

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

CIPLA LIMITED
Petitioner,

v.

GILEAD SCIENCES, INC.,
Patent Owner.

Case No. IPR2025-00033
U.S. Patent No. 11,744,802

PATENT OWNER'S PRELIMINARY SUR-REPLY

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LIST OF EXHIBITS

Exhibit No.	Description
2001	Biography of Rebecca T. Horwitz in Support of Patent Owner's Motion for Admission <i>Pro Hac Vice</i>
2002	Declaration of Rebecca T. Horwitz in Support of Patent Owner's Motion for Admission <i>Pro Hac Vice</i>
2003	Biography of Taylor Kelson in Support of Patent Owner's Motion for Admission <i>Pro Hac Vice</i>
2004	Declaration of Taylor Kelson in Support of Patent Owner's Motion for Admission <i>Pro Hac Vice</i>
2005	Biography of J. Scott McBride in Support of Patent Owner's Motion for Admission <i>Pro Hac Vice</i>
2006	Declaration of J. Scott McBride in Support of Patent Owner's Motion for Admission <i>Pro Hac Vice</i>
2007	U.S. Patent No. 10,548,846
2008	Stipulation and [Proposed] Order To Amend Scheduling Order, D.I. 159
2009	PACER Docket Report, <i>Gilead Sciences, Inc. v. Lupin Ltd. et al.</i> , No. 1:22-cv-00615-MN (D. Del.)
2010	Stipulation and Order To Amend Scheduling Order, D.I. 160
2011	Excerpt of Federal Court Management Statistics, Sep. 30, 2024
2012	Excerpt of Defendants Laurus Labs Limited, Cipla Limited, and Lupin Limited's Amended Initial Invalidity Contentions, Dec. 20, 2023
2013	Excerpt of Defendants Laurus Labs Limited, Cipla Limited, and Lupin Limited's Final Invalidity Contentions, July 2, 2024
2014	Defendants' '802 Patent Claim Chart, July 11, 2024
2015	Excerpt of Plaintiff Gilead Sciences, Inc's Final Validity Contentions, Aug. 2, 2024

Exhibit No.	Description
2016	Stipulation and Order To Amend Scheduling Order, D.I. 200
2017	Excerpt of Opening Expert Report of Prassana Jagannathan, M.D., Jan. 31, 2025
2018	Excerpt of Opening Expert Report of Jeffrey Winkler, Ph.D., Jan. 29, 2025
2019	Annotated Excerpt of Declaration of Prassana Jagannathan, M.D., Oct. 23, 2024
2020	Excerpt of Rebuttal Expert Report of David W.C. MacMillan, Ph.D. in <i>ViiV Healthcare Co. v. Gilead Sciences, Inc.</i> , No. 1:18-cv-00224-CFC-CJB, Jan. 10, 2020
2021	Excerpt of Hal Martin Deposition Transcript, May 2, 2024 [Confidential – Filed Under Seal]
2022	Gilead GS-9883 STR Development PDCS Group Meeting Presentation, Aug. 12, 2015 [Confidential – Filed Under Seal]
2023	Annotated U.S. Patent No. 11,744,802
2024	Brian A. Johns, et al., <i>Chapter 6: HIV Integrase Inhibitors</i> , in RSC DRUG DISCOVERY SERIES NO. 32: SUCCESSFUL STRATEGIES FOR THE DISCOVERY OF ANTIVIRAL DRUGS (Manoj C. Desai and Nicholas A. Meanwell eds., 2013)
2025	W. Spreen, et al., <i>Pharmacokinetics, Safety, and Monotherapy Antiviral Activity of GSK1265744, an HIV Integrase Strand Transfer Inhibitor</i> , 14(5) HIV Clin. Trials 192 (2013)

Gilead put forward two independent and compelling reasons to deny institution of Cipla's petition: *Fintiv* and § 325(d). The Reply fails to provide any reason why the Board should not exercise its discretion.

This is a textbook case for *Fintiv* denial. The '802 patent is asserted in a district court case involving additional defendants and patents that will go to trial six months before a final written decision is expected. The advanced stage of that proceeding and complete overlap of issues favors denial. Cipla does not even argue that four of the factors favor institution (Factors 1-3 and 5). Instead, it focuses on its hollow *Sotera* stipulation (Factor 4) and unconvincing merits (Factor 6). Cipla's *Sotera* stipulation fails to "mitigate[] any concerns of duplicative efforts" because the other defendants will continue to assert the same invalidity grounds at the district court. *Sotera Wireless, Inc. v. Masimo Corp.*, No. IPR2020-01019, 2020 WL 7049372, at *7 (PTAB Dec. 1, 2020) (precedential). On Factor 6, Cipla's Petition fails to make out a *prima facie* case of obviousness, much less present compelling evidence. Indeed, Cipla's obviousness arguments are fatally flawed, both because of what was known (75 mg dosage in Gilead's clinical trial) and what was unknown (the effect of combining three active ingredients into one tablet). "[T]he efficiency and integrity of the system are best served by denying review." *Motorola Sols. Inc. v. Stellar, LLC*, No. IPR2024-01205, Paper 19 at 4 (PTAB Mar. 28, 2025).

The grounds for denial under § 325(d) are equally strong. Cipla's Petition fails

to analyze whether the same or substantially the same prior art was before the Patent Office during prosecution and fails to show that the Office erred in evaluating that art. This dooms the Petition under § 325(d). Beyond a single conclusory paragraph, Cipla’s Reply again essentially ignores these issues. Because Cipla failed to carry its burden, the Board could deny institution under § 325(d) without even reaching the *Fintiv* arguments. *See Advanced Med. Designs, Inc. v. Corbin Clinical Res., LLC*, No. PGR2023-00041, 2024 WL 249517, at *15 (PTAB Jan. 23, 2024).

I. Each *Fintiv* Factor Favors Denying Institution Under § 314(a)

A. Factors 1-5 Favor Denial

Factor 1 Favors Denial: Cipla does not argue that Factor 1 favors institution but instead attempts to characterize it as “neutral.” Reply at 2. Cipla concedes that the district court has not entered a stay and Cipla has not requested one. While Cipla speculates that a stay is possible, a stay request would likely be denied for all the reasons articulated in Gilead’s preliminary response, including the proximity to trial, that two defendants (Laurus and Lupin) have not joined Cipla’s Petition, and only one of four asserted patents is challenged in the Petition. POPR at 15. *See Exact Scis. Corp. v. Geneoscopy, Inc.*, No. 1:23-cv-1319-MN (D. Del. Nov. 1, 2024) (no stay where only one asserted patent was in *inter partes* review); *PureWick Corp. v. Sage Prods., LLC*, No. 1:19-cv-1508-MN (D. Del. May 4, 2021) (same); *Ferring Pharms. Inc. v. Eugia Pharma Specialties Ltd.*, No. 1:22-cv-0017-MN, D.I. 139 (D. Del. May

10, 2024) (no stay where all defendants had not joined the petition).

Cipla's speculation is solely based on the district court's amended scheduling order, which moved trial from December 9, 2024 to October 6, 2025. Reply at 3; Ex. 2010. But the court moved all deadlines (not just trial) at the joint request of the parties to allow Gilead to amend its complaint to assert the '802 patent. No such reason exists now. Hence, it is highly unlikely that the district court will move the current trial date, much less stay a case that has been pending for three years and is now a few months from trial. Factor 1 favors denial.

Factor 2 Favors Denial: Cipla concedes that Factor 2 "slightly" favors denial but there is nothing "slight" about it. Reply at 3. If *inter partes* review is instituted, the deadline for the Board's final written decision would be six months after the district court trial. Cipla's unsupported conjecture that the trial date will be moved has no bearing here because this factor assesses the impact of the current schedule, not an imaginary one. Factor 2 strongly favors denial.

Factor 3 Favors Denial: As with the majority of the *Fintiv* factors, Cipla concedes that this factor does not favor institution. *Id.* It admits that significant "time and resources [have been] invested in the parallel litigation," including fact discovery, infringement and invalidity contentions, claim construction, and expert discovery. *Id.* Despite this, Cipla says Factor 3 is neutral because this work involved three other patents in addition to the '802 patent. Notably, Cipla does not dispute

that considerable work has been done on the '802 patent. Nor can it. The fact that the district court case includes other patents does not diminish the considerable fact discovery and expert work already completed on the '802 patent (including six expert reports). The parties have invested substantial time and effort, which strongly favors denial. *See Apple Inc. v. Haptic, Inc.*, No. IPR2024-01475, Paper 11 at 10 (PTAB Apr. 4, 2025) (Factor 6 favored denial where case was in expert discovery); *Motorola Sols.*, No. IPR2024-01205, Paper 19 at 2-3 (same).

Factor 4 Favors Denial: This is only one of two factors Cipla says favors institution. Cipla relies heavily on its *Sotera* stipulation. But that stipulation is effectively meaningless for at least two reasons.

First, Gilead has asserted all '802 patent claims against two other defendants who have each raised *exactly* the same district court invalidity defenses and arguments as Cipla (with the same experts and the same reports) but have not joined Cipla's Petition or *Sotera* stipulation. Ex. 1066; POPR at 24-26. While Cipla disputes that "a complete overlap of issues" remains, Reply at 4, the *same* claims, grounds, arguments, and evidence raised in the Petition will have to be adjudicated by the district court regardless of what happens before the Board.

Second, even with a *Sotera* stipulation, Cipla's Petition is not a "true alternative" to the district court proceedings because Cipla's own "invalidity arguments in the district court [for the '802 patent] are more expansive and include"

obviousness-type double patenting, “which Petitioner’s stipulation is not likely to moot.” *Motorola Sols.*, IPR2024-01205, Paper 19 at 3-4 (*Sotera* stipulation did not ensure *inter partes* review “would be a ‘true alternative’” where petitioner relied on additional invalidity arguments in the district court); see *SAP Am., Inc. v. Cyandia, Inc.*, No. IPR2024-01496, Paper 13 at 8-9 (PTAB Apr. 7, 2025) (same).

Cipla speculates that the overlap of claims will be eliminated through routine case narrowing as the parties get closer to trial. Reply at 4. Whether and to what extent narrowing will occur is uncertain at best. Cipla points to no rules requiring such narrowing. Despite some preliminary discussions, the parties have not yet reached an agreement, and one defendant has refused to engage in such discussions. All ’802 patent claims remain in the district court case and will likely need to be tried. Because a complete overlap of issues remain, this factor strongly favors denial. See *SAP*, No. IPR2024-01496, Paper 13 at 8-9 (rejecting argument that “most of the challenged claims will be dropped from the district court”).

Factor 5 Favors Denial: Cipla argues this factor is “neutral.” *Id.* Cipla is the petitioner and defendant, i.e., the same party. Rather than conceding this factor, Cipla repeats its assumption that the parties will eventually narrow the claims in the district court case at some unidentified date. *Id.* at 4-5. Claim narrowing has no relevance to Factor 5. Therefore, this factor favors denial.

B. Factor 6 Favors Denial

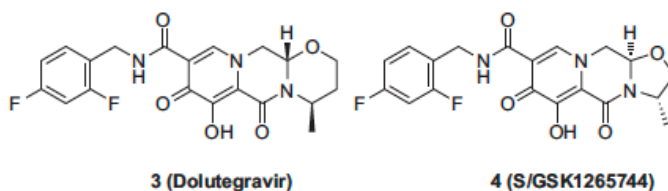
Since Factors 1-5 favor denying institution, the merits of the Petition do not outweigh the other factors. *See Motorola Sols.*, No. IPR2024-01205, Paper 19 at 4 (vacating institution where Factors 1-5 favored denial, notwithstanding that merits favored petitioner). In any event, Cipla fails to show that “the merits of [its] challenges are compelling” because its evidence does not support obviousness. *Samsung Display Co. v. Pictiva Displays Int’l Ltd.*, No. IPR2024-00855, 2024 WL 4827385, at *6 (PTAB Nov. 19, 2024).

Gilead’s preliminary response identified a glaring defect in the Petition: there was no motivation to dose bictegravir at 50 mg. POPR at 29-33. Cipla’s hindsight-driven obviousness theory for the 50 mg dose limitation depends on: (1) selecting compound 42 over others in WO ’323, (2) identifying purported structural similarities between compound 42 and dolutegravir, (3) assuming that important structural differences between the compounds do not matter, and (4) dosing compound 42 at 50 mg like dolutegravir. Petition at 47-56. To get there, a person of skill would have to cherry-pick compound 42 and dolutegravir’s dose while blinding herself to all other compounds, dosing information of other integrase inhibitors, and WO ’323’s teachings.

As of the priority date, the following was known. Gilead was developing a once-daily integrase inhibitor that it called “GS-9883” and indicated that GS-9883

was to be dosed at 75 mg in Phase 2 trials. Petition at 17; Ex. 1035. The structure of GS-9883 was not publicly known nor was the name bictegravir. Reply at 7. Gilead's WO '323 identified several compound structures, including seven that might be considered preferred, one of which is the GS-9883 compound that later became known as bictegravir (compound 42). Ex. 1005 at 240-41. WO '323 included broad dosing suggestions for these compounds, ranging from "about 25 mg to about 500 mg," "about 100 mg to about 300 mg," and "about 25 mg, 50 mg, 100 mg, 200 mg, 300 mg, 400 mg or about 500 mg" but did not specify dosing for any particular compound. *Id.* at 35.

A skilled artisan would know that even small structural differences between compounds can lead to significant changes in dosing. For instance, cabotegravir (known then as "GSK1265744") was another integrase inhibitor that was similar to dolutegravir but for three structural differences. Ex. 2024 at 6.



Yet cabotegravir's pharmacokinetic profile supported a significantly different proposed dose than dolutegravir's (between 5 and 30 mg). Ex. 2025 at 2.

Cipla concedes that bictegravir and dolutegravir have structural differences but unsurprisingly downplays those differences. Petition at 41-42. Yet a person of

skill would not be able to predict with any certainty that the chemical and biological properties between bictegravir and dolutegravir would be similar given the known dosing differences between dolutegravir and cabotegravir. Indeed, Gilead concluded from its own work and dose-ranging study that 50 mg would not be effective for viral suppression in the full range of patients and proceeded with 75 mg as the optimal dosage in Phase 2 trials. POPR at 29-30.

Cipla's Reply emphasizes that a person of skill would not know that GS-9883 was bictegravir or know the structure of GS-9883 or bictegravir.¹ Reply at 6-7. It is unclear why Cipla thinks that strengthens the Petition. Indeed, without the knowledge of the structure of GS-9883, it is even less likely that the skilled artisan would have selected compound 42 from WO '323. Instead, a person of skill would have expected that *one* of the preferred compounds in WO '323 (a 2014 Gilead patent application on compounds that "may be used to inhibit the activity of HIV integrase and may be used to reduce HIV replication," Ex. 1005 at 3) to be the compound dosed at 75 mg in Gilead's Phase 2 clinical trials. But nothing more.

Moreover, Cipla does not dispute that Gilead ran into an unknown problem

¹ Cipla accuses Gilead of misleading the Board because *Cipla's* Exhibit 1035 (Gilead's 2015 Phase 2 protocol) "uses the name 'bictegravir'" but is dated April 4, 2020. Reply at 7. Any confusion was thus introduced by *Cipla*.

when it combined bictegravir, emtricitabine, and tenofovir into a single tablet—an over-exposure of bictegravir—or that Gilead’s solution was unknown. Instead, Cipla argues that the ’802 patent shows the problem was solved by using a bilayer tablet “with 75 mg of bictegravir in its own layer.” Reply at 8 (emphasis in original) (citing ’802 patent). But Cipla misreads the data in the patent: it was the bilayer tablet with 75 mg of bictegravir and tenofovir/emtricitabine that resulted in over-exposure of bictegravir by approximately 30%. *See, e.g.*, Ex. 1001 at 60:52-67 (AUC_{last} for single bilayer tablet (151,844.0) vs. two tablets (119,619.4)). The ’802 patent solves that problem by determining the appropriate 50 mg dosage of bictegravir in a single tablet with tenofovir/emtricitabine.

Cipla attempts to brush away this evidence that the ’802 patent was a solution to an unknown problem, arguing it is not “dispositive” of obviousness. Reply at 8. But the question for Factor 6 is whether there is a “genuinely-disputed issue” that “casts doubt” Cipla is “highly likely” to prevail. *Samsung*, 2024 WL 4827385, at *6. Public information and real-world evidence known before the priority date cast significant doubt on Cipla’s ability to prevail. Factor 6 favors denial.

II. The Board Should Deny The Petition Under § 325(d)

For part one of *Advanced Bionics*’ two-part framework, Cipla admits that its primary references, WO ’323 and WO ’351, were before the examiner. Petition at 32. *See Advanced Bionics, LLC v. MED-EL-Elektromedizinische Geräte GmbH*, No.

IPR2019-01469, 2020 WL 740292, at *3 (PTAB Feb. 13, 2020) (precedential). As to Cipla's secondary references (Bowker, Paulekuhn, and US '079), Cipla's Reply (just like its Petition) simply asserts they have "non-cumulative details" without any meaningful analysis. Reply at 10. Cipla's conclusory say-so that these references are "different" is not enough. This is especially true because Cipla relies on its secondary references in the alternative for the *same* teachings it says are in WO '323 and WO '351. *Id.*; POPR at 40-41 (demonstrating cumulateness and collecting cases).

Under part two of the *Advance Bionics* framework, Cipla fails to demonstrate that the examiner made a material error in finding WO '323 does not teach bictegravir, tenofovir, and emtricitabine within the same tablet. Neither the Petition nor Cipla's Reply identifies any specific example or statement in WO '323 that combined those three drugs within the same tablet because, as explained in Gilead's preliminary response, no such teaching is in WO '323. Petition at 33-34; Reply at 10; POPR at 46. Petitioner's conclusory statement that "the Examiner's misreading of WO '323 materially impacted the Examiner's analysis of that reference" is not enough to meet its burden. Reply at 10. *See Siemens Mobility, Inc. v. Metrom Rail, LLC*, No. IPR2024-00947, 2024 WL 4827396, at *8 (PTAB Nov. 19, 2024) ("five conclusory sentences" failed to "flesh out any material error the Examiner made").

III. Conclusion

For these reasons, the Board should deny institution.

Dated: April 9, 2025

Respectfully submitted,

By: Katherine E. Rhoades

Meg E. Fasulo (Reg. No. 75,820)

J. Scott McBride (*pro hac vice* requested)

Rebecca T. Horwitz (*pro hac vice* requested)

Katherine E. Rhoades (Reg. No. 75,109)

BARTLIT BECK LLP

54 West Hubbard Street, Suite 300

Chicago, IL 60654

(312) 494-4400

Taylor Kelson (*pro hac vice* requested)

BARTLIT BECK LLP

1801 Wewatta Street, Suite 1200

Denver, CO 80202

(303) 592-3100

Counsel for Patent Owner

CERTIFICATE OF SERVICE

The undersigned certifies, that on this 9th day of April, 2025, the foregoing document is being served by e-mail on counsel of record for Petitioner as follows:

alarsen@merchantgould.com
csorenson@merchantgould.com
CiplaBictegravirIPR@merchantgould.com

By: Katherine E. Rhoades
Katherine E. Rhoades (Reg. No. 75,109)
BARTLIT BECK LLP
54 West Hubbard Street, Suite 300
Chicago, IL 60654

Counsel for Patent Owner