MIDATECH PHARMA US INC.

8601 Six Forks Road
Suite 400
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September 6, 2018

Donna Griebel, MD, Director
Division of Gastroenterology and Inborn Errors Products
Center for Drug Evaluation and Research
Food and Drug Administration
5901-B Ammendale Road
Beltsville, MD 20705-1266

Re: NDA #22,524 ZUPLENZ® (ondansetron) Oral Soluble Film
SN0094
RESPONSE TO PREA NON-COMPLIANCE LETTER
DEFERRAL EXTENSIONS REQUESTED (PMRs 1664-1, 1664-2, 1664-3, 1664-4)

Dear Dr. Griebel:

Reference is made to NDA #22,524 approved July 2, 2010 and to submission SN0047 in which the ownership of this NDA was transferred from Galena Biopharma, Inc. to Midatech Pharma US Inc. effective January 28, 2016.

Reference is also made to the following:

- Sponsor's Type C Meeting Request to discuss amending the Pediatric Study Plan (July, 2017; SN0072),
- Meeting briefing package (September, 2017; SN 0076),
- FDA's written responses (October, 2017),
- Sponsor's Type C Meeting Request (February 2018; SN0086),
- FDA's Meeting Request Granted letter (March, 2018),
- Meeting briefing package (March, 2018; SN0088),
- FDA's preliminary comments (April, 2018),
- Minutes of FDA-Sponsor telephonic meeting of May 2, 2018, and
- Submission SN0093, which included the full protocol for Study 1664-3 (August 31, 2018).

These interactions between the Agency and Sponsor have redefined the approach to obtaining PK information on Zuplenz in pediatric subjects (1664-1 and 1664-3); and further discussion may lead to data-driven decisions about the need for clinical efficacy studies in pediatric subjects (1664-2 and 1664-4). Per these interactions, the pediatric plan has been revised as follows:

- The Sponsor will initiate a PK study in pediatric surgical subjects aged 4 – 17 years (PONV), starting with the submission of the full protocol by September 4, 2018. It is noted that this work is underway, with the submission SN0093, which provided, for the purposes of FDA review and comment, the full protocol for Study 1664-3, (b) (4) [redacted]

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- [redacted] (b) (4)
- The Sponsor will utilize the PK results from the PONV setting along with modeling and simulations to evaluate exposures resulting from multi-dose administration of various dose levels to inform what dose of Zuplenz will provide exposures most comparable to [redacted] (b) (4) the CINV/HEC indication [redacted] (b) (4)
- Further assessment for the need for additional clinical studies (1664-1, 1664-2, and 1664-4) will be done upon review of the clinical PK results (1664-3) and the simulation results.

We respectfully request deferral extensions as follows:

- For PMR 1664-3 until October 2020 (25 months after PONV protocol 1664-3 submission to FDA, as agreed on May 2, 2018),
- For PMRs 1664-1, 1664-2, and 1664-4 until March 2021 (to permit time for the Agency to review study results for 1664-3, and for Sponsor to propose further clinical work and/or prepare partial waiver requests for these PMRs).

Midatech Pharma US Inc. is committed to working closely with the FDA to meet the highest and most ethical standards pertaining to pediatric research as owners of NDA #22,524 and we appreciate the Agency's assistance in these matters. If you have questions or require additional information, please contact me at 919-861-0226 by telephone, 919-861-0239 by facsimile, or at MaryKay.Delmedico@MidatechPharmaUS.com by e-mail.

Sincerely,

Mary Kay Delmedico
Digitally signed by Mary Kay Delmedico
Date: 2018.09.05 15:25:12 -04'00'

Mary Kay Delmedico, Ph.D.
Vice President, Scientific & Regulatory Affairs

ELECTRONIC SUBMISSION SPECIFICATIONS

This application is submitted in compliance with the "*Guidance for Industry – Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*" (April 2018).

ELECTRONIC DESCRIPTION

Contents of the media: one (1) transmission through the Electronic Submissions Gateway (ESG).

VIRUS VERIFICATION

This submission is virus-free and confirmed via Kaspersky Total Security - Anti-Virus Software.

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