UNITED STATES OF AMERICA
BEFORE FEDERAL TRADE COMMISSION

In the Matter of **WATSON PHARMACEUTICALS INC.,** a corporation; **ACTAVIS INC.,** a corporation; **ACTAVIS PHARMA HOLDING 4 EHF.,** a private limited liability company; and **ACTAVIS S.Á.R.L.,** a limited liability corporate entity.	Docket No. C-4373

PETITION OF RESPONDENT TEVA PHARMACEUTICAL INDUSTRIES LTD. TO REOPEN AND MODIFY DECISION AND ORDER

Pursuant to Section 5(b) of the Federal Trade Commission Act, 15 U.S.C. § 45(b), and Section 2.51(b) of the Commission's Rules of Practice and Procedure, Teva Pharmaceutical Industries Ltd. ("Teva"), a Respondent in the above-captioned matter as a successor to the merged parties Watson and Actavis,[1] hereby petitions the Federal Trade Commission (the "Commission") to reopen this matter for the limited purpose of modifying and setting aside the Commission's Decision and Order ("Order"), dated December 14, 2012 (attached as Exhibit 1), as it applies to Teva's agreement to supply the abuse-resistant opioid painkiller morphine sulphate naltrexone extended release capsules (brand name Embeda®) to Pfizer Inc. ("Pfizer") (the "Embeda Supply Arrangement"). Specifically, Teva hereby petitions the Commission to

[1] Capitalized terms not otherwise defined in this report have the meanings given to such terms in the Decision and Order issued in the above-captioned matter. Teva became a Respondent when it completed the acquisition of the Allergan Generic Pharmaceutical Entities from Allergan plc. *See* Paragraph XIII, Decision and Order, In the Matter of Teva Pharmaceutical Industries, Ltd. and Allergan plc.

modify the provision in Paragraph I.III.6 of the Order stating that the Embeda Supply Arrangement shall "not . . . exceed four years" from the date Pfizer reintroduced Embeda into the commercial market (the "Four-Year Supply Limitation"). At Pfizer's request, Teva is seeking modification of the Order to extend the Embeda Supply Arrangement for an additional period and, thereby, to avoid supply interruption and preserve competition for Embeda until such time as Pfizer is able to manufacture Embeda independently of Teva.

The Embeda Supply Arrangement did not arise out of a generic product divestiture. Rather, it was a pre-existing agreement between Pfizer and Actavis at the time of Actavis's merger with Watson, pursuant to which Actavis was working to re-launch, and supply Pfizer with, *branded* Embeda—a complex extended release product in capsule form. Watson, by contrast, had filed an Abbreviated New Drug Application with the FDA, seeking approval to sell a generic version of Embeda. Thus, and as a condition to approving Watson's merger with Actavis, the Commission required Actavis to amend the Embeda Supply Arrangement: (1) to allow supply to continue long enough for Pfizer to re-launch branded Embeda; but (2) to include the Four-Year Supply Limitation, to ensure that Watson retained the incentive to develop and launch its competing generic product; and (3) to grant Pfizer the right to qualify an alternative supplier, and to require Actavis to assist in transfer of the manufacturing technology in the event Pfizer were to exercise that right, so that Pfizer could, at its option, receive supply of Embeda independent of Watson/Actavis even before the Embeda Supply Arrangement expired pursuant to the Four-Year Supply Limitation.

The continuation of the Embeda Supply Arrangement was in large part successful: Pfizer reintroduced Embeda in January 2015 and, according to IMS, had gross sales of approximately $53 million in 2017, and Teva is currently planning to introduce generic Embeda [redacted]

[redacted]. Presently, however, Pfizer has not yet been able to complete the active and ongoing tech transfer of Embeda manufacturing to a third party. And due to the Four-Year Supply Limitation, Teva cannot supply Pfizer after December 2018, potentially threatening patients' ability to fill their Embeda prescriptions. Therefore, at Pfizer's request, Teva is petitioning the Commission to modify the Order to remove the Four-Year Supply Limitation or extend it for a limited period of time, so that Teva and Pfizer may amend their Development and Manufacturing Services Agreement and extend the Embeda Supply Arrangement until [redacted] (the "Proposed Fourth Amendment") (attached as Exhibit 7).

The Commission should grant Teva's Petition for either of two independently sufficient reasons. ***First***, changed circumstances—namely, the fact that Pfizer will not be able to manufacture Embeda independently of Teva by December 2018, when the Embeda Supply Arrangement is presently slated to expire—warrant removing or extending the Four-Year Supply Limitation. ***Second***, the public interest heavily favors removing or extending the Four-Year Supply Limitation because doing so (1) will preserve Pfizer's ability to supply patients with Embeda, and (2) will not impact Teva's plans to introduce a generic version of Embeda, which Teva remains fully incentivized to do.

I. Summary of Relevant Facts

A. The Pre-Order Market for Embeda

1. Actavis's Embeda Supply Agreement

In February 2008, Alpharma Pharmaceuticals LLC ("Alpharma") and Actavis Elizabeth LLC entered into a Development and Manufacturing Services Agreement (the "Embeda Supply Agreement") (attached as Exhibit 2), under which Actavis agreed to "assist in the scale-up, validation for commercialization, commercial manufacturing and packaging" of Embeda.

Alpharma submitted a new drug application ("NDA") for Embeda to the FDA on or about June 30, 2008, and the FDA approved Alpharma's NDA on or about August 13, 2009.

King Pharmaceuticals, Inc. ("King"), which acquired Alpharma in December 2008, launched Embeda in September 2009. Pfizer acquired King in March 2011. Shortly thereafter, due to formulation and safety concerns, Pfizer voluntarily recalled Embeda with a plan to reintroduce the product "as quickly as possible."[2] Embeda remained off the market at the time that Actavis announced its merger with Watson in 2012.

2. Watson's Proposed Generic Version of Embeda

In 2011, Watson filed an abbreviated new drug application ("ANDA") to market a generic version of Embeda. Watson's ANDA included a Paragraph IV certification, 21 U.S.C. § 355(j)(2)(A)(vii)(IV), that the Pfizer patents protecting Embeda were invalid or not infringed by the proposed generic. Watson notified Pfizer of its Paragraph IV certification pursuant to 21 U.S.C. § 355(j)(2)(B), and Pfizer sued Watson in the United States District Court for the District of Delaware, alleging that Watson's proposed generic would infringe four patents covering Embeda.

B. The Commission's Order

On or about April 25, 2012, Watson announced that it had entered into an agreement to acquire Actavis. The Commission believed that this combination risked "reduc[ing] future competition in generic markets that do not yet exist," including the market for Embeda. *See* Analysis of Agreement Containing Consent Orders To Aid Public Comment. For this reason, the

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[2] *See* Press Release, Pfizer Reports Results From Three Phase 4 Studies Demonstrating EMBEDA® (morphine sulfate and naltrexone hydrochloride) Extended Release Capsules CII Impact On Drug Liking And Withdrawal Symptoms (Dec. 21, 2011), https://www.pfizer.com/news/press-release/press-release-detail/pfizer_reports_results_from_three_phase_4_studies_demonstrating_embeda_morphine_sulfate_and_naltrexone_hydrochloride_extended_release_capsules_cii_impact_on_drug_liking_and_withdrawal_symptoms.

Commission required Watson/Actavis to effectively "divest" the Embeda Supply Arrangement by giving Pfizer the right to qualify an alternate supplier, and by agreeing to tech transfer the relevant intellectual property and manufacturing know-how in the event Pfizer were to exercise that right. *See* Order ¶ I.III.1-5.

The Commission also sought to ensure that, during the interim period, Watson/Actavis would continue to supply Embeda to Pfizer in a way that was fair to both Pfizer and Respondents. Specifically, the Commission required Watson/Actavis to grant Pfizer "rights to extend" Actavis's supply of Embeda, for a period "not to exceed four (4) years" after Pfizer's reintroduction of the product. Order ¶ I.III.6 This Four-Year Supply Limitation was designed both to ensure that Watson/Actavis would continue to develop generic Embeda and also to give Pfizer the ability to become a "viable and effective" independent competitor. *See* Order ¶ IV.E.

To satisfy these obligations and address the Commission's concerns, Pfizer and Actavis entered into—and the Commission approved—the Second Amendment to the Development and Manufacturing Services Agreement (the "Second Amendment") (attached as Exhibit 4).[3] The Second Amendment provided that [redacted]. Further, in the Second Amendment, [redacted].[4]

[3] Actavis and King had entered into a First Amendment to the Development and Manufacturing Services Agreement in September 2009 (attached as Exhibit 3), which did not impact the duration of the Embeda Supply Agreement and thus is not the subject of this Petition.

[4] With the Commission's approval, Actavis and Pfizer also entered into the Third Amendment to the Development and Manufacturing Services Agreement (the "Third Amendment") (attached as Exhibit 5), executed on September 24, 2012 and approved by the Commission. The Third Amendment [redacted]

(cont'd)

C. Post-Order Developments

1. Teva Has Acquired Watson's ANDA and Actavis's Supply Obligations

In August 2016, Teva completed its acquisition of the generic pharmaceutical business of Allergan plc. As part of this acquisition, Teva both acquired the Watson ANDA for Embeda and assumed Actavis's rights and obligations under the Embeda Supply Agreement. Teva also became a Respondent for purposes of the Order.

2. Teva Is Currently Planning To Launch Generic Embeda in [redacted]

On July 31, 2014, Pfizer and Watson settled their patent infringement litigation by entering into the Embeda Settlement and License Agreement ("Embeda SLA") (attached as Exhibit 8). In the Embeda SLA, Pfizer granted Watson a license to the Embeda patents [redacted]

(cont'd from previous page) [redacted]

Put another way, the market and competitive dynamics today are just the same as they were when the Commission first approved the Order. And accordingly, Teva's incentives to bring generic Embeda to market as quickly as possible are just as strong now as Watson's were then.

3. The Tech Transfer is Challenging and Remains Ongoing

Using product manufactured and supplied by Watson/Actavis, Pfizer relaunched Embeda in January 2015. And [redacted]. But Pfizer, despite its best efforts, does not expect to complete the technically challenging Embeda tech transfer until [redacted] at the earliest.

The Commission recently recognized that extended-release products like Embeda are "complex" and "difficult to manufacture."[5] And Embeda's abuse-deterrent properties make manufacturing especially difficult. Embeda is an extended-release capsule that includes morphine sulphate and naltrexone hydrochloride that is sequestered from the morphine. If Embeda is taken as intended, the naltrexone remains sequestered and has no impact on the patient; if Embeda is crushed or chewed, the naltrexone is released and intermingles with—and reverses the subjective and analgesic effects of—the morphine.[6] Pfizer tested the efficacy of this abuse-deterrent technology in three clinical studies (two oral and one intranasal), and Embeda's FDA-approved labeling states that "in vitro and pharmacokinetic data . . . along with results from

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[5] *See, e.g.*, Analysis of Agreement Containing Consent Orders To Aid Public Comment, *In the Matter of Amneal Holdings, LLC, Amneal Pharmaceuticals LLC, Impax Laboratories, Inc., and Impax Laboratories, LLC*, Dkt. No. C-4650, at 4 (describing generic aspirin and dipyridamole extended release ("ER") capsules as "complex pharmaceutical products that are difficult to manufacture").

[6] *See generally* Embeda: Technology, https://www.pfizerpro.com/product/embeda/hcp/technology (last visited Aug. 7, 2018).

the oral and intranasal human abuse potential studies indicate that Embeda has properties that are expected to reduce abuse via the oral and intranasal route."[7] Manufacturing Embeda in a way that effects proper naltrexone sequestration—and the concomitant patient-safety benefits—is a complex and difficult operation.

Pfizer has been actively working on the technical transfer of the Embeda product from Actavis' Elizabeth, NJ manufacturing site to [redacted] manufacturing site for a number of years. *See* Affidavit of Adam Schwab (attached as Exhibit 11) ¶ 2. The transfer project has been highly active and has included: [redacted].

In sum, while Pfizer continues to do everything it can to complete the tech transfer as expeditiously as possible, the high technical risk associated with this very complex product—

[7] Embeda, Highlights of Prescribing Information, *available at* https://www.accessdata.fda.gov/drugsatfda_docs/label/2014/022321s016lbl.pdf.

including risk [redacted] —has made it impossible for Pfizer to complete the transfer any earlier than [redacted].

4. The Parties Wish To Enter into the Proposed Fourth Amendment

At Pfizer's request, Pfizer and Teva negotiated the Proposed Fourth Amendment. The Proposed Fourth Amendment, which is contingent on Commission approval pursuant to Paragraph IX.F of the Order, would extend Teva's obligation to supply Pfizer with Embeda until [redacted]. The Proposed Fourth Amendment would not alter other critical terms—including pricing or similar terms between Pfizer and Teva. Nor would the Proposed Fourth Amendment alter—either explicitly or implicitly—the terms of Teva's patent license pertaining to generic Embeda.

II. Changed Conditions of Fact and the Public Interest Warrant Reopening and Modifying the Order

Section 5(b) of the FTC Act, 15 U.S.C. § 45(b), and Section 2.51(b) of the Commission's Rules of Practice, 16 C.F.R. §2.51(b), provide that, upon a party's request, the Commission shall reopen an order and consider whether it should be modified if the party makes "a satisfactory showing that changed conditions of law or fact require the rule or order to be altered, modified, or set aside, in whole or in part, or that the public interest so requires." 16 C.F.R. § 2.51(b); *see also In the Matter of Eli Lilly & Co.*, Dkt. No. C-3594, 127 F.T.C. 577, 578 (1999) ("A satisfactory showing sufficient to require reopening is made when a request identifies significant changes in circumstances and shows that the changes eliminate the need for the order or make continued application if inequitable or harmful to competition.").

Here, Teva can readily show that the Commission should re-open the Order and modify it

to remove or extend the Four-Year Supply Limitation. Pfizer's inability, despite its efforts, to complete the tech transfer is a changed condition of fact that warrants modification. In addition, and in the alternative, removing or extending the Four-Year Supply Limitation is in the public interest because doing so—and allowing the Proposed Fourth Amendment—both (1) will ensure that Pfizer will remain on the market and also (2) will not impact Teva's internal plan to launch generic Embeda [redacted]. In any event, the Commission should modify the Order to remove or extend the Four-Year Supply Limitation and pave the way for the Proposed Fourth Amendment.

A. Pfizer's Inability To Complete the Tech Transfer Is a Changed Circumstance that Requires Modifying the Order

At the time of the Order, the Commission had no reason to doubt that Pfizer would be able to complete the tech transfer and become an effective manufacturer of Embeda within four years. However, due to Embeda's complexity, Pfizer has not been able to complete the tech transfer and become able to manufacture Embeda independently of Teva. *See supra*, Section I.C.3. In the past, the Commission has modified orders where continuing to apply them would inhibit market participation. *See, e.g.*, *In the Matter of California Med. Ass'n*, Dkt. No. C-2967, 120 F.T.C. 858, 862 (1995) (modifying, in light of changed circumstances, order provisions that "inhibit[ed] conduct that is necessary for CMA to participate in the managed care market"); *In the Matter of Gen. Motors Corp., et al.*, Dkt. No. C-3132, 116 F.T.C. 1276, 1284 (1993) (modifying, in light of changed circumstances, "the order's limitations on the output and the duration of [a] joint venture" between GM and Toyota); *In the Matter of Genstar Ltd.*, Dkt. No. C-3049, 104 F.T.C. 264 (1984) (modifying, in light of changed circumstances, "import restrictions [that] limit[ed] Genstar's ability to compete to its fullest in the relevant market"). Just so here, where, in light of changed circumstances, the Four-Year Supply Limitation

threatens to eliminate Pfizer's ability to remain on the market and provide Embeda to patients.

And importantly, the Proposed Fourth Amendment does not take advantage of changed circumstances to depart from the spirit of the Order. Instead, the Proposed Fourth Amendment will extend supply [redacted], so that Teva and Pfizer have additional time to address the unanticipated difficulties in completing the tech transfer and fulfilling the Order's goals. Pfizer will retain its ability to become "a viable and effective competitor, that is independent of Respondents, in the research, Development, and manufacture of" Embeda. Order ¶ IV.E.3. And Teva will continue to develop—[redacted]—a competing generic version of Embeda. *See supra*, Section I.C.2.

B. The Public Interest Requires Modifying the Order

Because changed circumstances independently warrant reopening and modification here, the Commission need not consider whether removing or extending the Four-Year Supply Limitation would serve the public interest. *See, e.g., In the Matter of Entergy Corp.*, Dkt. No. C-3998, 140 F.T.C. 1125, 1128 (2005) ("In this instance, however, we do not need to assess the sufficiency of Entergy's and EKLP's public interest showing because the Commission has determined that Entergy and EKLP have made the requisite satisfactory showing that changed conditions of fact require the Order to be reopened and set aside."). However, should the Commission deem it necessary to assess the public-interest impact of removing or extending the Four-Year Supply Limitation, Teva submits that doing so would be demonstrably procompetitive and, thus, the Order should be modified accordingly.

1. Without the Fourth Amendment, the Number of Embeda Competitors Will Be Reduced—Potentially to Zero

At present, Pfizer markets the lone Embeda product on the market. And [redacted]

[redacted]. This means that, starting in [redacted], there will be at most three versions of Embeda available to patients: Pfizer's brand, Pfizer's authorized generic (supplied by Teva, should Pfizer elect to launch an authorized generic), and Teva's generic. Without supply from Teva, however, Pfizer will no longer be able to continue supplying brand-name Embeda to the market, nor will it be able to launch an authorized generic. In other words, leaving the Four-Year Supply Limitation intact could result in patients having absolutely no Embeda available to them from as early as December 2018 until Teva introduces its generic.[8] The abuse of opioids is so severe and well-documented that President Trump has declared it a "public health emergency."[9] Today, more than ever, it is critical to preserve the availability of abuse-resistant formulations such as Embeda.

2. *Teva Currently Plans to Launch Generic Embeda in [redacted] Irrespective of the Four-Year Supply Limitation or the Proposed Fourth Amendment*

Watson and Pfizer settled their patent infringement litigation related to Embeda in July 2014, and, in the Embeda SLA, Watson obtained a patent license that begins [redacted]. The parties negotiated that license date and executed the Embeda SLA years before the Proposed Fourth Amendment was ever contemplated. The license date is and has been the

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[8] Pfizer could even opt to discontinue Embeda altogether. Under these circumstances, the Watson ANDA likely would remain approvable. *See* Office of Generic Drugs, Referencing Approved Drug Products in ANDA Submissions, at 5 (explaining that the FDA "will remove [a] listed drug from the Orange Book and . . . will not . . . approve ANDAs that refer to the drug product" if the agency "determines that the listed drug was withdrawn from sale for reasons of safety or effectiveness"), *available at* https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM536962.pdf. But withdraw of a reference listed drug can result in outdated labeling—including safety—information for patients. *See, e.g.*, Remarks from FDA Commissioner Scott Gottlieb, M.D., as Prepared for Testimony Before a U.S. Senate Committee on Appropriations on FDA's Fiscal Year 2019 Budget, *available at* https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm605539.htm (last visited Aug. 10, 2018).

[9] *See, e.g.*, Louise Radnofsky & Jon Kamp, *Trump Announces Opioid Crisis a Public Health Emergency*, WALL ST. J., Oct. 26, 2017, *available at* https://www.wsj.com/articles/president-trump-to-announce-opioid-crisis-a-public-health-emergency-1509024286; *see also* U.S. Food & Drug Administration, Timeline of Selected FDA Activities and Significant Events Addressing Opioid Misuse and Abuse, https://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm338566.htm (last visited Aug. 9, 2018).

primary driver of Teva's planned launch. And indeed, Teva's current plan, subject to FDA requirements, is to launch the product [redacted]. Teva [redacted] (*see supra*, Section I.C.2), and remains fully committed to launching as quickly as possible both to ensure patient access to a generic and to prolong Teva's de facto generic exclusivity. And no changes to the Embeda Supply Arrangement in the Proposed Fourth Amendment—including extending the term of supply—would affect Teva's incentives to launch generic Embeda.

At bottom, the Proposed Fourth Amendment does nothing more than maintain the status quo as it existed when the Commission approved the Order. Accordingly, here, the Commission should modify the Order to remove or extend the Four-Year Supply Limitation.

III. Conclusion

For the foregoing reasons, Teva respectfully requests that the Commission grant Teva's Petition to Reopen and Modify Decision and Order and remove or extend the Four-Year Supply Limitation from the Order.

Pursuant to 28 U.S.C. § 1746, I declare under penalty of perjury that the foregoing is true and correct to the best of my knowledge.

Executed this 4th day of October, 2018.

Respectfully submitted

Brian P. Savage
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Teva Pharmaceuticals USA, Inc.

INDEX OF EXHIBITS

Exhibit No.	Description
1	Decision and Order, *In re Watson Pharmaceuticals, Inc. and Actavis Inc. et al.*
2	Development and Manufacturing Services Agreement
3	First Amendment to Development and Manufacturing Services Agreement
4	Second Amendment to Development and Manufacturing Services Agreement
5	Third Amendment to Development and Manufacturing Services Agreement
6	Notice of Extension of Term
7	Fourth Amendment to Manufacturing and Development Services Agreement
8	Settlement and License Agreement
9	Complete Response letter from U.S. Food & Drug Administration to Actavis Laboratories, FL, Inc. dated July 27, 2018
10	Affidavit of Vance Russell
11	Affidavit of Adam Schwab