DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 125522/S-001, S-004

SUPPLEMENT APPROVAL

Amgen, Inc.
Attention: Adam Rupert
Senior Manager, Regulatory Affairs
One Amgen Center Drive, Mail Stop 17-2-B
Thousand Oaks, CA 01320-1799

Dear Mr. Rupert:

Please refer to the following Supplemental Biologics License Applications (sBLAs) submitted under section 351(a) of the Public Health Service Act for Repatha (evolocumab) injection, 140 mg/mL:

1. Supplement -001 (S-001), dated and received September 10, 2015, proposes to market the Repatha Pushtronex system consisting of a Repatha (evolocumab) injection 420 mg/3.5 mL prefilled cartridge co-packaged with on-body infusion device, and associated labeling revisions.

2. Supplement -004 (S-004), dated and received February 29, 2016, submitted as a Changes Being Effected, as described under 21 CFR 601.12(f)(2), proposes to revise the Instructions for Use (IFU) for the approved SureClick® Autoinjector. Specifically, text and pictures have been added to convey that upon removal of the orange cap, the product should be injected within 5 minutes, and associated minor labeling revisions.

MANUFACTURING LOCATIONS

The final formulated prefilled cartridge drug product will be manufactured (b) (4)

DATING PERIOD

The dating period for the Repatha Pushtronex system shall be 24 months from the date of manufacture when stored at 2-8C. The date of manufacture shall be defined as the date of sterile filtration of the formulated drug product. The expiration date for the Repatha Pushtronex system shall not exceed the shortest shelf life of any of the Repatha Pushtronex system components.

Results of ongoing stability studies should be submitted to the annual report.

We have approved the stability protocols in your supplemental application for the purpose of extending the expiration dating period of your drug product under 21 CFR 601.12.

APPROVAL & LABELING

We have completed our review of these supplemental applications, as amended. They are 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, via the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 601.14(b)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the enclosed labeling (text for the package insert, text for the patient package insert, and Instructions for Use [IFU]) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements. 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.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this BLA, including pending "Changes Being Effected" (CBE) supplements, for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 601.12(f)] in MS Word format that includes the changes approved in these supplemental applications.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the enclosed carton and immediate container labels, 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 "**Product Correspondence – Final Printed Carton and Container Labels for approved BLA 125522/S-001**." Approval of this submission by FDA is not required before the labeling is used.

Marketing the product with final printed labeling (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(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your application, you are exempt from this requirement.

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

We remind you of your postmarketing commitments:

3105-1 Conduct Real Time Aging/Shelf-Life Studies for Device Performance for the interim 1-year timepoint. These studies should use the methods equivalent to those used to evaluate device performance in the accelerated aging studies. The interim report must include results from the following shelf life tests: Device Function Test, Deliverable Volume Test, Injection Time Test, Sterile (b) (4) Integrity Test, (b) (4) Function Test, and Adhesive Function Test.

The timetable you submitted on July 6, 2016, states that you will conduct this study according to the following schedule:

Interim Report (1-year timepoint) Submission: July 2017

3105-2 Conduct Real Time Aging/Shelf-Life Studies for Device Performance for the interim 2-year and 31-day timepoint. These studies should use methods equivalent to those used to evaluate device performance in the accelerated aging studies. The final report must include results from the following shelf life tests: Device Function Test, Deliverable Volume Test, Injection Time Test, Sterile (b) (4) Integrity Test, (b) (4) Function Test, and Adhesive Function Test.

The timetable you submitted on July 6, 2016, states that you will conduct this study according to the following schedule:

Interim Report (2-year and 31-day timepoint) Submission: July 2018

3105-3 Conduct Real Time Aging/Shelf-Life Studies for Device Performance for the final 3-year and 31-day timepoint. These studies should use methods equivalent to those used to evaluate device performance in the accelerated aging studies. The final report must include results from the following shelf life tests: Device Function Test, Deliverable Volume Test, Injection Time Test, Sterile (b) (4) Integrity Test, (b) (4) Function Test, and Adhesive Function Test.

The timetable you submitted on July 6, 2016, states that you will conduct this study according to the following schedule:

Interim Report (3-year and 31-day timepoint) Submission: July 2019

Submit clinical protocols to your IND 105188 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this BLA. In addition, under 21 CFR 601.70 you should include a status summary of each commitment in your annual progress report of postmarketing studies to this BLA. 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**."

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved BLA (in 21 CFR 600.80 and in 21 CFR 600.81).

If you have any questions, call Kati Johnson, Senior Regulatory Project Manager, at (301) 796-1234.

Sincerely,

{See appended electronic signature page}

James P. Smith, MD, MS
Deputy Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURES:
Content of Labeling
Package Insert (S-001, S-004)

Patient Information (S-001)
Instructions for Use (S-001)
Instructions for Use (S-004)
Carton and Container Labeling (S-001)
Prefilled Cartridge Label
(b) (4) Lid Labeling
Carton (Trade)
Carton (Replacement)
Device Labeling

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

/s/

JAMES P SMITH
07/08/2016