May 24, 2013

Norman Stockbridge, MD, PhD
Director, Division of Cardiovascular and Renal Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research
Food and Drug Administration
5901-B Ammendale Road
Beltsville, MD 20705-1266

RE: **NDA 22-127 Renvela® (sevelamer carbonate) Tablets, Sequence 0073**
NDA 22-318 Renvela® (sevelamer carbonate) for Oral Suspension, Sequence 0056

Subject: **RESPONSE TO PREA NON-COMPLIANCE LETTER**
PMR# 233-1, NDA 22-127
PMR# 1555-1, NDA 22-318

Cross Reference: **Renvela® (sevelamer carbonate) Tablet IND 66,710, Serial 0065**
Renvela® (sevelamer carbonate) for Oral Suspension IND 71,878, Serial 0057

Dear Dr. Stockbridge:

Reference is made to NDA 22-127 for Renvela (sevelamer carbonate) Tablets approved on October 19, 2007. A deferral for pediatric studies for NDA 22-127 was granted on February 21, 2007 with a deferral date of October 20, 2009 due to the ongoing development of the Renvela (sevelamer carbonate) for Oral Suspension formulation. Reference is also made to NDA 22-318 for Renvela for Oral Suspension submitted on March 30, 2008 and approved on August 12, 2009, and to the post marketing commitment set forth in the approval of NDA 22-318, requiring a study in pediatric patients with Renvela tablets and powder and the final clinical study report due December 31, 2011. Additional reference is also made to the April 11, 2013 letter denying Genzyme's December 5, 2012 deferral extension request for the post-marketing requirement of the pediatric study under PREA.

Genzyme remains committed to completing a pediatric study that provides clinically meaningful information on the use of Renvela in children and this study (SVCARB00706) is well underway with both tablet and powder formulations. Genzyme's correspondence with the FDA regarding pediatric plans and design of this study began in 2006 and included a face to face meeting with FDA in May 2009. Genzyme submitted 8 revisions of the pediatric study design based on feedback from FDA including that received in 4 General Advice Letters. The Advice Letter dated February 17, 2011 contained further recommendations on the study design, yet still required the final clinical study report by December 31, 2011.

As a result of the discussions and correspondence with FDA, Genzyme submitted a pediatric study protocol to the FDA on June 28, 2011 and received a response from FDA on August 12, 2011 informing Genzyme that the design was a "generally reasonable approach" and including further suggested revisions to the protocol. An amendment to the protocol incorporating the changes suggested by FDA was submitted on November 16, 2011. With a final protocol agreed upon, Genzyme then followed our internal processes to initiate the study, supply planning, and selection and opening of clinical sites.

In May 2012 the first patient consented for the study. Currently there have been 40 patients randomized in the US and clinical sites in Europe are preparing for start-up.

As stated previously, Genzyme remains committed to completing this pediatric post-marketing study. We acknowledge that we could not meet the December 2011 date for the clinical study report given that the final FDA agreement on the study design was received less than 6 months before the commitment due date. However, Genzyme has made every effort to successfully conduct this clinical study once the final study design was deemed acceptable by the FDA. We will continue to update the FDA on the status of the study as it progresses. Genzyme anticipates a submission date of June 2016 for the completed clinical study report.

Should you have any questions, please feel free to contact me at (617) 768-9467. For technical questions concerning this transmission, please contact Penny Dowd at (617) 768-6264.

Sincerely,

Melanie Govignon, MS, RAC
Principal Associate, Regulatory Affairs

CC: CDER's Pediatric and Maternal Health Staff