



Our STN: BLA 125846/0

**LATE-CYCLE  
MEETING MEMORANDUM**  
July 24, 2025

Fondazione Telethon ETS  
Attention: Mike Yefimenko (US Agent)

(b) (4)

Dear Mike Yefimenko:

Attached is a copy of the memorandum summarizing your June 26, 2025, Late-Cycle Meeting with CBER. This memorandum constitutes the official record of the meeting. If your understanding of the meeting outcomes differs from those expressed in this summary, it is your responsibility to communicate with CBER in writing as soon as possible.

Please include a reference to the appropriate Submission Tracking Number (STN) in future submissions related to the subject product.

If you have any questions, please contact Cecilia Crowley at (240) 402-2810.

Sincerely,

Mara Miller, MA  
Director  
Division of Review Management and Regulatory Review 2  
Office of Review Management and Regulatory Review  
Office of Therapeutic Products  
Center for Biologics Evaluation and Research

### **Late-Cycle Meeting Summary**

**Meeting Date and Time:** June 26, 2025, at 11:00-12:00 pm  
**Meeting Location:** WO 71, Room 6244

**Application Number:** BLA 125846  
**Product Name:** etuvetidigene autotemcel; WASKYRA  
**Proposed Indications:** Treatment of patients aged 6 months and older with Wiskott-Aldrich Syndrome (WAS) who have a mutation in the WAS gene and for whom no suitable human leukocyte antigen (HLA)-matched related haematopoietic stem cell donor is available.

**Applicant Name:** Fondazione Telethon ETS (Telethon)  
**Meeting Chair:** Laura DeMaster, PhD  
**RPM:** Cecilia Crowley

### **FDA ATTENDEES**

Afsah Amin, MD, MPH, CBER/OTP/OCE/DCEGM  
Judith Badoo, CBER/OD  
Rabia Ballica, PhD, CBER/OCBQ/DMPQ  
Jessica Boehmer, MBA, CBER/OTP/ORMRR  
Colleen Caldwell, MS, MPH, CBER/OTP/ORMRR  
David Cantu, PhD, CBER/OTP/OPT  
Jennifer Chan, PharmD, CBER/OCBQ/DIS  
CDR Stephen Chang, PharmD, CBER/OBPV/DABRA/ARWEB  
Freda Cooner, PhD, CBER/OBPV/DB  
Cecilia Crowley, CBER/OTP/ORMRR  
Rochelle DalsanVaughn, MD, MS, CBER/OBPV/DPV  
Asha Das, MD, CBER/OTP/OCE/DCEO  
Brendan Day, MD, CBER/OBPV/DPV  
Laura DeMaster, PhD, CBER/OTP/OGT  
Varsha Garnepudi, MS, RAC, CBER/OCBQ/DBSQC  
Denise Gavin, PhD, CBER/OTP/OGT  
Jared Greenleaf, CBER/OCBQ/DMPQ  
Weidong Gu, MD, PhD, CBER/OBPV/DABRA/ARWEB  
Jiang Hu, PhD, CBER/OBPV/DB  
Ning Hu, MD, CBER/OTP/OCE/DCEGM  
Xing Jing, PhD, CBER/OTP/OCE/DCEH  
Alla Kachko, PhD, CBER/OCBQ/DMPQ  
Beatrice Kallungal, MS, CBER/OTP/ORMRR  
George Kastanis, MS, CBER/OCBQ/DBSQC  
CAPT Simleen Kaur, MSc, CBER/OCBQ/DBSQC  
Stella Lee, PhD, CBER/OTP/OGT  
Wei Liang, PhD, CBER/OTP  
Gumei Liu, MD, PhD, CBER/OTP/PSPS  
Namangolwa Jane Mutanga, MD, MPH, PhD, CBER/OBPV/DABRA/ARWEB

Renuka Miller, PhD, CBER/OTP/OGT  
Xinyi Ng, PhD, CBER/OBPV/DABRA/BRAB  
Manuel Osorio, CBER/OD  
Tao Pan, PhD, CBER/OTP/OGT  
Lori Peters, MS, CBER/OCBQ/DMPQ  
CDR Kenneth Phillips, CBER/OCBQ/DBSQC  
Gopa Raychaudhuri, PhD, CBER/OD  
Teisha Rowland, PhD, CBER/OTP/OGT  
Andrey Sarafanov, PhD CBER/OTP/OPPT  
Kimberly Schultz, PhD, CBER/OTP/OGT  
Rosa Sherafat-Kazemzadeh, MD, CBER/OTP/OCE/DCEGM  
Lisa Stockbridge, PhD, CBER/OCBQ/DCM/APLB  
Ekaterini Tsilou, MD, CBER/OTP/OCE/DCEGM  
Wei Tu, CBER/OCBQ/DBSQC/LBVI  
Ramjay Vatsan, PhD, CBER/OTP/OGT  
Debra Vause, RN, BSN, CBER/OCBQ/DMPQ  
CAPT Teresa Vu, PharmD, MBA, CBER/OCBQ/DCM/APLB  
Claire Wernly, PhD, CBER/OCBQ/DBSQC  
Hong Yang, PhD, CBER/OBPV/DABRA/BRAB  
Boguang Zhen, PhD, CBER/OBPV/DB  
Tingting Zhou, PhD, CBER/OBPV/DB

**EMA/EU Attendees**

Patrick Celis PhD  
Joseph deCourcey, PhD  
Caroline Pothet, PharmD, Msc  
Dolca Rogers, PhD  
Anabela Marcal, PharmD  
Catherine Draï PharmD MSc  
Thomas Castelnovo PharmD, MSc  
Mihaela Bogatu Ms.  
Paolo Petracci Mr.  
Guillaume Belliard, PhD  
Solène Maitenaz, PhD  
Badis-Lakhdar Bensaad Mr  
Marianne Delville, PhD  
Gabriela Ullio-Gamboa, PhD  
Monika Jarzabek, PhD  
Gavin McGauran, PhD  
Jayne Crowe, MD  
Ailise Carleton, MD  
Sarah Brophy, PhD  
Sean Barry, PhD  
Simona Teodosiu

**APPLICANT (Telethon) ATTENDEES**

Francesca Ferrua, Investigator, San Raffaele Hospital

(b) (4), CMC Consultant

Michela Palmisano, Senior Manager, CMC Regulatory Affairs

Sean Russell, Head of Regulatory Affairs

Celeste Scotti, Head of R&D

Stefano Zancan, Head of Clinical Development

Federica Miotto, Head of Medical Affairs

**BACKGROUND**

BLA 125846/0 was submitted on January 10, 2025, for etuvetidigene autotemcel (TL003).

Proposed indication: Treatment of patients aged 6 months and older with Wiskott-Aldrich Syndrome (WAS) who have a mutation in the WAS gene and for whom no suitable human leukocyte antigen (HLA)-matched related haematopoietic stem cell donor is available.

PDUFA goal date: September 10, 2025

In preparation for this meeting, FDA issued the Late-Cycle Meeting Materials on June 17, 2025.

## DISCUSSION

### 1. Discussion of Substantive Review Issues

#### **Chemistry, Manufacturing, and Controls**

The proposed submission date for responses to many of the identified review issues is after the PDUFA Action Due Date (ADD) of September 10, 2025. In order to complete our review within this timeline, it is important that the requested information is provided with enough time to review prior to the ADD.

1. Regarding the DP sterility assay, we have concerns with the amount of sample tested and the storage of the test samples.

#### **Meeting Discussion for #1:**

FDA suggested the Applicant combine the (b) (4) DP sample to test according to (b) (4). This will become the release test for the DP. Data from the suitability test for this method must be submitted and reviewed by CBER within the review clock.

Regarding the (b) (4) sterility assay, testing (b) (4) in (b) (4) using the (b) (4) method will be the release test. CBER does not need to review data from the suitability test for this method.

2. Regarding the DP mycoplasma assay, we are concerned that you are testing final DP rather than (b) (4) material. Moreover, you have not included the (b) (4) part of the mycoplasma test in your validation study.

#### **Meeting Discussion for #2:**

Mycoplasma testing should be performed on (b) (4) material. CBER will temporarily accept results using (b) (4) (b) (4) material validation is complete. Validation as per (b) (4) may be submitted as a PMC. Validation using the (b) (4) material must show how (b) (4) was overcome. The validation must also include an equivalency test between (b) (4) method and (b) (4) method. Once successfully validated, the mycoplasma test using (b) (4) material will be used for release testing.

3. Additional information is needed for the DP WAS protein (WASP) assay validation and to support DP potency assurance.

#### **Meeting Discussion for #3:**

FDA stated that additional information is needed on the intermediate precision (IP) assessment that was submitted in response to IR #15. As discussed at the teleconference on June 18, 2025, FDA requested information on the assay runs in the IP assessment to understand assay performance and sources of variability. Telethon responded that the requested information will be submitted by the end of June.

4. Regarding the DP transduction efficiency (TE) assay, we are concerned that intermediate precision was not assessed using DP material that is representative of the commercial etu-cel manufacturing process. Additionally, the validation study did not assess assay robustness.

**Meeting Discussion for #4:**

The applicant response to the Late Cycle Meeting (LCM) materials have been received and are under review.

5. We are concerned that the DP immunophenotype assay validation does not evaluate analytical parameters with respect to the (b) (4) and that the %CD34 (b) (4) does not adequately cover the relevant clinical range.

**Meeting Discussion for #5:**

Applicant response to this LCM agenda item has been received and is under review.

6. Regarding the (b) (4) sterility assay, we have concerns with the test sample to (b) (4) and the storage of the test samples.

**Meeting Discussion for #6:**

For sterility testing of commercial (b) (4) lots, Telethon has previously agreed to test (b) (4) and implement (b) (4) storage for (b) (4) sterility samples. However, FDA needs additional information on the (b) (4) lots that will be used initially for commercial DP manufacturing. FDA will send an IR requesting this information. FDA noted that this information will need to be provided before the ADD. FDA acknowledges that only (b) (4) samples are available for clinical (b) (4) lots and can work with Telethon on a plan to ensure that all (b) (4) lots used in commercial DP manufacturing have been tested adequately for sterility.

7. You have not demonstrated that (b) (4) process-related impurities are adequately reduced in the etu-cel manufacturing process.

**Meeting Discussion for #7:**

Applicant response to this LCM agenda item has been received and is under review.

8. The submitted leachables study is not adequate. Specifically, you should perform a real-time study to assess the cumulative leachables profile in the final DP.

**Meeting Discussion for #8:**

This agenda topic has been previously discussed, and Telethon has committed to perform an additional real-time study.

9. In your response to IR#23 dated June 6, 2025, you committed to provide supplemental CCIT validation and shipping validation results by August 2025. The CCIT study will include a positive control with a qualified critical defect and the shipping study will include a post shipment CCIT. We agree with your proposal provided the results are made available no later than the first week of August (i.e., COB August 8, 2025). The results from these studies are needed to ensure the microbial control of your final DP following filling and transport.

**Meeting Discussion for #9:**

FDA found the Applicant's response to be acceptable.

2. Additional Applicant Data

**Pharmacologic Class:** autologous hematopoietic stem cell-based gene therapy

**USAN:** etuvetidigene autotemcel

**Tradename:** WASKYRA

No suffix due to autologous product.

3. Information Requests

Responses to all information requests sent to date have been received.

Additional information requests will be sent out during the review process.

4. Discussion of Upcoming Advisory Committee Meeting

Currently, an advisory committee meeting is not planned.

5. Risk Management Actions (e.g., REMS, the ability of adverse event reporting and CBER's Sentinel Program to provide sufficient information about product risk)

Currently, there is no anticipation for REMS.

6. Postmarketing Requirements/Postmarketing Commitments

The review of the BLA is on-going. PMCs/PMRs will be conveyed to the Applicant by August 11, 2025, and July 30, 2024, respectively.

7. Major Labeling Issues

Labeling review is ongoing.

8. Review Plans

The review of the BLA is on-going. We will continue to send information requests as necessary to get clarification on any submitted information. We will communicate anticipated PMR's by July 30, 2025, and anticipated PMCs will be communicated on August 11, 2025. FDA plans to start label negotiations no later than August 11, 2025.

9. Applicant Questions

FDA reviewed the remaining timeline with Applicant.

10. Wrap-up and Action Items

This application has not yet been fully reviewed by the signatory authorities, Division Directors and Review Committee Chair and therefore, this meeting did not address the final regulatory decision for the application.