

## COMBINATION FIRST COMMITTEE AND FILING MEETING SUMMARY

**Application Type and STN:** BLA 125789/0

**Product Name:** afamitresgene autoleucel

**Proposed indication:** Treatment of adult patients with unresectable or metastatic synovial sarcoma who have received prior systemic therapy.

**Applicant:** Adaptimmune LLC

**Meeting Date & Time:** January 10, 2024, 11:00 AM – 12:00 PM

**Meeting Chair:** Elvira Argus, PhD

**Background:** Adaptimmune was granted rolling review for afamitresgene autoleucel for the treatment of adult patients with unresectable or metastatic synovial sarcoma who have received prior systemic therapy on December 22, 2022. Adaptimmune submitted the non-clinical module on December 23, 2022, Clinical module on March 30, 2023, and CMC module on December 5, 2023. The Applicant requested a priority review. The product was granted Orphan Drug Designation on August 26, 2016. RMAT was granted on November 27, 2019, under IND 17235.

**Table 1: Review Committee and Discipline Filing Decision Summary**

Discipline/Organization	Name	Attended meeting	Fileable	RTF		Deficiencies Identified
Regulatory Project Manager	Tigist Assefa, PharmD	Y	Y			
Chair	Elvira Argus, PhD	Y	Y			
Division Director/Deputy	Beatrice Kallungal, MS	Y				
Office Director/Deputy	Ramani Sista, PhD	Y				
Clinical Reviewer	Katherine Barnett, MD	Y	Y			
	Abigail Johnson, RN, BSN	Y	Y			
OCE MORE TL/Reviewer	Doros Leslie, MD	N				

Discipline/Organization	Name	Attended meeting	Fileable	RTF		Deficiencies Identified
Clinical Pharmacology Reviewer	Xiaofei Wang, PhD	Y	Y			
Toxicology Reviewer	Yves (Maurice) Morillon, PhD	Y	Y			
CMC Reviewer	Alan Baer, PhD	N	Y			
	Laura DeMaster, PhD	Y	Y			
	Y Nguyen, PhD	N	Y			
OCBQ/DMPQ RPM	Maureen DeMar	Y				
OCBQ/DMPQ Reviewer	Viviana Ramirez	N	Y			
OCBQ/APLB Reviewer	CAPT Teresa Vu, PharmD, BCSCP, MBA, RAC	Y	Y			
OCBQ/BIMO Reviewer	LCDR Malcolm Nasirah, PharmD, MS	Y	Y			
OCBQ/DBSQC	Simleen Kaur, MSc	Y	Y			
	Salil Ghosh, MS, PhD	Y	Y			
	Most Nahid Parvin	Y	Y			
	Marie Anderson, PhD	Y	Y			
Statistical Reviewer of clinical data	Cong Wang, PhD	Y				
Statistical Reviewer of non-clinical data		Y	Y			
Clinical Data Analyst	Elin Cho, MS	Y				
Epidemiology/ Pharmacovigilance	Brendan Day, MD, MPH	Y	Y			
Consult Reviewers	OBRR – Meihong Liu, PhD	Y				
	CDRH – Rupali Sharma, PhD	Y				
Other Attendees	Rachael Anatol, PhD Nirjal Bhattarai, PhD Peter Bross, MD Dennis Cato Asha Das, MD Maryna Eichelberger, PhD Chaohong Fan, MD, PhD Alyssa Galaro, PhD Varsha Garnepudi, MS					

Discipline/Organization	Name	Attended meeting	Fileable	RTF		Deficiencies Identified
	Denise Gavin, PhD Alifiya Ghadiali, Christine Harman, PhD Gaya Hettiarachchi, PhD Anna Kwilas, PhD Jessica Lee, MD, PhD Fengmin Li, Wei Liang, PhD Zhugong (Jason) Liu, PhD Narayan Nair, MD Yasmin Philips Kimberly Schultz, PhD Muhammad Shahabuddin, PhD Jason Steinberg, MD Nadia Whitt, MS Boguang Zhen, PhD					

## **REGULATORY CONCLUSIONS / DEFICIENCIES**

- 1. Does the application, on its face, appear to be suitable for filing or is the application unsuitable for filing and require an RTF letter?**

This application is fileable.

- 2. If fileable, list any substantive deficiencies or issues that have significant impact on the ability to complete the review or approve the application:**

- a. CMC – Fileable
- b. Clinical – Fileable
- c. Clinical Pharmacology – Fileable
- d. P/T – Fileable
- e. Biostats – Fileable
- f. Pharmacovigilance/ Epidemiology – Fileable
- g. BIMO – Fileable
- h. APLB – Fileable
- i. DBSQC – Fileable
- j. DMPQ – Fileable

- 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. Ensure that all Review Committee Members are appropriately assigned (including whether any consult reviewers are needed), they have received the appropriate documents or electronic links, and they have a clear understanding of their review responsibilities.**

All review members have been assigned.

CMC – Extractables and Leachables consult may be requested.

Clinical Pharmacology – A consult request will be submitted to CDER/OCP/Division of Pharmacometrics.

- 5. Confirm that the application is compliant with 21 CFR 601.2 for BLAs and 21 CFR 314.101 for NDAs.**

Application is compliant with 21 CFR 601.2

- 6. Indicate any comments on the status of the proprietary name review (PNR).**

FDA issued a PNR acceptable “at this time” letter for the proposed proprietary name TECELRA, on October 4, 2021. A request for a second review of the proprietary name was received on December 5, 2023. The review is ongoing by APLB.

- 7. Confirm review schedule for the application. If priority review was requested, include justification to grant or deny from clinical reviewer filing review checklist.**

Priority review was requested and granted by clinical.

- The product is intended to treat adult patients with unresectable or metastatic synovial sarcoma (SS) who have received prior systemic therapy. This is a serious condition with unmet medical need and there are no FDA approved therapies specifically for the proposed indication.
- The primary evidence to support the efficacy of afamitresgene autoleucel in subjects with advanced (unresectable/ metastatic) SS is provided by Study ADP-0044-002, Cohort 1. The sponsor reports the overall response rate (ORR) by independent review among the SS group was 38.6% with a median DOR of 11.6 months. This would be an improvement in the effectiveness of treatment for this serious condition.
- Afamitresgene autoleucel was granted RMAT designation on November 27, 2019, for the treatment of HLA-A\*02 allele-positive patients with synovial sarcoma and whose tumor expresses the ADP-A2M4 tumor antigen.

**8. Review/confirm if Orphan Drug designation was granted.**

Orphan Drug designation was granted on August 26, 2016.

**9. Indicate whether the submission triggers PREA or if it is in response to an outstanding PREA PMR. Verify whether the applicant has an initial pediatric study plan (iPSP) in place. Discuss timeframe for scheduling the PeRC meeting as applicable.**

The submission triggers PREA. The Applicant submitted an Agreed iPSP under IND 17235 on March 4, 2021.

The Applicant is requesting a partial waiver of pediatric subjects under the age of 2 years and a deferral on pediatric assessment for children aged 2-17 years old.

The PeRC meeting will be scheduled June 10 - June 21, 2024.

**10. Indicate whether the product should or would be subject to lot release, surveillance, or exempt from lot release. Verify sample availability.**

This product is exempt from lot release.

**11. Indicate the decision regarding the need for an Advisory Committee.**

There is no need for an Advisory Committee at this time.

**12. 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.**

The submission does not contain a proposed REMS.

**13. Is a comprehensive and readily located list of all clinical sites included or referenced in the application?**

Yes

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

Yes

**15. Indicate need for pre-license inspection, pre-approval inspection, or BIMO sites requiring inspections:**

- **Is the establishment(s) ready for inspection?**
- **Confirm that our intent to inspect has been / will be communicated at least 60 days in advance of the inspection and no later than mid-cycle.**

DMPQ will inspect 2 facilities domestically, including (b) (4) and Adaptimmune sites. BIMO will inspect facilities domestically and internationally.

**16. Is the application affected by the Application Integrity Policy (AIP)?**

No

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

The Applicant provided an updated lentiviral vector and drug product stability data as late components of BL125789/0 (within 30 calendar days of BLA Part 3 submission) on December 20, 2023.

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

Yes, CMC sent an information request to the applicant requesting the report of the risk assessment conducted to determine the suitability of LV manufacturing process version (b) (4), LV comparability report, and LV DS and DP batch analyses data in a format that is easily exportable on January 9, 2024.

**19. Review the Milestone Schedule and indicate if there are any issues with the schedule.**

<b><u>BLA Milestone Due Date</u></b> <b><u>Priority Review</u></b>	
Combined First Committee and Filing Meeting	January 10, 2024
Internal Mid-cycle Meeting	March 20, 2024
Mid-cycle Applicant t-con	April 3, 2024
Internal Late-cycle Meeting	May 2, 2024
Late-cycle Meeting	May 20, 2024

60-day filing date	February 3, 2024
PDUFA Action Date	August 4, 2024

The Application orientation meeting (11:00 AM – 12:00 PM) and data walkthrough meeting (12:15 PM – 1:00PM) has been scheduled on January 26, 2024.