DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

IND 78,227

WRITTEN REQUEST

Omeros Corporation
Attention: Catherine A. Melfi, Ph.D
Vice President, Regulatory Affairs & Quality Systems
201 Elliott Avenue West
Seattle, WA 98119

Dear Dr. Melfi:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for OMS302 (phenylephrine-ketorolac injection) 1%/0.(b)(4)%. We also refer to your submission dated August 27, 2013, received August 28, 2013, containing your Pediatric Study Plan (PSP).

To obtain needed pediatric information on phenylephrine and ketorolac , the Food and Drug Administration (FDA) is hereby making a formal Written Request, pursuant to Section 505A of the Federal Food, Drug, and Cosmetic Act (the Act), as amended by the Food and Drug Administration Amendments Act of 2007, that you submit information from the study described below.

Clinical Trial: The trial must be double masked, randomized, parallel group, trial of patients with childhood cataracts. Study arms should consist of an OMS302 drug formulation arm (final dilution (b)(4) µM phenylephrine/(b)(4) µM ketorolac), and a phenylephrine-only arm (final dilution (b)(4) µM phenylephrine). The use of postoperative anti-infectives should be standardized.

Objective: The primary objective of the trial should be to evaluate the safety and the efficacy of OMS302 compared to a concurrent active control for intraoperative mydriasis and the reduction of ocular pain in patients who have undergone cataract surgery. Enrolled patients must include male and female patients with a clinical diagnosis of childhood cataract.

Age Groups/Number of Patients: Pediatric patients undergoing cataract surgery must be aged 0 to 3 years of age. At least 60 subjects (30 subjects per arm) must be enrolled, treated, and followed for three months postoperatively in this study.

Representation of Ethnic and Racial Minorities: This study must take into account adequate (e.g., proportionate to study population) representation of children of ethnic and racial minorities, or if it is not possible, a description of the efforts to do so and an explanation for why they were unsuccessful must be provided.

Trial endpoints: The primary study endpoints must be: 1) change in pupil diameter over time from surgical baseline (immediately prior to surgical incision) to the end of the surgical procedure (wound closure); and 2) postoperative pain as measured at a pre-determined timepoint within 24 hours of surgical initiation.

Statistical: The study should have the ability to detect adverse events which occur in the post-operative cataract surgery population at an incidence of 10% or greater.

Extraordinary results: In the course of conducting these trials, you may discover evidence to indicate that there are unexpected safety concerns, unexpected findings of benefit in a smaller sample size, or other unexpected results. In the event of such findings, there may be a need to deviate from the requirements of this Written Request. If you believe this is the case, you must contact the Agency to seek an amendment. It is solely within the Agency's discretion to decide whether it is appropriate to issue an amendment.

Drug information: OMS302 (phenylephrine 12 (b) (4) mg/mL and ketorolac 4.24 mg/mL) (b) (4) solution (b) (4) and administered as irrigation solution during surgery, resulting in a final dilution (b) (4) µM phenylephrine and (b) (4) µM ketorolac; and phenylephrine 12 (b) (4) mg/mL (b) (4) solution (b) (4) resulting in a final dilution (b) (4) µM phenylephrine.

Labeling that may result from the trials: You must submit proposed pediatric labeling to incorporate the findings of the trials. Under section 505A(j) of the Act, regardless of whether the trials demonstrate that phenylephrine and ketorolac are safe and effective, or whether such trial results are inconclusive in the studied pediatric population(s) or subpopulation(s), the labeling must include information about the results of the trials. Under section 505A(k)(2) of the Act, you must distribute to physicians and other health care providers at least annually (or more frequently if FDA determines that it would be beneficial to the public health), information regarding such labeling changes that are approved as a result of the trial.

Format and types of reports to be submitted: You must submit full trial reports (which have not been previously submitted to the Agency) that address the issues outlined in this request, with full analysis, assessment, and interpretation. In addition, the reports must include information on the representation of pediatric patients of ethnic and racial minorities. All pediatric patients enrolled in the trials should be categorized using one of the following designations for race: American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or other Pacific Islander or White. For ethnicity, you should use one of the following designations: Hispanic/Latino or Not Hispanic/Latino. If you choose to use other categories, you should obtain agency agreement.

Under section 505A(d)(2)(B) of the Act, when you submit the trial reports, you must submit all postmarketing adverse event reports regarding this drug that are available to you at that time. All post-market reports that would be reportable under section 21 CFR

314.80 should include adverse events occurring in an adult or a pediatric patient. In general, the format of the post-market adverse event report should follow the model for a periodic safety update report described in the Guidance for Industry E2C Clinical Safety Data Management: Periodic Safety Update Reports for Marketed Drugs and the Guidance addendum. You are encouraged to contact the reviewing Division for further guidance.

Although not currently required, we request that trial data be submitted electronically according to the Study Data Tabulation (SDTM) standard published by the Clinical Data Interchange Standards Consortium (CDISC) provided in the document "Study Data Specifications," which is posted on the FDA website at http://www.fda.gov/CDER/REGULATORY/ersr/Studydata.pdf and referenced in the FDA Guidance for Industry, *Providing Regulatory Submissions in Electronic Format - Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications* at http://www.fda.gov/Cder/guidance/7087rev.htm.

Timeframe for submitting reports of the trials:

- Protocol submission: December 2013
- First subject visit: June 2014
- Last subject visit: Thirty months following first subject visit
- Clinical study report: Nine months following last subject visit

Please keep in mind that pediatric exclusivity attaches only to existing patent protection or exclusivity that would otherwise expire nine (9) months or more after pediatric exclusivity is granted, and FDA has 180 days from the date that the trials reports are submitted to make a pediatric exclusivity determination. Therefore, to ensure that a particular patent or exclusivity is eligible for pediatric exclusivity to attach, you are advised to submit the reports of the trials at least 15 months (9 months plus 6 months/180 days for determination) before such patent or exclusivity is otherwise due to expire.

Response to Written Request: Under section 505A(d)(2)(A)(i), within 180 days of receipt of this Written Request you must notify the Agency whether or not you agree to the Written Request. If you agree to the request, you must indicate when the pediatric trials will be initiated. If you do not agree to the request, you must indicate why you are declining to conduct the trials. If you decline on the grounds that it is not possible to develop the appropriate pediatric formulation, you must submit to us the reasons it cannot be developed.

Furthermore, if you agree to conduct the trials, but have not submitted the trial reports on or before the date specified in the Written Request, the Agency may utilize the process discussed in section 505A(n) of the Act.

Submit protocols for the above study to an investigational new drug application (IND) and clearly mark your submission "**PEDIATRIC PROTOCOL SUBMITTED FOR PEDIATRIC EXCLUSIVITY STUDY**" in large font, bolded type at the beginning of the cover letter of the submission.

Reports of the study must be submitted as a new drug application (NDA) or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF PEDIATRIC STUDY REPORTS - PEDIATRIC EXCLUSIVITY DETERMINATION REQUESTED**" in large font, bolded type at the beginning of the cover letter of the submission and include a copy of this letter. Please also send a copy of the cover letter of your submission to the Director, Office of Generic Drugs, HFD-600, Metro Park North IV, 7519 Standish Place, Rockville, MD 20855-2773. If you wish to fax it, the fax number is 240-276-9327.

In accordance with section 505A(k)(1) of the Act, *Dissemination of Pediatric Information*, FDA must make available to the public the medical, statistical, and clinical pharmacology reviews of the pediatric studies conducted in response to this Written Request within 210 days of submission of your study report. These reviews will be posted regardless of the following circumstances:

1. the type of response to the Written Request (i.e. complete or partial response);
2. the status of the application (i.e. withdrawn after the supplement has been filed or pending);
3. the action taken (i.e. approval, complete response); or
4. the exclusivity determination (i.e. granted or denied).

FDA will post the medical, statistical, and clinical pharmacology reviews on the FDA website at http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/UCM049872

If you wish to discuss any amendments to this Written Request, please submit proposed changes and the reasons for the proposed changes to your application. Submissions of proposed changes to this request should be clearly marked "**PROPOSED CHANGES IN WRITTEN REQUEST FOR PEDIATRIC STUDIES"** in large font, bolded type at the beginning of the cover letter of the submission. You will be notified in writing if any changes to this Written Request are agreed upon by the Agency.

Please note that, if your trial is considered an "applicable clinical trial" under section 402(j)(1)(A)(i) of the Public Health Service Act (PHS Act), you are required to comply with the provisions of section 402(j) of the PHS Act with regard to registration of your trial and submission of trial results. Additional information on submission of such information can be found at www.ClinicalTrials.gov.

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

Sincerely,

{See appended electronic signature page}

Edward M. Cox, MD, MPH
Director
Office of Antimicrobial Products
Center for Drug Evaluation and Research

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

/s/

EDWARD M COX
10/03/2013