

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

UNITED THERAPEUTICS CORPORATION,
Petitioner,

v.

ACTELION PHARMACEUTICALS, LTD.,
Patent Owner.

Case IPR2025-01139
U.S. Patent No. 8,268,847

**PETITIONER'S RESPONSE TO PATENT OWNER'S
REQUEST FOR DISCRETIONARY DENIAL**

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I. INTRODUCTION

Actelion's request for discretionary denial should be rejected. Three independent Actelion-induced material errors during prosecution warrant review on the merits. Further, UTC filed its Petition as soon as practicable, before Actelion could have any alleged "settled expectations."

First, the Office erred by ignoring that Actelion's narrow alleged "unexpected results" were grossly disproportionate to the broad scope of the '847 patent's claims. If the Office had properly analyzed the results, the claims would not have issued.

Second, the Office's belief that certain results were "unexpected" rests solely on Actelion's one-sided and incomplete characterization of the prior art. *See* EX1002, 205-06, 238-39. When the teachings of the prior art (*e.g.*, Keyser) are accurately understood (EX1003, 214), the results were expected and cannot rebut *prima facie* obviousness.

Third, the claimed invention was already disclosed—and dedicated to the public—by Actelion's own publication, Bolli. The record contains no indication that the examiner considered whether the person of ordinary skill in the art (POSA) would have understood Bolli to describe the use of macitentan with tadalafil or sildenafil—blockbuster PDE5 inhibitors then widely used as vasodilators for vasoconstrictive diseases. *See* Pet. 18; EX1003, 263-64. The only appropriate outcome on these unique facts is to institute *inter partes* review and correct the

material errors that occurred during prosecution of the '847 patent.

“**Settled expectations**” that the patent would remain in force do not exist where Actelion *repeatedly* misled the Office during prosecution about what qualified as prior art, giving rise to material errors. *Infra* pp. 16. By attempting to salvage the patent via reexamination, Actelion conceded that its patent was weak and would likely be challenged.

There are no time-based settled expectations either. UTC brought its IPR challenge as early as practicable—even earlier than district court litigation would be permitted under the Hatch-Waxman Act, which was specifically designed to encourage *early* litigation of patents involving approved drugs. In fact, Actelion’s decision to list the '847 patent in the Orange Book indicates that it *expected* validity challenges upon Paragraph IV notice letter receipt. Because Actelion had no justifiable expectations that the '847 patent would not be challenged, and because UTC petitioned for *inter partes* review as early as practicable, the request for discretionary denial should be denied.

The Office’s *ultra vires* “settled expectations” rule also violates due process and any application of “discretion” on this record is arbitrary and capricious.

II. ARGUMENT

The Office should not exercise its discretion to deny institution. The Petition provides the first opportunity to correct material errors committed during

prosecution. Allowing it to stand—as a matter of discretion—impedes rather than “promote[s] the Progress of Science and useful Arts” by insulating weak blocking patents from scrutiny. U.S. Const. art. I, § 8, cl. 8. Contrary to Actelion’s assertions, the Petition advances, *inter alia*, three independent dispositive grounds that have never been considered and which justify cancelling all 57 claims. Moreover, there are no parallel proceedings posing a risk of inconsistent outcomes or duplication of efforts. Actelion disregards this factor that weighs in UTC’s favor. *See Belden Inc. v. Commscope, Inc.*, IPR2025-00833, Paper 13 at 2 (Director Sept. 12, 2025) (explaining that where final written decision will issue before district court trial occurs “counsel[s] against discretionary denial”).

A. The Office materially erred.

Discretionary denial should be rejected because the Office materially erred in allowing the challenged claims. *See Xencor, Inc. v. Merus N.V.*, IPR2025-00604, Paper 12 at 2-3 (July 17, 2025) (denying discretionary denial request where examiner overlooked material disclosure in prior art); *Advanced Bionics v. MED-EL Elektromedizinische Geräte GmbH*, IPR2019-01469, Paper 6 at 8, n.9 (Feb. 13, 2020) (precedential) (material error includes “misapprehending or overlooking specific teachings of the relevant prior art where those teachings impact patentability”).

The Office has never considered UTC’s arguments (supported by expert testimony) that: (1) Actelion’s alleged unexpected results are not commensurate in

scope with the '847 patent claims; (2) the POSA would have known macitentan and a PDE5 inhibitor to be therapeutically complementary; and (3) post-priority date publications cannot change the scope and content of the prior art available to the POSA as of the priority date. Pet. § V.B.8. These errors are material because the examiner relied on unexpected results alone to overcome *prima facie* obviousness.

1. Failure to analyze whether the scope of the claims is commensurate to “unexpected” results.

The Office first erred by failing to even acknowledge the requirement, let alone analyze, that the evidence of alleged unexpected results must be commensurate with the full scope of the claims. *See* Pet. 45-49. Actelion’s disclosure—the sole source of the supposed supporting data—covers only narrow examples, not the thousands of embodiments encompassed by the claims. *Id.* at 46-49. As the Federal Circuit has held, unexpected results must provide a “basis to support the conclusion that other embodiments ... will behave in the same manner.” *In re Huai-Hung Kao*, 639 F.3d 1057, 1068 (Fed. Cir. 2011); *see also* Pet. 45-49. No such basis exists here.

The '847 patent’s written description reports very limited data. Examples 1-3 address combinations of macitentan with one of only two tested PDE5 inhibitors (sildenafil or tadalafil), in one species (rats), each at only a single dose (measured in mg/kg), administered once and simultaneously. *See* Pet. 45-49. The claims, however, cover thousands of permutations—*any* PDE5 inhibitor in *any* animal or human at *any* dose in combination with *any* dose of macitentan, all administered *once, few, or*

many times, and administered *simultaneously, separately, or over a period of time*. See *id.* The data does not support the claims’ overwhelming breadth.

Despite the limited nature of the data, the Office failed to analyze whether the disclosed results were commensurate with the claims. MPEP § 716.02(d) (“the showing of unexpected results *must be reviewed* to see if the results occur over the entire claimed range”) (emphasis added); *Kao*, 639 F.3d at 1068; *see also* Pet. 45-49. Under the proper legal analysis, the Board would have determined that the specification’s narrow examples are not even close to commensurate with the sweeping scope of the claims and rejected them. *See, e.g.*, Pet. 46-49; *Application of Lindner*, 457 F.2d 506, 508 (C.C.P.A. 1972) (affirming obviousness where limited testing did not support “great number and variety of compositions included by the claims”).

Actelion’s attempt to recast the broad ’847 patent’s claims as commensurate with the patent’s limited data, citing *Rambus*, fails. While “objective evidence ... for every potential embodiment of the claim” may not be required, that is a far cry from the present circumstance where there is no “objective evidence” commensurate with the full scope of *any* claim. *Compare Rambus Inc. v. Rea*, 731 F.3d 1248, 1257 (Fed. Cir. 2013), *with* Pet. 49 (citing *Genetics Inst., LLC v. Novartis Vaccines & Diagnostics, Inc.*, 655 F.3d 1291, 1308 (Fed. Cir. 2011) and *In re Peterson*, 315 F.3d 1325, 1331 (Fed. Cir. 2003)). For objective evidence of secondary considerations to even be “relevant” there “*must* be a nexus between the merits of the claimed invention

and the objective evidence.” *Bayer Pharma Aktiengesellschaft v. Mylan Pharms. Inc.*, No. 2023-2434, 2025 WL 2698408 (Fed. Cir. Sept. 23, 2025) (emphasis added) (citations omitted). Notably, Actelion fails to assert that unexpected results support any specific claim.

Actelion cites *Kao* and *Rambus* for the proposition that objective evidence “need only be ‘reasonably commensurate with the scope of the claims.’” DD Req. 17. But *Kao* makes clear that “reasonably commensurate” requires both an unexpected result *and* disclosure of “an adequate basis to support the conclusion that other embodiments falling within the claim will behave in the same manner.” *Kao*, 639 F.3d at 1068. Actelion has not met this standard. The specification provides no basis, and Actelion has offered none, to conclude that the multitude of other claimed embodiments would “behave in the same manner” as the narrow, one-time rat studies of macitentan with sildenafil or tadalafil. *See* Pet. 45-49.

With respect to UTC’s cases, Actelion argues they concern only numerical ranges and that no ranges appear in the prior art. Neither argument has merit.

First, the Federal Circuit case law cited in the Petition stands for the well-established rule that unexpected results cannot support nonobviousness of patent claims when the results are “plainly disproportionate to the scope of the claims.” *Genetics Inst.*, 655 F.3d at 1308. Actelion does not—and cannot—point to any aspect of UTC’s cited cases that would limit their applicability only to claims and prior

art involving numerical ranges. This fictional distinction fails, as does Actelion's attempt to distinguish numerical ranges from claimed genera such as classes of pharmaceutically active ingredients (*e.g.*, PDE5 inhibitors). Whether a claim defines a numerical range or a large genus of subgenera or discrete species, the full breadth of that claim must be proportional to the purportedly unexpected results. *See Lindner*, 457 F.2d at 508 (affirming obviousness of claims "covering mixtures of numerous compounds" because there was "no 'adequate basis for reasonably concluding that the great number and variety of compositions included by the claims would behave in the same manner as the [single] tested composition.'" (citation omitted); *Application of Greenfield*, 571 F.2d 1185, 1189 (C.C.P.A. 1978) (similar).

Second, Actelion is simply wrong that "there is no range ... in the prior art." DD Req. 17. UTC cites prior art references that expressly teach amounts and ranges of macitentan doses, tadalafil doses, and sildenafil doses falling within or overlapping the ranges recited in claims 23-37 and 43-57 of the '847 patent. *See, e.g.*, Pet. 27-29 (noting that Bolli discloses "dosages of 0.1-50 mg/kg body weight per day"); *see also id.*, 43-44, 67-69 (noting that Keyser discloses "[d]aily amounts for ET_A antagonists will be in the range of 5 mg to 125 mg"). Demonstrably false assertions cannot be the basis to grant discretionary denial.

2. Flawed reliance upon Actelion's mischaracterization of the POSA's knowledge and expectations.

The Office also materially erred by relying on post-priority art to find that the

POSA would have understood macitentan to be insufficiently selective for ET_A receptors. Actelion repeats that farce here. DD Req. 13. As the Petition states, the prior art record before the Office shows that as of the priority date the POSA would have understood macitentan to be selective for ET_A receptors. Pet. § V.B.8.

a) Actelion mischaracterized Keyser.

The Office materially erred by adopting Actelion's mischaracterization of Keyser. Pet. 55; *see* EX1002, 205-06, 238-39. Keyser explicitly teaches that “[s]elective compounds for ET_A antagonists according to this invention, *in general*, *should* display a relative receptor binding ratio of *at least 100*, ... *if* they are going to act at only one of the receptor subtypes, *e.g.* ET_A.” EX1005, [059] (emphases added). The only “nonselective” antagonist Keyser specifically discusses is bosentan, with a selectivity ratio of 20: “bosentan ... has an ET_A:ET_B *selectivity ratio of 20* and is classified as a nonselective antagonist. ... Therefore, for the purposes of this invention, *bosentan or any other non-specific endothelin receptor antagonist would not represent an ET_A-specific antagonist.*” EX1005, [060] (emphasis added). Actelion does not dispute that macitentan has a ratio of 683. DD Req. 19-20. Therefore the POSA would understand macitentan to be selective as of the priority date, and it was error to find otherwise.

Instead of accepting Keyser's express preference for any compound with an *in vitro* selectivity ratio above 100, Actelion offers attorney argument that the POSA

would infer a litigation-inspired, brightline rule selectivity cutoff from Tables 2-3—which neither Actelion nor the examiner cited during prosecution. Not so. For Table 2, Keyser cites a paper by Cheng et al. *See* EX1005, [063]. The POSA would not infer a cutoff from Cheng’s data, however, when Keyser—knowing Cheng’s data—*nevertheless* taught combinations with compounds having a ratio of 100 or higher. Further, Keyser’s selectivity guidance is based on *in vitro* selectivity ratios. *E.g.*, EX1005, [059]; EX1013, ¶ 368. By contrast, Table 3 recites endothelin receptor antagonists that “have undergone *clinical* development”—*i.e.*, that were tested in humans (*in vivo*). The POSA would not ignore Keyser’s *in vitro* teaching based on an unjustified inference from a table of external *in vivo* data. *Id.*

Keyser’s disclosure certainly falls far short of discouraging, let alone precluding, or “explicitly teach[ing] away” (EX1002, 205) from the use of macitentan in combinations. *See Meiresonne v. Google, Inc.*, 849 F.3d 1379, 1382 (Fed. Cir. 2017) (“A reference that ‘merely expresses a general preference for an alternative invention but does not criticize, discredit, or otherwise discourage investigation into’ the claimed invention does not teach away.”) (citation omitted). The POSA would not be discouraged from using macitentan when it has an *in vitro* selectivity ratio greater than bosentan and the “general” lower threshold ratio of 100. Actelion’s argument that an arbitrary tenfold higher selectivity ratio of at least 1000 would be “require[ed]” is baseless and not supported by Keyser’s explicit disclosure. DD Req.

19-20. The factual record, as explained by Dr. Shebuski, flatly rebuts Actelion’s attorney argument. *See* EX1013, ¶¶ 358-374.

b) Impermissible post-priority “expectation” evidence.

The Office legally erred by relying on post-prior art publications to inform the POSA’s expectation. *See, e.g.,* Pet. 52-53. The Board erroneously adopted Actelion’s post-priority argument during prosecution, concluding that the POSA “*would not have expected* the administration of a *nonselective* ET antagonist, such as the compound of formula (I), and a PDE5 antagonist to have produced the synergistic results provided in Appellant’s Specification.” EX1006, 464-65 (emphasis added). That was legal error. The law does not permit such post-priority art to retroactively infect the mind of the POSA. *See Forest Labs., v. Sigmapharm Labs., LLC*, 918 F.3d 928, 937 (Fed. Cir. 2019) (“the results must be ‘unexpected by one of ordinary skill in the art *at the time of [the] application.*’”) (emphasis added)); *Janssen Pharms., Inc. v. Teva Pharms. USA, Inc.*, 97 F.4th 915, 934-35 (Fed. Cir. 2024).

Actelion’s motion relies on false assertions. Actelion argues the Board “relied on *Keyser*” for the “POSA’s expectations” at the time of the invention. DD Req. 18 (emphasis added) (citing EX1006, 464-65). That is wrong. Actelion submitted non-prior-art-publications Iglarz and Bolli 2012 to argue for unexpected results in order to rebut *prima facie* obviousness, telling the Office that the POSA “would not have any *expectation* of success in the use of Macitentan” because *post-priority* references

Iglarz and Bolli 2012 establish that macitentan is “a dual ET_A-ET_B receptor antagonist.” EX1006, 386 (emphasis added). Actelion did not rely on Keyser for that point.

Actelion’s only argument is that “[i]t is well established that the ‘propert[ies] of a claimed compound need not be fully recognized as of the filing date’” to support unexpected results. DD Req. 18. But that bald statement of law is only half the story. The only reason Actelion argued that selectivity was relevant to “unexpected results” was to retroactively alter the POSA’s “expectation.” Even assuming “that macitentan is a dual antagonist, which is an inherent property of the compound” (DD Req. 18), as a matter of law, *post-priority* art cannot alter the POSA’s expectation as of the priority date. Thus, the POSA would understand a relative receptor binding ratio of “at least 100” was sufficiently selective. EX1005, [059].

To be clear, whether macitentan is “nonselective” is *only* relevant to the POSA’s “expectation” in combining it with a PDE5 inhibitor. Ultimately, Actelion’s logic implodes, admitting that the POSA “combin[ing] a dual antagonist with a PDE5 inhibitor ... would have *expected* inferior results.” DD Req. 18 (emphasis added). Evident by the Office’s reliance on post-priority art, the POSA would have no reason to consider macitentan “nonselective” or a “dual antagonist” as of the priority date. *Supra* pp. 8-9 (comparing macitentan’s 683 ratio to Keyser’s selectivity ratio “of at least 100”). The Office’s *post-priority* and *post-hoc* understanding of what the POSA would have expected as of the relevant date is clear material error.

B. Unique art and arguments present a strong case of unpatentability.

UTC's Petition includes arguments and prior art that the Office has not yet considered, weighing against discretionary denial.

1. No consideration of anticipation by Bolli.

The Office has never considered that Bolli alone, as understood by the POSA, anticipates the claims of the '847 patent. Bolli teaches that macitentan is an effective compound in "combination" with "vasodilators" for the treatment of diseases wherein vasoconstriction is involved. Pet. 17-19. The POSA would understand that vasodilators included PDE5 inhibitors such as sildenafil (*e.g.*, Viagra[®]), which were well-known vasodilators that were *already* being used to treat vasoconstriction diseases like ED or hypertension. *Id.* In view of Bolli's explicit instruction to use macitentan "combined with" vasodilators for diseases such as ED or hypertension, it would be immediately apparent to the POSA to combine macitentan with sildenafil and tadalafil. *Id.* Had the Office considered how the POSA would understand Bolli as of the priority date, it would have found the claims anticipated.

Actelion admits that the Office "did not explicitly consider anticipation." DD Req. 16. This confirms the error. Trying to sidestep it, Actelion argues that during prosecution, the examiner read a sentence from Bolli that UTC cited in the Petition. *Id.* But this argument misses the point. Neither the Board nor the examiner did more than look for explicit disclosure of a PDE5 inhibitor. *Cf. In re Bond*, 910 F.2d 831,

832 (Fed. Cir. 1990) (anticipation does not require *ipsis verbis* disclosure). The Office never considered whether the POSA would understand the term “vasodilator” to include PDE5 inhibitors or addressed whether a blockbuster PDE5 inhibitor like Viagra[®] would have been “immediately apparent” to the POSA treating ED. Rather, in reiterating the examiner’s obviousness rejection based on Bolli and Keyser, the Board merely found that Bolli’s black letter text “does not *specifically* teach that the ‘other therapeutics’ may be PDE5 inhibitors.” EX1006, 460-61 (emphasis added). The Board did not determine whether the POSA reading Bolli would *already understand* PDE5 inhibitors to be vasodilators.

It is undisputed that Bolli explicitly directs the POSA to “combin[e]” macitentan with a vasodilator. Pet. 17-18; DD Req. 12; EX1004, 18. All that remains is what the POSA would have understood from “vasodilators” within the context of Bolli—an essential inquiry the examiner failed to undertake. This does not require combining “multiple references.” DD Req. 19. As a matter of law, “[g]eneral knowledge may still be used in an IPR to ... demonstrate the knowledge of a person having ordinary skill in the art.” Memorandum, Acting Dir. Stewart, *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 1-2 (citing *Unification Techs. LLC v. Micron Tech., Inc.*, 2024 WL 3738401, at *7 (Fed. Cir. Aug. 9, 2024)). As Dr. Shebuski explained, the Petition’s discussion of blockbuster drugs in Ground 1

is evidence of the state of the art and corroboration for what the POSA—or even a layperson—would have already known. Pet. 18-19; *In re Graves*, 69 F.3d 1147, 1152 (Fed. Cir. 1995) (“A reference anticipates a claim if it discloses the claimed invention ‘such that a skilled artisan could take its teachings *in combination with his own knowledge of the particular art and be in possession of the invention.*’” (emphasis in original)). Actelion asks the Office to cover its eyes and pretend the POSA is unaware of two of the largest blockbuster vasodilators—and drugs—ever to exist. The POSA is not so blind. The Board should consider anticipation for the first time.

2. No consideration of Hoeper or Morice.

The Office did not analyze or rely upon Hoeper or Morice, material references describing human studies involving specific dosing of bosentan with sildenafil (Hoeper) and tadalafil (Morice). UTC’s Petition explains that the POSA would have reason to replace bosentan from Hoeper and Morice with macitentan as taught by Bolli—yielding the obvious combination of a PDE5 inhibitor with macitentan. That Hoeper and Morice were cited in an IDS is insufficient to support discretionary denial, because they were overlooked and not substantively addressed. *See Motorola Mobility et al. v. Multifold Int’l Inc.*, IPR2025-00040, Paper 10 at 32-34 (May 21, 2025) (declining to exercise discretion where prior art asserted in the Petition was “not ‘addressed in any way by the examiner’ or ‘considered substantively’”).

Actelion’s arguments regarding Morice and Hoeper fall flat. First, UTC did

not argue that Hoeper reports administration to “one patient.” DD Req. 11. Hoeper states “[t]he combination of bosentan and sildenafil was surprisingly well tolerated by *all patients* and resulted in marked clinical improvement,” and reported that 6 out of 9 patients reached the pre-defined treatment goals. EX1009, 3 (emphasis added). Second, Actelion wrongly asserts that “Morice and Hoeper add nothing new to what Keyser disclosed.” DD Req. 11. This is plainly false. According to Actelion, Keyser “teaches away” from bosentan and mentions (but does not describe) a study combining bosentan with sildenafil that was terminated due to drug interaction problems. DD Req. 11. By contrast, Morice and Hoeper present human data suggesting safe and effective treatment with combinations of bosentan and sildenafil or tadalafil. *See* EX1009, 3. Their studies were not terminated and in fact produced promising results that would have led the POSA to investigate bosentan and other endothelin receptor antagonists such as macitentan. *See* EX1013, ¶ 363. Further, Actelion’s reliance on a Canadian court’s consideration of Hoeper (DD Req. 15) is meritless and contrary to the Federal Circuit’s explicit “[c]aution” regarding relying on foreign proceedings. *See Heidelberg Druckmaschinen AG v. Hantscho Commercial Prods., Inc.*, 21 F.3d 1068, 1072 n.2 (Fed. Cir. 1994).

Lastly, Actelion asserts that one cherry-picked comment from Dr. Shebuski’s Declaration is unsupported and cumulative to Keyser. DD Req. 20. Wrong again. Dr. Shebuski has decades of experience and provided a fulsome explanation of the

ET_A and ET_B pathways and the effects of inhibiting each to explain why the POSA would have known targeting both pathways would produce complementary and/or synergistic effects. *See* EX1013, ¶¶ 26-34.

C. There are no “settled expectations” favoring discretionary denial.

Contrary to Actelion’s arguments, settled expectations do not justify discretionary denial. First, Actelion does not deserve the benefit of settled expectations where its misleading conduct contributed to the errors leading to the issuance of the ’847 patent. Second, UTC had no reason to monitor—much less challenge—the ’847 patent before Actelion listed its patent in the Orange Book for OPSYNVI® on April 18, 2024. Fairness compels consideration of UTC’s Petition on the merits.

Actelion’s prosecution strategy and related errors. Actelion’s actions before the Office undermine its purported expectations. For example, claims 1-11 were originally granted because Actelion incorrectly claimed—and the examiner mistakenly accepted—that a key prior art reference (Bolli) did not qualify as prior art. Pet. 3; EX1002, 239 (“Applicants *again confirm* that Bolli et al. does not qualify as prior art[.]” (emphasis added)); DD Req. 11. Actelion took no action to fix the error it created for nearly *five years*, and that time should not accrue to Actelion’s favor. Similarly, Actelion misled the Board during *ex parte* prosecution of a separate application to establish allowance of its *prima facie* obvious claims by misrepresenting what the POSA would have understood as of the relevant date. *Supra* pp. 8-11. Those

representations are false and caused material error. *Supra* pp. 3-11. Despite this, Actelion strategically chose not to raise any issue with the '847 patent until it achieved its desired result in the '148 application. This strategic prosecution led to the allowance of 46 reexamination claims that have no nexus to the alleged “unexpected” results. Actelion’s repeated misconduct ought to deprive Actelion of any “settled expectation” of enforceability. Actelion relies heavily on the age of its patent, but there is no basis for “settled” expectations on the unique facts at issue here.

Expectations are different in pharmaceutical litigation. The Hatch-Waxman Act incentivizes pharmaceutical patent litigation earlier than other fields, providing standing to sue even before a putative competitor launches its product. *See, e.g., Caraco Pharm. Labs., Ltd. v. Novo Nordisk A/S*, 566 U.S. 399, 404-09 (2012). The competitor’s drug development is generally protected from infringement by the 35 U.S.C. § 271(e)(1) safe harbor, so parties rely on the Hatch-Waxman Act for standing. *Id.* Litigated before launch, the six-year limitation on damages does not typically apply. *See* 35 U.S.C. § 286.

Patent holders obtain approval and then list patents covering their product in the Orange Book. Putative competitors cannot compete without FDA approval, and they cannot get FDA approval without addressing any Orange Book-listed patents first. Thus, because of the time it takes the patent holder to secure approval of its own product, pharmaceutical companies expect litigation based on when they obtain

approval and list patents in the Orange Book, not based on when the patents issued. Indeed, right now, Actelion has at least three pending patent litigations filed in April 2024, August 2025, and September 2025 on patents issued 11-19 years earlier: in 2012 and 2013, 2006, and 2007, respectively. EX1050, 1-6. It bears emphasis: Actelion asserted on September 2 that it has “settled expectations” that its ’847 patent would never be challenged because it issued in 2012 (DD Req. 6), and then on September 3—*one day later*—Actelion filed a complaint alleging infringement of a patent that issued in 2007 where the defendants dispute validity. EX1051, ¶ 38. The only legitimate “settled expectation” Actelion could have had is that listing its patent in the Orange Book was an invitation to litigate at any point during the patent’s term.

As a result, it is unsurprising that Actelion’s alleged “settled expectations” rely on attorney argument only. Its request for discretionary denial notably lacks any sworn testimony by an Actelion declarant that Actelion believed no one would ever contest its ’847 patent, and that it therefore had “settled expectations.” And it is unlikely that any Actelion employee would swear as much under penalty of perjury.

UTC had no reason to challenge the ’847 patent any earlier. “[T]here is no bright-line rule on when expectations become settled.” *Dabico Airport Sols. Inc. v. AXA Power ApS*, IPR2025-00408, Paper 21 at 3 (Director June 18, 2025). UTC just recently began pursuing a combination drug product with macitentan. EX1052, ¶ 6. UTC has not marketed or filed an FDA application for any macitentan product, alone

or in combination with other active ingredients. *Id.*, ¶ 4. Thus, UTC had no reason to monitor or challenge any patent claiming macitentan or the use thereof since UTC had (and still has) no macitentan products. *See Home Depot U.S.A., Inc. v. H2 Intellect LLC*, IPR2025-00480, Paper 11 at 2-3 (Director Sept. 4, 2025) (denying discretionary denial request because the petitioner would not have been reasonably concerned that it might inadvertently infringe the patent at issue).

Further, the '847 patent was first listed in the Orange Book for a combination product containing macitentan and a PDE5 inhibitor (OPSYNVI®) on April 18, 2024—only *fourteen months* prior to UTC's Petition. Actelion cites the Orange Book listing for OPSUMIT®, a macitentan-monotherapy product (*i.e.*, no additional PDE5 inhibitor or other actives). DD Req. 7-8. There is no evidence UTC had knowledge of the patent until it decided to pursue a combination product, and even if UTC had notice from the OPSUMIT® listing sooner, UTC “did not have reason to anticipate assertion of the patent against it” because it had no macitentan monotherapy product. *See Home Depot*, Paper 11 at 2-3; EX1052, ¶¶ 4, 6.

Applying settled expectations here is backwards. A pharmaceutical petitioner cannot reasonably be expected to divert resources to investigate and challenge the validity of patents not relevant to its business plans. Nor can a drug developer like UTC reasonably invest in bringing a new competitive drug to market—as encouraged by Congress in the Hatch-Waxman Act—without the ability to challenge weak

blocking patents. It is UTC that had a settled expectation to rely on the statutes establishing IPRs as a streamlined method to litigate unpatentability challenges.

D. The “settled expectations” rule exceeds the Office’s authority.

The Office lacks authority to deprive UTC of *inter partes* review based on its *ultra vires* “settled expectation” rule. Retroactive application of the brand-new 6-year settled expectations rule here, without notice of how the rule would apply or ability to comment, deprives UTC of due process. That the ’847 patent is arguably “old” should not insulate it from the fact that it should never have issued. Any “discretion” that favors settled expectations for a patent recently Orange Book-listed (thus encouraging early litigation) over correcting the Office’s errors would be arbitrary and capricious. Actelion’s “Request” is also procedurally deficient under the Board’s rules. Under 37 C.F.R. § 42.20(a), “[r]elief ... must be requested in the form of a motion.” *See also* § 42.2. Even if Patent Owner’s “Request” is considered a “motion” under the rules, it exceeds the 15-page limit. *See* § 42.24(a)(1)(v).

Similarly, and for at least these reasons, the Director’s Mar. 26, 2025, interim processes and guide exceed the Director’s authority under the AIA, were issued without notice-and-comment rulemaking (*see* 5 U.S.C. § 553(b), (c); 35 U.S.C. §§ 2(b)(2), 316(a)), and are arbitrary and capricious.

For all these reasons, the Director should not exercise discretion to deny the Petition and should instead refer the Petition to a merits panel.

Date: October 1, 2025

Respectfully submitted,

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CERTIFICATE OF SERVICE

Pursuant to 37 C.F.R. §§42.6 and 42.105, I hereby certify that the foregoing PETITIONER'S RESPONSE TO PATENT OWNER'S REQUEST FOR DISCRETIONARY DENIAL, together with all exhibits, was served via electronic mail on the attorneys of record for the patent owner at the following addresses of record:

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