IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

AVEO PHARMACEUTICALS, INC. and KYOWA KIRIN CO., LTD., *Plaintiffs*, v. GLENMARK PHARMACEUTICALS LIMITED and GLENMARK PHARMACEUTICALS INC., USA, *Defendants*.	C.A. No. 25-735-MN

GLENMARK'S ANSWER, SEPARATE DEFENSES, AND COUNTERCLAIMS

Defendants Glenmark Pharmaceuticals Limited ("GPL") and Glenmark Pharmaceuticals Inc., USA ("Glenmark USA") (collectively, "Glenmark"), by and through the undersigned attorneys, hereby answer the Complaint of Plaintiffs AVEO Pharmaceuticals, Inc. and Kyowa Kirin Co., Ltd. (collectively, "Plaintiffs") as follows. Every allegation not expressly admitted herein is denied.

RESPONSE TO "NATURE OF ACTION"

1. This is an action for infringement of United States Patent No. 11,504,365 ("the '365 Patent") and 7,166,722 ("the '722 Patent") (collectively, "the Patents-in-Suit") in relation to Glenmark's Abbreviated New Drug Application ("ANDA") No. 220307 (the "Glenmark ANDA"), which seeks approval from the U.S. Food & Drug Administration ("FDA") to make a generic version of AVEO's FOTIVDA® (tivozanib) product.

ANSWER: Paragraph 1 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that Plaintiffs' Complaint purports to state a claim for alleged infringement of United States Patent Nos. 11,504,365 ("the '365 patent") and 7,166,722 ("the '722 patent"). Glenmark further admits that this action purports to relate to GPL's

Abbreviated New Drug Application ("ANDA") No. 220307 to the U.S. Food and Drug Administration ("FDA") seeking approval to manufacture, use, sell, or import tivozanib capsules, 0.89 mg and 1.34 mg, before the expiration of the '365 and '722 patents. Glenmark further admits that the reference listed drug ("RLD") identified in GPL's ANDA No. 220307 is FOTIVDA® (tivozanib) Capsules, 0.89 mg and 1.34 mg. Glenmark denies any and all remaining allegations of Paragraph 1.

2. Plaintiffs also seek a declaratory judgment under the Patent Laws of the United States, 35 U.S.C. § 100 *et seq.*, and the Declaratory Judgment Act, 28 U.S.C. § 2201 *et seq.*, that Glenmark's commercial manufacture, use, offer for sale, sale, and/or importation into the United States of its ANDA No. 220307 would directly and indirectly infringe the Patents-in-Suit.

ANSWER: Paragraph 2 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that Plaintiffs' Complaint purports to state a claim for declaratory judgment of infringement under 28 U.S.C. §§ 2201 and 2202. Glenmark denies any and all remaining allegations of Paragraph 2.

RESPONSE TO "PARTIES"

3. Plaintiff AVEO is a corporation organized and existing under the laws of the State of Delaware, having a principal place of business at One Marina Park Drive, 12th Floor, Boston, Massachusetts 02210. AVEO develops, manufactures, and markets pharmaceutical products in the United States. AVEO is the owner of the '365 Patent and exclusive licensee of the '722 Patent.

ANSWER: Paragraph 3 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark lacks knowledge or information sufficient to form a belief as to the truth of the allegations of Paragraph 3 and therefore denies them.

4. Plaintiff KKC is a corporation organized and existing under the laws of Japan, having a principal place of business at 1-9-2, Otemachi, Chiyoda-Ku, Tokyo Japan 100-0004. KKC develops, manufactures, and markets pharmaceutical products. KKC is the owner of the '722 Patent.

ANSWER: Paragraph 4 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark lacks knowledge or information sufficient to form a belief as to the truth the allegations of Paragraph 4 and therefore denies them.

5. On information and belief, Defendant Glenmark USA is a corporation organized under the laws of the State of Delaware, having a principal place of business at 750 Corporate Drive, Mahwah, New Jersey 07430. On information and belief, Glenmark USA has a registered agent for service of process, Corporation Service Company, located at 251 Little Falls Drive, Wilmington, Delaware 19808. On information and belief, Glenmark USA is in the business of, among other things, manufacturing and selling generic versions of branded pharmaceutical products for the United States market, including in this judicial district. On information and belief, Glenmark USA is the United States Regulatory Agent for Glenmark Pharmaceuticals. On information and belief, Glenmark USA is a wholly owned subsidiary of Glenmark Pharmaceuticals.

ANSWER: Paragraph 5 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that Glenmark USA is a Delaware corporation with a place of business at 750 Corporate Drive, Mahwah, New Jersey 07430. Glenmark further admits that Glenmark USA is the United States regulatory agent for GPL for ANDA No. 220307. Glenmark further admits that Glenmark USA markets and sells pharmaceutical products in the United States, including quality generic medicines. Glenmark further admits that Glenmark USA is an indirect subsidiary of GPL. Glenmark denies any and all remaining allegations of Paragraph 5.

6. On information and belief, Defendant Glenmark Pharmaceuticals is a corporation organized under the laws of India, having corporate headquarters at Glenmark House, HDO-Corporate Building, Wing-A, B D Sawant Marg, Chakala, Off Western Express Highway, Mumbai 400099, Maharashtra, India. On information and belief, Glenmark Pharmaceuticals is in the business of, among other things, manufacturing and selling generic versions of branded pharmaceutical products for the United States market, including in this judicial district.

ANSWER: Paragraph 6 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark states that GPL is a corporation organized and existing under the laws of India, having a registered office at B/2, Mahalaxmi Chambers, 22, Bhulabhai

Desai Road, Mumbai 400026, India. Glenmark further admits that GPL develops and manufactures pharmaceutical products, including quality generic medicines. Glenmark denies any and all remaining allegations of Paragraph 6.

7. On information and belief, Defendants hold themselves out as affiliated entities within the same corporate family for purposes of manufacturing, marketing, selling, and distributing generic drug products through the United States, including in this judicial district.

ANSWER: Paragraph 7 contains legal conclusions to which no answer is required. To the extent an answer is required, denied.

8. On information and belief, Defendants acted in concert to prepare and submit ANDA No. 220307 to the FDA.

ANSWER: Paragraph 8 contains legal conclusions to which no answer is required. To the extent an answer is required, denied.

9. On information and belief, upon FDA approval, Defendants will work in concert with one another to make, use, offer to sell, and/or sell the drug products that are the subject of ANDA No. 220307 throughout the United States, and/or import such drug products into the United States, including in this judicial district.

ANSWER: Paragraph 9 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that GPL's ANDA No. 220307 seeks approval to manufacture, use, sell, or import tivozanib capsules, 0.89 mg and 1.34 mg. Glenmark denies any and all remaining allegations of Paragraph 9.

10. On information and belief, Defendants will each derive significant financial benefit resulting from the FDA's approval of ANDA No. 220307 and subsequent marketing and use of Glenmark's ANDA product throughout the United States, including in this judicial district.

ANSWER: Paragraph 10 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that GPL's ANDA No. 220307 seeks approval

to manufacture, use, sell, or import tivozanib capsules, 0.89 mg and 1.34 mg. Glenmark denies any and all remaining allegations of Paragraph 10.

RESPONSE TO "JURISDICTION AND VENUE"

11. This Court has subject matter jurisdiction over this action pursuant to 28 U.S.C. §§ 1331, 1338(a), 2201, and 2202.

ANSWER: Paragraph 11 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that subject matter jurisdiction is proper solely for claims alleging infringement the '365 and '722 patents under 35 U.S.C. § 271(e)(2)(A). Glenmark denies any and all remaining allegations of Paragraph 11.

12. This Court has personal jurisdiction over Glenmark USA because, on information and belief, Glenmark USA is a Delaware corporation. On information and belief, Glenmark USA maintains pervasive, continuous, and systematic contacts with the State of Delaware through the marketing, distribution, and sale of generic versions of branded pharmaceutical products in the State of Delaware and by deriving substantial revenue from the importation and sale of its products in the State of Delaware.

ANSWER: Paragraph 12 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that Glenmark USA is a Delaware corporation. Answering further, Glenmark does not contest personal jurisdiction in the District of Delaware solely for the limited purpose of this action only. Glenmark denies any and all remaining allegations of Paragraph 12.

13. This Court has personal jurisdiction over Glenmark Pharmaceuticals because, on information and belief, it maintains pervasive, continuous, and systematic contacts with the State of Delaware through the marketing, distribution, and sale of generic versions of branded pharmaceutical products in the State of Delaware, directly and through its affiliates, and by deriving substantial revenue from the importation and sale of its products in the State of Delaware.

ANSWER: Paragraph 13 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark does not contest personal jurisdiction in the District of

Delaware solely for the limited purpose of this action only. Glenmark denies any and all remaining allegations of Paragraph 13.

14. Alternatively, this Court may also exercise jurisdiction over Glenmark Pharmaceuticals pursuant to Fed. R. Civ. P. 4(k)(2) to the extent that Glenmark Pharmaceuticals, as a foreign defendant, is not subject to personal jurisdiction in any state's court of general jurisdiction, based on Glenmark Pharmaceuticals's contacts with the United States as a whole, including without limitation through the manufacture, importation, distribution, and sales of its pharmaceutical products throughout the United States, including in this judicial district.

ANSWER: Paragraph 14 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that GPL is a corporation organized and existing under the laws of India. Answering further, Glenmark does not contest personal jurisdiction in the District of Delaware solely for the limited purpose of this action only. Glenmark denies any and all remaining allegations of Paragraph 14.

15. Venue is proper in this district as to Glenmark USA, pursuant to 28 U.S.C. §§ 1391 and 1400(b), because Glenmark USA is incorporated in the State of Delaware and thus resides in this judicial district.

ANSWER: Paragraph 15 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that Glenmark USA is a Delaware corporation. Answering further, Glenmark does not contest venue in the District of Delaware solely for the limited purpose of this action only. Glenmark denies any and all remaining allegations of Paragraph 15.

16. Venue is proper as to Glenmark Pharmaceuticals, pursuant to 28 U.S.C. § 1391(c)(3), because Glenmark Pharmaceuticals is a foreign corporation not residing in any judicial district and may be sued in any judicial district that has personal jurisdiction, including this judicial district.

ANSWER: Paragraph 16 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that GPL is a corporation organized and existing under the laws of India. Answering further, Glenmark does not contest venue in the District of

Delaware solely for the limited purpose of this action only. Glenmark denies any and all remaining allegations of Paragraph 16.

RESPONSE TO "THE DRUG APPROVAL PROCESS"

17. A company seeking to market a new pharmaceutical drug in the United States must first obtain approval from the FDA, typically through the filing of a New Drug Application ("NDA"). *See* 21 U.S.C. § 355(a). The sponsor of the NDA is required to submit to FDA information on all patents claiming the drug that is the subject of the NDA, or a method of using that drug, and FDA then lists the patent information in its publication, the *Approved Drug Products with Therapeutic Equivalence Evaluations*, which is referred to as the "Orange Book." *See* 21 U.S.C. §§ 355(b)(1) and (c)(2).

ANSWER: Paragraph 17 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that 21 U.S.C. § 355(b)(1) states, in part:

> (A) Any person may file with the Secretary an application with respect to any drug subject to the provisions of subsection (a). Such persons shall submit to the Secretary as part of the application—
>
> > (viii) the patent number and expiration date of each patent for which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug, and that—
> >
> > > (I) claims the drug for which the applicant submitted the application and is a drug substance (active ingredient) patent or a drug product (formulation or composition) patent; or
> >
> > > (II) claims a method of using such drug for which approval is sought or has been granted in the application.

See 21 U.S.C. § 355(b)(1)(A)(viii)(I-II). Glenmark further admits that 21 U.S.C. § 355(c)(2) states, in part, that "[u]pon the submission of patent information under this subsection, the Secretary shall publish it." Glenmark further admits that FDA's publication, *Approved Drug Products with Therapeutic Equivalence Evaluations*, commonly is referred to as the "Orange Book." Glenmark denies any and all remaining allegations of Paragraph 17.

18. Alternatively, a company seeking to market a generic version of a previously approved drug is not required to submit a full NDA. Instead, it may file an Abbreviated New Drug Application ("ANDA"). *See* 21 U.S.C. § 355(j). The generic drug approval process is

considered "abbreviated" because the generic manufacturer may piggyback on the innovator company's data and FDA's prior finding of safety and efficacy by demonstrating, among other things, that the generic product is bioequivalent to the previously approved drug (the "reference listed drug" or "branded drug").

ANSWER: Paragraph 18 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that 21 U.S.C. § 355 states, *inter alia*:

> (j) Abbreviated new drug applications
>
> (4) Subject to paragraph (5), the Secretary shall approve an application for a drug unless the Secretary finds—
>
> (F) information submitted in the application is insufficient to show that the drug is bioequivalent to the listed drug referred to in the application or, if the application was filed pursuant to a petition approved under paragraph (2)(C), information submitted in the application is insufficient to show that the active ingredients of the new drug are of the same pharmacological or therapeutic class as those of the listed drug referred to in paragraph (2)(A)(i) and that the new drug can be expected to have the same therapeutic effect as the listed drug when administered to patients for a condition of use referred to in such paragraph;

See 21 U.S.C. § 355(j)(4)(F). Glenmark denies any and all remaining allegations of Paragraph 18.

19. In conjunction with this "abbreviated" application process, Congress has put in place a process for resolving patent disputes relating to generic drugs, pursuant to which an ANDA filer must provide certifications addressing each of the patents listed in the Orange Book for the branded drug. *See* 21 U.S.C. § 355(j)(2)(A)(vii); 21 C.F.R. § 314.94(a)(12). An ANDA filer may certify, for instance, that it believes a patent is invalid or will not be infringed by the manufacture, use, or sale of the generic drug for which the ANDA is submitted. *See* 21 U.S.C. § 355(j)(2)(A)(vii)(IV); *see also* 21 C.F.R. § 314.94(a)(12)(i)(A)(4). This is known as a "Paragraph IV Certification."

ANSWER: Paragraph 19 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that 21 U.S.C. § 355 states, *inter alia*:

> (j) Abbreviated new drug applications
>
> (2)
>
> (A) An abbreviated application for a new drug shall contain—

> (vii) a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the listed drug referred to in clause (i) or which claims a use for such listed drug for which the applicant is seeking approval under this subsection and for which information is required to be filed under subsection (b) or (c)—
>
> (I) that such patent information has not been filed,
>
> (II) that such patent has expired,
>
> (III) of the date on which such patent will expire, or
>
> (IV) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted;

See 21 U.S.C. § 355(j)(2)(A)(vii)(I-IV). Glenmark denies any and all remaining allegations of Paragraph 19.

20. The filer of an ANDA with a Paragraph IV Certification must also provide notice to both the owner of the listed patents and the holder of the NDA for the referenced listed drug. This "Paragraph IV Notice" must include a detailed statement of the factual and legal bases for the applicant's belief that the challenged patent is invalid or not infringed by the proposed generic product. *See* 21 U.S.C. § 355(j)(2)(B); 21 C.F.R. § 314.95.

ANSWER: Paragraph 20 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that 21 U.S.C. § 355 states, *inter alia*:

> (j) Abbreviated new drug applications
>
> (2)
>
> (B) Notice of opinion that patent is invalid or will not be infringed.—
>
> (iv) Contents of notice.—A notice required under this subparagraph shall—
>
> (I) state that an application that contains data from bioavailability or bioequivalence studies has been submitted under this subsection for the drug with respect to which the certification is made to obtain approval to engage in the commercial manufacture,

> use, or sale of the drug before the expiration of the patent referred to in the certification; and
>
> (II) include a detailed statement of the factual and legal basis of the opinion of the applicant that the patent is invalid or will not be infringed.

See 21 U.S.C. § 355(j)(2)(B)(iv)(I-II). Glenmark denies any and all remaining allegations of Paragraph 20.

21. If the patentee or NDA holder files a patent infringement action within 45 days of receiving a Paragraph IV Notice from an ANDA filer, final approval of the ANDA is subject to a litigation stay. *See* 21 U.S.C. § 355(j)(5)(B)(iii); 21 C.F.R. § 314.107(b)(3). When the NDA holder is awarded New Chemical Entity ("NCE") exclusivity, the litigation stay runs to the later of 30 months from receipt of the notice letter or seven-and-a-half years from the approval date of the NDA. 21 U.S.C. §§ 355(c)(3)(E)(ii), (j)(5)(F)(ii). The stay provides an innovator company with the opportunity to resolve any patent dispute before the generic product enters the market. *See* 21 U.S.C. 355(j)(5)(B)(iii).

ANSWER: Paragraph 21 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that 21 U.S.C. § 355 states, *inter alia*:

> (j) Abbreviated new drug applications
>
> (5)
>
> (B) The approval of an application submitted under paragraph (2) shall be made effective on the last applicable date determined by applying the following to each certification made under paragraph (2)(A)(vii):
>
> (iii) If the applicant made a certification described in subclause (IV) of paragraph (2)(A)(vii), the approval shall be made effective immediately unless, before the expiration of 45 days after the date on which the notice described in paragraph (2)(B) is received, an action is brought for infringement of the patent that is the subject of the certification and for which information was submitted to the Secretary under subsection (b)(1) or (c)(2) before the date on which the application (excluding an amendment or supplement to the application), which the Secretary later determines to be substantially complete, was submitted. If such an action is brought before the expiration of such days, the approval shall be made effective upon the expiration of the thirty-month period beginning on the date of the receipt of the notice provided under paragraph (2)(B)(i)

or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action, except that—

(I) if before the expiration of such period the district court decides that the patent is invalid or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity), the approval shall be made effective on—

(aa) the date on which the court enters judgment reflecting the decision; or

(bb) the date of a settlement order or consent decree signed and entered by the court stating that the patent that is the subject of the certification is invalid or not infringed;

* * *

(F)

(ii) If an application submitted under subsection (b) for a drug, no active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) of which has been approved in any other application under subsection (b), is approved after September 24, 1984, no application may be submitted under this subsection which refers to the drug for which the subsection (b) application was submitted before the expiration of five years from the date of the approval of the application under subsection (b), except that such an application may be submitted under this subsection after the expiration of four years from the date of the approval of the subsection (b) application if it contains a certification of patent invalidity or noninfringement described in subclause (IV) of paragraph (2)(A)(vii). The approval of such an application shall be made effective in accordance with subparagraph (B) except that, if an action for patent infringement is commenced during the one-year period beginning forty-eight months after the date of the approval of the subsection (b) application, the thirty-month period referred to in subparagraph (B)(iii) shall be extended by such amount of time (if any) which is required for seven and one-half years to have elapsed from the date of approval of the subsection (b) application.

See 21 U.S.C. §§ 355(j)(5)(B)(iii), (j)(5)(F)(ii). Glenmark denies any and all remaining allegations of Paragraph 21.

RESPONSE TO "FACTUAL BACKGROUND"

Response to "The Patents-in-Suit"

22. On November 22, 2022, the United States Patent and Trademark Office ("USPTO") duly and legally issued the '365 Patent, entitled "Use of Tivozanib to Treat Subjects with Refractory Cancer," to AVEO as the assignee. A true and correct copy of the '365 Patent is attached as Exhibit A.

ANSWER: Paragraph 22 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that a purported copy of the '365 patent is attached to the Complaint as Exhibit A; that the '365 patent is titled "Use of Tivozanib to Treat Subjects with Refractory Cancer"; and that it bears an issuance date of November 22, 2022. Glenmark further admits that the online records of the USPTO lists the current assignee for the '365 patent as AVEO Pharmaceuticals, Inc. Glenmark denies any and all remaining allegations of Paragraph 22.

23. The claims of the '365 Patent are generally directed to methods of treating patients with refractory advanced renal cell carcinoma ("RCC") having previously received at least two anti-cancer therapies, at least one of which included a tyrosine kinase inhibitor ("TKI").

ANSWER: Paragraph 23 contains legal conclusions to which no answer is required. To the extent an answer is required, denied.

24. On January 23, 2007, the USPTO duly and legal issued the '722 Patent, entitled "N-{2-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-n′-(5-methyl-3-isoxazolyl) urea salt in crystalline form," to Kirin Beer Kabushiki Kaisha. The '722 Patent was subsequently assigned to KKC. A true and correct copy of the '722 Patent is attached as Exhibit B.

ANSWER: Paragraph 24 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that a purported copy of the '722 patent is

attached to the Complaint as Exhibit B; that the '722 patent is titled "N-{2-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N′-(5-methyl-3-isoxazolyl) urea salt in crystalline form"; and that it bears an issuance date of January 23, 2007. Glenmark further admits that the online records of the USPTO lists the current assignee for the '722 patent as Kyowa Kirin Co., Ltd. Glenmark denies any and all remaining allegations of Paragraph 24.

25. The claims of the '722 Patent are generally directed to crystalline forms of tivozanib hydrochloride, including crystalline forms having certain characteristic peaks as determined by X-ray powder diffractometry ("XRPD").

ANSWER: Paragraph 25 contains legal conclusions to which no answer is required. To the extent an answer is required, denied.

Response to "FOTIVDA®"

26. AVEO is the holder of NDA 212904, including all supplements thereto, for FOTIVDA.

ANSWER: Paragraph 26 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that, according to FDA's online records, "AVEO PHARMACEUTICALS INC" is the holder of NDA No. 212904 for FOTIVDA (tivozanib hydrochloride), capsules; oral, EQ 0.89 mg Base and EQ 1.34 mg Base. Glenmark denies any and all remaining allegations of Paragraph 26.

27. On March 31, 2020, AVEO submitted NDA No. 212904, under Section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act ("FDCA"), seeking FDA approval for an oral tivozanib hydrochloride product for the treatment of patients with relapsed or refractory RCC. On March 10, 2021, the FDA approved NDA No. 212904. NDA No. 212904 was also awarded NCE exclusivity, which expires March 10, 2026.

ANSWER: Paragraph 27 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that, according to FDA's online records, FDA approved NDA No. 212904 for FOTIVDA (tivozanib hydrochloride), capsules; oral, EQ 0.89 mg Base and EQ 1.34 mg Base, on or about March 10, 2021. Answering further, Glenmark states that,

according to the approved label for FOTIVDA (tivozanib hydrochloride), Capsules, 0.89 mg and 1.34 mg, currently available from the online records of FDA:

> **1 INDICATIONS AND USAGE**
>
> FOTIVDA is indicated for the treatment of adult patients with relapsed or refractory advanced renal cell carcinoma (RCC) following two or more prior systemic therapies.

Answering further, Glenmark states that the online records of the FDA provide the following "Exclusivity Data" for NDA No. 212904:

Exclusivity Data

Product No	Exclusivity Code	Exclusivity Expiration
001	NCE	03/10/2026

Glenmark denies any and all remaining allegations of Paragraph 27.

28. Plaintiffs timely submitted information regarding the '365 Patent for Listing in FDA's Orange Book with respect to FOTIVDA, for strengths EQ 0.89MG BASE (Product 001), and EQ 1.34MG Base (Product 002), pursuant to 21 U.S.C. §§ 355(b)(1) and (c)(2). The FDA thereafter listed the '365 Patent in the Orange Book with respect to those products, pursuant to 21 C.F.R. § 314.53(e).

ANSWER: Paragraph 28 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that the electronic version of FDA's publication, *Approved Drug Products with Therapeutic Equivalence Evaluations* ("Orange Book") identifies "AVEO PHARMACEUTICALS INC." as the holder of NDA No. 212904 for FOTIVDA; lists the '365 patent in connection with NDA No. 212904; and lists the "Submission Date" for the '365 patent as "12/01/2022." Glenmark denies any and all remaining allegations of Paragraph 28.

29. Plaintiffs timely submitted information regarding the '722 Patent in the Orange Book with respect to FOTIVDA, for strengths EQ 0.89MG BASE (Product 001), and EQ 1.34MG Base (Product 002), pursuant to 21 U.S.C. §§ 355(b)(1) and (c)(2). The FDA thereafter listed the '722 Patent in the Orange Book with respect to those products, pursuant to 21 C.F.R. § 314.53(e).

ANSWER: Paragraph 29 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that the Orange Book identifies "AVEO PHARMACEUTICALS INC." as the holder of NDA No. 212904 for FOTIVDA; lists the '722 patent in connection with NDA No. 212904; and lists the "Submission Date" for the '722 patent as "04/06/2021." Glenmark denies any and all remaining allegations of Paragraph 29.

30. Plaintiffs timely submitted information regarding U.S. Patent No. 6,821,987 (the "'987 patent") in the Orange Book with respect to FOTIVDA, for strengths EQ 0.89MG BASE (Product 001), and EQ 1.34MG Base (Product 002), pursuant to 21 U.S.C. §§ 355(b)(1) and (c)(2). The FDA thereafter listed the '987 Patent in the Orange Book with respect to those products, pursuant to 21 C.F.R. § 314.53(e).

ANSWER: Paragraph 30 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that the Orange Book identifies "AVEO PHARMACEUTICALS INC." as the holder of NDA No. 212904 for FOTIVDA; lists the '987 patent in connection with NDA No. 212904; and lists the "Submission Date" for the '987 patent as "04/06/2021." Glenmark denies any and all remaining allegations of Paragraph 30.

31. The FDA-approved label for FOTIVDA, among other things, provides information and instructions for the safe and effective use of FOTIVDA by healthcare providers and patients. A true and correct copy of the FOTIVDA label is attached as Exhibit C.

ANSWER: Paragraph 31 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that what purports to be a true and correct copy of the current approved label for FOTIVDA is attached to Plaintiffs' Complaint as Exhibit C. Glenmark denies any and all remaining allegations of Paragraph 31.

32. The FOTIVDA label states that "FOTIVDA is indicated for the treatment of adult patients with relapsed or refractory advanced renal cell carcinoma (RCC) following two or more prior systemic therapies." Ex. C § 1, Indications and Usage.

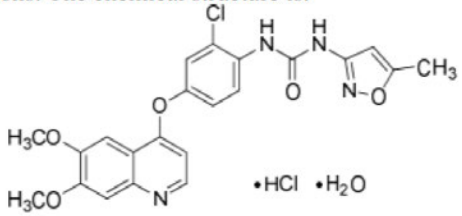
ANSWER: Paragraph 32 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that the FOTIVDA label attached as Exhibit C to Plaintiffs' Complaint states in part:

> **1 INDICATIONS AND USAGE**
>
> FOTIVDA is indicated for the treatment of adult patients with relapsed or refractory advanced renal cell carcinoma (RCC) following two or more prior systemic therapies.

Glenmark denies any and all remaining allegations of Paragraph 32.

33. According to the FOTIVDA label, the active ingredient in FOTIVDA is tivozanib hydrochloride, which has the chemical name 1-{2-chloro-4-[(6,7-dimethoxyquinolin-4-yl)oxy]phenyl}-3-(5-methylisoxazol-3-yl)urea hydrochloride hydrate. *Id.* § 11, Description. It is alternatively referred to as N-{2-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N′-(5-methyl-3-isoxazolyl)urea monohydrochloric acid salt monohydrate.

ANSWER: Paragraph 33 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that the FOTIVDA label attached as Exhibit C to Plaintiffs' Complaint states in part:

> **11 DESCRIPTION**
>
> Tivozanib is a kinase inhibitor. Tivozanib hydrochloride, the active ingredient, has the chemical name 1-{2-chloro-4-[(6,7-dimethoxyquinolin-4-yl)oxy]phenyl}-3-(5-methylisoxazol-3-yl)urea hydrochloride hydrate. The molecular formula is $C_{22}H_{19}ClN_4O_5 \cdot HCl \cdot H_2O$ and the molecular weight is 509.34 Daltons. The chemical structure is:
>
> 
>

Glenmark denies any and all remaining allegations of Paragraph 33.

34. Tivozanib hydrochloride is a "white to light brown crystalline powder." Ex. C § 11, Description.

ANSWER: Paragraph 34 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that the FOTIVDA label attached as Exhibit C

to Plaintiffs' Complaint states in part: "Tivozanib hydrochloride is a white to light brown crystalline powder that is practically insoluble in water (0.09 mg/mL)." Glenmark denies any and all remaining allegations of Paragraph 34.

35. Tivozanib hydrochloride is a tyrosine kinase inhibitor ("TKI") targeting specific proteins that tumors rely on to grow new blood vessels, namely vascular endothelial growth factor receptor ("VEGFR")-1, VEGFR-2, and VEGFR-3. *See* Ex. C § 12.1, Mechanism of Action. This growth of new blood vessels, known as angiogenesis, supplies tumors with the oxygen and nutrients they need to grow and spread. *Id.* By inhibiting angiogenesis, tivozanib acts to slow the growth of a tumor or cause it to shrink. *Id.* Tivozanib exhibits high selectivity for these proteins, which means it interferes less with other cellular functions and can reduce side effects compared to broader systemic treatments.

ANSWER: Paragraph 35 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that the FOTIVDA label attached as Exhibit C to Plaintiffs' Complaint states in part:

> **12.1 Mechanism of Action**
>
> Tivozanib is a tyrosine kinase inhibitor. In vitro cellular kinase assays demonstrated that tivozanib inhibits phosphorylation of vascular endothelial growth factor receptor (VEGFR)-1, VEGFR-2 and VEGFR-3 and inhibits other kinases including c-kit and PDGFR β at clinically relevant concentrations. In tumor xenograft models in mice and rats, tivozanib inhibited angiogenesis, vascular permeability, and tumor growth of various tumor cell types including human renal cell carcinoma.

Glenmark denies any and all remaining allegations of Paragraph 35.

36. Hepatic impairment refers to the reduction in liver function due to liver disease or damage. It affects the liver's ability to metabolize drugs and can lead to increased bioavailability of orally administered drugs. Among the patients with RCC who are treated with tivozanib hydrochloride are those who have hepatic impairment or develop hepatic impairment during the treatment cycle.

ANSWER: Paragraph 36 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark lacks knowledge and information sufficient to form a belief as to the truth of the remaining allegations of Paragraph 36 and therefore denies them.

37. The "recommended dosage of FOTIVDA is 1.34 mg taken orally once daily for 21 days on treatment followed by 7 days off treatment for a 28-day cycle." Ex. C § 2.1, Recommended Dosing. The label states that the "1.34 mg capsule contains 1.5 mg of tivozanib hydrochloride (equivalent to 1.34 mg tivozanib)." *Id.* § 11, Description.

ANSWER: Paragraph 37 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that the FOTIVDA label attached as Exhibit C to Plaintiffs' Complaint states in part:

> **2.1 Recommended Dosing**
>
> The recommended dosage of FOTIVDA is 1.34 mg taken orally once daily for 21 days on treatment followed by 7 days off treatment for a 28-day cycle.
>
> Continue treatment until disease progression or until unacceptable toxicity occurs.
>
> Take FOTIVDA with or without food. Swallow the FOTIVDA capsule whole with a glass of water. Do not open the capsule.
>
> If a dose is missed, the next dose should be taken at the next scheduled time. Do **not** take two doses at the same time.

* * *

> FOTIVDA 1.34 mg capsule contains 1.5 mg of tivozanib hydrochloride (equivalent to 1.34 mg tivozanib) with inactive ingredients: mannitol and magnesium stearate. Capsule composition: gelatin, titanium dioxide, FDA yellow iron oxide, and Blue SB-6018 (ink).

Glenmark denies any and all remaining allegations of Paragraph 37.

38. The FOTIVDA label provides further instructions for "use in specific populations," including patients with moderate hepatic impairment. Ex. C, Highlights of Prescribing Information. Specifically, the FOTIVDA label instructs monitoring patients for hepatic impairment and making certain dose modifications for patients exhibiting moderate hepatic impairment. *Id.* § 2.3 Dosage Modifications for Moderate Hepatic Impairment; § 8.7 Hepatic Impairment. For such patients, the "recommended dosage of FOTIVDA [is a] 0.89 mg capsule taken orally once daily for 21 days on treatment followed by 7 days off treatment for a 28-day cycle." *Id.* § 2.3. The Dosage and Administration section from the Highlights of Prescribing Information portion of the label also instructs healthcare providers and patients to "reduce the dose to 0.89 mg" for patients with moderate hepatic impairment. *Id.*, Highlights of Prescribing Information. The label states that the "0.89 mg capsule contains 1.0 mg of tivozanib hydrochloride (equivalent to 0.89 mg tivozanib)." *Id.* § 11, Description.

ANSWER: Paragraph 38 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that the FOTIVDA label attached as Exhibit C to Plaintiffs' Complaint states in part: "Hepatic Impairment: Adjust dosage in patients with moderate hepatic impairment. Avoid use in patients with severe hepatic impairment." Glenmark further admits that the FOTIVDA label attached as Exhibit C to Plaintiffs' Complaint states, *inter*

alia: "Reduce the recommended dosage of FOTIVDA to 0.89 mg capsule taken orally once daily for 21 days on treatment followed by 7 days off treatment for a 28-day cycle for patients with moderate hepatic impairment." Glenmark further admits that the FOTIVDA label attached as Exhibit C to Plaintiffs' Complaint states, *inter alia*: "Reduce the dosage when administering FOTIVDA in patients with moderate (total bilirubin greater than 1.5 to 3 times ULN with any AST) hepatic impairment [ ]. No dosage modification is recommended for patients with mild (total bilirubin less than or equal to ULN with AST greater than ULN or total bilirubin greater than 1 to 1.5 times ULN with any AST) hepatic impairment. The recommended dosage of FOTIVDA in patients with severe (total bilirubin greater than 3 to 10 times ULN with any AST) hepatic impairment has not been established [ ]." Glenmark denies any and all remaining allegations of Paragraph 38.

39. The FOTIVDA label also provides that "[t]he safety of FOTIVDA was evaluated in TIVO-3, a randomized, open-label trial in 350 patients with relapsed or refractory advanced RCC who received 2 or 3 prior systemic treatments *[see CLINICAL STUDIES (14)]*," and directs the reader to the clinical studies section of the label. Ex. C. § 6.1, Clinical Trial Experience. The clinical studies section states that the "efficacy of FOTIVDA was evaluated in TIVO-3 (NCT02627963), a randomized (1:1), open label, multicenter trial of FOTIVDA versus sorafenib in patients with relapsed or refractory advanced RCC who received 2 or 3 prior systemic treatments including at least one VEGFR kinase inhibitor other than sorafenib or tivozanib." *Id.* § 14 Clinical Studies. Further, the FOTIVDA label, sets forth a summary of the patient demographics for the clinical trial, stating that "[p]rior therapy included two KIs (45%), a KI plus an immune checkpoint inhibitor (26%), and a KI plus another systemic agent (29%)." *Id.* Thus, all patients in the TIVO-3 trial described in the FOTIVDA label received a TKI prior to treatment with tivozanib as a monotherapy. *See id.* § 6.1, Clinical Trial Experience and § 14, Clinical Studies.

ANSWER: Paragraph 39 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that the FOTIVDA label attached as Exhibit C to Plaintiffs' Complaint states, *inter alia*: "The safety of FOTIVDA was evaluated in TIVO-3, a randomized, open-label trial in 350 patients with relapsed or refractory advanced RCC who received 2 or 3 prior systemic treatments [ ]. Patients were randomized (1:1) to receive FOTIVDA

1.34 mg orally once daily for 21 days on treatment followed by 7 days off treatment for a 28-day cycle, or to receive sorafenib 400 mg orally twice a day continuously until disease progression or unacceptable toxicity. Among patients who received FOTIVDA, 53% were exposed for 6 months or longer and 31% were exposed for greater than one year." Glenmark further admits that the FOTIVDA label attached as Exhibit C to Plaintiffs' Complaint states, *inter alia*: "The median age was 63 years (range: 30 to 90 years), 73% were male, 95% were Caucasian, ECOG performance status was 0 in 48% and 1 in 49% of patients (respectively), and 98% of patients had clear cell or clear cell component histology. Prior therapy included two KIs (45%), a KI plus an immune checkpoint inhibitor (26%), and a KI plus another systemic agent (29%). At the time of study entry, 20% of patients had favorable, 61% intermediate, and 19% poor IMDC prognoses." Glenmark denies any and all remaining allegations of Paragraph 39.

40. The FOTIVDA label reports the efficacy results of the TIVO-3 clinical trial, providing, among other things, that the median duration of progression free survival in patients receiving FOTIVDA is 5.6 months. Ex. C § 14, Table 4, Efficacy Results in TIVO-3 (ITT).

ANSWER: Paragraph 40 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that the FOTIVDA label attached as Exhibit C to Plaintiffs' Complaint states, *inter alia*: "The safety of FOTIVDA was evaluated in TIVO-3, a randomized, open-label trial in 350 patients with relapsed or refractory advanced RCC who received 2 or 3 prior systemic treatments [ ]. Patients were randomized (1:1) to receive FOTIVDA 1.34 mg orally once daily for 21 days on treatment followed by 7 days off treatment for a 28-day cycle, or to receive sorafenib 400 mg orally twice a day continuously until disease progression or unacceptable toxicity. Among patients who received FOTIVDA, 53% were exposed for 6 months or longer and 31% were exposed for greater than one year." Glenmark further admit that the FOTIVDA label attached as Exhibit C to Plaintiffs' Complaint states, *inter alia*, that the "main

efficacy outcome measure was progression-free survival (PFS) assessed by a blinded independent radiology review committee." Glenmark denies any and all remaining allegations of Paragraph 40.

Response To "Glenmark's Infringing Tivozanib Hydrochloride Products"

41. On information and belief, on or before May 2, 2025, Glenmark USA and Glenmark Pharmaceuticals, submitted ANDA No. 220307 pursuant to 21 U.S.C. § 355(j), seeking FDA approval to engage in the commercial manufacture, importation, use, marketing, and sale of proposed generic tivozanib hydrochloride (eq. 1.34 mg and 0.89 mg base), referencing AVEO's FOTIVDA product as the reference listed drug (the "Proposed ANDA Product").

ANSWER: Paragraph 41 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that GPL's ANDA No. 220307 was submitted to the FDA pursuant to 21 U.S.C. § 355(j) and that GPL's ANDA contains a certification pursuant to § 505(j)(2)(A)(vii)(IV) of the Federal Food, Drug, and Cosmetic Act for the '365 and '722 patents. Glenmark further admits that the RLD identified in GPL's ANDA No. 220307 is FOTIVDA® (tivozanib) Capsules, 0.89 mg and 1.34 mg. Glenmark denies any and all remaining allegations of Paragraph 41.

42. Glenmark sent Plaintiffs a notice letter, dated May 2, 2025, stating that Glenmark had submitted the Glenmark ANDA seeking approval to manufacture, import, use, market, and/or sell the Proposed ANDA Product prior to the expiration of the '365 Patent and '722 Patent (the "Paragraph IV Notice Letter").

ANSWER: Paragraph 42 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that GPL's ANDA No. 220307 was submitted to the FDA pursuant to 21 U.S.C. § 355(j) and that GPL's ANDA contains a certification pursuant to § 505(j)(2)(A)(vii)(IV) of the Federal Food, Drug, and Cosmetic Act for the '365 and '722 patents. Glenmark further admits that it sent a letter on May 2, 2025 via Federal Express to AVEO Pharmaceuticals, Inc., and Kyowa Kirin Co., Ltd. pursuant to 21 U.S.C. § 355(j)(2)(B)

("Glenmark's Notice Letter"), which provided written notification of the paragraph IV certification for the '365 and '722 patents. Glenmark denies any and all remaining allegations of Paragraph 42.

43. Plaintiffs received the Notice Letter on May 5, 2025.

ANSWER: Paragraph 43 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that it sent Glenmark's Notice Letter on May 2, 2025 via Federal Express to AVEO Pharmaceuticals, Inc. and Kyowa Kirin Co., Ltd. Glenmark denies any and all remaining allegations of Paragraph 43.

44. The Paragraph IV Notice Letter asserts that the '365 Patent and the '722 Patent are invalid and not infringed by the Proposed ANDA Product but makes no such assertions with respect to the '987 Patent.

ANSWER: Paragraph 44 contains legal conclusions and allegations to which no answer is required. To the extent an answer is required, Glenmark admits that GPL's ANDA contains a certification pursuant to § 505(j)(2)(A)(vii)(IV) of the Federal Food, Drug, and Cosmetic Act for the '365 and '722 patents. Glenmark denies any and all remaining allegations of Paragraph 44.

45. The Paragraph IV Notice Letter included an offer of confidential access to the Glenmark ANDA pursuant to 21 U.S.C. § 355(j)(5)(C). The offer only committed to provide unspecified information from Glenmark's ANDA and was subject to unreasonably restrictive confidentiality provisions.

ANSWER: Paragraph 45 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark states that the Offer of Confidential Access ("OCA") to Application sent with Glenmark's Notice Letter complied with all statutory and regulatory requirements. Glenmark further states that Plaintiffs did not make a good faith request for any information from GPL's ANDA No. 220307. Glenmark denies any and all remaining allegations of Paragraph 45.

46. Glenmark's submission of the Glenmark ANDA to the FDA, including any amendments or supplements thereto, and any commercial manufacture or sale by Glenmark of the Proposed ANDA Product, constitutes infringement of the '365 Patent and the '722 Patent, as detailed below.

ANSWER: Denied.

47. This action is being commenced before the expiration of forty-five days from the date Plaintiffs received Glenmark's Paragraph IV Notice Letter.

ANSWER: Paragraph 47 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that it sent Glenmark's Notice Letter on May 2, 2025 via Federal Express to AVEO Pharmaceuticals, Inc. and Kyowa Kirin Co., Ltd. Glenmark denies any and all remaining allegations of Paragraph 47.

RESPONSE TO "COUNT I INFRINGEMENT OF THE '365 PATENT"

48. Plaintiffs incorporate each of the preceding paragraphs as if fully set forth herein.

ANSWER: Glenmark restates and incorporates each of its responses to the preceding Paragraphs 1-47 as if fully set forth herein.

49. The submission of the Glenmark ANDA to the FDA, including the Paragraph IV Certification submitted therewith, which seeks approval to engage in the commercial manufacture, use, marketing, offer for sale, sale, and/or importation of the Proposed ANDA Product prior to the expiration of the '365 Patent, constitutes infringement by Glenmark of the '365 Patent under 35 U.S.C. § 271(e)(2)(A).

ANSWER: Denied.

50. The commercial manufacture, use, marketing, offer for sale, sale, and/or importation into the United States of the Proposed ANDA Product by Glenmark before the expiration of the '365 Patent would instruct, direct, recommend, encourage, and/or promote direct infringement, contributory infringement, and/or active inducement of infringement of the '365 Patent under 35 U.S.C. §§ 271(a)-(c).

ANSWER: Denied.

51. On information and belief, and subject to Plaintiffs' ongoing investigation and discovery efforts, if Glenmark's Proposed ANDA Product is approved, Glenmark will make, offer for sale, sell, or import Glenmark's ANDA Product in a manner that, when used in

accordance with its proposed labeling would infringe at least, by way of example, independent claims 1 and 7 of the '365 Patent, which recite as follows:

> **1. A method of treating a human subject with refractory advanced renal cell carcinoma (RCC) having previously received at least two anti-cancer therapies, at least one of which included a tyrosine kinase inhibitor (TKI), the method comprising:**
>
> > **administering to the subject treatment cycles consisting essentially of:**
> >
> > **orally administering a pharmaceutical composition comprising an active agent consisting essentially of 1.5 mg tivozanib hydrochloride daily for 21 days followed by 7 days without administration of tivozanib hydrochloride until the subject experiences moderate hepatic impairment, upon which the amount of tivozanib hydrochloride in each treatment cycle is reduced from 1.5 mg to 1.0 mg,**
> >
> > **thereby to achieve a progression free survival in the subject of at least 5 months.**
>
> **7. A method of treating a human subject with refractory advanced renal cell carcinoma (RCC) having previously received at least two anti-cancer therapies, at least one of which included a tyrosine kinase inhibitor (TKI), and experiencing moderate hepatic impairment, the method comprising:**
>
> > **administering to the subject one or more treatment cycles consisting essentially of:**
> >
> > **orally administering a pharmaceutical composition comprising an active agent consisting essentially of 1.0 mg tivozanib hydrochloride daily for 21 days followed by 7 days without administration of tivozanib hydrochloride**
> >
> > **thereby to treat RCC.**

ANSWER: Paragraph 51 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that claims 1 and 7 of the '365 patent recite:

> 1. A method of treating a human subject with refractory advanced renal cell carcinoma (RCC) having previously received at least two anti-cancer therapies, at least one of which included a tyrosine kinase inhibitor (TKI), the method comprising:
>
> administering to the subject treatment cycles consisting essentially of:
>
> orally administering a pharmaceutical composition comprising an active agent consisting essentially of 1.5 mg tivozanib hydrochloride daily for 21 days followed by
>
> 7 days without administration of tivozanib hydrochloride until the subject experiences moderate hepatic impairment, upon which the amount of tivozanib hydrochloride in each treatment cycle is reduced from 1.5 mg to 1.0 mg,
>
> thereby to achieve a progression free survival in the subject of at least 5 months.

* * *

> 7. A method of treating a human subject with refractory advanced renal cell carcinoma (RCC) having previously received at least two anti-cancer therapies, at least one of which included a tyrosine kinase inhibitor (TKI), and experiencing moderate hepatic impairment, the method comprising:
>
> administering to the subject one or more treatment cycles consisting essentially of:
>
> orally administering a pharmaceutical composition comprising an active agent consisting essentially of 1.0 mg tivozanib hydrochloride daily for 21 days followed by 7 days without administration of tivozanib hydrochloride,
>
> thereby to treat the RCC.

Glenmark denies any and all remaining allegations of Paragraph 51.

52. On information and belief, Glenmark's Proposed ANDA Product will substantively copy the FOTIVDA label. *See* 21 C.F.R. § 314.94(a)(8)(iv). Accordingly, on information and belief and subject to Plaintiffs' ongoing investigation and discovery efforts, by virtue of Glenmark's submission of the proposed product label and other conduct, Glenmark proposes to instruct, direct, recommend, encourage, and/or promote direct infringement of at least claims 1 and 7 of the '365 Patent by patients, physicians, prescribers and/or other healthcare providers.

ANSWER: Denied.

53. Glenmark's Proposed ANDA Product is indicated for the treatment of adult patients with relapsed or refractory advanced RCC following two or more prior systemic therapies.

ANSWER: Paragraph 53 contains legal conclusions to which no answer is required. To the extent an answer is required, denied.

54. On information and belief, the label for Glenmark's Proposed ANDA Product, including its indication for patients with refractory advanced RCC would actively direct, instruct, recommend, encourage, and/or promote that patients, physicians, prescribers, and/or healthcare providers administer tivozanib hydrochloride to patients with refractory advanced RCC.

ANSWER: Denied.

55. On information and belief, many patients with relapsed or refractory advanced RCC who have had two or more prior systemic therapies would have received at least one TKI prior to treatment with tivozanib hydrochloride.

ANSWER: Paragraph 55 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark lacks knowledge or information sufficient to form a belief as to the truth of the allegations of Paragraph 55 and therefore denies them.

56. On information and belief, the label for Glenmark's Proposed ANDA Product, including its description of the TIVO-3 study conducted on patients who all received a TKI prior to receiving tivozanib hydrochloride, would actively direct, instruct, recommend, encourage, and/or promote that patients, physicians, prescribers, and/or healthcare providers administer tivozanib hydrochloride to patients with refractory advanced RCC who have had two or more prior systemic therapies including at least one TKI.

ANSWER: Denied.

57. The recommended dosage of Glenmark's Proposed ANDA Product is 1.34 mg once daily 21 days on treatment followed by 7 days off treatment. On information and belief, the 1.34 mg dosage form of Glenmark's Proposed ANDA Product contains 1.5 mg of tivozanib hydrochloride.

ANSWER: Paragraph 57 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that the FOTIVDA label attached as Exhibit C to Plaintiffs' Complaint states in part:

----------DOSAGE AND ADMINISTRATION----------

- Recommended Dose: 1.34 mg once daily with or without food for 21 days on treatment followed by 7 days off treatment (28-day cycle) until disease progression or unacceptable toxicity. (2.1)
- Dose interruptions and/or dose reduction may be needed to manage adverse reactions. (2.2)
- For patients with moderate hepatic impairment, reduce the dose to 0.89 mg for 21 days on treatment followed by 7 days off treatment (28-day cycle). (2.3)

----------DOSAGE FORMS AND STRENGTHS----------

Capsules: 1.34 mg and 0.89 mg (3)

Answering further, Glenmark states that GPL's ANDA meets all statutory and regulatory requirements. Glenmark denies any and all remaining allegations of Paragraph 57.

58. On information and belief, among the patients who are administered Glenmark's Proposed ANDA Product according to the instructions in its label are those who will have moderate hepatic impairment at the onset of treatment or develop moderate hepatic impairment during treatment.

ANSWER: Paragraph 58 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark lacks knowledge or information sufficient to form a belief as to the truth of the allegations of Paragraph 58 and therefore denies them.

59. Glenmark's Proposed ANDA Product label includes instructions to reduce the dose of tivozanib for patients with moderate hepatic impairment. On information and belief, based on these label instructions, physicians or healthcare providers will assess the patients' liver function for hepatic impairment before and during treatment.

ANSWER: Paragraph 59 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that the FOTIVDA label attached as Exhibit C to Plaintiffs' Complaint states in part:

----------DOSAGE AND ADMINISTRATION----------

- Recommended Dose: 1.34 mg once daily with or without food for 21 days on treatment followed by 7 days off treatment (28-day cycle) until disease progression or unacceptable toxicity. (2.1)
- Dose interruptions and/or dose reduction may be needed to manage adverse reactions. (2.2)
- For patients with moderate hepatic impairment, reduce the dose to 0.89 mg for 21 days on treatment followed by 7 days off treatment (28-day cycle). (2.3)

----------DOSAGE FORMS AND STRENGTHS----------

Capsules: 1.34 mg and 0.89 mg (3)

Answering further, Glenmark states that GPL's ANDA meets all statutory and regulatory requirements. Glenmark denies any and all remaining allegations of Paragraph 59.

60. On information and belief, physicians or healthcare providers will consult and follow the instructions of Glenmark's Proposed ANDA Product label and adjust the dose of tivozanib hydrochloride from 1.5 mg to 1.0 mg for patients with moderate hepatic impairment. On information and belief, the 0.89 mg dosage form of Glenmark's Proposed ANDA Product contains 1.0 mg of tivozanib hydrochloride. Accordingly, Glenmark's Proposed ANDA Product label would actively direct, instruct, recommend, encourage, and/or promote, that patients, physicians, prescribers, and/or healthcare providers reduce the dose of tivozanib hydrochloride from 1.5 mg to 1.0 mg for patients with moderate hepatic impairment.

ANSWER: Denied.

61. Glenmark's Proposed ANDA Product label provides instructions and safety information regarding the use and administration of tivozanib as a monotherapy. Accordingly, Glenmark's Proposed ANDA Product label would actively direct, instruct, recommend, encourage, and/or promote that patients, physicians, prescribers, and/or healthcare providers administer or take tivozanib hydrochloride as a monotherapy.

ANSWER: Denied.

62. Glenmark's Proposed ANDA Product label reports the efficacy results of clinical trials involving the treatment of RCC patients with tivozanib, where the median duration of progression free survival in patients receiving tivozanib is 5.6 months. Accordingly, Glenmark's Proposed ANDA Product label would actively direct, instruct, recommend, encourage, and/or promote that patients, physicians, prescribers, and/or healthcare providers administer or take tivozanib hydrochloride to achieve a progression free survival in the subject of at least 5 months.

ANSWER: Denied.

63. On information and belief, and subject to Plaintiffs' ongoing investigation and discovery efforts, the manufacture, use (including as directed in Glenmark's proposed labeling for Glenmark's Proposed ANDA Product), offer for sale, sale, marketing, distribution, and/or importation of Glenmark's Proposed ANDA Product will satisfy each of the recited elements of the methods recited in at least claims 1 and 7, either literally or under the doctrine of equivalents.

ANSWER: Denied.

64. On information and belief, if the FDA were to approve the Glenmark ANDA, Glenmark's commercial manufacture, use, marketing, offer for sale, sale, and/or importation into the United States of the Proposed ANDA Product, including administration of Glenmark's Proposed ANDA Product according to the foregoing label instructions, would necessarily or inevitably cause patients, physicians, prescribers, and/or other healthcare providers to directly infringe at least claims 1 and 7. Glenmark would actively induce and contribute to such direct infringement.

ANSWER: Denied.

65. Glenmark has knowledge of the claims of the '365 Patent. Despite this knowledge, Glenmark has continued to assert its intent to engage in the manufacture, use, offer for sale, sale, marketing (including marketing Glenmark's Proposed ANDA Product as a generic substitute for FOTIVDA to be used and administered in the same manner as FOTIVDA), distribution, and/or importation of Glenmark's Proposed ANDA Product with the proposed labeling to be included for the Proposed ANDA Product, immediately and imminently upon approval of ANDA No. 220307. On information and belief, and subject to Plaintiffs' ongoing investigation and discovery efforts, by engaging in the forgoing activities, Glenmark specifically intends to infringe the '365 Patent.

ANSWER: Denied

66. On information and belief, Glenmark's specific intent to actively induce and/or contribute to infringement of at least claims 1 and 7 of the '365 Patent includes Glenmark's decision to proceed with its plan to engage in the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of Glenmark's Proposed ANDA Product, despite being aware that the proposed labeling to be included for the Proposed ANDA Product instructs, directs, recommends, encourages, and/or promotes direct infringement of at least claims 1 and 7 of the '365 Patent.

ANSWER: Denied.

67. On information and belief, and with full knowledge of the '365 Patent, Glenmark intends to and will actively induce infringement of the '365 Patent when Glenmark's Proposed ANDA is approved and will do so immediately and imminently upon approval.

ANSWER: Denied.

68. FOTIVDA and any corresponding generic tivozanib hydrochloride product is not a staple article of commerce and has no substantial approved uses that do not infringe at least claims 1 and 7 of the '365 Patent. On information and belief, Glenmark's Proposed ANDA Product is not a staple article of commerce and has no substantial uses that do not infringe at least claims 1 and 7 of the '365 Patent. Upon information and belief, and subject to Plaintiffs' ongoing investigation and discovery efforts, Glenmark, with full knowledge of the '365 Patent, knows that its Proposed ANDA Product is especially adapted for use in a manner that infringes the '365 Patent, is not a staple article of commerce, and has no substantial uses that do not infringe at least claims 1 and 7 of the '365 Patent.

ANSWER: Denied.

69. Any launch by Glenmark of the Proposed ANDA Product before expiration of the '365 Patent would cause Plaintiffs to suffer immediate and irreparable harm.

ANSWER: Denied.

70. Unless Glenmark is enjoined from infringing the '365 Patent, actively inducing infringement of the '365 Patent, and contributing to the infringement of others of the '365 Patent, Plaintiffs will suffer irreparable injury. Plaintiffs have no adequate remedy at law.

ANSWER: Denied.

71. Glenmark's infringement of the '365 Patent is willful.

ANSWER: Denied.

RESPONSE TO "COUNT II DECLARATORY JUDGMENT OF INFRINGEMENT OF THE '365 PATENT"

72. Plaintiffs incorporate each of the preceding paragraphs as if fully set forth herein.

ANSWER: Glenmark restates and incorporates each of its responses to the preceding Paragraphs 1-71 as if fully set forth herein.

73. These claims arise under the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202.

ANSWER: Paragraph 73 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that Plaintiffs' Complaint purports to state a

claim for declaratory judgment of infringement under 28 U.S.C. §§ 2201 and 2202. Glenmark denies any and all remaining allegations of Paragraph 73.

74. For the reasons explained in Count I above, if the FDA were to approve the Glenmark ANDA, Glenmark's commercial manufacture, use, marketing, offer for sale, sale, and/or importation into the United States of the Proposed ANDA Product would instruct, direct, recommend, encourage, and/or promote direct infringement, contributory infringement, and/or active inducement of infringement of at least, by way of example, claims 1 and 7 of the '365 Patent under 35 U.S.C. §§ 271(a)-(c).

ANSWER: Denied.

75. With full knowledge of the '365 Patent, Glenmark submitted ANDA No. 220307 to obtain approval under the FDCA to engage in the commercial manufacture, use, offer for sale, and/or sale of Glenmark's ANDA Product with its proposed labeling prior to expiration of the '365 Patent.

ANSWER: Paragraph 75 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that GPL's ANDA contains a certification pursuant to § 505(j)(2)(A)(vii)(IV) of the Federal Food, Drug, and Cosmetic Act for the '365 and '722 patents. Glenmark denies any and all remaining allegations of Paragraph 75.

76. Any launch by Glenmark of the Proposed ANDA Product before expiration of the '365 Patent would cause Plaintiffs to suffer immediate and irreparable harm.

ANSWER: Denied.

77. Glenmark's infringement of the '365 Patent would be willful.

ANSWER: Denied.

78. A definite and concrete controversy exists between Plaintiffs and Glenmark as to whether Glenmark's commercial manufacture, use, marketing, offer for sale, sale, and/or importation into the United States of the Proposed ANDA Product prior to the expiration of the '365 Patent would infringe the '365 Patent. Accordingly, Plaintiffs are entitled to a declaratory judgment that it would.

ANSWER: Paragraph 78 contains legal conclusions to which no answer is required. To the extent an answer is required, denied.

RESPONSE TO "COUNT III INFRINGEMENT OF THE '722 PATENT"

79. Plaintiffs incorporate each of the preceding paragraphs as if fully set forth herein.

ANSWER: Glenmark restates and incorporates each of its responses to the preceding Paragraphs 1-78 as if fully set forth herein.

80. The submission of the Glenmark ANDA to the FDA, including the Paragraph IV Certification submitted therewith, which seeks approval to engage in the commercial manufacture, use, marketing, offer for sale, sale, and/or importation of the Proposed ANDA Product prior to the expiration of the '722 Patent, constitutes infringement by Glenmark of the '722 Patent under 35 U.S.C. § 271(e)(2)(A).

ANSWER: Denied.

81. The commercial manufacture, use, marketing, offer for sale, sale, and/or importation into the United States of the Proposed ANDA Product by Glenmark before the expiration of the '722 Patent would constitute infringement by Glenmark of the '722 Patent under 35 U.S.C. §§ 271(a)-(c), and (g).

ANSWER: Denied.

82. On information and belief, and subject to Plaintiffs' ongoing investigation and discovery efforts, if Glenmark's Proposed ANDA Product is approved, Glenmark will make, offer for sale, sell, or import Glenmark's ANDA Product, comprising crystalline tivozanib hydrochloride, and would infringe at least, by way of example, independent claims 1 and 13 of the '722 Patent, which recite as follows:

> **1. Crystalline N-{2-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N′-(5-methyl-3-isoxazolyl)urea monohydrochloric acid salt monohydrate.**
>
> **13. A process for producing a crystal N-{2-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N′-(5-methyl-3-isoxazolyl)urea, monhydrochloric acid salt monohydrate, said process comprising the steps of:**
>
> > **adding hydrochloric acid to a solution of N-{2-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N′-(5-methyl-3-isoxazolyl)urea in an aprotic polar solvent selected from N,N-dimethylformamide and N,Ndimethylacetamide; adding ethanol and water to the above solution to precipitating crystals from the solution.**

ANSWER: Denied.

83. Glenmark did not set forth any theory of noninfringement with respect to any claim of the '722 patent in its Paragraph IV Notice Letter.

ANSWER: Denied.

84. On information and belief, Glenmark's Proposed ANDA Product, upon manufacture, formulation, and/or storage during its shelf life, will contain the same active ingredient as FOTIVDA, crystalline tivozanib hydrochloride, also referred to as N-{2-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N′-(5-methyl-3-isoxazolyl)urea monohydrochloric acid salt monohydrate. *See* 21 C.F.R. § 314.94(a)(1). Accordingly, on information and belief and subject to Plaintiffs' ongoing investigation and discovery efforts, the manufacture, use (including as directed in Glenmark's proposed labeling for Glenmark's Proposed ANDA Product), offer for sale, sale, marketing, distribution, and/or importation of Glenmark's Proposed ANDA Product will satisfy each of the recited elements of the compound recited in at least claim 1 of the '722 Patent, and thus directly infringe claim 1 of the '722 patent, either literally or under the doctrine of equivalents.

ANSWER: Denied.

85. On information and belief, and subject to Plaintiffs' ongoing investigation and discovery efforts, the crystalline tivozanib hydrochloride in Glenmark's Proposed ANDA Product will be manufactured by a process comprising the steps of (1) adding hydrochloric acid to a solution of N-{2-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N′-(5-methyl-3-isoxazolyl)urea in an aprotic polar solvent selected from N,N-dimethylformamide and N,Ndimethylacetamide; and (2) adding ethanol and water to the above solution to precipitating crystals from the solution. Accordingly, on information and belief and subject to Plaintiffs' ongoing investigation and discovery efforts, the manufacturing and/or importation of Glenmark's Proposed ANDA Products will satisfy each of the recited elements of the method described in claim 13 of the '722 Patent, and thus directly infringe claim 13 of the '722 patent, either literally or under the doctrine of equivalents.

ANSWER: Denied.

86. On information and belief, if the FDA were to approve the Glenmark ANDA, Glenmark's commercial manufacture, use, marketing, offer for sale, sale, and/or importation into the United States of the Proposed ANDA Product, including administration of Glenmark's Proposed ANDA Product according to the label instructions, would cause patients, physicians, prescribers, and/or other healthcare providers to directly infringe at least claims 1 and 13 of the '722 Patent. Glenmark would actively induce and contribute to such direct infringement.

ANSWER: Denied.

87. Glenmark has knowledge of the claims of the '722 Patent. Despite this knowledge, Glenmark has continued to assert its intent to engage in the manufacture, use, offer for sale, sale, marketing (including marketing Glenmark's Proposed ANDA Product as

a generic substitute for FOTIVDA to be used and administered in the same manner as FOTIVDA), distribution, and/or importation of Glenmark's Proposed ANDA Product with the proposed labeling to be included for the Proposed ANDA Product, immediately and imminently upon approval of ANDA No. 220307. On information and belief, and subject to Plaintiffs' ongoing investigation and discovery efforts, by engaging in the forgoing activities, Glenmark specifically intends to infringe the '722 Patent.

ANSWER: Denied.

88. On information and belief, Glenmark's specific intent to actively induce and/or contribute to infringement of at least claims 1 and 13 of the '722 Patent includes Glenmark's decision to proceed with its plan to engage in the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of Glenmark's Proposed ANDA Product, despite being aware that the proposed labeling to be included for the Proposed ANDA Product instructs, directs, recommends, encourages, and/or promotes direct infringement of the '722 Patent.

ANSWER: Denied.

89. On information and belief, and with full knowledge of the '722 Patent, Glenmark intends to and will actively induce infringement of the '722 Patent when Glenmark's Proposed ANDA is approved and will do so immediately and imminently upon approval.

ANSWER: Denied.

90. FOTIVDA and any corresponding generic tivozanib hydrochloride product is not a staple article of commerce and has no substantial approved uses that do not infringe at least claims 1 and 13 of the '722 Patent. Upon information and belief, and subject to Plaintiffs' ongoing investigation and discovery efforts, Glenmark, with full knowledge of the '722 Patent, knows that its Proposed ANDA Product is especially adapted for use in a manner that infringes the '722 Patent, is not a staple article of commerce, and has no substantial uses that do not infringe at least claims 1 and 13 of the '722 Patent.

ANSWER: Denied.

91. Any launch by Glenmark of the Proposed ANDA Product before expiration of the '722 Patent would cause Plaintiffs to suffer immediate and irreparable harm.

ANSWER: Denied.

92. Unless Glenmark is enjoined from infringing the '722 Patent, actively inducing infringement of the '722 Patent, and contributing to the infringement of others of the '722 Patent, Plaintiffs will suffer irreparable injury. Plaintiffs have no adequate remedy at law.

ANSWER: Denied.

93. Glenmark's infringement of the '722 Patent is willful.

ANSWER: Denied.

RESPONSE TO "COUNT IV DECLARATORY JUDGMENT OF INFRINGEMENT OF THE '722 PATENT"

94. Plaintiffs incorporate each of the preceding paragraphs as if fully set forth herein.

ANSWER: Glenmark restates and incorporates each of its responses to the preceding Paragraphs 1-93 as if fully set forth herein.

95. These claims arise under the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202.

ANSWER: Paragraph 95 contains legal conclusions to which no answer is required. To the extent an answer is required, Glenmark admits that Plaintiffs' Complaint purports to state a claim for declaratory judgment of infringement under 28 U.S.C. §§ 2201 and 2202. Glenmark denies any and all remaining allegations of Paragraph 95.

96. For the reasons explained in Count III above, if the FDA were to approve the Glenmark ANDA, Glenmark's commercial manufacture, use, marketing, offer for sale, sale, and/or importation into the United States of the Proposed ANDA Product would constitute, instruct, direct, recommend, encourage, and/or promote direct infringement, contributory infringement, and/or active inducement of infringement of at least, by way of example, claims 1 and 13 of the '722 Patent under 35 U.S.C. §§ 271(a)-(c), (g).

ANSWER: Denied.

97. With full knowledge of the '722 Patent, Glenmark submitted ANDA No. 220307 to obtain approval under the FDCA to engage in the commercial manufacture, use, offer for sale, and/or sale of Glenmark's ANDA Product prior to expiration of the '722 Patent.

ANSWER: Denied.

98. Any launch by Glenmark of the Proposed ANDA Product before expiration of the '722 Patent would cause Plaintiffs to suffer immediate and irreparable harm.

ANSWER: Denied.

99. Glenmark's infringement of the '722 Patent would be willful.

ANSWER: Denied.

100. A definite and concrete controversy exists between Plaintiffs and Glenmark as to whether Glenmark's commercial manufacture, use, marketing, offer for sale, sale, and/or importation into the United States of the Proposed ANDA Product prior to the expiration of the '722 Patent would infringe the '722 Patent. Accordingly, Plaintiffs are entitled to a declaratory judgment that it would.

ANSWER: Paragraph 100 contains legal conclusions to which no answer is required. To the extent an answer is required, denied.

* * *

Glenmark denies any and all allegations not expressly admitted herein. Glenmark further denies that Plaintiffs are entitled to any of the relief requested or to any relief whatsoever. Glenmark respectfully requests that the Court: (a) dismiss this action with prejudice; (b) enter judgment in favor of Glenmark; (c) award Glenmark its reasonable attorneys' fees and costs incurred in defending this action pursuant to 35 U.S.C. § 285; and (d) award Glenmark such further relief as the Court deems just and appropriate.

DEFENSES

Without prejudice to the denials set forth in its Answer, without admitting allegations of the Complaint not otherwise admitted (and, for purposes of clarity, those allegations not specifically admitted are denied), and without undertaking any of the burdens imposed by law on Plaintiffs, Glenmark asserts the following defenses to the Complaint:

First Defense

The Complaint fails to state a claim upon which relief can be granted.

Second Defense

The proposed manufacture, use, sale, offer for sale, importation, and/or marketing of the tivozanib capsules, 0.89 mg and 1.34 mg, products described in GPL's ANDA No. 220307 ("GPL's ANDA Products") has not infringed, does not infringe, and will not—if made, used, sold, offered for sale, imported, or marketed—infringe either directly or indirectly, any valid and/or enforceable claim of the '365 and/or '722 patents.

Third Defense

Glenmark has not induced, does not induce, and will not induce infringement of any valid and/or enforceable claim of the '365 and/or '722 patents.

Fourth Defense

Glenmark has not contributed, does not contribute, and will not contribute to infringement of any valid and/or enforceable claim of the '365 and/or '722 patents.

Fifth Defense

The claims of the '365 and '722 patents are invalid for failure to comply with one or more of the requirements in 35 U.S.C. §§ 101, 102, 103, and/or 112, and/or for obviousness-type double patenting.

Sixth Defense

The Court lacks subject matter jurisdiction over any and all claims asserted under 35 U.S.C. § 271(a), (b), and/or (c).

Seventh Defense

The Complaint fails to state a claim for willful infringement and/or exceptional case.

Eighth Defense

Any additional defenses or counterclaims that discovery may reveal.

* * *

COUNTERCLAIMS

Defendants/Counterclaim-Plaintiffs Glenmark Pharmaceuticals Limited ("GPL") and Glenmark Pharmaceuticals Inc., USA ("Glenmark USA") (collectively, "Glenmark") for their Counterclaims against Plaintiffs/Counterclaim-Defendants AVEO Pharmaceuticals, Inc. and Kyowa Kirin Co., Ltd. (collectively, "Plaintiffs"), allege as follows:

THE PARTIES

1. GPL is a corporation organized and existing under the laws of India, having a registered office at B/2, Mahalaxmi Chambers, 22, Bhulabhai Desai Road, Mumbai 400026, India.

2. Glenmark USA is a corporation organized and existing under the laws of the State of Delaware, having a principal place of business at 750 Corporate Drive, Mahwah, New Jersey 07430.

3. On information and belief, and according to Plaintiffs' Complaint, AVEO Pharmaceuticals, Inc. is a corporation organized and existing under the laws of the State of Delaware, having a principal place of business at One Marina Park Drive, 12th Floor, Boston, Massachusetts 02210. (Complaint at ¶ 3).

4. On information and belief, and according to Plaintiffs' Complaint, Kyowa Kirin Co., Ltd. is a corporation organized and existing under the laws of Japan, having a principal place of business at 1-9-2, Otemachi, Chiyoda-Ku, Tokyo Japan 100-0004. (Complaint at ¶ 4).

JURISDICTION

5. These Counterclaims arise under the Patent Law of the United States, 35 U.S.C. § 1 *et seq.*; the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202; and the Medicare Prescription

Drug, Improvement, and Modernization Act of 2003, Pub. L. No. 108-173, 117 Stat. 2066 (2003) ("MMA") (21 U.S.C. § 355(j) and 35 U.S.C. § 271(e)(5)).

6. This Court has original jurisdiction over the subject matter of these Counterclaims under 28 U.S.C. §§ 1331 and 1338(a); under the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202; and under the MMA (21 U.S.C. § 355(j) and 35 U.S.C. § 271(e)(5)).

7. This Court has personal jurisdiction over Plaintiffs because: (i) Plaintiffs have availed themselves of the rights and privileges—and subjected themselves to the jurisdiction—of this forum by suing Glenmark in this District; (ii) AVEO Pharmaceuticals, Inc. is organized and existing under the laws of the State of Delaware; and/or (iii) Plaintiffs conduct substantial business in, and have regular and systematic contact with, this District.

FACTUAL BACKGROUND

FOTIVDA® (tivozanib hydrochloride)

8. AVEO Pharmaceuticals, Inc. purports to be the holder of approved New Drug Application ("NDA") No. 212904, under which the United States Food and Drug Administration ("FDA") granted approval for tivozanib hydrochloride, 0.89 mg and 1.34 mg, capsules marketed in the United States under the trade name FOTIVDA®.

9. At the time the Complaint was filed, the *Approved Drug Products with Therapeutic Equivalence Evaluations* ("Orange Book"), which is published by FDA, listed U.S. Patent Nos. 11,504,365 ("the '365 patent") and 7,166,722 ("the '722 patent"), *inter alia*, in connection with NDA No. 212904.

Patents-in-Suit

The '365 Patent

10. The '365 patent issued on or about November 22, 2022, from U.S. Patent Application Serial No. 17/720,619 ("the '619 application"), filed on April 14, 2022, as a purported continuation of U.S. Patent Application Serial No. 17/289,913 ("the '913 application"), filed as International Application No. PCT/US2019/059904 ("PCT '904") on November 5, 2019. What purports to be a true and correct copy of the '365 patent is attached to Plaintiffs' Complaint as Exhibit A.

11. The '365 patent is titled "Use of Tivozanib to Treat Subjects with Refractory Cancer."

12. The face of the '365 patent identifies Michael P. Bailey and Michael N. Needle as the purported inventors.

13. AVEO Pharmaceuticals, Inc. is listed as "assignee" of the '365 patent on the face of the '365 patent.

14. AVEO Pharmaceuticals, Inc. purports and claims to be the owner of the '365 patent.

15. On information and belief, AVEO Pharmaceuticals, Inc. claims and purports to have the right to enforce the '365 patent.

16. On information and belief, and according to Plaintiffs' Complaint, Plaintiffs submitted information regarding the '365 patent in the Orange Book with respect to FOTIVDA, for strengths EQ 0.89MG BASE (Product 001), and EQ 1.34MG BASE (Product 002). (Complaint at ¶ 28).

17. By listing the '365 patent in the Orange Book, Plaintiffs maintain that an infringement suit can reasonably be asserted against any generic Abbreviated New Drug

Application ("ANDA") applicant—including GPL—that attempts to seek approval for, and market, a generic version of FOTIVDA® before the expiration of the '365 patent.

The '722 Patent

18. The '722 patent issued on or about January 23, 2007, from U.S. Patent Application Serial No. 10/532,104 ("the '104 application"), filed as a National Stage Entry of International Application No. PCT/JP03/13439 ("PCT '439") on October 21, 2003. What purports to be a true and correct copy of the '722 patent is attached to Plaintiffs' Complaint as Exhibit B.

19. The '722 patent is titled "N-{2-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(5-methyl-3-isoxazolyl)urea salt in crystalline form."

20. The face of the '722 patent identifies Naoki Matsunaga, Satoshi Yoshida, Ayako Yoshino, and Tatsuo Nakajima as the purported inventors.

21. Kirin Beer Kabushiki Kaisha is listed as "assignee" of the '722 patent on the face of the '722 patent.

22. Kyowa Kirin Co., Ltd. purports and claims to be the owner of the '722 patent.

23. AVEO Pharmaceuticals, Inc. purports and claims to be the exclusive licensee of the '722 patent.

24. On information and belief, Kyowa Kirin Co., Ltd. and/or AVEO Pharmaceuticals, Inc. claims and purports to have the right to enforce the '722 patent.

25. On information and belief, and according to Plaintiffs' Complaint, Plaintiffs submitted information regarding the '722 patent in the Orange Book with respect to FOTIVDA, for strengths EQ 0.89MG BASE (Product 001), and EQ 1.34MG Base (Product 002). (Complaint at ¶ 29).

26. By listing the '722 patent in the Orange Book, Plaintiffs maintain that an

infringement suit can reasonably be asserted against any generic ANDA applicant—including GPL—that attempts to seek approval for, and market, a generic version of FOTIVDA® before the expiration of the '722 patent.

GPL's ANDA Products

27. GPL has filed ANDA No. 220307 ("GPL's ANDA") with the FDA.

28. Because GPL's ANDA seeks FDA approval to engage in the commercial manufacture, use or sale of Tivozanib Capsules, 0.89 mg and 1.34 mg ("GPL's ANDA Products") prior to the expiration of the '365 and '722 patents, GPL's ANDA includes a certification under 21 U.S.C. § 355(j)(2)(A)(vii)(IV) to the '365 and '722 patents.

29. On June 13, 2025, Plaintiffs filed the above-captioned action against Glenmark asserting infringement of the '365 and '722 patents.

COUNT I
Declaration of Non-Infringement of the '365 Patent

30. Glenmark realleges and incorporates by reference the allegations in the preceding paragraphs as if fully set forth herein.

31. A present, genuine, and justiciable controversy exists between Plaintiffs and Glenmark regarding, *inter alia*, whether the manufacture, use, offer for sale, sale, or importation of GPL's ANDA Products would infringe any valid and enforceable claim of the '365 patent.

32. The manufacture, use, offer for sale, sale, or importation of GPL's ANDA Products would not directly or indirectly infringe any valid and enforceable claim of the '365 patent, either literally or under the doctrine of equivalents.

33. Glenmark is entitled to a declaration that the manufacture, use, offer for sale, sale, or importation of GPL's ANDA Products would not infringe any valid and enforceable claim of the '365 patent.

COUNT II
Declaration of Invalidity of the '365 Patent

34. Glenmark realleges and incorporates by reference the allegations in the preceding paragraphs as if fully set forth herein.

35. A present, genuine, and justiciable controversy exists between Plaintiffs and Glenmark regarding, *inter alia*, the invalidity of the '365 patent.

36. The claims of the '365 patent are invalid for failure to satisfy one or more of the conditions for patentability in Title 35 of the United States Code, including, but not limited to, 35 U.S.C. §§ 101, 102, 103, 112, and/or for obviousness-type double patenting, the bases for which include, at the very least, one or more of the following:

a. The alleged invention of the '365 patent does no more than combine familiar elements according to known methods to yield predictable results. Any alleged improvement set forth in the '365 patent over the prior art is no more than the predictable use of prior art elements according to their established functions. A person of ordinary skill in the art would have been motivated to combine the teachings of the prior art to achieve the alleged invention of the '365 patent and would have had a reasonable expectation of success in doing so.

b. The subject matter claimed in the '365 patent fails to comply with, *inter alia*, 35 U.S.C. §§ 102 and/or 103 at least in that the claimed subject matter as a whole was anticipated by the prior art and/or any differences between the subject matter claimed in the patent and the prior art are such that the claimed invention as a whole would have been obvious at the time the alleged invention was made, and/or before the effective filing date of the claimed invention, would have been obvious before the effective filing date of the claimed invention to a person having knowledge of

such prior art and having ordinary skill in the art to which the claimed invention pertains. Non-limiting examples of prior art rendering each of the claims of the '365 patent invalid under, at least, 35 U.S.C. §§ 102 and/or 103, include, but are expressly not limited to, one or more (or a combination of one or more) of the references and/or products set forth, and discussed, in Glenmark's Notice Letter.

37. Glenmark is entitled to a declaration that the claims of the '365 patent are invalid for failure to satisfy one or more of the conditions for patentability in Title 35 of the United States Code, and/or for obviousness-type double patenting.

COUNT III
Declaration of Non-Infringement of the '722 Patent

38. Glenmark realleges and incorporates by reference the allegations in the preceding paragraphs above as if fully set forth herein.

39. A present, genuine, and justiciable controversy exists between Plaintiffs and Glenmark regarding, *inter alia*, whether the manufacture, use, offer for sale, sale, or importation of GPL's ANDA Products would infringe any valid and enforceable claim of the '722 patent.

40. The manufacture, use, offer for sale, sale, or importation of GPL's ANDA Products would not directly or indirectly infringe any valid and enforceable claim of the '722 patent, either literally or under the doctrine of equivalents.

41. Glenmark is entitled to a declaration that the manufacture, use, offer for sale, sale, or importation of GPL's ANDA Products would not infringe any valid and enforceable claim of the '722 patent.

COUNT IV
Declaration of Invalidity of the '722 Patent

42. Glenmark realleges and incorporates by reference the allegations in the preceding paragraphs as if fully set forth herein.

43. A present, genuine, and justiciable controversy exists between Plaintiffs and Glenmark regarding, *inter alia*, the invalidity of the '722 patent.

44. The claims of the '722 patent are invalid for failure to satisfy one or more of the conditions for patentability in Title 35 of the United States Code, including, but not limited to, 35 U.S.C. §§ 101, 102, 103, 112, and/or for obviousness-type double patenting, the bases for which include, at the very least, one or more of the following:

a. The alleged claimed invention of the '722 patent does no more than combine familiar elements according to known methods to yield predictable results. Any alleged improvement set forth in the '722 patent over the prior art is no more than the predictable use of prior art elements according to their established functions. A person of ordinary skill in the art would have been motivated to combine the teachings of the prior art to achieve the alleged invention of the '722 patent and would have had a reasonable expectation of success in doing so.

b. The subject matter claimed in the '722 patent fails to comply with, *inter alia*, 35 U.S.C. §§ 102 and/or 103 at least in that the claimed subject matter as a whole was anticipated by the prior art and/or any differences between the subject matter claimed in the patent and the prior art are such that the claimed invention as a whole would have been obvious at the time the alleged invention was made, and/or before the effective filing date of the claimed invention, to a person having knowledge of such prior art and having ordinary skill in the art to which the claimed invention pertains. Non-limiting examples of prior art rendering each of the claims of the '722 patent invalid under, at the very least, 35 U.S.C. §§ 102 and/or 103, include,

but are expressly not limited to, one or more (or a combination of one or more) of the references and/or products set forth and discussed in Glenmark's Notice Letter.

c. The claims of the '722 patent are not patentably distinct from the subject matter claimed in the '987 patent—an earlier patent having a different expiration date—and thus, the '722 patent claims impermissibly extend the patentee's right to exclude the public from practicing the invention in the now-expired '987 patent.

45. Glenmark is entitled to a declaration that the claims of the '722 patent are invalid for failure to satisfy one or more of the conditions for patentability in Title 35 of the United States Code, and/or for obviousness-type double patenting.

PRAYER FOR RELIEF

WHEREFORE, Glenmark respectfully requests that this Court enter a Judgment and Order in its favor and against Plaintiffs/Counterclaim-Defendants as follows:

(a) Declaring that the manufacture, sale, offer for sale, use, or importation of GPL's ANDA Products do not and will not infringe (either literally or under the doctrine of equivalents), directly or indirectly (either by inducement or contributorily), any valid and enforceable claim of the '365 patent;

(b) Declaring that the claims of the '365 patent are invalid;

(c) Declaring that the manufacture, sale, offer for sale, use, or importation of GPL's ANDA Products do not and will not infringe (either literally or under the doctrine of equivalents), directly or indirectly (either by inducement or contributorily), any valid and enforceable claim of the '722 patent;

(d) Declaring that the claims of the '722 patent are invalid;

(e) Ordering that Plaintiffs' Complaint be dismissed with prejudice and judgment entered in favor of Glenmark;

(f) Declaring that this is an exceptional case under 35 U.S.C. § 285 and awarding Glenmark its attorneys' fees, costs, and expenses in this action; and

(g) Awarding Glenmark any further and additional relief as the Court deems just and proper.

DEMAND FOR JURY TRIAL

Glenmark hereby demands a jury trial on all issues so triable.

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