DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

ANDA 208061

ANDA APPROVAL

Lupin Pharmaceuticals, Inc.
U.S. Agent for Lupin Limited
111 South Calvert Street
Harborplace Tower, 24th Floor
Baltimore, MD 21202
Attention: Mr. Sudhir Kaushal
Director of Regulatory Affairs

Dear Sir:

This letter is in reference to your abbreviated new drug application (ANDA) received for review on April 13, 2015, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Testosterone Topical Solution, 30 mg per actuation.[1]

Reference is also made to the complete response letter issued by this office on June 17, 2016, and to any amendments thereafter.

We have completed the review of this ANDA and have concluded that adequate information has been presented to demonstrate that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, the ANDA is **approved**, effective on the date of this letter. The Office of Bioequivalence has determined your Testosterone Topical Solution, 30 mg per actuation, to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug (RLD), Axiron Topical Solution, 30 mg per actuation, of Eli Lilly and Company (Lilly).

The RLD upon which you have based your ANDA, Lilly's Axiron Topical Solution, 30 mg per actuation, is subject to periods of patent protection. The following patents and expiration dates are currently listed in the Agency's publication titled *Approved Drug Products with Therapeutic Equivalence Evaluations* (the "Orange Book"):

U.S. Patent Number	Expiration Date
8,419,307 (the '307 patent)	February 26, 2027
8,435,944 (the '944 patent)	September 27, 2027
8,784,878 (the '878 patent)	July 13, 2023
8,807,861 (the '861 patent)	February 26, 2027

8,993,520 (the '520 patent)	June 2, 2026
9,180,194 (the '194 patent)	June 2, 2026
9,289,586 (the '586 patent)	February 26, 2027

Your ANDA contains paragraph IV certifications to each of the patents under section 505(j)(2)(A)(vii)(IV) of the FD&C Act stating that the patents are invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Testosterone Topical Solution, 30 mg per actuation, under this ANDA. You have notified the Agency that Lupin Limited (Lupin) complied with the requirements of section 505(j)(2)(B) of the FD&C Act and that litigation was initiated within the statutory 45-day period against Lupin for infringement of the '307, '944, '861 and '520 patents in the United States District Court for the Southern District of Indiana [Eli Lilly and Company, Eli Lilly Export S.A., Acrux DDS PTY Ltd. vs. Perrigo Company, Perrigo Israel Pharmaceuticals Ltd., Actavis Laboratories UT, Inc. formerly known as Watson Laboratories Inc., Amneal Pharmaceuticals, LLC, Lupin Pharmaceuticals, Inc. Lupin Ltd., Civil Action No. 13-0851 (consolidated)] and the United States District Court for the Eastern District of Virginia [Eli Lilly and Company, Eli Lilly Export S.A., and Acrux DDS PTY Ltd. v. Lupin Pharmaceuticals, Inc. and Lupin Ltd., Civil Action No. 15-0877]. You have also notified the Agency that on August 22, 2016, the court issued a decision in CA No. 13-0851 (consolidated) of non-infringement of the patent claims at issue in the litigation[2], and that CA No. 15-0877 was subsequently dismissed.

Under section 506A of the FD&C Act, certain changes in the conditions described in this ANDA require an approved supplemental application before the change may be made.

RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENTS

Section 505-1 of the FD&C Act authorizes FDA to require the submission of a risk evaluation and mitigation strategy (REMS), if FDA determines that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks [section 505-1(a)]. In accordance with section 505-1(i) of the FD&C Act, a drug that is the subject of an ANDA under section 505(j) is subject to certain elements of the REMS required for the applicable listed drug.

Your final proposed REMS submitted on April 28, 2017 and appended to this letter is approved with your application. The REMS consists of a Medication Guide.

We remind you that you must include an adequate rationale to support a proposed REMS modification for the addition, modification, or removal of any goal or element of the REMS, as described in section 505-1(g)(4) of the FD&C Act.

Prominently identify the submission containing proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

NEW SUPPLEMENT FOR ANDA 208061/S-000
CHANGES BEING EFFECTED IN 30 DAYS
PROPOSED MINOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR ANDA 208061/S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED MAJOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR ANDA 208061/S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED REMS MODIFICATIONS DUE TO SAFETY LABELING CHANGES SUBMITTED IN SUPPLEMENT XXX

Should you choose to submit a REMS revision, prominently identify the submission containing the REMS revisions with the following wording in bold capital letters at the top of the first page of the submission:

REMS REVISION FOR ANDA 208061

To facilitate review of your submission, we request that you submit your proposed modified REMS and other REMS-related materials in Microsoft Word format.

Under section 506A of the FD&C Act, certain changes in the conditions described in this ANDA require an approved supplemental application before the change may be made.

REPORTING REQUIREMENTS

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98 and at section 506I of the FD&C Act. The Office of Generic Drugs should be advised of any change in the marketing status of this drug or if this drug will not be available for sale after approval. In particular, under section 506I(b) of the FD&C Act, you are required to notify the Office of Generic Drugs in writing within 180 days from the date of this letter if this drug will not be available for sale within 180 days from the date of approval. [As part of such written notification, you must include (1) the identity of the drug by established name and proprietary name (if any); (2) the ANDA number; (3) the strength of the drug; (4) the date on which the drug will be available for sale, if known; and (5) the reason for not marketing the drug after approval.].

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling materials prior to publication or dissemination. Please note that these submissions are voluntary. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert (PI), Medication Guide, and patient PI (as applicable) to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf).

You must also submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

ANNUAL FACILITY FEES

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions[3] with respect to self-identification of facilities and payment of annual facility fees. Your ANDA identifies at least one facility that is subject to the self-identification requirement and payment of an annual facility fee. Self-identification must occur by June 1st of each year for the next fiscal year. Facility fees must be paid each year by the date specified in the *Federal Register* notice announcing facility fee amounts. All finished dosage forms (FDFs) or active pharmaceutical ingredients (APIs) manufactured in a facility that has not met its obligations to self-identify or to pay fees when they are due will be deemed misbranded. This means that it will be a violation of federal law to ship these products in interstate commerce or to import them into the United States. Such violations can result in prosecution of those responsible, injunctions, or seizures of misbranded products. Products misbranded because of failure to self-identify or pay facility fees are subject to being denied entry into the United States.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical in content to the approved labeling (including the package insert, and any patient package insert and/or Medication Guide that may be required). Information on submitting SPL files using eLIST may be found in the guidance for industry titled “SPL Standard for Content of Labeling Technical Qs and As” at

http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf. The SPL will be accessible via publicly available labeling repositories.

The Electronic Common Technical Document (eCTD) is CDER's standard format for electronic regulatory submissions. Beginning May 5, 2017, ANDAs must be submitted in eCTD format and beginning May 5, 2018, drug master files must be submitted in eCTD format. Submissions that do not adhere to the requirements stated in the eCTD Guidance will be subject to rejection. For more information please visit: www.fda.gov/ectd.

Sincerely yours,

{See appended electronic signature page}

For Vincent Sansone, PharmD
Acting Deputy Director
Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research

ENCLOSURE: REMS

[1] We note that the reference listed drug (RLD) upon which you have based this ANDA, Eli Lilly and Company's (Lilly's) Axiron Topical Solution, 30 mg per actuation, is no longer being marketed in the United States and is currently listed in the discontinued section of FDA's *Approved Drug Products With Therapeutic Equivalence Evaluations* (the "Orange Book"). The Agency has determined that Lilly's Axiron Topical Solution, 30 mg per actuation, was not withdrawn from sale for reasons of safety or effectiveness. FDA will publish this determination in the *Federal Register* as soon as is practicable. This determination allows the Agency to approve ANDAs for the discontinued drug product(s).

[2] *Findings of Fact and Conclusions of Law and Final Judgment Based Thereon*, at 208-10, Civil Action No. 13-0851 (S.D. Ind. Aug. 22, 2016).

[3] Some of these provisions were amended by the Generic Drug User Fee Amendments of 2017 (GDUFA II) (Public Law 115-52, Title III).

Sarah Kurtz

Digitally signed by Sarah Kurtz
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