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June 27, 2024

Rigoberto Roca, M.D.
Director, Division of Anesthesiology, Addiction Medicine, and Pain Medicine (DAAP)
Office of Neuroscience
Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-1266

RESPONSE TO PREA NON-COMPLIANCE LETTER

Re: **NDA 211988; SN0211**
ZYNRELEF® (Bupivacaine and Meloxicam) Extended-Release Solution
Response to Pediatric Research Equity Act Non-Compliance Letter for Postmarketing Requirements 4059-3 and 4059-4

Attn: Rita K. Joshi, PharmD, Regulatory Project Manager

Dear Dr. Roca:

Reference is made to the New Drug Application (NDA) 211988 for ZYNRELEF® (bupivacaine and meloxicam) extended-release solution, approved in adults for postsurgical analgesia for up to 72 hours after soft tissue and orthopedic surgical procedures by DAAP on January 23, 2024. Further reference is made to the Notification of Non-compliance with Pediatric Research Equity Act (PREA) letter dated May 16, 2024 (Reference ID: 5382293) regarding pediatric assessments not submitted for the following PREA Postmarketing Requirements (PMR) 4059-3 and PMR 4059-4 issued at the time of approval of the ZYNRELEF Original NDA 211988 (Reference ID: 4794625, dated May 12, 2021) for nonclinical studies to support pediatric use of ZYNRELEF:

4059-3 A juvenile animal study in an appropriate model to characterize the impact of meloxicam on the developing kidney, liver, lung, and testes to support clinical studies in pediatric patients from birth to less than two years of age.

Draft Protocol Submission:	12/2022
Final Protocol Submission:	05/2023
Study Completion:	09/2023
Final Report Submission:	03/2024

4059-4 A juvenile animal study in the rodent model to characterize the impact of DMSO on the developing brain to support clinical studies in pediatric patients from birth to less than three years of age.

Final Protocol Submission:	11/2022
Study Completion:	04/2023
Final Report Submission:	12/2023

The purpose of this submission is to provide the Division with a Response to Non-compliance Letter in Section 1.17.2 regarding PMR 4059-3 and PMR 4059-4. The response provides explanations for the delayed pediatric assessments, including the expected assessment submission date for PMR 4059-3 and the assessment submission date for PMR 4059-4.

If you have any questions regarding this submission, please contact me at jhart@herontx.com or by mobile at (858) 229-0447.

Sincerely,

{See appended electronic signature page}

Jelane Hart, MPH, MBA
Director, Regulatory Affairs
Heron Therapeutics, Inc.

This submission was scanned using Symantec Endpoint Protection (version 12.1.6) and is confirmed to be virus free.

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Approval Task	Jelane Hart Regulatory 27-Jun-2024 16:44:19 GMT+0000

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