DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 206406

NDA APPROVAL

Veloxis Pharmaceuticals, Inc.
Attention: Mr. Ronald Guido
Vice President, Global Regulatory Affairs
Chief Compliance Officer
499 Thornall Street
3rd Floor
Edison, NJ 08837

Dear Mr. Guido:

Please refer to your New Drug Application (NDA) dated December 28, 2013, received December 30, 2013, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Envarsus XR (tacrolimus extended-release tablets), 0.75 mg, 1 mg and 4 mg.

We acknowledge receipt of your amendments dated

November 17, 2014	January 21, 2015	June 12, 2015	July 2, 2015
December 2, 2014	February 16, 2015	June 18, 2015	July 6, 2015
December 8, 2014	March 10, 2015	June 25, 2015	July 7, 2015
December 12, 2014	April 2, 2015	June 26, 2015	
December 16, 2014	April 13, 2014	July 1, 2015(2)	

Your application was tentatively approved on October 30, 2014. You submitted an amendment on June 12, 2015, after receiving advice provided in the December 5, 2014, teleconference, the December 12, 2014, advice letter and the two January 12, 2015, advice letters.

This new drug application provides for the use of Envarsus XR (tacrolimus extended-release tablets) for prophylaxis of organ rejection in kidney transplant patients converted from tacrolimus immediate-release formulations in combination with other immunosuppressants.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

WAIVER OF HIGHLIGHTS SECTION

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the package insert, Medication Guide). Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*, available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE CONTAINER LABELS

We acknowledge your September 26, 2014, October 9, 2014 and October 16, 2014, submissions containing final printed overwrap, carton and container labels.

Submit final printed carton and immediate container labels that are identical to the enclosed carton, overwrap and immediate container labels as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008)*. Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 206406**." Approval of this submission by FDA is not required before the labeling is used.

Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the

product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Tacrolimus, the active moiety in Envarsus XR, has orphan designation for the indication of prophylaxis of organ rejection in patients receiving allogeneic kidney transplant; therefore, PREA requirements do not apply to this application.

POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

2925-1 Develop and validate a regulatory X-Ray Powder Diffraction (XRPD) test, with a limit of detection of not more than (b) (4) for determination of crystalline tacrolimus content in tacrolimus extended-release tablets. Revise 3.2.P.5 Drug Product Specification accordingly. Submit a supplemental NDA to add the XRPD testing facility.

Add XRPD testing to the on-going drug product stability protocol (first three commercial batches of each strength or next three consecutive commercial batches of each strength and annual stability commitment batches).

The timetable you submitted on July 1, 2015 and July 6, 2015, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	09/2015
Study/Trial Completion:	04/2016
Final Report Submission:	07/2016
Interim Report:	01/2016

2925-2 Develop and validate an X-Ray Powder Diffraction (XRPD) test, with a limit of detection of not more than (b) (4)

Add XRPD testing to tacrolimus (b) (4) stability protocol.

The timetable you submitted on July 1, 2015 and July 6, 2015, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	09/2015
Study/Trial Completion:	04/2016

Final Report Submission: 07/2016
Interim Report: 01/2016

2925-3 Evaluate the crystalline content of available legacy batches of tacrolimus [redacted] and of drug product stability batches by XRPD.

The timetable you submitted on July 1, 2015 and July 6 2015, states that you will conduct this study according to the following schedule:

Final Protocol Submission: 09/2015
Study/Trial Completion: 04/2016
Final Report Submission: 07/2016
Interim Report: 01/2016

2925-4 Evaluate conditions that might be expected to promote crystallization of tacrolimus in [redacted] tablets, including:

1. Any relationship between [redacted] and crystalline Tacrolimus content in tacrolimus extended-release tablets.
2. The [redacted] stability of tacrolimus in [redacted] tablets under accelerated and stress conditions.

The timetable you submitted on July 6, 2015, states that you will conduct this study according to the following schedule:

Final Protocol Submission: 10/2015
Study/Trial Completion: 10/2016
Final Report Submission: 01/2017
Interim Report: 04/2016

2925-5 Evaluate the effect of [redacted] manufacturing process parameters on crystalline content of [redacted] tablets.

The timetable you submitted on July 6, 2015, states that you will conduct this study according to the following schedule:

Final Protocol Submission: 10/2015
Study/Trial Completion: 10/2016
Final Report Submission: 01/2017
Interim Report: 04/2016

Submit clinical protocols to your IND 75250 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each

study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled "**Postmarketing Commitment Protocol**," "**Postmarketing Commitment Final Report**," or "**Postmarketing Commitment Correspondence**."

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. 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, 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 20705-1266

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).

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. 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.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Lois Almoza, M.S., Regulatory Project Manager, at (301) 796-1600.

Sincerely,

{See appended electronic signature page}

Renata Albrecht, M.D.
Director
Division of Transplant and Ophthalmology Products
Office of Antimicrobial Products
Office of New Drugs
Center for Drug Evaluation and Research

Enclosure(s):
Content of Labeling (Package Insert)
Medication Guide
Carton, Overwrap and Container Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

RENATA ALBRECHT
07/10/2015