

Filed on behalf of Petitioner CIPLA LIMITED

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

Issued: September 5, 2023

Title: THERAPEUTIC COMPOSITIONS FOR TREATMENT OF HUMAN
IMMUNODEFICIENCY VIRUS

REPLY TO PATENT OWNER'S PRELIMINARY RESPONSE

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EXHIBIT LIST

<u>Exhibit No.</u>	<u>Description</u>
EX-1064	Supplemental Information for Patent Cases Involving an Abbreviated New Drug Application (ANDA), DI 003 of Case No. 22-cv-00615-MN, dated May 9, 2022
EX-1065	Memorandum Order, DI 280 of Case No. 22-cv-00615-MN, dated February 21, 2025
EX-1066	Defendant Cipla Limited's Notice of Sotera Stipulation, DI 286 of Case No. 22-cv-00615-MN, dated March 27, 2025
EX-1067	Email regarding proposal of stay for Case No. 22-cv-00615 from Defendants to Plaintiffs, dated November 14, 2024
EX-1068	Email regarding Narrowing and Extension of Deadlines, dated February 20, 2025
EX-1069	Cover Page and Table of Contents for Defendants' Amended Invalidity Contentions regarding U.S. Patent Nos. 10,548,846, 10,385,067, 9,708,342 and 11,744,802
EX-1070	Orange Book Patent and Exclusivity list for Bictegravir Sodium, Emtricitabine, Tenofovir Alafenamide Fumarate (BIKTARVY®) Tablet EQ 50 mg base, 200 mg, EQ 25 mg base, retrieved on March 31, 2025
EX-1071	Joint Claim Construction Brief, DI 263 of Case No. 22-cv-00615-MN, dated November 22, 2024
EX-1072	Joint Submission in Response to January 3, 2022 Oral Order, DI 180 in Case No. 20-cv-00431-MN, dated January 6, 2022

I. INTRODUCTION

The Leahy-Smith America Invents Act, 35 U.S.C. § 100 *et seq.*, was enacted to provide a mechanism to “improve patent quality and restore confidence in the presumption of validity that comes with issued patents.” *Cuozzo Speed Techs., LLC v. Lee*, 579 U.S. 261, 272 (2016) (quoting H.R. Rep. No. 112–98, pt. 1, at 45, 48 (2011)). The ’802 Patent should not enjoy the presumption of validity it presently holds. It is precisely the type of patent the AIA intended for *inter partes* review. Cipla respectfully submits that the Board should not exercise its discretion to deny institution.

II. THE DISTRICT COURT LITIGATION

The parallel litigation began more than a year before the application for the ’802 Patent was filed. EX-2009 at 13 (D.I. 1). Gilead initially asserted three Orange Book patents not at issue here. POPR at 8. One asserted patent -- the ’846 Patent -- is a predecessor of the ’802 Patent presenting narrow claims to multilayer tablets. Pet. at 27-28 EX-1012, ¶ 47. The other two patents claim bictegravir sodium crystalline forms, compositions comprising them, and methods of treating HIV infection with those forms and compositions. See EX-1012, ¶¶ 41-45.

The parties’ contentions, fact witnesses depositions, document productions, claim construction proceedings, and expert discovery involve *substantial* efforts that have *nothing* to do with the ’802 Patent. Indeed, ~500 pages of the final

invalidity contentions are primarily directed to the patents not at issue in this proceeding. EX-1069. Moreover, the Districts Court’s recent claim construction proceedings did not involve any claim terms of the ’802 Patent. EX-1065 at 5.

When the parallel litigation began, Gilead advised the Court of a “thirty-month stay deadline” of August 7, 2025. EX-1064. The District Court then *sua sponte* set a trial date nine months before that deadline -- December 9, 2024. EX-2009 at 14-15 (D.I. 19). The litigation then proceeded as scheduled until the ’802 Patent listed in the Orange Book on October 4, 2023. EX-1070. Soon thereafter, the parties agreed to request a trial date after the thirty-month deadline -- October 6, 2025. EX-2010. The same stipulation notes that the District Court defendants could not market their generic products until *after* December 19, 2033, the expiration date of an unchallenged Orange Book patent. *Id.* at 1-2. The District Court then rescheduled trial to after the thirty-month deadline as requested. *Id.* at 5.

III. THE EFFICIENCY AND INTEGRITY OF THE PATENT SYSTEM WOULD NOT BE SERVED BY DISCRETIONARY DENIAL

A holistic application of the *Fintiv* factors, as applied to the facts now before the Board, favor granting institution.

A. Factor 1 is Neutral: The District Court May Grant a Stay (POPR Section V.A)

In Delaware, filing an opposed motion to stay a case *before institution* of an IPR Petition is considered premature – and would most likely be denied outright.

See IOENGINE, LLC v. PayPal Holdings, Inc., 2019 U.S. Dist. LEXIS 141545, at *19-20 (D. Del. Aug. 21, 2019). Shortly after the Petition was filed, all parallel litigation defendants inquired whether Gilead would be willing to jointly request a stay of the litigation. EX-1067. To date, Gilead has not formally responded to this inquiry, even though no Defendant will have FDA approval of a generic product until 2033. EX-2010 at 1-2.

Given the District Court's prior willingness to postpone trial, there is reason to believe that a motion to stay trial until after the Board's decision deadline – May 19, 2026 – would be granted. No party would be prejudiced by this later trial date.

B. Factor 2 Slightly Favors Denial: Current Trial Date favors Denial, but that may Change (POPR Section V.B)

It is true that the current trial date is set to occur before the Board's May 19, 2026 decision deadline. However, as explained above in Section II, there is reason to believe the Court would be willing to again accommodate a later trial date.

C. Factor 3 is Neutral: The Parallel Litigation is Advanced based Primarily on Three Other Patents (POPR Section V.C)

Gilead's POPR is accurate about the time and resources invested in the parallel litigation. But most of that investment focused on other patents-in-suit. EX-1069. And, the District Court's only significant investment (to date) pertained to claim construction proceedings having nothing to do with the '802 Patent. EX-1065.

D. Factor 4 Strongly Favors Institution: Cipla's Sotera Stipulation Eliminates Overlap (POPR Section V.D)

On March 27, 2025, Cipla filed a *Sotera* stipulation in the parallel litigation stating that Cipla will not seek an adjudication of '802 Patent invalidity on any ground raised or that reasonably could have been raised in the Petition. EX-1066 (D.I. 286). Gilead's assertion that a complete overlap of issues will nonetheless occur before the district court "because two other defendants . . . are raising the same invalidity defenses" is not accurate and is, nonetheless, no longer supported.

In Delaware, it is common for the Court to require parties to narrow the number of patent claims to be adjudicated at trial. *See e.g.*, EX-1072 (example of claim narrowing in response to oral order by Judge Noreika in Hatch-Waxman matter). Consistent with this policy, Gilead has proposed asserting only 3 claims of the '802 Patent. EX-1068 (Feb. 20, 2025 email). Gilead's proposal came with conditions that have not been accepted by any Defendant. However, the court eventually will require that all parties to the parallel litigation narrow the claims to be adjudicated at trial, which means the validity all claims of the '802 will not be assessed in the parallel litigation in any event.

E. Factor 5 is Neutral: Not All Claims of the '802 Patent Will Be Adjudicated at Trial (POPR Section V.E)

It is simply not true that Cipla will be able to "fully litigate the invalidity" of the '802 Patent in the parallel litigation. POPR at 26. Instead, it is virtually certain

that only some of the claims will be adjudicated due to case narrowing, which will apply to all Defendants. *See* EX-1072. Moreover, Gilead initially asserted only a subset of the '802 Patent claims against Cipla in the parallel litigation, whereas Cipla's Petition challenges all of them.

F. Factor 6 Strongly Favors Institution: The Petition Presents Compelling Merits (POPR Section V.F)

Substantial evidence, if unrebutted in trial, has been presented in the Petition that would “plainly lead to a conclusion that one or more claims [of the '802 Patent] are unpatentable by a preponderance of the evidence.” *See Opensky Indus., LLC v. VLSI Tech. LLC*, No. IPR2021-01064, 2022 WL 4963049, at *20 (PTAB Oct. 4, 2022) (precedential). The POPR does not challenge any of the substantial substantive evidence supporting obviousness under *Graham* in the Petition (Pet. at § IX), and the other circumstances presented in the POPR fail to disrupt the strong merits of Cipla's obviousness Grounds 1-3.

1. POSA would have arrived at 50 mg of claimed Formula I compound using only disclosures in the prior art.

The POPR challenges the merits of the Petition, but only as applied to a 50 mg dose of bictegavir. POPR at 29-33. The Petition provides substantial evidence addressing this limitation, including that WO '323 discloses a collection of active CGRP receptor antagonists (including Compound 42), routine methods for dose determination, and specific doses including 25, 50, and 100 mg. Pet. at

53-56 (citing EX-1005, 35:14-23; EX-1003, ¶¶ 143, 194). The Petition also explains that multiple doses of other INSTIs were found (via routine early clinical trials) effective for reducing viral load when combined with other antiretroviral drugs. Pet. at 54 (citing EX-1045 and EX-1056). The POPR presents no evidence suggesting that 50 mg of Compound 42 identified using routine dose ranging studies would not also be sufficient to reduce viral load when combined into a tablet with TAF and FTC. Pet. at 54; EX-1003, ¶¶ 194-97; EX-1005, 16:8-32, 16:19-21, 36:31-37:5.

The POPR largely ignores this substantial evidence, electing instead to change the subject and professes that obviousness of the '802 Patent depends upon refuting Gilead's own private struggle in selecting a 50 mg bicitgravir dose for a specific bilayer tablet. POPR at 29, 33. This argument is not supported by the facts before the Board or current legal precedent. *ImmunoGen, Inc. v. Stewart*, 2025 U.S. App. LEXIS 5215, at *7 (Fed. Cir. Mar. 6, 2025) (rejecting the maxim that "a claimed solution to an unknown problem is *necessarily* non obvious").

2. The POPR Misrepresents Prior Art in the Petition's Background

Gilead states that by 2015, it "had started early clinical trials with bicitgravir." POPR at 29 (emphasis added) (citing EX-1003 at ¶ 94 and EX-1029 at 4). Gilead repeats this assertion often, suggesting that the prior art supports Gilead's choice of 75 mg as "the appropriate dose" for bicitgravir, and disclosed

this to the public in a Phase 2 protocol on February 6, 2015. *Id.* at 30-31 (citing EX-1035) (emphasis added). Although Gilead’s 2015 protocol (EX-1035) was surely in the public record, it only identified an investigational drug “GS-9883,” not “bictegravir.” EX-1035 at 2. Gilead did not tie “GS-9883” to the name “bictegravir” in any public disclosure until June of 2016. *See e.g.*, EX-1061.

There was also no prior art disclosure associating “GS-9883” with the chemical structure of Formula I required by the ’802 Patent claims. EX-1001 at 77:28-40 (claim 1). In 2015, that structure was only known as “Compound 42” in WO ’323, and was not associated with “GS-9883” or “bictegravir” until 2016. EX-1005, 99:8-101:25, 223-24; EX-1061; *see also* Pet. at 19, fn. 11.

The POPR’s deception is subtle. The first page of EX-1035 uses the name “bictegravir,” but that title is from the April 4, 2020 update of the NCT trial record – not the March 20, 2015 protocol, which Petitioner uses to identify a routine early clinical study in HIV therapy on “GS-9883.” Pet. at 17, 54 (citing EX-1035); EX-1035 at 2 (brief and official titles for version 1). No connection between GS-9883 and bictegravir (or its claimed chemical structure) was available to a POSA in 2015. Pet. at 17; EX-1003, ¶¶ 93-95 (reviewing EX-1035 in addition to the prior dose ranging study, EX-1029).

The February 6, 2015 version of Gilead’s dose ranging study from the Petition’s background also speaks to “GS-9883” alone, and not in connection with

“bictegravir” or its chemical structure. Pet. at 17, 54; EX-1029 at 4 (brief and official titles for version 7). Neither of these study protocols even identified “GS-9883” as an INSTI compound – much less do they support the statement that “Gilead determined that 75 mg of bictegravir was the appropriate dose to compare to 50 mg of dolutegravir,” as alleged in the POPR. POPR at 31.

3. Solution to Unknown Problem not Dispositive

Gilead may have identified its own issues and addressed them with a different bictegravir dose. POPR at 33-36. However, Gilead’s path does not detract from a POSA’s use of prior art to arrive at 50 mg bictegravir (and the tablet claims as a whole) using disclosures, suggestions, and routine practices. Pet. at § IX; *ImmunoGen, Inc.*, 2025 U.S. App. LEXIS 5215, at *7 (that the *specific* problem the inventors purported to solve was unknown does not necessarily mean that claim was not obvious; motivation analysis not limited by problem recognized by inventors). And, if the Board were to consider the avowed purpose and reasoning of Gilead in eventually arriving at the 50 mg dose, the so-called “previously unknown problem here” was (according to Gilead) ultimately solved by a specific multilayer tablet with **75 mg of bictegravir** in its own layer, segregated from the other active ingredients -- not the tablet claimed by the ’802 Patent. Ex. 1001 at 58:29-59:8 (bilayer tablet construction), 61:24-42 (pharmacokinetic results); *see also* EX-1003, ¶¶ 107-09.

Further, the POPR and its emphasis on Dr. Martin’s purported “surprise” simply reinforces another fundamental oversight made by the Examiner before allowing the ’802 Patent. POPR at 34-35. As explained in the Petition, the Examiner (when allowing the ’802 Patent) erroneously attributed the alleged surprising increase in bioavailability to a simple tablet with all three ingredients. EX-1002 at 1051-52; *see also* Pet. at § X (explaining materiality of Examiner’s error). The POPR provides no evidence establishing any enhanced performance when using a tablet not constructed in a bilayer manner.

4. PTAB has Rules and Tools Available to Provide Appropriate Fact-Finding and Due Process.

The POPR’s assertion that the district court is “uniquely situated” to evaluate the credibility of Dr. Martin or other Gilead witnesses such as the person(s) who made Gilead’s allegedly novel bilayer tablet, is of no moment. POPR at 37 (citing *Samsung Display Co., Ltd. v. Pictiva Displays Int’l Ltd.*, No. IPR2024-00855, 2024 WL 4827385, at *8 (PTAB Nov. 19, 2024)). To be sure, after review of the institution denial in *Samsung Display*, Acting Director Brent found error in the panel’s view that such credibility determinations cannot be made during live testimony in an AIA trial. *Samsung Display*, No. IPR2024-00855, Paper 13 at 6-7 (Director Brent Jan. 10, 2025).

5. POPR Incorporation of Response on 325(d)

Contrary to the POPR, the “teachings Petitioner pulls from [Bowker, Paulekuhn, and US ’079]” were not before the Examiner. POPR at 37-38, 40-44. These references provide non-cumulative details that *enhance the motivation* to prepare a sodium salt of bictegravir (Ground 2) and prepare lower weight tablets (Ground 3). Pet. at 32-33 (citing reference summaries in Sections V.C-E and Grounds 2-3 in Sections IX.B-C). Those specific teachings were addressed in the Petition (*id.*) and are distinctly different from any reference teachings identified in the POPR. *Id.* at 41-44. In addition, the Examiner’s misreading of WO ’323 materially impacted the Examiner’s analysis of that reference in the context of obviousness, e.g., combined with WO ’351 the other references in Petition Grounds 1-3. Pet. at 33-34 (citing WO ’323 summary in Section V.A and its application to obviousness in Sections IX.A-C); *see also* 68-69 (§ X) (explaining material impact of Examiner’s erroneous assessment of unexpected results).

IV. CONCLUSION

For the reasons explained herein, Cipla respectfully requests the Board institute review of the ’802 Patent.

Respectfully submitted,

Date: April 2, 2025

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CERTIFICATION OF SERVICE

The undersigned hereby certifies that this REPLY TO PATENT OWNER'S PRELIMINARY RESPONSE, PETITIONER'S UPDATED EXHIBIT LIST and Exhibits 1064-1072 were served in their entirety this second day of April, 2025 on the Patent Owner by service via e-mail to Patent Owner's counsel of record.

Date: April 2, 2025

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