RESPONSE PREA NON-COMPLIANCE LETTER

December 26, 2019

Rigoberto Roca, MD, Acting Division Director
Division of Anesthesiology, Addiction Medicine and Pain Medicine
Center for Drug Evaluation and Research
Food and Drug Administration
Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-1266

Product Name:	**Zipsor® (diclofenac potassium) Tablets, (b) (4)**
NDA #:	**022202**
Sequence No:	**0137**
Subject:	**Response to PREA Non-Compliance letter and Deferral Extension Requested**

Dear Dr. Roca:

Reference is made to the Noncompliance letter received on November 5, 2019 regarding the deferred pediatric assessment PMR 1053-3 assigned to NDA 022202 under the Pediatric Research Equity Act (PREA). The deferred PMR requested Assertio to complete a pharmacokinetic, efficacy and safety study in pediatric patients 1-2 years and the final study report submitted by September 30, 2019. Reference is also made to the deferral extension requested on September 24, 2012 and granted by the Agency on April 12, 2013. Reference is also made to a second request for a deferral extension made in July 2016 and denied in September 2016. It was stated not enough evidence was provided to describe the reason for the delay and how the timelines were affected.

The deferred pediatric study requirements have been revised over the course of time to reflect the current program of:

PMR 1053-1- pk and safety of Zipsor in Pediatric patients ages 12-17.
PMR 1053-2 pk and safety of Zipsor in pediatric patients ages 2-12.
PMR 1053-3 pk, efficacy and safety of Zipsor in pediatric patients ages 1-2.

Ownership of NDA 022202 has transferred several times since the original approval on June 16, 2009. In 2018, Depomed, underwent a significant change. The new company became Assertio Therapeutics and moved Headquarters from California to Lake Forest, Illinois. As a result of the company move, a new leadership team and new employees took over. This has led to delays in understanding the historical interactions and background with the Agency. However, Assertio has and continues to be diligent in understanding the status of the program and provided below are milestones steps taken to address the pediatric program requirements.

Depomed, discussed the current PMR program in August 2017 to gain feedback and acceptance, and committed to submitting two separate supplemental NDA's (sNDA). (b) (4) is currently under active review.

In line with the current strategy, the new Assertio leadership attempted to develop an oral pediatric formulation bioequivalent to the approved product. Using this approach, efficacy can be extrapolated based on a bioequivalent product. The current, approved drug product is a 25 mg oral solid soft capsugel, which is not feasible to give in the 1-2 year age group. Formulation development challenges have caused delays to the clinical program

(b) (4)

(b) (4)

Our next steps include continued development work that optimizes the formulation for which we can then use in a clinical study to complete the objectives of PMR 105-3. In parallel to the ongoing formulation development work, we also plan to seek Agency advice regarding proposed changes to PMR 105-3.

Finally, Assertio requests a Deferral extension to the timelines. The proposed extension dates are based on our successful ability to develop a formulation to use in a clinical trial for the age group of 1-2 year and the feasibility to enroll this patient population.

We request the following date changes:
Draft Protocol: May 2020
Final Protocol: July 2020
Study Completion: October 2021
Final Report: April 2022

Assertio has shown continued diligence in progressing the pediatric program and respectfully requests the Agency grant a deferral extension based on the reasons listed above.

If you have questions concerning this correspondence, please do not hesitate to contact me at (224) 441-6560 or via email at RA@assertiotx.com.

(b) (4)

Sincerely,

Clorey Toombs

Clorey Toombs, RAC
Director, Regulatory Affairs

Electronic Submission Specifications

This submission is compliant with FDA's Guidelines for Industry and current eCTD specifications.

All files were checked and verified to be free of viruses prior to transmission through the electronic submission gateway.

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The IT point of contact for this submission is:

Name	Clorey Toombs
Phone Number	224-441-6560
Email Address	RA@assertiotx.com