

FILING MEETING SUMMARY

Application type and number: BLA 125720/0
Product name: valoctocogene roxaparvovec
Proposed indication: For adults with severe hemophilia A (congenital factor VIII deficiency) (b) (4)
 without antibodies to adeno-associated virus serotype 5 detected by an FDA approved test.
Sponsor: BioMarin Pharmaceutical Inc.
Meeting date & time: January 31, 2020, 9:00 am- 10:00 am
Meeting Chair: Angela Whatley, PhD
Meeting Recorder: Leyish Minie, MSN, RN

Background:

BioMarin Pharmaceutical Inc. has submitted an original BLA on December 23, 2019 for treatment of severe hemophilia A. The applicant has also submitted a PMA on Dec 23, 2019 to CDRH. The product has been granted an Orphan Drug Designation on February 29, 2016 and Breakthrough Therapy designation on October 4, 2017 under IND 17659. The sponsor has requested a priority review.

Table 1: Review Committee and Discipline Filing Decision Summary

Discipline/Organization	Name	Attended meeting	Fileable	RTF	Deficiencies Identified
Regulatory Project Manager (RPM)	Leyish Minie, MSN, RN	Y	Y		
Chair	Angela Whatley, PhD	Y	Y		
Clinical Reviewer	Mona Elmacken, MD	Y	Y		
CMC Reviewer	Andrew Harmon, PhD	Y	Y		
CMC Reviewer	Mikhail Ovanesov, PhD	Y	Y		
CMC Reviewer	Emmanuel Adu-Gyamfi, PhD	Y	Y		
Animal Pharmacology Reviewer	N/A				
Clinical Pharmacology Reviewer	Xiaofei Wang, PhD	Y	Y		
Toxicology Reviewer	Feorillo Galivo, MD, PhD	Y	Y		
Developmental Toxicology Reviewer	N/A				
OCBQ/DMPQ RPM	Marian Ortiz-Rodriguez	Y			
OCBQ/DMPQ Reviewer	Bradley Dworak	Y	Y		
OCBQ/DMPQ Reviewer	Donald Lech	Y	Y		

Discipline/Organization	Name	Attended meeting	Fileable	RTF	Deficiencies Identified
OCBQ/DMPQ/PRB Reviewer					
Statistical Reviewer of clinical data	Yuqun Luo	Y	Y		
Statistical Reviewer of non-clinical data	N/A				
Postmarketing Safety Epidemiological Reviewer	Graca Dores, MD	N			
OCBQ/APLB PNR Reviewer	Oluchi Elekwachi	N			
OCBQ/BIMO Reviewer	Colonious King	Y	Y		
BIMO team Lead	Denise Cato	Y	Y		
CBQ/DBSQC Reviewer	Simleen Kaur James Kenney	Y	Y		
DBSQC Reviewer	Nahid Parvin Muhammad Shahabuddin	Y	Y		
DBSQC Reviewer	Tao Pan Lori Francis	Y	Y		
DBSQC Reviewer	Varsha Garnepudi Suzanne Carter	Y	Y		
Consult Reviewer	Natasha Thorne -CDRH	Y			
Discipline (Office/ Division)	Additional Meeting Attendees				
Office Director CBER/OTAT	Wilson Bryan, MD	Y	Y		
OTAT Office Deputy Director	Kim Benton, PhD	Y	Y		
OTAT/DRPM	Ramani Sista, PhD, RAC	Y	Y		
OTAT/DRPM	Lori Tull	Y	Y		
OTAT/DCEPT	Bindu George, MD	Y	Y		
OTAT/DCEPT	Poornima Sharma, MD	Y	Y		
OTAT/DCEPT	Tejashri Purohit-Sheth, MD	Y	Y		
OTAT/DCGT	Raj Puri, MD, PhD	Y	Y		
OTAT/DCGT	Stephan Oh, PhD	Y	Y		
OTAT/DCGT	Denise Gavin, PhD	Y	Y		
OTAT/DCG	Zenobia Taraporewala, PhD	Y			
OTAT/DCGT	Carolyn Laurencot, PhD	Y			
CBER/OCBQ/DMPQ/BI	Carolyn Renshaw	Y			

REGULATORY CONCLUSIONS / DEFICIENCIES

- 1. Does the application, on its face, appear to be suitable for filing or is the application unsuitable for filing and will require an RTF letter?**
The application is suitable for filing.
- 2. If fileable, list any substantive deficiencies or issues that have significant impact on the ability to complete the review or approve the application:**
No
- 3. If RTF, list any substantive deficiencies or issues that would make this application unsuitable for filing:**
N/A

FILING MEETING DISCUSSION, IF FILED:

- 4. Indicate any comments on the status of the proprietary name review (PNR).**
ROCTAVIAN as a potential. name is currently under review. Non-acceptance of the previously proposed proprietary name (b) (4) , was communicated to the sponsor on December 16, 2019.
- 5. Indicate whether the product sh/would be subject to lot release, surveillance, or exempt from lot release. Verify sample availability.**
The team will decide at the later.
- 6. Confirm review schedule of this application.**
Priority Review
- 7. Indicate the decision regarding the need for an Advisory Committee.**
No, there is no need for advisory committee meeting.
- 8. Indicate whether the submission triggers PREA; if yes, a PeRC meeting is needed. Verify whether the applicant has an initial pediatric study plan (iPSP) in place.**
No, the submission does not trigger PREA. The application has orphan designation.
- 9. Indicate whether the submission contains a proposed REMS. If yes, or if a REMS may be needed as a condition of approval, schedule an internal REMS meeting between the Product Office and OBE/DE.**
This submission does not contain REMS. The sponsor has submitted proposed pharmacovigilance plan.
- 10. Is a comprehensive and readily located list of all clinical sites included or referenced in the application?**
Yes.

11. Is a comprehensive and readily located list of all manufacturing facilities included or referenced in the application?

Yes.

12. Indicate any updates since the First Committee Meeting on pre-license inspection, pre-approval inspection, or BIMO sites requiring inspections (Is the establishment(s) ready for inspection?)

BIMO will identify inspection sites and will inform the team.

13. If the application is affected by the Application Integrity Policy (AIP), has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance?

No

14. Is the product an Original Biological Product or a New Molecular Entity (NME) for an NDA?

Yes, original BLA

FOR APPLICATIONS IN THE PDUFA PROGRAM (NME NDAs/Original BLAs), IF FILED

15. Confirm that any late submission components were submitted within 30 days. List any late submission components that arrived after 30 days.

Yes, submitted on Jan 22, 2020 as agreed at pre-BLA meeting.

16. Was the application otherwise complete upon submission, including those applications where there were no agreements regarding late submission components?

N/A

ADMINISTRATIVE DETAILS, IF FILED:

17. Review the Milestone Schedule and indicate if there are any issues with the schedule. Note: This is a confirmation to capture any changes made since the First Committee Meeting.

AOM and Data set walk through: February 7, 2020; 1:00 pm -3:00 pm

Filing action: February 22, 2020

Weekly CMC meetings: Wednesdays 1:00p.m.- 2:00 p.m.

Bi weekly Clinical meeting: Tuesdays and Fridays

CDISC – Feb 12, 2020

Internal Mid-cycle: March 31, 2020

Sponsor Mid-cycle: April 20, 2020

Sponsor late cycle: June 1, 2020

Internal goal date: August 7, 2020

Labeling meeting: Will schedule bimonthly labeling meeting after the late cycle meeting.