CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

202408Orig1s000

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

NDA 202408

MEETING MINUTES

Fera Pharmaceuticals, L.L.C.
Attention: Sadie M. Ciganek
Vice President, Regulatory Affairs
134 Birch Hill Road
Locust Valley, New York 11560

Dear Ms. Ciganek:

Please refer to your Pre-New Drug Application for Acyclovir Ophthalmic Ointment.

We also refer to the Pre-NDA Meeting between representatives of your firm and the FDA on December 6, 2010.

The official minutes of that meeting are enclosed. You are responsible for notifying us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, call Michael Puglisi, Project Manager, at (301) 796-0791.

Sincerely,

{See appended electronic signature page}

Wiley A. Chambers, M.D.
Acting Director
Division of Anti-Infective and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosure

MEMORANDUM OF MEETING MINUTES

MEETING DATE: December 6, 2010
MEETING TIME: 2:00 pm

APPLICATION (DRUG): NDA 202408
Acyclovir Ophthalmic Ointment

SPONSOR: Fera Pharmaceuticals, L.L.C. (Fera)

TYPE OF MEETING: Type-B, Pre-NDA Meeting

MEETING CHAIR: Wiley A. Chambers, M.D.

MEETING RECORDER: Michael Puglisi

FDA PARTICIPANTS: Division of Anti-Infective and Ophthalmology Products (Agency)
Wiley Chambers/ Acting Director
William Boyd/ Clinical Team Leader
Lucious Lim/ Medical Officer
Martin Nevitt/ Medical Officer
Jennifer Harris/ Medical Officer
Sonal Wadhwa/ Medical Officer
Rhea Lloyd/ Medical Officer
Linda Ng/ Premarketing CMC Pharmaceutical Assessment Lead
Yan Wang/ Statistics Team Leader
Dongliang Zhuang/ Statistics Reviewer
Amy Nostrandt/ Pharmacology/Toxicology Reviewer
Charles Bonapace/ Clinical Pharmacology Team Leader
Kimberly Bergman/ Clinical Pharmacology Reviewer
Michael Puglisi/ Project Manager

INDUSTRY PARTICIPANTS:
Representing Fera Pharmaceuticals, L.L.C. (Fera)
Frank DellaFera/ President
Sue Augello-Vaisey/ Senior Partner
Edward Lane/ Medical Director
Dave Cobb/ Vice President, Ophthalmics
Sadie M. Ciganek/ Vice President, Regulatory Affairs

MEETING OBJECTIVE: To discuss Fera's planned NDA submission of Acyclovir Ophthalmic Ointment (b) (4)

SUMMARY OF DISCUSSION:
Agency responses to the questions outlined in the November 6, 2010, background package were provided to Fera in an email sent on December 1, 2010 (see text in italics below). This meeting served to clarify those responses.

Questions for the Agency:

1. Will summary data from the scientific literature be acceptable in the overall meta analysis?

   Agency Response: *No. The clinical evidence to support an NDA needs to be derived from adequate and well controlled studies as defined in 21 CFR 314.126. Submissions to the NDA need to include sufficient information to be able to determine whether the clinical trial was an adequate and well controlled trial. In addition to being able to determine whether they are adequate and well controlled studies it is recommended that the NDA submission include sufficient descriptions of the studies to determine whether the studies can be combined.*

   Please note that we consider (b) (4)

   In addition,

   - *It was stated in the Meta Analysis Plan that 'If the proportion healed in the acyclovir group and the comparator group was the same, the odds ratio could not be computed. These studies were excluded (by the program) for computing the overall odds ratio in the meta-analysis.' We don't recommend the exclusion of these studies. If the studies were excluded by the program because of zero cells, alternative methods of analysis should be considered, such as Peto's odds ratio.*
   - *The primary outcome is the proportion of participants healed at Day 7. The proportions of participants healed at other time points are considered supportive endpoints. The meta-analysis of the primary outcome should be presented separately by the type of ulcer (dendritic and geographic) and the comparator (idoxuridine, arabinoside, ganciclovir, trifluorothymidine, interferon, and bromovinyldeoxyuridine). The current Meta Analysis Plan included the analysis of the proportions healed either combining all days for a particular comparator, or combining all types of ulcers at a particular time point.*
   - *In addition to odds ratio, the treatment difference in the proportion of participants healed at Day 7 and Day 14 and its two-sided 95% exact confidence interval should be provided for each individual study and for the meta-analysis.*

   You may find it useful to review the Medical Officer's Reviews for ganciclovir ophthalmic gel found on FDA's website.

Meeting Comments: The Agency stated that it believes published studies have sufficient information to support an indication of treatment of dendritic ulcers. The Agency stated that there is no need to perform a Meta Analysis on the data from the published studies. The Agency stated that labeling will include ocular events from the published ocular studies and systemic events from the oral administration studies.

2. Will process validation on three commercial batches be required at the time of NDA filing or will it be sufficient to submit an interim validation report with one batch then supplement the NDA with the final report (three batches) while the application is under review?

   Agency Response: *An interim process validation report for one batch may be submitted together with an executed batch record and master batch record at time of NDA filing. The final report of the three process validation batches should be stored on site, and do not need to be submitted to the NDA.*

   Comment: There was no further discussion of this matter.

3. How much accelerated and CRT stability data will be required at the time of NDA submission?

   Agency Response: *At least 12 months of room temperature and 6 months of accelerated stability data for 3 batches are recommended for NDA filing.*

   Meeting Comments: The Agency stated that it expects complete stability data at the time of NDA filing. The Agency may or may not review additional stability data submitted while the NDA is under review.

4. Draft labeling will be based on data from the scientific literature in addition to the package insert labeling for acyclovir (Zirgan). What additional sources, if any, will the agency require from Fera to be incorporated into the product labeling?

   Agency Response: *No additional sources would be required to be in the label, but the annotated label should identify all of the specific sources utilized for your labeling statements.*

   We anticipate that the acyclovir label (Zovirax) and the data from the scientific literature will provide the information for the label. Zirgan is the trade name for ganciclovir and not acyclovir.

   Comment: There was no further discussion of this matter.

5. Since the safety and toxicity profile of acyclovir is well established and there exists an abundance of information for the same, Fera intends to submit summary data of the scientific literature with a corresponding bibliography to support its 505(b)(2)

application. Will the agency accept this approach without the need for Fera to undertake additional animal and/or pharmacology studies?

Agency Response: *The application needs to include adequate and well controlled studies either directly or by reference. Additional studies (clinical or non-clinical) are not expected to be needed as long as you are able to reference the Agency's findings through a 505(b)(2) application and can link your product to the products in previous studies. Please provide copies of summarized and referenced publications.*

Comment: There was no further discussion of this matter.

Action Items:
The Agency agreed to issue minutes of this meeting within 30 days.

Minutes Prepared by: *{See appended electronic signature page}*

Michael Puglisi
Project Manager

Concurrence by: *{See appended electronic signature page}*

Wiley A. Chambers, M.D.
Acting Division Director

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
12/17/2010