Incyte Corporation
1801 Augustine Cut-Off
Wilmington, Delaware 19803
Tel 302.498.6700
Fax 302.425.2734
Web www.incyte.com

June 7, 2024

Jill A. Lindstrom, MD, Director
Division of Dermatology and Dentistry
Food and Drug Administration
Center for Drug Evaluation and Research
5901-B Ammendale Road
Beltsville, MD 20705-1266

Re: NDA 215309
Serial No. 0084
OPZELURA® (ruxolitinib) Cream
RESPONSE TO PREA
NON-COMPLIANCE LETTER

Dear Dr. Lindstrom,

Reference is made to the NDA Approval letter dated September 21, 2021 for OPZELURA® (ruxolitinib) cream for the short-term and non-continuous chronic treatment of mild to moderate atopic dermatitis in non-immunocompromised adult and pediatric patients 12 years of age and older whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable and to the postmarketing requirements included in the letter.

Further reference is made to the Notification of Non-Compliance with PREA letter dated April 23, 2024 for failure to submit either a pediatric assessment or a request for a deferral extension for the following PMRs:

PMR 4147-1: Conduct a randomized, double-blind, 8-week trial of ruxolitinib 1.5%, ruxolitinib 0.75%, and vehicle, followed by a 44-week long-term safety extension where vehicle subjects are randomized to either ruxolitinib 1.5% or ruxolitinib 0.75%. The trial should enroll 250 subjects ages ≥ 2 to < 12 years with atopic dermatitis of at least 3 months duration, a baseline Investigator's Global Assessment (IGA) score of 2 to 3, and % body surface area (BSA) involvement (excluding scalp) of 3% to 20% (Study INCB 18424-305).

- Final Report Submission: 02/2024

PMR 4147-2: Conduct a maximal use pharmacokinetic (PK) study in pediatric subjects with atopic dermatitis ages ≥ 2 years to < 12 and target at least 16 completers.

- Final Report Submission: 12/2023

Incyte is strongly committed to fulfilling the postmarketing studies required under PREA. The delay in the completion of the required pediatric studies was initially communicated to FDA in the briefing package submitted on October 2, 2023 (IND 077101; SQ0561) to support a Type B meeting with the FDA Division of Dermatology and Dentistry scheduled for November 1, 2023. Incyte requested agreement from the Agency on the proposed submission plan to fulfill the

postmarketing study requirements for pediatric patients with atopic dermatitis ages ≥ 2 to < 12 years (Question 5) and provided the anticipated dates. FDA feedback was provided in the Meeting Preliminary Comments dated October 27, 2023.

Incyte subsequently submitted an Annual Report for NDA 215309 on November 20, 2023 (SQ0076). The submission included the newly released Form FDA 3989 (PMR/PMC Annual Status Report for Drugs and Biological Products) which was used to request revised milestone dates for Final Report Submission for PMR 4147-1 and PMR 4147-2. Reasons for the proposed revised dates were provided in Section 11.j. of Form FDA 3989 for the respective PMR studies.

On March 8, 2024, Incyte was advised to submit a formal request to the NDA to change the final report submission dates for PMR 4147-1 and PMR 4147-2 in an email communication received from the FDA Regulatory Project Manager in response to a request for confirmation regarding the revised milestone dates proposed in the Annual Report with Form FDA 3989.

The deferral extension request for PMR 4147-1 and PMR 4147-2 was submitted to NDA 215309 (SQ0079) on March 14, 2024. In an email communication received May 20, 2024, FDA requested a response to the April 23, 2024 non-compliance letter by June 7, 2024. FDA also advised that submission of another deferral extension request was not required as the March 14, 2024 deferral extension request was received and is currently under review.

The purpose of this submission is to provide a response to the PREA non-compliance letter as requested. The response provided in Module 1.17.2 contains the information provided in the deferral extension request submitted to NDA 215309 on March 14, 2024, including the reasons for the delayed pediatric assessments and the date by which we expect to submit the assessments.

A cross-reference letter for this submission is provided to IND 077101 to which the protocols for PMR 4147-1 and PMR 4147-2 have been submitted (SQ0581).

This electronic submission is approximately 3 MB and has been scanned using Microsoft Defender, Antivirus version 1.413.114.0. All files were checked and verified to be free of viruses prior to transmission through the Electronic Submissions Gateway. For technical inquiries related to this electronic submission or its transmission, please contact Rob Connelly at 302-274-4776 or rconnelly@incyte.com.

The confidentiality of this submission, and all information contained herein, is claimed by Incyte Corporation under all applicable laws and regulations. Disclosure of any such information is not authorized without the prior written authorization of Incyte Corporation.

Should you have any comments or questions related to this submission, please contact me, or in my absence Deb McGill, Executive Director, Global Regulatory Affairs, at 302-498-6894 or dmcgill@incyte.com.

Sincerely,

Digitally signed by Fiona Lee
DN: c=US, st=DE, l=Wilmington, o=Incyte Corporation, ou=Global Regulatory Affairs, cn=Fiona Lee, email=flee@incyte.com
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Fiona Lee
Director, Global Regulatory Affairs
Office: 302-498-6747; Fax: 302-425-2734; Email: flee@incyte.com