₄₇ that would have been tolerated (*i.e.*, a PH20₁₋₄₄₇ with that single substitution would

retain its enzymatic activity).” Pet., 85. 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”).

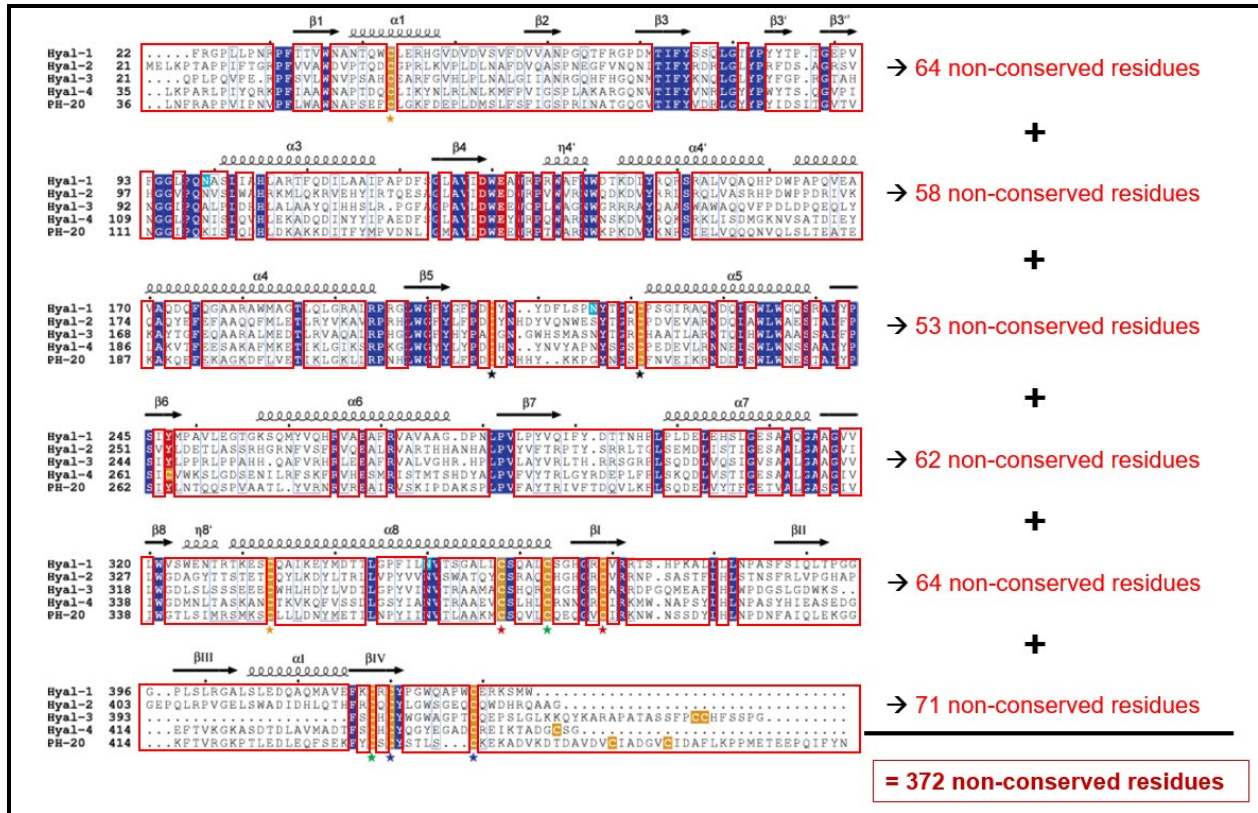
For example, Merck never argues that making a modification in non-essential regions of PH20 would have improved or increased hyaluronidase enzymatic activity. Rather, Merck states that such a modification would have the “same utility [and] therapeutic applications” as wild-type PH20. Pet., 88; EX2001, ¶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 PH20_{1,447} and not alter existing enzymatic activity. Pet., 112; *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 317 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., 94. To illustrate the point, Merck annotates and crops Chao’s Figure 3 below to visualize position 317 relative to its bounding essential residues at positions 316 and 327:



Pet., 94; 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 317 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 L317Q Modification.

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 leucine (L) at position 317 with glutamic acid (Q), Merck utilizes hindsight and relies almost exclusively on the counsel-directed testimony of both Hecht and Park instead of the asserted prior art. Pet., 94-98. *First*, Merck uses hindsight to lead Park to the claimed modifications at position 317. In fact, Park concedes he was “*asked by counsel* to report [his] conclusions with respect to position 317.” EX1004, ¶103; EX2001, ¶100. Park never provides a reason why POSAs would have focused on position 317 among the 300 or so non-conserved residues. EX1004, ¶32. Instead, Park simply states that he believes that “position 317, 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 317. 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 317 only because counsel directed him to that position. EX1004, ¶103. Neither of Merck’s declarants provide a concrete reason to identify position 317 apart from Merck’s counsel instructing Park to analyze position 317 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 317 as an amino acid to

modify. EX2001, ¶¶93-117.

Only hindsight—provided by counsel instructions—led Park and Hecht to position 317. *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 *eleven other* PGRs alleging that Halozyme’s patents claiming other modifications are invalid as obvious. EX2001, ¶¶133-136. In these eleven 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, 320, and 324.

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
PGR2025-00017	12,110,520	324
PGR2025-00024	12,060,590	307
PGR2025-00033	12,049,652	320
PGR2025-00039	12,104,185	320
PGR2025-00042	12,037,618	309
PGR2025-00046	12,091,692	313
PGR2025-00053	12,195,773	320

EX2023, 91-107; EX2024, 85-111; EX2025, 92-108; EX2026, 86-113; EX2027, 85-114; EX2028, 84-113; EX2029-EX2034; EX2036; EX2037, 85-109; EX2038,

EX2039, 89-110; EX2001, ¶¶133-136; EX2056-EX2057; EX2060, 90-110;
EX2061; EX2064; EX2065, 89-109¹².

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 317, such testimony was directed by counsel and strictly hindsight-based with no reason articulated for arriving at position 317 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

¹² In 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=.

L317Q modification. To do so, a POSA would have had to perform nearly *thirty* different steps—beyond the disclosures in the '429 patent and Chao—to make these modifications. Pet., 94-98; EX1003, ¶¶83, 195, 217-222; EX1004, ¶¶20-145, Appendix C, Appendix D-1. 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 317, just to arrive at the alleged conclusion that it was obvious to replace leucine with glutamine at position 317 of PH20. Pet., 94-98; 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 L317Q modification 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., 99-107. 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, 44-110, 112-138, 147-150, 152, 162-163; 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 L317Q modification 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., 87-88; 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 L317Q modification 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.

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 affecting patentability of the challenged claims. 35 U.S.C. §325(d); *Advanced Bionics, LLC v. MED-EL Elektromedizinische Geräte GmbH*, 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., 114-115.

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

Merck's Ground III alleges that the claims "would have been obvious over the '429 patent in view of Chao and the knowledge of a skilled artisan." Pet., 84. However, the Examiner considered art the same as or cumulative to the '429 patent and Chao. *Becton, Dickinson* factors (a), (b), and (c) warrant discretionary denial here. *Advanced Bionics*, IPR2019-01469, Paper 6 at 9-10 (citing *Becton, Dickinson v. Braun Melsungen*, IPR2017-01586, Paper 8 at 17-18 (P.T.A.B. Dec. 15, 2017) (informative)); *Monolithic Power Systems, Inc. v. Volterra Semiconductor LLC*, IPR2020-01348, Paper 19 at 10-14 (P.T.A.B. Mar. 4, 2021).

Merck's Cited Reference	Prior Consideration by Examiner
'429 patent	Included in IDS (reference CK) considered by the Examiner
Chao	Substantially the same art as Stern, Zhang, and Arming 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, 513 (initialed IDS, reference CK); EX1001, 70:10, 71:47, 73:49-50, 74:18, 128:51-52, 174:44, 184:29, 188:11. This satisfies *Advanced Bionics* part one. *Ecto World, LLC v. RAI Strategic Holdings, Inc.*, IPR2024-01280, Paper 10 at 9-11 (P.T.A.B. Mar. 6, 2025).

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

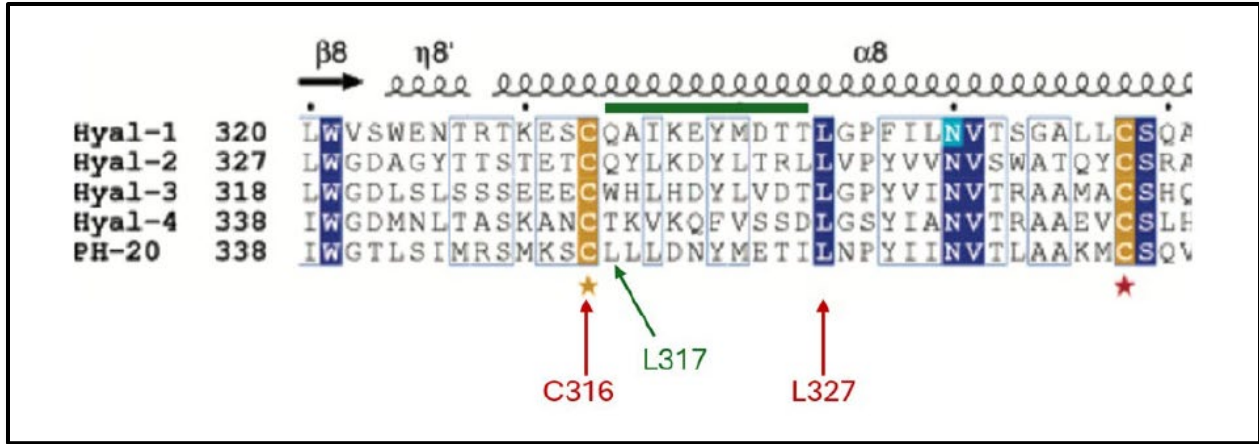
The Examiner considered Stern (EX1008), Zhang (EX1010), and Arming (EX1011). Stern alone includes teachings substantially similar and cumulative to the relevant teachings in Chao. EX2001, ¶¶142-156. Zhang and Arming provide teachings that, considered in combination with Stern, further confirm the cumulative 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 like PH20.” Pet., 89. Dr. Park relies upon structural data for PH20 that he states was reported in Chao, Zhang, Stern, and Arming. EX1004, ¶¶88-101. 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, 517 (reference HE), 526 (reference OB), 527 (reference PK). EX2001, ¶¶139-140.

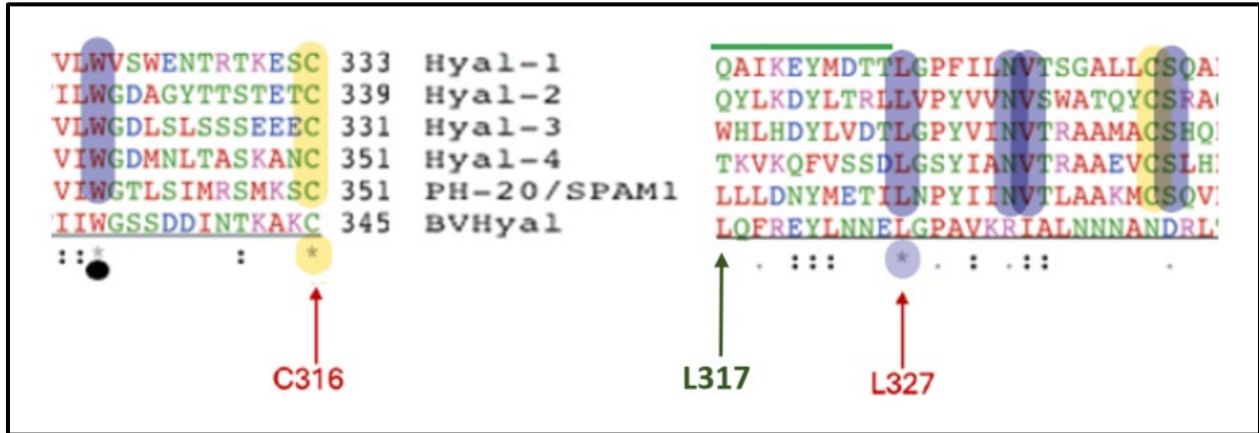
Chao adds nothing materially new to what the Examiner considered, because these references include the same teachings regarding PH20's structure that are relevant to Merck's obviousness challenge. EX2001, ¶¶142-165.

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 317 is in a non-essential region. Pet., 92-93, 96-97.



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

But this alignment and (allegedly) “non-essential” region (green line annotation) were disclosed in Stern. EX2001, ¶¶146-148.



EX1008, 826, FIG. 3 (excerpted and annotated with green line, purple and yellow highlighting, and arrows identifying residues C316, L317, L327¹⁴); EX2001, ¶¶148-149.

¹⁴ Triggs-Raine explains that the residue numbers in Stern’s and Chao’s

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, discloses a glutamine (Q) at residue 317 in Hyal-1 and 2¹⁵. 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, ¶¶147-149.

Second, Merck relies on Chao’s alignment to identify predicted secondary structures. Pet., 90-92. 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.

sequences differ because Stern’s sequences disclose more of the N and C-termini than in Chao and Chao does not include a line for bee venom hyaluronidase (bvHyal). EX2001, ¶149.

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.

Stern also provides other relied-upon teachings of Chao:

Relied-Upon Teaching of Chao	Same Teaching in Stern
<p>“There are five homologous hyaluronidases encoded in the human genome: hHyal-1 through -4 and the sperm adhesion molecule 1 (termed PH-20.” EX1006, 6911; Pet., 11, 12-13.</p>	<p>“All models of human Hyals-1—4 as well as HPH-20 are of high quality and are essentially identical to one another in the structure of their main domain (Figures 4, 5). These five models, therefore, represent reliable structural models for all five human Hyal enzymes.” EX1008, 828.</p>
<div data-bbox="232 1056 743 1388"> </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</p>	<div data-bbox="841 1062 1268 1539"> </div> <p>“(B) Comparison of the 3D structures of Hyal-1 and BVHyl enzymes. ... The positions of the catalytic Glu and</p>

Relied-Upon Teaching of Chao	Same Teaching in Stern
color scheme: red, oxygen; blue, nitrogen; gray (hHyal-1) and yellow (bvHyal), carbon.” EX1006, 6917, FIG. 4; Pet., 90-91.	carbonyl positioning residues are essentially identical in the two structures (data not shown). The BVHyal does not have a C-terminal 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.

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, Inc. v. Metrom Rail, LLC*, IPR2024-00947, Paper 12 at 12-17 (P.T.A.B. Nov. 19, 2024); EX2001, ¶¶138-165.

* * *

Merck alleges “[t]he present obviousness grounds also rely on Chao (EX1006), which was not cited or considered during examination.” Pet., 114-115. But Petitioner ignores that the ’429 patent, Stern, Zhang, and Arming were all considered by the Examiner, and Chao is cumulative to these references. 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., 114-115. Accordingly, Ground III lacks merit. *Advanced Bionics*, IPR2019-01469, Paper 6 at 8–9; *Ecto World*, IPR2024-01280, Paper 10 at 11.

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, Inc. v. Bardy Diagnostics, Inc.*, IPR2023-00381, Paper 7 at 19-20 (P.T.A.B. July 11, 2023); *Siemens Mobility*, IPR2024-00947, Paper 12 at 17-19 (“the Petition does not try to flesh out any material error the Examiner made”); *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”. *PowerOasis, Inc. v. T-Mobile USA, Inc.*, 522 F.3d 1299, 1304 (Fed. Cir. 2008); *Advanced Bionics*, IPR2019-01469, Paper 6 at 9; 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 ’758 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, *six* separate Examiners with specialized technical expertise properly assessed the patentability of Halozyme’s family of patents, including the ’758 patent. *See supra* Section III. Accordingly, it would be an inefficient use of the Board’s resources to revisit patentability of the ’758 patent. The Director should deny institution.

VI. 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 America¹⁶. 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

¹⁶ 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.

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 patent portfolio, which includes the '758 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 *thirteen* PGR Petitions Merck has filed back-to-back within the last seven 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 13 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 (thirteen 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 *six* separate Examiners who have properly assessed the patentability of the family of patents, including the '758 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; PGR2025-00053 EX1002, 454. Granting institution would amount to accepting that six 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 '758 patent claims are unpatentable. Merck's efforts to eliminate Halozyme's justly awarded patent portfolio warrants discretionary denial here

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 discretionary denial.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX PLLC

/Eldora L. Ellison/

Eldora L. Ellison, Ph.D.
Registration No. 39,967
Lead Attorney for Patent Owner

Date: June 17, 2025

1101 K Street, NW, 10th Floor
Washington, DC 20005
(202) 371-2600

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 13,991 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,

STERNE, KESSLER, GOLDSTEIN & FOX PLLC

/Eldora L. Ellison/

Eldora L. Ellison, Ph.D.
Registration No. 39,967
Lead Attorney for Patent Owner

Date: June 17, 2025

1101 K Street, NW, 10th Floor
Washington, DC 20005
(202) 371-2600

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, 2046-2048, 2050-2054, and 2056-2065 were served in their entireties on June 17, 2025, upon the following parties via electronic mail:

Jeffrey P. Kushan (Lead Counsel)
Leif Peterson (Back-up Counsel)
SIDLEY AUSTIN LLP
jkushan@sidley.com
leif.peterson@sidley.com
HalozymePGRs@sidley.com

Mark Stewart (Back-up Counsel)
MERCK SHARP & DOHME LLC
mark.stewart@merck.com

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX PLLC

/Eldora L. Ellison/

Eldora L. Ellison, Ph.D.
Registration No. 39,967
Lead Attorney for Patent Owner

Date: June 17, 2025

1101 K Street, NW, 10th Floor
Washington, DC 20005
(202) 371-2600