BLA 761032/S-020

**SUPPLEMENT APPROVAL**

Bausch Health Ireland, Limited
c/o: Bausch Health US, LLC
Attention: James Harn
Director, Global Regulatory Affairs
400 Somerset Corporate Boulevard
Bridgewater, NJ 08807

Dear James Harn:

Please refer to your supplemental biologics license application (sBLA) received September 2, 2025, and your amendments, submitted under section 351(a) of the Public Health Service Act for Siliq (brodalumab) injection.

This Prior Approval sBLA provides for introduction of a Siliq sample program and proposed modifications to the approved Siliq (brodalumab) injection risk evaluation and mitigation strategy (REMS).

## 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.

## 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 FDA.gov,[1] that is identical to the enclosed labeling (text for the Prescribing Information, and Medication Guide) 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 *SPL Standard for Content of Labeling Technical Qs and As*.[2]

The SPL will be accessible via publicly available labeling repositories.

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm
[2] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

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 Microsoft Word format that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

We request that the labeling approved today be available on your website within 10 days of receipt of this letter.

## CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling, as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*. For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved BLA 761032/S-020**." Approval of this submission by FDA is not required before the labeling is used.

## RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENTS

The REMS for Siliq (brodalumab) was originally approved on February 15, 2017, and the most recent REMS modification was approved on July 19, 2023. The REMS consists of elements to assure safe use, an implementation system, and a timetable for submission of assessments of the REMS.

Your proposed modifications to the REMS consists of changes to incorporate requirements for participants who dispense or distribute Siliq samples (i.e., healthcare providers who dispense and distributors).

Your proposed modified REMS, submitted on September 2, 2025, amended and appended to this letter, is approved.

The timetable for submission of assessments of the REMS remains the same as that approved on February 15, 2017.

The revised REMS assessment plan must include, but is not limited to, the following:

1. **Siliq Stakeholder data** (prescribers, pharmacies, patients, and wholesalers-distributors) per reporting period and cumulatively:
   a. Numbers of each certified/enrolled stakeholder, status of certification, and method of certification including:

i. Number of certified prescribers by medical degree, geographic location, prescriber specialty, method of certification (email, fax, online), and the number and percentage of enrolled health care providers who have prescribed Siliq.
   1) Number of certified prescribers who dispense
   2) Number of certified prescribers who were active (i.e., prescribed at least once during the reporting period)

ii. Number of certified pharmacies by pharmacy type (inpatient, outpatient) and method of certification (email, fax, online).
   1) Number of certified pharmacies that were active (i.e., dispensed at least once during the reporting period)

iii. Number of authorized distributors and wholesalers.
   1) Number of distributors that were active (i.e., distributed at least once during the reporting period)

iv. Number of enrolled patients and their demographics (age, sex, race, geographic location).

b. Listing and categorization of reasons enrollment is incomplete for each stakeholder category.

2. **Utilization Data,** per reporting period and cumulatively:
   a. Number of Siliq prescriptions (new and refills) dispensed stratified by:
      i. Pharmacy type
      ii. Number of samples dispensed by certified prescribers
      iii. Method of dispensing authorization (on-line versus phone)
      iv. Prescriber specialty
      v. Patient demographics (age, race, sex)

3. **Compliance Metrics**, per reporting period and cumulatively:
   a. A copy of the audit plan for each stakeholder (certified pharmacies, distributors, and prescribers).
   b. Provide a copy of the non-compliance plan, including the criteria for non-compliance for each stakeholder, actions taken to address non-compliance for each case, and which event led to de-certification from the REMS.
   c. Report of audit findings for each stakeholder including:
      i. The number of audits expected, and the number of audits performed.
      ii. The number and types of deficiencies noted for each group of audit stakeholders.
      iii. For those with deficiencies noted, report the number that successfully completed a corrective and preventative action (CAPA) plan.
      iv. For any that did not complete the CAPA, describe actions taken.

v. Include a unique ID for each stakeholder that has had deviations to track deviations by stakeholder over time.

vi. Documentation of completion of training for relevant staff.

vii. The existence of documented processes and procedures for complying with the REMS.

viii. Verification that each audited stakeholder's site has retained the same designated authorized representative. If different, include the number of new authorized representative and verification of the site's recertification.

d. Report of annual audit findings from wholesalers-distributors for audits conducted during the reporting period, including:
   i. What processes and procedures the REMS and distributors-wholesalers have in place to verify, prior to dispensing Siliq, that the pharmacies and prescribers who dispense are certified. This report is to include, the source of the report, a description of the event, the root cause analysis of any findings of non-compliance, any corrective actions taken to address findings, the status of corrective actions, and any resulting preventative actions taken.

e. Report of audit findings from the certified pharmacies that have dispensed Siliq
   i. This report is to include, the source of the report, a description of the event, the root cause analysis of any findings of non-compliance, any corrective actions taken to address findings, the status of corrective actions, and any resulting preventative actions taken.

f. Report of audit findings from certified prescribers that dispense, after they have placed their first order of Siliq
   i. This report is to include, the source of the report, a description of the event, the root cause analysis of any findings of noncompliance, any corrective actions taken to address findings, the status of corrective actions, and any resulting preventative actions taken.

g. Report of findings from audit of the pilot prescription program specialty pharmacy
   i. This report is to include, the source of the report, a description of the event, the root cause analysis of any findings of non-compliance, and any resulting preventative actions taken.

h. Number of Siliq prescriptions dispensed that were written by non-certified prescribers, the root cause analysis of dispensing a prescription by a non-certified prescriber, whether the patients was enrolled or not enrolled, and the actions taken to prevent future occurrences. Include a unique ID for each pharmacy to track deviations over time.

i. Number of Siliq prescriptions that were dispensed to non-enrolled patients, the root cause analysis of dispensing a prescription to a non-enrolled patient, whether the prescriber was certified or non-certified, and the actions taken to prevent

future occurrences. Include a unique ID for each pharmacy to track deviations over time.

j. Number of Siliq prescriptions dispensed by non-certified pharmacies, the root cause analysis of how a non-certified pharmacy obtained Siliq, and the actions taken to prevent future occurrences.

k. Number of Siliq samples dispensed by non-certified prescribers, the root cause analysis of how a non-certified prescriber obtained Siliq, and the actions taken to prevent future occurrences

l. Number of times a Siliq prescription was dispensed because a certified pharmacy bypassed REMS authorization processes, the root causes analysis of why the pharmacy bypassed the REMS authorization process; to include a description of how the events were identified and any corrective actions taken.

m. Number and percentage of Siliq samples that were dispensed by certified prescribers without a corresponding signed and submitted Patient Enrollment Form out of all samples dispensed, the root cause analysis of dispensing a sample without a Patient Enrollment Form, and the actions taken to prevent future occurrences. Include a unique ID for each certified prescriber to track deviations over time.
    i. Number and percentage of unique certified prescribers who dispensed samples without submitting a Patient Enrollment Form out of all certified prescribers who dispensed samples

n. Number of shipments sent to non-certified pharmacies, the root cause analysis of shipping to a non-certified pharmacy, sources of the reports, and actions taken to prevent future occurrences.

o. Number of Siliq samples sent to non-certified prescribers, actions taken to prevent future occurrences, actions taken to recover the samples from these non-certified prescribers, and the outcome of such actions.

p. Number of prescribers, pharmacies, and distributors de-certified and reasons for decertification.

q. The number of and reasons for rejected prescription authorizations.

r. Failures of prescription dispensing authorization due to calls to the REMS for authorization when the call center was closed or when the prescriber/patient verification portion of the website was down.

s. The numbers of the most frequently asked questions to the Call Center organized by topic.

4. **Evaluation of knowledge via Knowledge, Attitude and Behavior (KAB) surveys**
    a. Prescribers
        i. An evaluation of knowledge of certified prescribers of the potential risk of suicidal ideation and behavior observed with Siliq therapy.

ii. An evaluation of prescriber practice or behavior with regards to counseling patients about the potential risk of suicidal ideation and behavior observed with Siliq therapy and patients' need to seek medical attention should they experience emergence or worsening of suicidal thoughts and behavior.
iii. An evaluation of certified prescriber knowledge of Siliq REMS requirements and processes.

b. Patients
i. An evaluation of knowledge of patients of the potential risk of suicidal ideation and behavior observed with Siliq therapy and patients' need to seek medical attention should they experience emergence or worsening of suicidal thoughts and behavior.
ii. An evaluation of patients' recall of counseling by prescriber, pharmacist, or both, on the potential risk of suicidal ideation and behavior observed with Siliq therapy and patients' need to seek medical attention should they experience emergence or worsening of suicidal thoughts and behavior.
iii. An evaluation of patient receipt of the wallet card.

5. The requirements for assessments of an approved REMS under section 505-1(g)(3) include with respect to each goal included in the strategy, an assessment of the extent to which the approved strategy, including each element of the strategy, is meeting the goal or whether one or more such goals or such elements should be modified.

We remind you that in addition to the REMS assessments submitted according to the timetable in the approved REMS, you must include an adequate rationale to support a proposed REMS modification for the addition, modification, or removal of any goal or element of the REMS, as described in section 505-1(g)(4) of the FDCA.

We also remind you that you must submit a REMS assessment when you submit a supplemental application for a new indication for use, as described in section 505-1(g)(2)(A) of the FDCA. This assessment should include:

a) An evaluation of how the benefit-risk profile will or will not change with the new indication;

b) A determination of the implications of a change in the benefit-risk profile for the current REMS;

c) *If the new indication for use introduces unexpected risks*: A description of those risks and an evaluation of whether those risks can be appropriately managed with the currently approved REMS.

d) *If a REMS assessment was submitted in the 18 months prior to submission of the supplemental application for a new indication for use*: A statement about whether

the REMS was meeting its goals at the time of that last assessment and if any modifications of the REMS have been proposed since that assessment.

e) *If a REMS assessment has not been submitted in the 18 months prior to submission of the supplemental application for a new indication for use:* Provision of as many of the currently listed assessment plan items as is feasible.

f) *If you propose a REMS modification based on a change in the benefit-risk profile or because of the new indication of use, submit an adequate rationale to support the modification, including*: Provision of the reason(s) why the proposed REMS modification is necessary, the potential effect on the serious risk(s) for which the REMS was required, on patient access to the drug, and/or on the burden on the health care delivery system; and other appropriate evidence or data to support the proposed change. Additionally, include any changes to the assessment plan necessary to assess the proposed modified REMS. *If you are not proposing REMS modifications*, provide a rationale for why the REMS does not need to be modified.

Additionally, we recommend that you submit your proposed audit plan and non-compliance plan for FDA review within 60 days of this letter. Prominently identify the submission containing the assessment instruments and methodology with the following wording in bold capital letters, at the top of your cover letter and at the top of the first page of the main submission document: "**REQUEST FOR REMS ASSESSMENT METHODOLOGY PROTOCOL REVIEW/ AUDIT AND NON-COMPLIANCE PLAN".**

If the assessment instruments and methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted assessment instruments or methodology, you should update the REMS supporting document to include specific assessment instrument and methodology information at least 90 days before the assessments will be conducted. Updates to the REMS supporting document may be included in a new document that references previous REMS supporting document submission(s) for unchanged portions. Alternatively, updates may be made by modifying the complete previous REMS supporting document, with all changes marked and highlighted.

Prominently identify the submission containing the assessment instruments and methodology with the following wording in bold capital letters at the top of the first page of the submission:

**BLA 761032 REMS ASSESSMENT METHODOLOGY**
**(**insert concise description of content in bold capital letters, e.g., **ASSESSMENT METHODOLOGY, PROTOCOL, SURVEY METHODOLOGIES, AUDIT PLAN, DRUG USE STUDY)**

Prominently identify any submission containing the REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

**BLA 761032 REMS ASSESSMENT**

***or***

**NEW SUPPLEMENT FOR BLA 761032/S-000**
**CHANGES BEING EFFECTED IN 30 DAYS**
**PROPOSED MINOR REMS MODIFICATION**

***or***

**NEW SUPPLEMENT FOR BLA 761032/S-000**
**PRIOR APPROVAL SUPPLEMENT**
**PROPOSED MAJOR REMS MODIFICATION**

***or***

**NEW SUPPLEMENT FOR BLA 761032/S-000**
**PRIOR APPROVAL SUPPLEMENT**
**PROPOSED REMS MODIFICATIONS DUE TO SAFETY LABELING CHANGES SUBMITTED IN SUPPLEMENT XXX**

***or***

**NEW SUPPLEMENT (NEW INDICATION FOR USE)**
**FOR BLA 761032/ S-000**
**REMS ASSESSMENT**
**PROPOSED REMS MODIFICATION (if included)**

Should you choose to submit a REMS revision, prominently identify the submission containing the REMS revisions with the following wording in bold capital letters at the top of the first page of the submission:

**REMS REVISIONS FOR BLA 761032**

To facilitate review of your submission, we request that you submit your proposed modified REMS and other REMS-related materials in Microsoft Word and PDF format. If certain documents, such as enrollment forms, or website screenshots are only in PDF format, they may be submitted as such, but Word and PDF format are preferred.

## SUBMISSION OF REMS DOCUMENT IN SPL FORMAT

As soon as possible, but no later than 14 days from the date of this letter, submit the REMS document in Structured Product Labeling (SPL) format using the FDA automated drug registration and listing system (eLIST). Content of the REMS document must be identical to the approved REMS document. The SPL will be publicly available.

Information on submitting REMS in SPL format may be found in the guidance for industry *Providing Regulatory Submission in Electronic Format – Content of the Risk Evaluation and Mitigation Strategies Document Using Structured Product Labeling.*

For more information on submitting REMS in SPL format, please email FDAREMSwebsite@fda.hhs.gov.

## 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).

Your product is a Part 3 combination product (21 CFR 3.2(e)); therefore, you must also comply with postmarketing safety reporting requirements for an approved combination product (21 CFR 4, Subpart B). Additional information on combination product postmarketing safety reporting is available at FDA.gov.

If you have any questions, contact Strother D. Dixon, Senior Regulatory Project Manager, at strother.dixon@fda.hhs.gov or (301) 796-1015.

Sincerely,

*{See appended electronic signature page}*

Tatiana Oussova, MD, MPH
Deputy Director for Safety
Division of Dermatology and Dentistry
Office of Immunology and Inflammation
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Medication Guide
- Carton and Container Labeling
- REMS

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**This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.**

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/s/

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TATIANA OUSSOVA
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