DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 203324/Original 2

NDA APPROVAL

Avedro, Inc.
Attention: Ms. Pamela Nelson
Vice President, Regulatory Affairs
230 Third Avenue
Waltham, MA 02451

Dear Ms. Nelson:

Please refer to your New Drug Application (NDA) dated September 16, 2013, received September 16, 2013, and your amendments, submitted under section 505(b)/ pursuant section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA), for Photrexa Viscous (riboflavin 5'-phosphate in 20% dextran ophthalmic solution) 0.146%, Photrexa (riboflavin 5'-phosphate ophthalmic solution) 0.146%, with the KXL System.

We acknowledge receipt of your amendment dated October 16, 2015, which constituted a complete response to our March 29, 2015, action letter. We also acknowledge receipt of your major amendment dated April 15, 2016, extending the goal date by three months to provide a full review of the submission.

NDA 203324 provides for the use of Photrexa Viscous (riboflavin 5'-phosphate in 20% dextran ophthalmic solution) 0.146%, Photrexa (riboflavin 5'-phosphate ophthalmic solution) 0.146%, with the KXL System for the following indications which, for administrative purposes, we have designated as follows:

- NDA 203324/Original 1 – treatment of progressive keratoconus
- NDA 203324/Original 2 – treatment of corneal ectasia following refractive surgery

NDA 203324/Original 1 was approved on April 15, 2016. The subject of this action letter is NDA 203324/Original 2.

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 with the following editorial revisions: the word "years" has been added to Section 8.4 of the package insert and to Section 1.9 of the operator's manual.

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 and operator's manual). 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.

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(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable. Because this drug product for this indication has an orphan drug designation, this requirement is not applicable.

POST MARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitment:

3106-1

A registry to provide long term evaluation of the durability of the treatment effect of the procedure in at least 100 corneal crosslinking-treated subjects at 3 years with a pre-treatment diagnosis of post-refractive corneal ectasia.

The timetable you submitted on July 13, 2016, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	01/2017
Enroll First Subject	10/2017
Study Completion:	07/2023
Final Report Submission:	12/2023

Submit clinical protocols to your IND 77,882 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 the 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 this postmarketing commitment 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 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 Jacquelyn Smith, MA, Senior Regulatory Project Manager at (301) 796-1600.

Sincerely,

{See appended electronic signature page}

Wiley A. Chambers, MD
Deputy Director
Division of Transplant and Ophthalmology Products
Office of Antimicrobial Products
Office of New Drugs
Center for Drug Evaluation and Research

{See appended electronic signature page}

Renata Albrecht, MD
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
Operator's Manual

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

/s/

WILEY A CHAMBERS
07/15/2016

RENATA ALBRECHT
07/15/2016