DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022542

NDA APPROVAL

Aptalis Pharma U.S., Inc.
Attention: Guy Rousseau, Ph.D.
Executive Director, Regulatory Affairs
22 Inverness Center Parkway, Suite 310
Birmingham, AL 35242

Dear Dr. Rousseau:

Please refer to your New Drug Application (NDA) dated October 29, 2009, received October 30, 2009, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Viokace (pancrelipase) Tablets.

We acknowledge receipt of your amendments dated October 30, 2009; November 2, 2009; November 19, 2009; November 23, 2009; November 27, 2009; December 11, 2009; January 27, 2010; January 28, 2010; March 1, 2010; March 9, 2010; March 22, 2010; May 27, 2010; June 21, 2010; June 30, 2010; July 8, 2010; July 9, 2010; July 12, 2010; August 13, 2010; August 20, 2010; August 27, 2010; September 15, 2010; September 17, 2010; October 8, 2010; October 26, 2010; November 19, 2010; November 23, 2010; September 1, 2011; September 29, 2011; October 12, 2011; October 14, 2011; October 17, 2011; November 16, 2011; December 5, 2011; December 29, 2011; January 9, 2012; January 12, 2012; January 24, 2012; February 2, 2012; February 3, 2012; February 6, 2012; February 14, 2012; and February 28, 2012.

The September 1, 2012, submission constituted a complete response to our November 28, 2010, action letter.

This new drug application provides for the use of Viokace (pancrelipase) Tablets, in combination with a proton pump inhibitor, for the treatment of exocrine pancreatic insufficiency in adults due to chronic pancreatitis or pancreatectomy.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at

http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the package insert, Medication Guide). Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the carton and immediate container labels submitted on January 9, 2012, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled "Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008)." Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 022542**." Approval of this submission by FDA is not required before the labeling is used.

Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for this application because this product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients and is not likely to be used in a substantial number of pediatric patients.

POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments in your submission dated February 28, 2012. These commitments are listed below.

Drug Substance:

1878-1 Provide an assessment of the viral inactivation capability of the cleaning agents currently used in the drug substance manufacturing facility.

Final Report Submission by September 1, 2012

1878-2 Develop and validate an infectivity assay for PCV1 (Porcine Circovirus 1).

Final Report Submission by March 1, 2013

1878-3 Establish lot release specifications for PPV (Porcine Parvovirus) and PCV2 (Porcine Circovirus 2) for the drug substance.

Final Report Submission by March 1, 2013

1878-4 Perform additional monitoring of viral load entering the drug substance manufacturing process. The control program should include the selection of human pathogenic viruses for monitoring by qPCR. An appropriate control strategy should be proposed.

Final Report Submission by May 15, 2013

1878-5 Improve the sensitivity of the qPCR assays used for drug substance release testing in order to provide adequate assurance that released drug substance will not contain EMCV, HEV, PEV-9, Reo1/3, Rota, Influenza, VSV-IND, and VSV-NJ viruses. The revised assays, assay validation data, and acceptance criteria should be submitted to the Agency.

Final Report Submission by April 15, 2013

1878-6 Assess the risk to product quality associated with hokovirus, and submit a control strategy for mitigating the risk to product quality.

Final Report Submission by June 1, 2012

1878-7 Revise the animal surveillance program and the risk assessment evaluation for source animals to capture new and emerging viral adventitious agents. The proposed program should include an example using Ebola virus, recently described in pigs from the Philippines, to illustrate how these programs will be implemented.

Final Report Submission by March 15, 2013

1878-8 Provide the results of leachable/extractable studies for the intermediate storage containers, a risk assessment evaluation and a proposed strategy to mitigate the risk to product quality.

Final Report Submission by June 1, 2012

1878-9 Revise release specifications after 30 lots of 1206 and 1252 drug substance have been manufactured.

Final Report Submission by May 15, 2013

Drug Product:

1878-10 Revise release and stability specifications after 30 lots of drug product have been manufactured.

Final Report Submission by July 2014

1878-11 Include accelerated and/or stressed stability conditions in the annual stability protocol.

Final Protocol Submission by June 2012

1878-12 Submit a stability protocol used to evaluate and extend the maximum cumulative storage time of the drug substance and drug product. The protocol will provide for placing on stability the first lot of drug product manufactured using drug substance aged beyond drug product manufacturing experience.

Final Protocol Submission by June 2012

1878-13 Perform *in vitro* studies to determine the feasibility of administering Viokace (pancrelipase) Tablets in an appropriate solution through a gastrostomy tube.

Final Report Submission by March 2013

Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled "**Postmarketing Commitment Protocol**," "**Postmarketing Commitment Final Report**," or "**Postmarketing Commitment Correspondence**."

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

We acknowledge receipt of your submission dated October 29, 2009, of a proposed risk evaluation and mitigation strategy (REMS). We have determined that, at this time, a REMS is not necessary for Viokace (pancrelipase) Tablets to ensure that its benefits outweigh its risks. We will notify you if we become aware of new safety information and make a determination that a REMS is necessary.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Jagjit Grewal, Regulatory Project Manager, at (301) 796-0846.

Sincerely,

{See appended electronic signature page}

Julie Beitz, M.D.
Director
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosures: Package Insert and Medication Guide

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

JULIE G BEITZ
03/01/2012