DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 761028

BLA APPROVAL

Amgen Inc.
Attention: Narae Bae, Ph.D.
Manager, Global Biosimilars Regulatory Affairs
One Amgen Center Drive
Mailstop 28-3-A
Thousand Oaks, CA 91320

Dear Dr. Bae:

Please refer to your Biologics License Application (BLA) dated November 14, 2016, received November 14, 2016, and your amendments, submitted under section 351(k) of the Public Health Service Act for Mvasi (bevacizumab-awwb) Injection, 100 mg/4 mL and 400 mg/16 mL.

LICENSING

We have approved your BLA for Mvasi (bevacizumab-awwb) effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Mvasi under your existing Department of Health and Human Services U.S. License No. 1080. Mvasi is indicated for:

- The treatment of patients with metastatic colorectal cancer, with intravenous 5 fluorouracil–based chemotherapy for first or second line treatment.
- The treatment of patients with metastatic colorectal cancer, with fluoropyrimidine irinotecan or fluoropyrimidine oxaliplatin based chemotherapy for second line treatment in patients who have progressed on a first line bevacizumab product-containing regimen.
- Patients with non-squamous non-small cell lung cancer, with carboplatin and paclitaxel for first line treatment of unresectable, locally advanced, recurrent or metastatic disease.
- The treatment of glioblastoma, as a single agent for adult patients with progressive disease following prior therapy.
- The treatment of patients with metastatic renal cell carcinoma with interferon alfa.
- The treatment of patients with cervical cancer, in combination with paclitaxel and cisplatin or paclitaxel and topotecan in persistent, recurrent, or metastatic disease.

Mvasi carries a limitation of use. Mvasi (bevacizumab-awwb) is not indicated for the adjuvant treatment of colon cancer.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture bevacizumab-awwb drug substance at Amgen Inc. Thousand Oaks, CA. The final formulated product will be manufactured and filled at [redacted] (b) (4) and labeled and packaged at Amgen Manufacturing Ltd, Juncos, Puerto Rico. You may label your product with the proprietary name, Mvasi, and will market it in 100 mg/4 mL (25 mg/mL) and 400 mg/16 mL (25 mg/mL) single dose vials.

DATING PERIOD

The dating period for Mvasi shall be 36 months from the date of manufacture when stored at 2-8°C and protected from light. The date of manufacture shall be defined as the date of final sterile filtration of the formulated drug product. The dating period for your drug substance shall be [redacted] (b) (4) months from the date of manufacture when stored at [redacted] (b) (4) °C.

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

FDA LOT RELEASE

You are not currently required to submit samples of future lots of Mvasi to the Center for Drug Evaluation and Research (CDER) for release by the Director, CDER, under 21 CFR 610.2. We will continue to monitor compliance with 21 CFR 610.1, requiring completion of tests for conformity with standards applicable to each product prior to release of each lot.

Any changes in the manufacturing, testing, packaging, or labeling of Mvasi, or in the manufacturing facilities, will require the submission of information to your biologics license application for our review and written approval, consistent with 21 CFR 601.12.

APPROVAL & LABELING

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.

WAIVER OF HIGHLIGHTS SECTION

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

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 [21 601.14(b)] in structured product labeling (SPL) format, 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). 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 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 — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (May 2015, Revision 3)." For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved BLA 761028**." Approval of this submission by FDA is not required before the labeling is used.

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 studies requirement for this application because necessary studies are impossible or highly impracticable as colorectal cancer, non-squamous non-small cell lung cancer, metastatic renal cell carcinoma, cervical cancer, and glioblastoma occur mostly in adults.

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

We remind you of your postmarketing commitments:

3261-1 Re-evaluate the drug substance (DS) stability acceptance criteria for stability samples held at the (b)(4)C condition after data from (b)(4)DS lots stored at (b)(4)C are available. The final report should include the corresponding data, the analysis, and

statistical plan used to evaluate the results and acceptance criteria and any proposed changes to the approved criteria.

The timetable you submitted on August 28, 2017, states that you will conduct this study according to the following schedule:

Final Report Submission: December 2022

3261-2 Perform method validation studies in support of the (b) (4) into the drug substance manufacturing control strategy.

The timetable you submitted on August 28, 2017, states that you will conduct this study according to the following schedule:

Final Report Submission: January 2018

3261-3 Perform method validation studies in support of the (b) (4) method into the drug substance manufacturing control strategy.

The timetable you submitted on August 28, 2017, states that you will conduct this study according to the following schedule:

Final Report Submission: January 2018

3261-4 Develop and implement a validated endotoxin detection method not subject to low endotoxin recovery for use in the release of the drug product.

The timetable you submitted on August 28, 2017, states that you will conduct this study according to the following schedule:

Final Report Submission: December 2018

Submit 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, and any changes in plans since the last annual report. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled "**Postmarketing Commitment Protocol**," "**Postmarketing Commitment Final Report**," or "**Postmarketing Commitment Correspondence**."

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 601.12(f)(4), you must submit final promotional materials, and the package insert, 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

You must submit adverse experience reports under the adverse experience reporting requirements for licensed biological products (21 CFR 600.80). You should submit postmarketing adverse experience reports to:

Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-1266

Prominently identify all adverse experience reports as described in 21 CFR 600.80.

You must submit distribution reports under the distribution reporting requirements for licensed biological products (21 CFR 600.81).

You must submit reports of biological product deviations under 21 CFR 600.14. You should promptly identify and investigate all manufacturing deviations, including those associated with processing, testing, packing, labeling, storage, holding and distribution. If the deviation involves a distributed product, may affect the safety, purity, or potency of the product, and meets the other criteria in the regulation, you must submit a report on Form FDA-3486 to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Compliance Risk Management and Surveillance
5901-B Ammendale Road
Beltsville, MD 20705-1266

Biological product deviations, sent by courier or overnight mail, should be addressed to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Compliance Risk Management and Surveillance
10903 New Hampshire Avenue, Bldg. 51, Room 4206
Silver Spring, MD 20903

If you have any questions, call Leah Her, M.S., Senior Regulatory Health Project Manager, at (240) 402-6611.

Sincerely,

{See appended electronic signature page}

Patricia Keegan, M.D.
Director
Division of Oncology Products 2
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling
Carton and Container Labeling

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

/s/

PATRICIA KEEGAN
09/14/2017