DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 125559/S-001

SUPPLEMENT APPROVAL

Sanofi-Aventis U.S. Inc.
Attention: Jeremy Dabbeekeh, Ph.D.
Senior Manager, Global Regulatory Affairs
55 Corporate Drive, Mail Stop: 55D-215A
Bridgewater, NJ 08807

Dear Dr. Dabbeekeh:

Please refer to your Supplemental Biologics License Application (sBLA) dated and received March 24, 2016, and your amendments, submitted under section 351(a) of the Public Health Service Act for Praluent (alirocumab) injection, 75 mg and 150 mg.

We acknowledge receipt of your major amendment dated January 19, 2017, which extended the goal date by three months.

This Prior Approval supplemental biologics application proposes a new dosing regimen for Praluent of 300 mg administered every 4 weeks (Q4W; monthly).

APPROVAL & LABELING

We have completed our review of this supplemental 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, 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 prescribing information and text for the patient package insert) 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 this supplemental application.

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.

We are waiving the pediatric study requirement for pediatric patients with clinical atherosclerotic cardiovascular disease because studies would be impossible or highly impractical as this condition rarely occurs in pediatric patients.

We are waiving the pediatric study requirement for patients with heterozygous familial hypercholesterolemia (HeFH) ages 0 through 9 years (inclusive) because studies would be impossible or highly impractical because the standard of care, which is highly effective, is based on diet and lifestyle modification.

We are deferring submission of your pediatric studies for patients with HeFH ages 10 to 17 years (inclusive) for this application because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 601.28 and section 505B(a)(3)(B) of the Federal Food, Drug, and Cosmetic Act. These required studies, which were previously required in the approval letter dated July 24, 2015, are listed below.

2927-1 Conduct a dose-finding study (Phase 2) and an efficacy and safety study (Phase 3) evaluating alirocumab in patients with heterozygous familial hypercholesterolemia (HeFH) ages 10 years to less than 18 years. If children younger than age 10 are included, the eligibility criteria should ensure that other available interventions to lower LDL-C have been insufficient. Phase 2 will be a randomized, open-label, 8-week, ascending repeated dose-finding study of alirocumab with an optional open-label extension study in patients 10 years to less than 18 years of age with HeFH on stable lipid modifying therapy with LDL-C $\geq$ 130 mg/dL. Phase 3 will be a randomized, 6-month, double-blind, placebo-controlled, parallel-group, multicenter efficacy and safety study followed by an 18-month open-label extension in patients 10 years to less than 18 years with

HeFH on stable lipid-modifying therapy with LDL-C ≥ 130 mg/dL. Patients treated in Phase 2, the dose-finding study, will be offered enrollment in Phase 3, the efficacy and safety study.

Final Protocol Submission (Phase 2):	January 2016
Final Protocol Submission (Phase 3):	December 2017
Study Completion (Phase 2):	December 2018
Study Completion (Phase 3):	April 2022
Final Report Submission (Phase 2 and 3):	September 2022

Submit the protocols to your IND 105574, with a cross-reference letter to this BLA.

Reports of these required pediatric postmarketing studies must be submitted as a BLA or as a supplement to your approved BLA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

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 prescribing information to:

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

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf).

As required under 21 CFR 601.12(f)(4), you must submit final promotional materials, and the prescribing information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. 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 BLA (in 21 CFR 600.80 and in 21 CFR 600.81).

If you have any questions, call Patricia Madara, Regulatory Project Manager, at (301) 796-1249.

Sincerely,

{See appended electronic signature page}

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

ENCLOSURES:
Prescribing Information
Patient Package Insert
Instructions for Use (versions approved on July 24, 2015)

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
04/24/2017