



Our STN: BL 125720/0

FILING NOTIFICATION
February 20, 2020

Biomarin Pharmaceutical Inc.
Attention: Sabrina Gu
Senior Director, Regulatory Affairs
105 Digital Drive
Novato, CA 94949

Dear Ms. Gu:

Please refer to your Biologics License Application (BLA) submitted and received on December 23, 2019, under section 351(a) of the Public Health Service Act (PHS Act) for valoctocogene roxaparvovec.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Under 21 CFR 601.2(a), we have filed your application today. The review classification for this application is **Priority**, the review action due date is August 21, 2020. This acknowledgment of filing does not mean that we have issued a license, nor does it represent any evaluation of the adequacy of the data submitted.

This application is also subject to the provisions of "the Program" under the Prescription Drug User Fee Act (PDUFA). Refer to <https://www.fda.gov/industry/prescription-drug-user-fee-amendments/pdufa-vi-fiscal-years-2018-2022>.

We are reviewing your application according to the processes described in the guidance for industry and review staff *Good Review Management Principles and Practices for New Drug Applications and Biologics License Applications* at <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/good-review-management-principles-and-practices-new-drug-applications-and-biologics-license>. Therefore, we have established internal review timelines as described in the guidance, which includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, mid-cycle, team and wrap-up meetings). We plan to hold our internal mid-cycle review meeting on March 31, 2020. Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing requirement/commitment requests by July 23, 2020.

We are not currently planning to hold an advisory committee meeting to discuss this application.

While conducting our filing review, we identified the following potential review issues:

Chemistry, Manufacturing, and Controls

1. We do not agree with the proposed shelf-life for the (b) (4) drug substance (b) (4) the drug product (DP). We note that the stability data provided in the BLA do not fully support the proposed expiry date for the (b) (4) (b) (4) DP. We also note that at the presentation provided as part of the application orientation meeting held on February 7, 2020, you stated that additional stability data will be provided in March and April of 2020. Please provide the data and justification to support the shelf-life of the (b) (4) DS and DP by the date agreed upon during the June 27, 2019, pre-BLA meeting. The data provided should demonstrate that you have at least 95% confidence that the (b) (4) DS and DP remain stable for the duration of the proposed shelf-life.
2. In Module 3.2R you reference a Post Approval Change Management Protocol for the introduction of a manufacturing process change that will allow the (b) (4)) lots for processing through to BMN 270 drug product (DP). This information is presented in the context of a MAA submission. Please submit a clarification of the approach and timeline for the submission of analytical data and/or studies to support the comparability of BMN270 manufacturing processes with regard to your BLA submission, if applicable.

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 the indication you are requesting has orphan drug designation PREA does not apply.

If you have any questions, please contact the Regulatory Project Manager,
Leyish Minie, at (301) 796-5522.

Sincerely,

Steven Oh -S

Digitally signed by Steven Oh -S
DN: c=US, o=U S Government, ou=HHS,
ou=FDA, ou=People, cn=Steven Oh -S,
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Date: 2020.02.20 15:51:18 -0500

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