

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

APOTEX INC.,
Petitioner,
v.
AGIOS PHARMACEUTICALS, INC.,
Patent Owner.

Case IPR2026-00351
U.S. Patent No. 11,878,049
Issued: January 23, 2024

Title: Mitapivat Therapy and Modulators of Cytochrome P450

**PETITIONER'S OPPOSITION TO PATENT OWNER'S
BRIEF ON DISCRETIONARY DENIAL**

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I. Introduction

The purpose of Apotex's IPR petition is simple: to cancel flimsy patent claims that keep the price of Agios' mitapivat products, Pyrukynd[®] and Aqvesme[®], far too high and thus out of reach of patients who need them. At \$552 *per tablet* for Pyrukynd[®] and \$699 *per tablet* for Aqvesme[®], these treatments are cost-prohibitive for many patients suffering from hemolytic anemia ("HA"). Apotex's Petition is thus consistent with the President's emphasis on "encouraging the development of generic . . . alternatives to higher cost brand name prescription drugs . . . to harness competitive forces and increase access to affordable medicines." Ex. 1019 (Exec. Order) at 1; *see also id.* ("The American people deserve better. It is time . . . to deliver lower prescription drug prices[.]"). Despite Apotex's Petition strongly favoring the public interest, Agios requests the Director to discretionarily deny institution. But it is Agios' request that should be denied.

As an initial matter, Agios has no settled expectations whatsoever given that the challenged patent issued only 2.5 years ago. And while Agios invokes Section 325(d), Agios ignores the Examiner's material error in misreading the prior art disclosures, not to mention the fact that a key reference was never even considered by the Examiner. And apart from disregarding the strong merits of the present Petition, Agios cannot dispute that (1) no forum has ever adjudicated the merits of the challenged patent, (2) the one parallel litigation involving this patent does not

involve Apotex, and (3) such litigation is not expected to be tried until August **2029**, well after a final written decision. Lastly, the public interest in the Petition is strong given the public health implications, not to mention Apotex's robust US presence. For these reasons, Agios' request should be denied.

II. Background

The claims of U.S. Patent No. 11,878,049 (the "challenged patent") are directed to methods of treating HA. Those methods employ a combination of two drugs, mitapivat and a "moderate inducer" of the liver enzymes cytochrome P450 3A4 or cytochrome P450 3A5 (collectively, "CYP3A4/5"). Mitapivat is the combination's primary drug, known to treat HA when administered alone. Paper No. 2 ("Pet.") at 7. But mitapivat is not only administered alone. It may commonly be administered with a secondary drug, which may have a variety of therapeutic effects, Ex. 1001 ('049 patent) at Abstract, 7:19-33, including treating HA, Pet. at 8. Secondary drugs will sometimes act as CYP3A4/5 inducers. Ex. 1001 ('049 patent) at Abstract, 7:26-33. That is problematic because such inducers lead the CYP3A4/5 enzymes to metabolize mitapivat. *Id.* at 2:3-8.

The solution that Agios claims to have invented to address that problem is nothing new: adjusting the dose of mitapivat to account for its metabolism by the CYP3A4/5 enzymes. Pet. at 1. Indeed, the prior art taught each aspect of that purported invention. For starters, the art taught the compound mitapivat **and** using

that compound as a treatment for HA. *Id.* at 7. The art also taught formulations for HA, *id.* at 55, with Phase 2 trials confirming the dosing of mitapivat for that disease, *id.* at 26. The art additionally taught co-administering mitapivat with other drugs, with logical options including certain moderate CYP3A4 inducers, as the art also taught administration of those inducers to HA patients. *Id.* at 29–30.

Even the problem the inventors sought to solve—the metabolism of mitapivat by CYP3A4—was recognized by the prior art. *Id.* at 7. And that problem was by no means unique. *Id.* Many other drugs were known to be metabolized by that enzyme, and such metabolism was known to give rise to interactions with drugs that modulate CYP3A4 activity. *Id.* The art also taught a common way to combat reduced drug concentration due to increased metabolism from such interactions: increase the drug’s dose. *Id.* at 8. Together, the art taught the claimed invention, and at a minimum, rendered it obvious.

III. Legal Standards

The Director’s March 26, 2025 Memorandum outlined a non-exhaustive list of relevant considerations for discretionary denial including:

1. Whether the PTAB or another forum has already adjudicated the validity or patentability of the challenged patent claims;
2. Whether there have been changes in the law or new judicial precedent issued since issuance of the claims that may affect patentability;
3. The strength of the unpatentability challenge;
4. The extent of the petition’s reliance on expert testimony;

5. Settled expectations of the parties, such as the length of time the claims have been in force;
6. Compelling economic, public health, or national security interests; and
7. Any other considerations bearing on the Director's discretion.

Stewart Mem., *Interim Processes for PTAB Workload Management* (Mar. 26, 2025) ("Stewart Mem.") at 2–3; *see also Magnolia Med. Techs., Inc. v. Kurin, Inc.*, IPR2026-00097, Paper No. 17 at 2–9 (PTAB May 14, 2026) (precedential) (summarizing discretionary denial policy and factors). Those considerations add to those relating to overlap with parallel litigation, *see Apple Inc. v. Fintiv, Inc.*, IPR2020-00019, Paper No. 11 (PTAB Mar. 20, 2020) (precedential), and prior USPTO evaluation of the petition's art and arguments under 35 U.S.C. § 325(d), *see Advanced Bionics, LLC v. MED-EL Elektromedizinische Geräte GmbH*, IPR2019-01469, Paper No. 6 (PTAB Feb. 13, 2020) (precedential). As explained below, the pertinent factors above all weigh against Agios' request.

IV. Agios Has No Settled Expectations in Its 2.5-Year-Old Patent

As an initial matter, Agios has no settled expectations whatsoever with respect to the challenged patent. When a challenged patent has "not been in force for a significant period of time," the patent owner does not develop "strong settled expectations that favor discretionary denial." *Samsung Elecs. Co., Ltd. v. Wilus Inst. of Standards & Tech. Inc.*, IPR2025-00933, Paper No. 11 at 3 (PTAB Oct. 10, 2025). In fact, challenging such a patent "weigh[s] *against* discretionary denial."

Id. (emphasis added); *see also Tesla, Inc. v. Charge Fusion Techs., LLC*, IPR2025-00152, Paper No. 11 at 3 (PTAB June 12, 2025) (“Early challenges to patents favor robust, predictable patent rights and weigh against discretionary denial.”). Apotex brings such an early challenge, as the patent here issued roughly 2.5 years ago in January 2024. Ex. 1001 (’049 patent), Cover. The timing of Apotex’s challenge thus weighs strongly against discretionary denial. *Samsung*, IPR2025-00933, Paper No. 11 at 3; *Tesla*, IPR2025-00152, Paper No. 11 at 3.

V. Apotex’s New Art and Arguments and the Examiner’s Error Weigh Against Discretionary Denial

Citing Section 325(d), Agios asserts that Apotex now presents substantially the same art or arguments as presented during prosecution and fails to identify any material error by the Examiner. Paper No. 7 (“DDB”) at 5–13. The Director should reject these arguments in view of Apotex’s new art and arguments, coupled with the Examiner’s error, which together weigh against discretionary denial.

A. Apotex Presents Substantially Different Art and Arguments Than Those Considered During Prosecution

Apotex presents substantially different prior art and arguments from those previously presented and considered by the Examiner. As to prior art, Apotex relies upon a new reference, Dana-Farber, Ex. 1007, in each of its obviousness grounds. Pet. at 6, 16 n.4. That is why this case is distinguishable from *Ecto World*, where the petition only relied on art cited in an IDS. *See Motorola Mobility*

LLC v. Multifold Int'l Inc. PTE Ltd., IPR2025-00040, Paper No. 10 at 30–31 (PTAB May 21, 2025). Significantly, Agios does not dispute that Dana-Farber was not before the Examiner during prosecution. *See* DDB at 6–8.

Agios instead asserts that Dana-Farber is cumulative of Sizemore, Ex. 1004, arguing that both references provide similar teachings. DDB at 7–8. But Agios incorrectly views Dana-Farber’s teachings alone, rather than in the proper context of the other combination references. *See Apple Inc. v. SpaceTime3D, Inc.*, IPR2023-00344, Paper No. 11 at 15–18 (PTAB July 17, 2023) (determining prior art to be not cumulative, considering the combined teachings of the references).

Unlike Sizemore’s teachings, Dana-Farber’s teachings interrelate with the teachings of the other combination references as to a Phase 2 mitapivat clinical study. Pet. at 32–33, 45–46. Notably, Dana-Farber provides inclusion and exclusion criteria permitting enrollment of patients taking moderate CYP3A4 inducers, while Grace Abstract, Ex. 1009, and Grace Presentation, Ex. 1008 (collectively the “Grace References”) disclose positive results for study patients overall. *Id.* Together these references show that a POSA would have been able to co-administer a moderate CYP3A4 inducer with mitapivat and it would have been obvious to do so. *Id.* Those combined teachings, and Apotex’s arguments based upon them, are new.

For the foregoing reasons, the same art and arguments were not previously presented during prosecution. As such, *Advanced Bionics* part 1 is not satisfied, weighing against discretionary denial. See *ResMed, Inc. v. N.Y. Univ.*, IPR2022-00990, Paper No. 16 at 15–16 (PTAB Dec. 7, 2022) (declining to exercise discretionary denial based upon *Advanced Bionics* part 1, reasoning “there are no rejections based on the combination of references asserted here”).

B. The Examiner Materially Erred During Prosecution

Moreover, the Examiner materially erred by overlooking the critical teachings of two sets of prior art references when allowing the claims: (1) Sizemore and Dana-Farber and (2) the Grace References.

In the case of Sizemore and Dana-Farber, the Examiner overlooked their key disclosures of a combination of a moderate inducer of CYP3A4/5 with mitapivat to treat HA. See Ex. 1002 (’049 prosecution history, Aug. 30, 2023 Notice of Allowance) at 451–52 (“[T]here are no teaching[s] or suggestions within the prior art to combine a moderate inducer of [CYP3A4/5] with the claimed doses of mitapivat . . . to treat hemolytic anemia”); Pet. at 17. Specifically, those references teach exclusion of strong CYP3A4 inducers **but permit** administration of moderate CYP3A4 inducers when administering mitapivat. Pet. at 22–23, 29–33; § V.A, *supra*. Such teachings are bolstered by the positive results of the Grace References. Pet. at 29–33, 45; § V.A, *supra*. They are further bolstered by Dr.

Thirman’s testimony, supported by additional prior art, which provides examples of moderate CYP3A4 inducers that would have been suitable for administration with mitapivat. Pet. at 16 & n.4, 29–32; Ex. 1003 (Thirman Decl.) ¶¶ 92–97.

The record is clear as to why the Examiner overlooked the foregoing teachings. As to Dana-Farber, the reference was simply not before the Examiner. § V.A, *supra*; *Oticon Med. AB v. Cochlear Ltd.*, IPR2019-00975, Paper No. 15 at 19–20 (PTAB Oct. 16, 2019) (precedential as to sections II.B and II.C) (determining examiner erred where “[t]he Petition . . . presents different prior art than the Office was aware of”). As to Sizemore, the Examiner narrowly utilized it for its inactive ingredient disclosures, Ex. 2001 at 1281–83, thus disregarding the pertinent teachings regarding CYP3A4, Pet. at 22-23; *Samsung*, IPR2025-00933, Paper No. 11 at 3–4. Not surprisingly, Agios does not identify anywhere the Examiner addressed those pertinent teachings. See DDB at 5–13.

In the case of the Grace References, the Examiner overlooked their key teachings regarding positive clinical results, as evidenced by his failure to apply those references in any office action. See Ex. 1002 (’049 prosecution history); *Wybotics, Co. Ltd. v. Zodiac Pool Sys. LLC*, IPR2026-00158, Paper No. 12 at 2–3 (PTAB May 6, 2026) (determining examiner erred in evaluating reference found in IDS but not utilized in any office action). Indeed, Agios does not identify any office action where those references were used. See DDB at 11–12.

And of course the Examiner could not have considered Dr. Thirman's testimony, including his interpretation of these references and why they render the claims unpatentable, as it was not before the Examiner. *Therabody, Inc. v. Hyperice IP Subco, LLC*, PGR2024-00053, Paper No. 8 at 10–11 (PTAB Apr. 21, 2025) (relying upon expert declaration in determining examiner erred).

Unable to meaningfully challenge the foregoing errors, Agios resorts to a grab bag of meritless arguments. Agios first argues that Apotex improperly relied upon an incorrect inference from Sizemore rather than its explicit disclosure. DDB at 9–10. But Apotex's reliance upon Sizemore was proper. Not only does it adhere to guidance from a Director memorandum, Section VI, *infra*, but as shown by Dr. Thirman's testimony, Apotex's reading of the reference is correct, *id.*; Pet. at 22–23. Further, Agios' case is off point, as the issue with petitioner's arguments was not reliance on an inference, but conclusory expert testimony, *Samsung Elecs. Co., Ltd. v. Neodron Ltd.*, IPR2020-00334, Paper No. 11 at 10–12, 15–16 (PTAB July 10, 2020), which is plainly not an issue here, Section VI, *infra*.

Agios next asserts that Apotex cannot show error based upon Dana-Farber because it is cumulative of Sizemore, which the Examiner already considered. DDB at 11. But Dana-Farber is not cumulative of Sizemore given Dana-Farber's Phase 2 clinical study disclosures. § V.A, *supra*. And, in any event, the Examiner overlooked Sizemore's key teachings, as discussed above.

Agios further contends that Apotex cannot show error based upon the Grace References' teachings, because the Examiner located those teachings in the Agresta reference, Ex. 1005, and utilized them in an office action. DDB at 11–12. But the Grace References' teachings are not the same as Agresta's. Unlike Agresta, the Grace References teach positive Phase 2 clinical study results, which interrelate with Dana-Farber's teachings about the same study. § V.A, *supra*.

Agios lastly asserts that the additional prior art supporting Dr. Thirman's testimony cannot support material error because they do not form part of the asserted grounds. DDB at 12–13. As noted above and set forth in the Petition, these references provide examples of moderate CYP3A4 inducers that would have been suitable for administration with mitapivat. Pet. at 29–32; Ex. 1003 (Thirman Decl.) ¶¶ 92–97. Such evidence may show examiner error even if not part of the asserted grounds. *Therabody*, PGR2024-00053, Paper No. 8 at 10–11. Thus, Dr. Thirman's declaration and supporting references, not considered during prosecution, may be used to show that the Examiner erred for the reasons above.

For the foregoing reasons, the Examiner materially erred during prosecution and *Advanced Bionics* part 2 is not satisfied, weighing against discretionary denial.

VI. The Petition's Strong Merits and Appropriate Use of Expert Testimony Weigh Against Discretionary Denial

The Petition's strong merits weigh against discretionary denial. See Stewart Mem. at 2–3. Evidencing its strength, each ground is robustly supported by prior

art teaching every limitation of the challenged claims, Pet. at 20–40, 43–52, 53–56, including most centrally, the key limitation the Examiner incorrectly identified as missing: co-administration of mitapivat and a moderate CYP3A4/5 inducer (the “co-administration limitation”), Section V, *supra*. The obviousness grounds further demonstrate motivation to combine and reasonable expectation of success, with fulsome support by prior art and expert testimony. Pet. at 40–42, 52, 56–57.

Agios nonetheless argues that Apotex’s unpatentability challenge is “weak” and “fails to show a reasonable likelihood of prevailing as to any claim.” DDB at 13. In support of those assertions, Agios argues that all four grounds “impermissibly rel[y]” on Dr. Thirman’s testimony to supply the co-administration claim limitation. *Id.* at 14. Agios also dismisses Dr. Thirman’s testimony as “*ipse dixit*” and as running afoul of 37 C.F.R. § 42.104(b)(4). *Id.* at 13–15. Each of these arguments is unsupported by the facts and the law.

To be clear, the co-administration teaching arises from the asserted references, **not** from Dr. Thirman. Pet. at 23, 29–33. In Apotex’s anticipation ground, Sizemore teaches that mitapivat may be administered “alone or in combination with other therapies.” Ex. 1004 ¶ 0046; Pet. at 23. Sizemore then excludes certain “other therapies” such as strong CYP3A4 inducers. Ex. 1004 ¶ 0053. Dr. Thirman explains that a POSA would understand that this exclusion of **strong** inducers means that the “other therapies” do include **moderate** CYP3A4

inducers. Ex. 1003 ¶ 73. In Apotex’s obviousness grounds, the Dana-Farber trial criteria exclude only strong inducers, and Exs. 1010, 1013–16 name specific moderate CYP3A4 inducers applicable to mitapivat patients. Pet. at 29–33. Again, Dr. Thirman explains that a POSA would understand from those disclosures that Dana-Farber permits administration of mitapivat in combination with moderate CYP3A4 inducers. Ex. 1003 ¶¶ 73, 96, 100.

Significantly, Acting Director Stewart’s memorandum expressly permits the very type of testimony Dr. Thirman supplies. Stewart Mem., *Enforcement and Non-Waiver of 37 C.F.R. § 42.104(B)(4) and Permissible Uses of General Knowledge in Inter Partes Reviews* (July 31, 2025) at 1. The memorandum states that general knowledge, e.g., expert testimony, “may still be used in an IPR . . . to demonstrate the knowledge of a [POSA].” *Id.* The memorandum supplies the example of *Unification Technologies*, which it describes as affirming the use of expert testimony to show “how a skilled artisan would have understood a prior art reference’s disclosure as teaching a claim limitation.” *Id.* at 1–2 (citing *Unification Techs. LLC v. Micron Tech. Inc.*, 2024 WL 3738401, at *7 (Fed. Cir. Aug. 9, 2024)). That is exactly what Apotex uses Dr. Thirman’s testimony for here. Ex. 1003 ¶¶ 73, 96, 100; *see also Sage Prods., LLC v. Stewart*, 133 F.4th 1376, 1384 n.5 (Fed. Cir. 2025) (explaining that even without express words, a

reference anticipates if a skilled artisan “would understand the prior art to disclose the limitation”).

Agios also argues that Dr. Thirman’s declaration is “conclusory and warrants little weight” because it mirrors the petition. DDB at 15–16. But “[t]he relevant issue is not how similar an expert declaration is to a petition, but whether the declarant’s expert testimony is supported by evidence.” *Abbott Diabetes Care Inc. v. DexCom, Inc.*, IPR2024-00859, Paper No. 12 at 34 (PTAB Nov. 20, 2024); *see also Hum Indus. Tech., Inc. v. Amsted Rail Co., Inc.*, IPR2023-00540, Paper No. 10 at 37 (PTAB Aug. 11, 2023) (“If declaration testimony is supported sufficiently and, in turn, supports contentions in the Petition, we do not give it little to no weight simply because it is repeated in the Petition.”).

Far from conclusory, Dr. Thirman’s declaration, including his opinions pertinent to the co-administration limitation, is in fact robustly supported by documentary evidence. His declaration contains **over 100** citations to prior art exhibits. Ex. 1003 ¶¶ 67–175. And his opinions about co-administration specifically are likewise backed by many prior art citations. Ex. 1003 ¶¶ 73, 96, 100. And as for the issue of mirroring, it only makes sense that the Petition and declaration align, as the arguments in the Petition should be supported by, *inter alia*, Dr. Thirman’s expert declaration and its robust citations.

Moreover, Agios’ cited cases are off-point and do not support its arguments that Apotex’s petition or Dr. Thirman’s declaration is deficient. In those cases, the petition or the expert’s opinions lacked sufficient support or explanation. *Xerox Corp. v. Bytemark, Inc.*, IPR2022-00624, Paper No. 9 at 15 (PTAB Aug. 24, 2022) (describing declaration as the “only evidence in support of [petitioner’s] assertion”); *TikTok Inc. v. Ntech Props., Inc.*, IPR2024-01339, Paper No. 9 at 15–16 (PTAB Feb. 25, 2025) (determining declaration lacked “supporting reasoning or evidence”); *CyberSecure IPS, LLC v. Network Integrity Sys., Inc.*, IPR2025-01441, Paper No. 18 at 2–3 (PTAB May 26, 2026) (determining that petitioner “does not explain sufficiently” its arguments). Here, by contrast, the Petition and Dr. Thirman’s opinions are supported by references and explanation as to what a POSA would understand them to teach, as discussed above.

For the foregoing reasons, Agios’ merits theory fails on the facts and on the law, such that discretionary denial is unwarranted.

VII. No Forum Has Adjudicated the Validity of the Challenged Patent and No Parallel Litigation Exists Between the Parties, Weighing Against Discretionary Denial

Turning to litigation involving the challenged patent, no forum has adjudicated its validity, which weighs against discretionary denial. *See* Stewart Mem. at 2–3. And no parallel litigation between Agios and Apotex currently exists, which likewise weighs against discretionary denial. *Multi-Color Corp. v.*

Brook & Whittle Ltd., PGR2025-00025, Paper No. 10 at 2 (PTAB July 16, 2025) (precedential). Agios nonetheless contends that this IPR is not an “alternative to litigation,” but will overlap with (1) a **future** Hatch-Waxman case between the parties and (2) a recently-filed case **not** involving Apotex. DDB at 16–19. But this IPR **is** a true alternative to litigation, given the lack of a prior or present litigation involving Apotex. Agios’ meritless, speculative contentions as to future litigation or litigation involving another party simply do not warrant discretionary denial.

As for future litigation against Apotex, Agios fails to cite a single case exercising discretionary denial based upon future litigation. Also notably absent from its brief is an analysis of the *Fintiv* factors, the proper framework for evaluating parallel litigation, IPR2020-00019, Paper No. 11 at 5–6. That is not surprising because *Fintiv* assumes the existence of pending litigation. Denial is thus unwarranted, as no litigation against Apotex has been filed. For the same reason, Agios’ reliance on *Magnolia* is unavailing, DDB at 16, 18, 19, because that case identifies “co-pending litigation” with overlapping prior art as a “sign” that an IPR “is not functioning as a litigation alternative.” IPR2026-00097, Paper No. 17 at 3–4. There is no such sign here, because there is no such co-pending litigation.

Agios nonetheless contends that litigation is imminent because Apotex will pursue a generic mitapivat product, and that will involve filing an abbreviated new drug application (“ANDA”) with a paragraph IV certification that will trigger

Hatch-Waxman litigation. DDB at 17–18. But filing a paragraph IV certification does not automatically “trigger” litigation; it is up to Agios if and when to sue. As for the timing of ANDA filing, Agios presents no evidence of when that may occur, rendering its contentions speculative. Agios suggests that Apotex could delay its ANDA filing until after institution to avoid discretionary denial. DDB at 18 n.7. But any such delay would be counterproductive, as it would in turn delay Apotex’s ability to bring its generic mitapivat product to market.

Agios asserts that the IPR will not avoid or simplify the parties’ disputes, because Apotex (1) raises defenses that cannot be resolved here and (2) has not agreed to a *Sotera* stipulation. DDB at 18–19. That is nonsense. Irrespective of the outcome, this IPR will simplify or eliminate future prior art-based disputes involving this patent. As for potential non-prior art disputes, they could be appropriately addressed in any potential district court litigation. *See Ingenico Inc. v. IOENGINE, LLC*, 136 F.4th 1354, 1367 (Fed. Cir. 2025) (holding that petitioners are not estopped from raising “different grounds that could not be raised during an IPR.”); *see also* 35 U.S.C. § 315(e)(2). And a *Sotera* stipulation would be premature given the absence of co-pending litigation against Apotex.

Lastly, Agios’ arguments about recently-filed litigation involving another generic, i.e., Annora, are also meritless. *See* DDB at 19; Ex. 2007. Such litigation does not involve Apotex and Agios again fails to address the *Fintiv* factors.

Instead, Agios merely asserts that institution would “risk inconsistent outcomes” and “waste the Board’s resources” in view of the Annora litigation. *See* DDB at 19. But there is no such risk or waste of resources given that Agios filed its litigation against Annora just three months ago on May 26, 2026, and Annora has not even filed its answer (and no trial date has been set). Ex. 1020 (Docket Report) at 1, 4. Looking at the 39-month median time to bench trial for Judge Connolly, *id.* at 1; Ex. 1021 (Connolly Milestones) at 2, a trial would not be expected until August 2029. That timing is far after the projected final written decision date of November 2027. Such timing “reduc[es] the risk of inconsistent outcomes or significant duplication of efforts.” *Samsung Elecs. Co., Ltd. v. CM HK Ltd.*, IPR2025-01023, Paper No. 12 at 2 (PTAB Oct. 17, 2025).

For the foregoing reasons, discretionary denial is unwarranted based upon future litigation or the Annora litigation.

VIII. The Public Interest Weighs Against Discretionary Denial

A. Apotex’s Petition Aims to Promote Public Health by Increasing Access to Generic Mitapivat for HA Patients

Apotex’s Petition serves the public interest, as it will facilitate access to generic mitapivat for patients suffering from HA. As Agios notes, HA is a devastating condition. DDB at 4. But the cost of its Pyrukynd[®] product is “out of reach of many” HA patients. Ex. 1022 (Wills) at 5. Agios’ other product, Aqvesme[®], is even more expensive. The “yearly price[s]” of Pyrukynd[®] and

Aqvesme[®] are about \$335,000 and \$425,000, respectively. Ex. 1023 (Mahatole) at 2; *see also* Ex. 1024 (Agiros Info.) at 1 (Agiros document listing average per-tablet wholesale prices of Pyrukynd[®] and Aqvesme[®] as \$552 and \$699, respectively); Ex. 1025 (Agiros Vt.) (Agiros website linking to Ex. 1024).¹ Those prices are higher than the prices for nearly all other products Agios has identified as being in the “same therapeutic class.” Ex. 1024 (Agiros Info.) at 1–3.

Apotex’s goal in filing its Petition is to cancel flimsy patent claims that keep the price of these medications artificially high, and thus facilitate access for HA patients. Indeed, Apotex’s mission as a company is to bring lower-cost drugs to patients. Ex. 1026 (Apotex) (“We improve everyday access to affordable, innovative medicines and health products for patients and consumers worldwide.”).

And this mission is fully consistent with the President’s goal of ensuring access to drugs such as Pyrukynd[®] and Aqvesme[®] for the patients who need them. To wit, the President has “encourage[ed] the development of generic . . . alternatives to higher cost brand name prescription drugs . . . to harness

¹ For a pharmacy to make a profit, the retail price would be even **higher** than the wholesale price. And even if health insurance lowers the retail price for some patients, the price would still be relatively higher than other drugs in the same class, and in any event, many patients lack health insurance.

competitive forces and increase access to affordable medicines.” Ex. 1019 (Exec. Order) at 1. And he has further noted that “[i]t is the policy of the United States that . . . intellectual property protections . . . are optimized to provide access to prescription drugs at lower costs to American patients and taxpayers.” *Id.* at 2. The present IPR represents such an optimization, ensuring that weak patent claims like those challenged here are cancelled to ensure lower-cost drugs for patients.

B. Apotex Has a Robust US Presence

Apart from this petition advancing public health, it is also in the public interest given Apotex’s substantial US footprint. While headquartered in Canada, Apotex is a top 10 player in the US generic pharmaceutical market and maintains a very robust US presence. Ex. 1027 (Baeder Decl.) ¶ 2. That presence includes about 200 US-based employees and two key sites for its US operations: Weston, Florida and Indianapolis, Indiana. *Id.* In Weston Apotex maintains its US headquarters, which performs a variety of functions including commercial operations, sales, marketing, regulatory affairs, and government affairs. *Id.* ¶ 3. In Indianapolis Apotex maintains a 156,000-square-foot pharmaceutical distribution facility responsible for supplying its many life-saving products to patients throughout the US. *Id.* ¶ 4. Those products include over 130 product families in fields such as oncology, neurology, hematology, ophthalmology, cardiovascular, respiratory, and anti-infectives. *Id.* It is also worth noting that in April 2026,

Apotex expanded its US presence via a partnership with Halo to manufacture sterile injectable pharmaceuticals in Whippany, NJ. *Id.* ¶ 5.

C. Agios’ Investment and Size Do Not Support Discretionary Denial

Agios asserts that its domestic investment and “small size” weigh in favor of discretionary denial. DDB at 19–20. Neither assertion supports discretionary denial. As for its domestic investment, as noted in Section VIII.B above, Apotex has likewise invested heavily in the US, maintaining a very robust US presence, rendering this consideration neutral. As for Agios being a “small” company, that characterization is belied by the facts. In its brief, Agios artfully claims to have “approximately 500 people,” *id.*, while its declaration plainly states that it has 509 employees, Ex. 2008 (Washburn Decl.) ¶ 4. Such a business is not “small.” According to the pertinent standard applied by the Patent Office, a small business must “not exceed 500 persons.” *See* 13 C.F.R. § 121.802; Squires Mem., *Additional Discretionary Institution Considerations - U.S. Manufacturing and Small Business Use of AIA Proceedings* (Mar. 11, 2026) at 3 (stating that the Director will rely on the size standards in 13 C.F.R. § 121.801-05). For these reasons, Agios’ investment and size do not weigh in favor of discretionary denial.

IX. Conclusion

For the foregoing reasons, the Director should not discretionarily deny institution of *inter partes* review.

CERTIFICATE OF SERVICE

I hereby certify that on August 26, 2026, I caused a true and correct copy of the foregoing PETITIONER'S OPPOSITION TO PATENT OWNER'S BRIEF ON DISCRETIONARY DENIAL to be served by electronic mail at the following addresses:

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