UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22314-1450
www.uspto.gov

Christopher J. Betti, Ph.D
Morgan, Lewis & Bockius LLP (CH-BSK)
1111 Pennsylvania Avenue, N.W.
Washington, DC 20004

In Re: Patent Term Extension
Application for
U.S. Patent No. 9,273,141
Filed: September 18, 2020

April 20, 2023

ORDER TO SHOW CAUSE

This is an order to show cause based on the apparent ineligibility of U.S. Patent No. 9,273,141 (the '141 patent) for patent term extension ("PTE") request under 35 U.S.C. § 156.

Factual Background

1. On March 1, 2016, the United States Patent and Trademark Office ("USPTO" or "Office") issued the '141 patent to Algate *et al.* The patent is assigned to Glaxo Group Limited ("Glaxo").[1]

2. On August 5, 2020 the Food and Drug Administration ("FDA") pursuant to § 351(a) of the Public Health Service Act, 42 U.S.C. § 262, approved the Biologics License Application (BLA), BLA-761158 for BLENREP® (belantamab mafodotin-blmf) to the Marketing Applicant Glaxo.[2]

3. BLENREP® (belantamab mafodotin-blmf) (BLA-761158) was approved by the FDA under the expedited regime called Accelerated Approval Program with the aim of providing treatment to patients with refractory myeloma cancer, 21 C.F.R. § 601.41.[3]

4. On September 18, 2020, Glaxo filed a PTE Application under 35 U.S.C. § 156 to extend the term of the '141 patent based on the regulatory review period under § 351 of the Public Health services Act (PHSA) for the human biological product BLENREP® (belantamab mafodotin-blmf).[4]

5. On December 8, 2020, pursuant to the Memorandum of Understanding ("MOU") between the USPTO and the FDA,[5] the USPTO requested assistance from the FDA in confirming that BLENREP® (belantamab mafodotin-blmf) was approved pursuant to BLA-761158.

6. On March 1, 2021, the FDA confirmed that BLENREP® (belantamab mafodotin-blmf) was approved pursuant to BLA-761158 on August 5, 2020.

---

[1] See the PTE application Appendix A.
[2] See the PTE application page 2, Appendix C.
[3] See the PTE application Appendix C and I.
[4] See the PTE application pages 1-2.
[5] See 52 Fed. Reg. 17830, May 12, 1987.

7. On December 8, 2021, the Office pursuant to 35 U.S.C. § 156(d)(2(A)(ii) asked the FDA to determine the applicable regulatory review period (RRP) for BLENREP® (belantamab mafodotin-blmf) and publish the determination as a notice in the Federal Register.

8. On July 13, 2022, the FDA published the RRP for BLENREP® (belantamab mafodotin-blmf) in the Federal Register Notice at Vol. 87 No. 133 starting at page no. 41727.

9. On March 30, 2023, the FDA published the revocation of BLENREP® (belantamab mafodotin-blmf) as requested by Glaxo in the Federal Register Notice at Vol. 88 No. 61, page no. 19153. Accordingly, Glaxo requested the revocation of BLA-761158 and "waived" its opportunity for a hearing.

Analysis

Pursuant to 21 U.S.C. § 301, the FDA is mandated by Congress to review BLA filings. The data gathered during the clinical trials of BLA become part of the approval process. The goal of the BLA approval process, *in part*, is to provide enough information to permit the FDA reviewer to determine whether the drug is safe and effective in its proposed use(s), and whether the benefits of the drug outweigh the risks.

The FDA has instituted the Accelerated Approval Program to allow for earlier approval of drugs that treat serious conditions, based on displaying proven efficacy at a designated future endpoint. An approved active ingredient under this program is still subject to final ratification by FDA officials where applicant is required to conduct studies to confirm the anticipated clinical benefit. If the confirmatory trial shows that the drug actually provides a clinical benefit then the FDA grants final approval for the drug. However, if the confirmatory trials do not verify the promised clinical benefit of a drug or do not demonstrate sufficient clinical benefit to justify the risks associated with the drug, then the drug's approval may be withdrawn or the label indication of the drug adjusted. *See*, 21 C.F.R. § 314.530.[6]

The human biological drug product BLENREP® (belantamab mafodotin-blmf) was approved under the FDA's Accelerated Approval Requirement which relies on a surrogate endpoint or an intermediate clinical endpoint pending final FDA approval based on due diligence and further clinical data. *See*, 21 C.F.R. § 601.41.

According to the PTE application, the FDA initially authorized introduction of BLENREP® (belantamab mafodotin-blmf) into interstate commerce under the condition that in order to obtain final FDA approval certain endpoint benchmarks must be met, otherwise the approval for BLENREP® (belantamab mafodotin-blmf) BLA-761158 will be withdrawn.[7]

[6] At www. FDA.gov: Accelerated Approval, last visited April 19, 2023.

[7] See the PTE application Exhibit I.

ACCELERATED APPROVAL REQUIREMENTS

Products approved under the accelerated approval regulations, 21 CFR 601.41, require further adequate and well-controlled studies/clinical trials to verify and describe clinical benefit. You are required to conduct such clinical trial with due diligence. If postmarketing studies/clinical trials fail to verify clinical benefit or are not conducted with due diligence, we may, following a hearing in accordance with 21 CFR 601.43(b), withdraw this approval. We remind you of your postmarketing requirement specified in your submission dated August 4, 2020. This requirement, along with required completion dates, is listed below.

3800-1 Submit the final study report and datasets from a randomized phase 3 clinical trial that verifies and describes the clinical benefit of belantamab mafodotin in patients with relapsed or refractory multiple myeloma. Patients should be randomized to receive belantamab mafodotin compared to standard therapy for relapsed or refractory multiple myeloma. The primary endpoint should be progression-free survival and secondary endpoints that include overall survival and overall response rate, as well as patient-reported outcomes. This trial should include a sufficient number of older patients (ages 65-74 and ≥75) and patients with extramedullary disease.

Draft Protocol Submission: 04/2020 (completed)
Final Protocol Submission: 09/2020
Trial Completion: 09/2022
Final Report Submission: 01/2023

According to the published Federal Register Notice of March 30, 2023, Glaxo requested withdrawal "(revocation)" of its BLA for the human biological product BLENREP® (belantamab mafodotin-blmf).[8] The Notice, in part, provided that the required clinical data did not meet the required threshold to receive final approval and Glaxo waived its oppurtunity for a hearing.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2023–N–0964]

GlaxoSmithKline Intellectual Property Development Ltd. England; Announcement of the Revocation of the Biologics License for BLENREP

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the revocation of the biologics license for BLENREP (belantamab mafodotin-blmf) powder for injection. GlaxoSmithKline

On November 2, 2022, FDA and GSK met to discuss the results of the confirmatory study required as a condition of BLENREP's accelerated approval, entitled "Study of Single Agent Belantamab Mafodotin Versus Pomalidomide Plus Low-dose Dexamethasone (Pom/Dex) in Participants with Relapsed/Refractory Multiple Myeloma (DREAMM-3 trial)" and considerations regarding

[8] See 88 Fed. Reg. 19153, March 30, 2023.

withdrawal (revocation) of the biologics license for BLENREP because the confirmatory DREAMM–3 trial did not meet its primary endpoint to demonstrate superior progression-free survival. On November 18, 2022, GSK requested withdrawal (revocation), in writing, of the biologics license for BLENREP (belantamab mafodotin-blmf) powder for injection (BLA 761158) under § 601.5(a) (21 CFR 601.5(a)) and waived its opportunity for a hearing. On February 6, 2023, the Agency issued a letter to GSK revoking the biologics license for BLENREP (belantamab mafodotin-blmf) powder for injection (BLA 761158).

Therefore, under § 601.5(a), the Agency revoked the biologics license for BLENREP (belantamab mafodotin-blmf) powder for injection (BLA 761158), effective as of February 6, 2023, the date of FDA's letter revoking the biologics license for BLENREP.

The right to extend the term of a patent is predicated on obtaining final FDA approval based upon regulatory review which is the result of the Drug Price Competition and Patent Term Restoration Act of 1984, Public Law 98-417, 98 Stat. 1585, commonly known as Hatch-Waxman Act. *See,* 21 U.S.C.§ 355(b), (j), (l); 35 U.S.C. § 156; and Manual of Patent Examination Procedure (MPEP) § 2750.

The PTE application is required to set forth an identification of the date on which the product received permission for commercial marketing or use under the provision of law under which the applicable regulatory review period occurred. *See,* 37 C.F.R. § 1.740(a).

The patent term extension determination is made based on the representations contained in the PTE application. 35 U.S.C. § 156(c) provides "[t]he term of a patent eligible for extension under subsection (a) shall be extended by the time equal to the regulatory review period for *the approved product* which period occurs after the date the patent is issued". Further information may be required or inquiry made of applicant before a final determination is made on whether a patent is eligible for extension. *See* 37 C.F.R. § 1.750.

Requirement to Show Cause

Since there is no longer an approved product, Glaxo is required to show cause with regard to its PTE application for BLENREP® (belantamab mafodotin-blmf) and establish: (1) why the USPTO should not terminate the PTE application based on the plain language of 35 U.S.C. § 156(c); and (2) why the PTE application for the '141 patent should remain under consideration despite Glaxo's express written request of withdrawal (revocation) of BLA-761158 and waiver of the opportunity for a hearing. In responding to the show cause request, Glaxo should identify statutory language in 35 U.S.C. § 156 or case law that would support extension of the '141 patent that claims the product despite revocation of the biologics license application. Moreover, Glaxo should explain how a PTE application for a withdrawn "revoked" biologics license application is in compliance with requirements of 37 C.F.R. § 1.740.

Time Period For Response

Applicant has **TWO MONTHS** from the date of this letter to reply to this requirement. Extensions of time under 37 C.F.R. § 1.136 are available.

Any correspondence from applicant with respect to this matter should be submitted via the USPTO's EFS Web system and should be addressed as follows:

By mail: Commissioner for Patents
Mail Stop Hatch-Waxman PTE
P.O. Box 1450
Alexandria, VA 22313-1450

Telephone inquiries related to this notice should be directed to the undersigned at (571) 272-0909.

/Ali Salimi/
Ali Salimi
Senior Legal Advisor
Office of Patent Legal Administration
Office of the Deputy Commissioner for Patents

cc: FDA, CDER, Office of Regulatory Policy
10903 New Hampshire Avenue,
Bldg. 51 Room 6250
Silver Spring MD 20993-0002

Attention: Beverly Friedman

RE: BLENREP® (belantamab mafodotin-blmf)
Docket No.: FDA-2020-E-2275