CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

205394Orig1s000

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

IND 110,753

MEETING MINUTES

IntelGenx Corp.
Attention: Tom Namsavanh
Manager, Regulatory Affairs and Compliance
6425 Abrams
Saint-Laurent, Quebec
H4S 1X9

Dear Mr. Namsavanh:

Please refer to your Pre-Investigational New Drug Application (PIND) file for rizatriptan oral film.

We also refer to the meeting between representatives of your firm and the FDA on November 7, 2012. The purpose of the meeting was to discuss your pre-NDA meeting package for migraine.

A copy of the revised official minutes of the meeting is enclosed for your information. Please notify us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, call me at (301) 796-1056.

Sincerely,

{See appended electronic signature page}

Russell Katz, M.D.
Director
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure:
Meeting Minutes

MEMORANDUM OF MEETING MINUTES

Meeting Type:	**Type B**
Meeting Category:	**Pre-NDA**
Meeting Date:	**November 7, 2012**
Meeting Location:	**Teleconference**
Application Number:	**IND 110,753**
Product Name:	**rizatriptan oral film**
Indication:	**Migraine**
Sponsor/Applicant Name:	**IntelGenx**
Meeting Chair:	**Russell Katz, MD**
Meeting Recorder:	**Lana Chen, RPh**

FDA ATTENDEES

Division of Neurology Products
Russell Katz, MD, Division Director
Eric Bastings, MD, Deputy Director
Nushin Todd, MD, Clinical Reviewer
Lois Fred, PhD, Nonclinical Team Leader
Donald Charles Thompson, PhD, Nonclinical Reviewer
Martha Heimann, PhD, Pharmaceutical Assessment Lead
Jeanine Best, MSN, RN, PNP, Senior Clinical Analyst, Pediatric and Maternal Health Staff
Xinning Yang, PhD, Acting Clinical Pharmacology Team Leader
Deepika Lakhani, Biopharmaceutics
Jared Lantzy, OBI/DDMSS
Neda Aghajani Memar, PharmD, Visiting Fellow
Lana Chen, RPh, Project Manager

SPONSOR ATTENDEES

Tom Namsavanh Manager, RA and Compliance IntelGenx Corp.
Nadine Paiement Director, R&D IntelGenx Corp.
Horst G. Zerbe President & CEO IntelGenx Corp.
Reza Fathi Senior VP, R&D RedHill Biopharma
Elkan R. Gamzu Product Manager RedHill Biopharma
Ira N. Kalfus Chief Medical Officer RedHill Biopharma

DISCUSSION

CMC

(b) (4)

4 Pages have been Withheld in Full as b4 (CCI/TS) immediately following this page

(b) (4)

[redacted]

CLINICAL

1. In the light of the clinical study (RZA-P9-688), the applicant believes bioequivalence has been demonstrated between the applicant's rizatriptan 10 mg release oral film and the reference rizatriptan orally disintegrating tablet under fasting conditions. The synopsis of the clinical study is provided in Appendix E.

   Q: Based on the synopsis, does the Agency agree on the conclusion of the study?

   FDA Preliminary Response:
   On face, the conclusion of bioequivalence was demonstrated. However, the final conclusion will depend on review of the detailed raw datasets, bioanalytical method and inspection of the study. All individual and summarized datasets should be submitted as a SAS transport files (*.xpt). A description of each data item should be provided in a Define.pdf file.

   Meeting Discussion: There was no meeting discussion.

2. The applicant will perform a literature search for unreported new adverse events published from January 2011 to one month prior the date of the submission (expected to be February 2013). As of September 17, 2012, a search in PubMed using the keywords "rizatriptan" AND "adverse event*" in the title/abstract field yielded 64 results from 1998/01/01 to 2013/12/31. A filter for publication dates from 2011/01/01 to 2013/12/31 then yielded **11 results**.

   Also, a search in PubMed using the keywords "rizatriptan" AND "adverse reaction*" in the title/abstract field yielded 1 (one) result from 1998/01/01 to 2013/12/31. A filter for publication dates from 2011/01/01 to 2013/12/31 then yielded 0 (no) result.

   The applicant believes such methodology will address the Agency's concerns pertaining to unreported new adverse events since Maxalt-MLT's Prescribing Information revision of December 2011 (see Appendix F).

   Q: Does the Agency agree?

   FDA Preliminary Response:
   We agree.

   Meeting Discussion: There was no meeting discussion.

Other

Q: Does the Agency agree?

FDA Preliminary Response:

Meeting Discussion: There was no meeting discussion.

2. The applicant will submit the 505(b)(2) NDA in paper CTD format. The applicant will also provide an electronic copy of the submission on disc(s). The applicant will not submit in eCTD format. As per 21 CFR 314.54, the applicant will submit three types of copies of the application: an archival copy, a review copy and a field copy. The contents of each copy will meet the requirements set in 21 CFR 314.54. The applicant will await further feedback from the Division's RPM on the number of copies of each type to be provided.

Q: Does the Agency agree?

FDA Preliminary Response:

If you choose to submit a paper NDA, we remind you that you should submit copies of the Methods Validation Section as required by 21 CFR 314.50(e)(1).

The 505(b)(2) NDA should be submitted entirely in paper CTD format with no additional electronic copy or should be submitted in an electronic NDA (eNDA - non-eCTD) "Hybrid" format with no additional paper copies. Instructions for preparing and submitting a non-eCTD "Hybrid" electronic submission are included here (attached). Please also send the following information to the CDER Electronic Submission Support Team, so they can issue a waiver (from eCTD format) for the application:

As per the docket, the following information is required for a waiver:

The following information should be contained in an e-mail requesting a waiver should be sent to CDER's Electronic Submission Coordinator at esub@fda.hhs.gov <mailto:esub@fda.hhs.gov>.

* **Contact Person Name - This will be the main contact:**
* **Contact Person's Company Name:**
* **Contact Person's Mailing Address:**
* **Contact Person's Phone Number:**
* **Contact Person's Email Address:**
* **Relevant Submission Types and Numbers:**
* **A description of the submitters plan to become compliant with the guidance "Providing Regulatory Submissions in Electronic Format--Human Pharmaceutical Applications and Related Submissions Using the eCTD Specifications", including relevant timeframes.:**

The CDER Electronic Submission Support Team is available to answer any questions you might have regarding the submission of your application in an electronic format. Please contact them at esub@fda.hhs.gov.

Meeting Discussion: There was no meeting discussion.

Additional FDA Comments

Your product is considered a new dosage form. As such, your application will trigger the Pediatric Research Equity Act (PREA). Therefore, please indicate how pediatric studies will be or have been addressed for each pediatric age group (ages 0 months to 6 years, ages 6 to 11 years and, ages 12 to17 years).

PREA PEDIATRIC STUDY PLAN

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. Since your product is a new dosage form, you will need to submit a Pediatric Study Plan.

The Food and Drug Administration Safety and Innovation Act of 2012 changes the timeline for submission of a PREA Pediatric Study Plan and includes a timeline for the implementation of these changes. You should review this law and assess if your application will be affected by these changes. If you have any questions, please email the Pediatric Team at Pedsdrugs@fda hhs.gov.

Meeting Discussion:

Merck & Co. received Waxman-Hatch Exclusivity (expires December 15, 2015) and Pediatric Exclusivity (expires June 15, 2015) for Maxalt for studies conducted in pediatric patients ages 6 to 17 years for the acute treatment of migraine. Consider the protected pediatric information that appears in Maxalt labeling and the ability to leverage this existing data when the Pediatric Exclusivity expires when planning the timeline for PREA required studies.

PRESCRIBING INFORMATION

Proposed prescribing information (PI) submitted with your application must conform to the content and format regulations found at 21 CFR 201.56 and 201.57.

Summary of the Final Rule on the Requirements for Prescribing Information for Drug and Biological Products, labeling guidances, sample tool illustrating Highlights and Table of Contents, an educational module concerning prescription drug labeling, and fictitious prototypes of prescribing information are available at: http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/LawsActsandRules/ucm084159.htm. We encourage you to review the information at this website and use it as you draft prescribing information for your application.

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

/s/

RUSSELL G KATZ
12/06/2012