



Our STN: BL 125868/0

**BLA APPROVAL**  
July 1, 2026

Orca Biosystems Inc.  
Attention: Karin Mcintosh, MPharm, RAC  
3475 Edison Way, Suite C  
Menlo Park, CA 94025

Dear Karin Mcintosh:

Please refer to your Biologics License Application (BLA) received August 6, 2025, submitted under section 351(a) of the Public Health Service Act (PHS Act) for allogeneic regulatory T cell immunotherapy with HSPC and T cells-vldq.

We also refer to our approval letter dated June 30, 2026, which contained the following error:

The letter referenced an incorrect manufacturing facility location of Menlo Park, California; the correct manufacturing facility location is Sacramento, California.

This replacement approval letter incorporates the correction of the error. The effective approval date will remain June 30, 2026, the date of the original approval letter.

## **LICENSING**

We are issuing Department of Health and Human Services U.S. License No. 2404 to Orca Biosystems Inc, Menlo Park, California, under the provisions of section 351(a) of the PHS Act controlling the manufacture and sale of biological products. The license authorizes you to introduce or deliver for introduction into interstate commerce, those products for which your company has demonstrated compliance with establishment and product standards.

Under this license, you are authorized to manufacture the product allogeneic regulatory T cell immunotherapy with HSPC and T cells-vldq, which is indicated for use in matched donor hematopoietic stem cell transplantation with myeloablative preparative regimen, for hematopoietic and immunologic reconstitution and to improve chronic graft-versus-host disease (cGVHD)-free survival, in the treatment of adults with hematological malignancies.

The review of this product was associated with the following National Clinical Trial (NCT) numbers: NCT04013685, NCT05316701.

## **MANUFACTURING LOCATIONS**

Under this license, you are approved to manufacture allogeneic regulatory T cell immunotherapy with HSPC and T cells-vldq at your facility located at Sacramento, California. You may label your product with the proprietary name TREGZI and market it in four individual infusion bags as follows for each of your drug product (DP) component:

- Regulatory T cell (Treg) infusion bag containing  $1.3 \times 10^6$  to  $3.5 \times 10^6$  viable cells per patient kilogram in approximately 100 mL of solution,
- Hematopoietic stem and progenitor cell (HSPC) infusion bag containing  $\geq 1.0 \times 10^6$  viable cells per patient kilogram in approximately 100 mL of solution,
- Conventional T cell (Tcon) infusion bag containing  $1.3 \times 10^6$  to  $6.9 \times 10^6$  viable cells per patient kilogram in approximately 15 mL of solution, and
- Tcon Diluent infusion bag containing approximately 38 mL of solution.

## **ADVISORY COMMITTEE**

We did not refer your application to the Cellular, Tissue, and Gene Therapies Advisory Committee because our review of information submitted in your BLA, including the clinical study design and trial results, did not raise concerns or controversial issues that would have benefited from an advisory committee discussion.

## **DATING PERIOD**

The dating period for allogeneic regulatory T cell immunotherapy with HSPC and T cells-vldq shall be 72 hours from the time of first apheresis collection when stored at  $2^{\circ}\text{C}$  to  $8^{\circ}\text{C}$  for your Treg and HSPC product components, and seven days from the time of first apheresis collection when stored at less than  $-125^{\circ}\text{C}$  for your Tcon product component. The time of apheresis collection shall be defined as the time of completion of the first apheresis collection. The dating period for your Tcon Diluent product component, supplied for use with your Tcon product component, shall be (b) (4) from the date of manufacture when stored at (b) (4)  $^{\circ}\text{C}$ . The date of manufacture shall be defined as the date the Tcon Diluent is filled in the final container closure. We have approved the stability protocol in your license application for the purpose of extending the expiration dating period of your Tcon Diluent product component under 21 CFR 601.12.

## **FDA LOT RELEASE**

You are not currently required to submit samples or protocols of future lots of allogeneic regulatory T cell immunotherapy with HSPC and T cells-vldq to the Center for Biologics Evaluation and Research (CBER) for release by the Director, CBER, under 21 CFR 610.2(a). We will continue to monitor compliance with 21 CFR 610.1 requiring completion of tests for conformity with standards applicable to each product prior to release of each lot.

## **BIOLOGICAL PRODUCT DEVIATIONS**

You must submit reports of biological product deviations under 21 CFR 600.14. You should identify and investigate all manufacturing deviations promptly, including those associated with processing, testing, packaging, labeling, storage, holding and distribution. If the deviation involves a distributed product, may affect the safety, purity, or potency of the product, and meets the other criteria in the regulation, you must submit a report on Form FDA 3486 to the Director, Office of Compliance and Biologics Quality, electronically through the eBPDR web application or at the address below. Links for the instructions on completing the electronic form (eBPDR) may be found on CBER's web site at <https://www.fda.gov/vaccines-blood-biologics/report-problem-center-biologics-evaluation-research/biological-product-deviations> :

Food and Drug Administration  
Center for Biologics Evaluation and Research  
Document Control Center  
10903 New Hampshire Ave.  
WO71-G112  
Silver Spring, MD 20993-0002

## **MANUFACTURING CHANGES**

You must submit information to your BLA for our review and written approval under 21 CFR 601.12 for any changes in, including but not limited to, the manufacturing, testing, packaging or labeling of allogeneic regulatory T cell immunotherapy with HSPC and T cells-vldq or in the manufacturing facilities.

## **LABELING**

We hereby approve the draft content of labeling including the Package Insert submitted under amendment 72, dated June 30, 2026, and the draft package and container labels submitted under amendment 71, dated June 29, 2026, and under amendment 72, dated June 30, 2026.

## **CONTENT OF LABELING**

As soon as possible, but no later than 14 days from the date of this letter, please submit the final content of labeling (21 CFR 601.14) in Structured Product Labeling (SPL) format via the FDA automated drug registration and listing system, (eLIST) as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Content of labeling must be identical to the Package Insert submitted on June 30, 2026. 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* at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>.

The SPL will be accessible via publicly available labeling repositories.

## **PACKAGE AND CONTAINER LABELS**

Please electronically submit final printed package and container labels identical to the package and container labels submitted on June 29, 2026 and June 30, 2026, according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications* at <https://www.fda.gov/downloads/drugs/guidancecompliance/regulatoryinformation/guidances/ucm333969.pdf>.

All final labeling should be submitted as Product Correspondence to this BLA, STN BL 125868/0 at the time of use and include implementation information on Form FDA 356h.

## **ADVERTISING AND PROMOTIONAL LABELING**

You may submit two draft copies of the proposed introductory advertising and promotional labeling with Form FDA 2253 to the Advertising and Promotional Labeling Branch at the following address:

Food and Drug Administration  
Center for Biologics Evaluation and Research  
Document Control Center  
10903 New Hampshire Ave.  
WO71-G112  
Silver Spring, MD 20993-0002

You must submit copies of your final advertising and promotional labeling at the time of initial dissemination or publication, accompanied by Form FDA 2253 (21 CFR 601.12(f)(4)).

All promotional claims must be consistent with and not contrary to approved labeling. You should not make a comparative promotional claim or claim of superiority over other products unless you have substantial evidence or substantial clinical experience to support such claims (21 CFR 202.1(e)(6)).

## **ADVERSE EVENT REPORTING**

You must submit adverse experience reports in accordance with the adverse experience reporting requirements for licensed biological products (21 CFR 600.80) and you must submit distribution reports as described in 21 CFR 600.81. For information on adverse experience reporting, please refer to the guidance for industry *Providing Submissions in Electronic Format — Postmarketing Safety Reports* at <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/providing-submissions-electronic-format-postmarketing-safety-reports> and FDA's Adverse Event reporting System website at <https://www.fda.gov/drugs/questions-and-answers-fdas->

[adverse-event-reporting-system-faers/fda-adverse-event-reporting-system-faers-electronic-submissions](https://www.fda.gov/vaccines-blood-biologics/lot-release/lot-distribution-database-idd). For information on distribution reporting, please refer to the guidance for industry *Electronic Submission of Lot Distribution Reports* at <https://www.fda.gov/vaccines-blood-biologics/lot-release/lot-distribution-database-idd>.

## **PEDIATRIC REQUIREMENTS**

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 in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because the biological product for this indication has an orphan drug designation, you are exempt from this requirement.

## **POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B**

We acknowledge your written commitment as described in your letter of June 26, 2026 as outlined below:

1. Orca Biosystems Inc. commits to complete and submit the final report and datasets for the Phase 3 component of Precision-T study with final analysis and formal hypothesis testing of the secondary endpoints including overall survival and GVHD- and relapse free survival (GRFS) as outlined in the statistical analysis plan.

Primary analysis report submission: May 31, 2027

Final Report Submission: September 30, 2030

Please submit clinical protocols to your IND 18873, and a cross-reference letter to this BLA, STN 125868/0 explaining that this protocol was submitted to the IND.

If the information in the final study report supports a change in the label, the final study report must be submitted as a supplement. Please use the following designators to prominently label all submissions, including supplements, relating to these postmarketing study commitments as appropriate:

- **Postmarketing Commitment – Correspondence**
- **Postmarketing Commitment – Final Study Report**
- **Supplement contains Postmarketing Commitment – Final Study Report**

For each postmarketing study subject to the reporting requirements of 21 CFR 601.70, you must describe the status in an annual report on postmarketing studies for this

product. Label your annual report as an **Annual Status Report of Postmarketing Requirements/Commitments** and submit it to the FDA each year within 60 calendar days of the anniversary date of this letter until all Requirements and Commitments subject to the reporting requirements of section 506B of the FDCA are fulfilled or released. The status report for each study should include:

- the sequential number for each study as shown in this letter;
- information to identify and describe the postmarketing commitment;
- the original schedule for the commitment;
- the status of the commitment (i.e., pending, ongoing, delayed, terminated, or submitted); and,
- an explanation of the status including, for clinical studies, the patient accrual rate (i.e., number enrolled to date and the total planned enrollment).

As described in 21 CFR 601.70(e), we may publicly disclose information regarding these postmarketing studies on our website at <http://www.fda.gov/Drugs/Guidance/ComplianceRegulatoryInformation/Post-marketingPhaseIVCommitments/default.htm>.

#### **POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B**

We acknowledge your written commitments as described in your letter of June 26, 2026 as outlined below:

2. Orca Biosystems Inc. commits to revise and update all method validation reports for (b) (4) [REDACTED] based on the revisions requested in information requests sent April 24, 2026 to June 18, 2026. Orca Biosystems Inc. will submit the final study report(s) as a Prior Approval Supplement by August 31, 2026.

Final Report Submission: August 31, 2026

3. Orca Biosystems Inc. commits to establish a system to improve the quality and integrity of data handling for future study data. Orca Biosystems Inc. will submit the proposal as a Product Correspondence by August 31, 2026. Orca Biosystems Inc. will submit the implementation report as a Product Correspondence by July 31, 2027.

Proposal Submission: August 31, 2026

Final Implementation Report: July 31, 2027

4. Orca Biosystems Inc. commits to perform a full risk assessment of the (b) (4) [REDACTED] Assay procedures and controls to evaluate the root cause of the repeatability validation parameter failures during the method validation studies

performed under VAL-0178 and reported in VAL-0212. After completion of the risk and root cause assessments, as necessary, corrective actions will be proposed, justified, and implemented. Orca Biosystems Inc. will submit the risk assessment and, if necessary, proposed corrective actions as Prior Approval Supplement by September 30, 2026. Orca Biosystems Inc. will submit a final study report summarizing the implemented corrective actions and, as needed, updated assay Standard Operating Procedures and/or Work Instructions as a Prior Approval Supplement by July 31, 2027.

Risk Assessment Submission: September 30, 2026

Final Report Submission: July 31, 2027

5. Orca Biosystems Inc. commits to perform supplemental validation of the (b) (4) Assay assessing all validation parameters using a statistically justified number of new batches. The validation study will incorporate any method procedure and control changes deemed necessary by the risk assessment in PMC #3. Orca Biosystems Inc. will submit the study protocol as Product Correspondence by December 31, 2026. Orca Biosystems Inc. will submit the final study report(s) as a Prior Approval Supplement by July 31, 2027.

Study Protocol Submission: December 31, 2026

Final Report Submission: July 31, 2027

6. Orca Biosystems Inc. commits to perform supplemental validation of the (b) (4) Assays using (b) (4) to evaluate intermediate precision of the assay when (b) (4). Orca Biosystems Inc. will submit the study protocol(s) as Product Correspondence by September 30, 2026. Orca Biosystems Inc. will submit the final study report(s) as a Prior Approval Supplement by July 31, 2027.

Study Protocol Submission: September 30, 2026

Final Report Submission: July 31, 2027

7. Orca Biosystems Inc. commits to perform supplemental validation of the following (b) (4) for the (b) (4) Assay:

(b) (4)

(b) (4)

[Redacted]

Orca Biosystems Inc. will submit study protocol(s) as Product Correspondence by September 30, 2026. Orca Biosystems Inc. will submit the final study report(s) as a Prior Approval Supplement by July 31, 2027.

Study Protocol Submission: September 30, 2026

Final Report Submission: July 31, 2027

8. Orca Biosystems Inc. commits to perform supplemental validation to assess all validation parameters for the (b) (4) across the range of (b) (4), unless otherwise indicated, using a (b) (4). Orca Biosystems Inc. will establish a LOD. Orca Biosystems Inc. will submit study protocol(s) as Product Correspondence by September 30, 2026. Orca Biosystems Inc. will submit the final study report(s) as a Prior Approval Supplement by July 31, 2027.

Study Protocol Submission: September 30, 2026

Final Report Submission: July 31, 2027

9. Orca Biosystems Inc. commits to perform supplemental validation of the following (b) (4) for the (b) (4) Assay:

(b) (4)

[Redacted]

(b) (4)

Orca Biosystems Inc. will submit study protocol(s) as Product Correspondence by September 30, 2026. Orca Biosystems Inc. will submit the final study report(s) as a Prior Approval Supplement by July 31, 2027.

Study Protocol Submission: September 30, 2026

Final Report Submission: July 31, 2027

10. Orca Biosystems Inc. commits to perform supplemental validation of the (b) (4)

[REDACTED] to evaluate intermediate precision of the assay when (b) (4)

[REDACTED]. Orca Biosystems Inc. will submit the study protocol(s) as Product Correspondence by September 30, 2026. Orca Biosystems Inc. will submit the final study report(s) as a Prior Approval Supplement by July 31, 2027.

Study Protocol Submission: September 30, 2026

Final Report Submission: July 31, 2027

11. Orca Biosystems Inc. commits to perform supplemental validation of the (b) (4)

[REDACTED] to evaluate intermediate precision of the assay when (b) (4)

[REDACTED] Orca Biosystems Inc. will submit the study protocol(s) as Product Correspondence by September 30, 2026. Orca Biosystems Inc. will submit the final study report(s) as a Prior Approval Supplement by July 31, 2027.

Study Protocol Submission: September 30, 2026

Final Report Submission: July 31, 2027

12. Orca Biosystems Inc commits to the following for the first two years of commercial manufacturing:

- a. Submit batch production records, including in-process test results, lot release data, and characterization data quarterly.
- b. Conduct extended characterization testing for (b) (4) commercial-scale lots.

Orca Biosystems Inc. will provide interim reports as Product Correspondence quarterly for 2 years after the start of commercial manufacturing. Orca Biosystems Inc. will submit the final study report(s) as a Prior Approval Supplement by November 30, 2028.

Interim Report Submission: Quarterly for 2 years after start of commercial manufacturing

Final Report Submission: November 30, 2028

13. Orca Biosystems Inc commits to conduct the following concerning the (b) (4) characterization assay:

(b) (4)

[Redacted]

[Redacted]

[Redacted]

[Redacted]

[Redacted]

[Redacted]

[Redacted]

[Redacted]

[Redacted]

[Redacted]

Orca Biosystems Inc. will submit the revised SOPs and/or WIs as Prior Approval Supplement by September 30, 2026. Orca Biosystems Inc. will submit the study protocol(s) as Product Correspondence by October 31, 2026. Orca Biosystems Inc. will submit the final study report(s) as a Prior Approval Supplement by September 30, 2027.

Revised SOPs/Wis Submission: September 30, 2026

Study Protocol Submission: October 31, 2026

Final Report Submission: September 30, 2027

14. Orca Biosystems Inc. commits to perform the following concerning the use of reference materials in their release assays:

- a. Qualification of reference materials for the (b) (4) [redacted] to establish defined operating ranges, release criteria, and acceptance limits.
- b. Revise the release method SOPs and/or WIs to include use of the reference material for the (b) (4) [redacted]

Orca Biosystems Inc. will submit the revised SOPs and/or WIs, and the final study report(s) as a Prior Approval Supplement by December 31, 2026.

Final Report Submission: December 31, 2026

15. Orca Biosystems Inc. commits to performing a study evaluating (b) (4) [redacted] to revise the (b) (4) [redacted] assay acceptance criteria of critical (b) (4) [redacted] manufacturing (b) (4) [redacted] and release testing (b) (4) [redacted]

[redacted]. Orca Biosystems Inc. will submit the study protocol(s) as Product Correspondence by October 31, 2026. Orca Biosystems Inc. will submit the final study report(s) as a Prior Approval Supplement by August 31, 2027.

Study Protocol Submission: October 31, 2026

Final Report Submission: August 31, 2027

16. Orca Biosystems Inc. commits to providing full leachables study results using validated analytical methods for compounds identified as extractables with high-risk levels. Orca Biosystems Inc. will submit the final study report(s) as a Prior Approval Supplement by November 30, 2026.

Final Report Submission: November 30, 2026

17. Orca Biosystems Inc. commits to update all eCTD Module 3 sections in BLA 125868, as applicable, to incorporate changes to your submission resulting from the interactive review process from the original BLA submission review period. The

Module 3 update will include a detailed summary table of all changes with hyperlinks. Orca Biosystems Inc. will submit the revised Module 3 as a PMC-Final Study Report by August 31, 2026.

Full Module 3 Update: August 31, 2026

We request that you submit information concerning chemistry, manufacturing, and control postmarketing commitments and final reports to your BLA, STN 125868/0. Please refer to the sequential number for each commitment.

Please use the following designators to prominently label all submissions, including supplements, relating to these postmarketing study commitments as appropriate:

- **Postmarketing Commitment – Status Update**
- **Postmarketing Commitment – Final Study Report**
- **Supplement contains Postmarketing Commitment – Final Study Report**

For each postmarketing commitment not subject to the reporting requirements of 21 CFR 601.70, you may report the status to FDA as a **Postmarketing Commitment – Status Update**. The status report for each commitment should include:

- the sequential number for each study as shown in this letter;
- the submission number associated with this letter;
- describe what has been accomplished to fulfill the non-section 506B PMC; and,
- summarize any data collected or issues with fulfilling the non-section 506B PMC.

When you have fulfilled your commitment, submit your final report as **Postmarketing Commitment – Final Study Report** or **Supplement contains Postmarketing Commitment – Final Study Report**.

## **POST APPROVAL FEEDBACK MEETING**

New biological products qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, please contact the Regulatory Project Manager for this application.

Sincerely,

Vincent Amatrudo, JD  
Acting Director  
Office of Compliance and Biologics Quality  
Center for Biologics Evaluation and  
Research

Asha Das, MD  
Director  
Office of Clinical Evaluation  
Office of Therapeutic Products  
Center for Biologics Evaluation and  
Research