



Our STN: BL 125845/0

BLA APPROVAL
September 17, 2026

Ultragenyx Pharmaceutical Inc.
Attention: Jad Adaimi
5000 Marina Blvd.
Brisbane, CA 94005

Dear Jad Adaimi:

Please refer to your Biologics License Application (BLA) received December 18, 2024, submitted under section 351(a) of the Public Health Service Act (PHS Act) for rebisufligene etisparovec-hopf.

We acknowledge receipt of your amendment dated March 20, 2026, which constituted a complete response to our July 7, 2025, action letter.

LICENSING

We have approved your BLA for rebisufligene etisparovec-hopf effective on this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, rebisufligene etisparovec-hopf under your existing Department of Health and Human Services U.S. License No. 2040. Rebisufligene etisparovec-hopf is indicated for the treatment of neurologic manifestations of mucopolysaccharidosis type IIIA (MPS IIIA, Sanfilippo Syndrome type A) in pediatric patients with preserved neurodevelopmental function.

The review of this product was associated with the following National Clinical Trial (NCT) number(s): NCT02716246, NCT04360265, and NCT04088734.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture rebisufligene etisparovec-hopf drug substance at Andelyn Biosciences, Inc., 1180 Arthur E Adams Dr., Columbus, OH 43221. The final formulated product will be manufactured and filled at Ultragenyx Pharmaceutical Inc., 170 Middlesex Turnpike, Bedford, MA 01730 and labeled and packaged at (b) (4).

You may label your product with the proprietary name FAYUVI and market it in single-dose vials containing 2.0 mL extractable volume at a concentration of 1.0×10^{13} vector genomes/mL (vg/mL).

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 rebisufligene etisparvovec-hopf shall be 24 months from the date of manufacture when stored at $\leq -60^{\circ}\text{C}$. The date of manufacture shall be defined as the date of (b) (4) of the formulated drug product. Following the (b) (4), no reprocessing/reworking is allowed without prior approval from the Agency. The dating period for your drug substance shall be (b) (4) when stored at (b) (4).

FDA LOT RELEASE

Please submit protocols showing results of all applicable tests. You may not distribute any lots of product until you receive a notification of release from the Director, Center for Biologics Evaluation and Research (CBER).

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 rebisufligene etisparvovec-hopf, or in the manufacturing facilities.

LABELING

We hereby approve the draft content of labeling including the Package Insert submitted under amendment 95, dated September 16, 2026 and the draft package and container labels submitted under amendment 91, dated September 10, 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 September 16, 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 September 10, 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 125845/0 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-G1122Silver 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. In addition to the reporting requirements in 21 CFR 600.80, you must submit adverse experience reports for cases of liver failure, thrombotic microangiopathy, and malignancy, regardless of whether they are considered as expected or unexpected, as 15-day expedited reports to the FDA Adverse Event Reporting System (FAERS) for 3 years following the date of product licensure.

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>.

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-ldd>.

RARE PEDIATRIC DISEASE PRIORITY REVIEW VOUCHER

We also inform you that you have been granted a rare pediatric disease priority review voucher (PRV), as provided under section 529 of the FDCA. This PRV has been assigned a tracking number, PRV BLA 125845. All correspondences related to this voucher should refer to this tracking number.

This voucher entitles you to designate a single human drug application submitted under section 505(b)(1) of the FDCA or a single biologic application submitted under section 351 of the Public Health Service Act as qualifying for a priority review. Such an application would not have to meet any other requirements for a priority review. The list

below describes the sponsor responsibilities and the parameters for using and transferring a rare pediatric disease priority review voucher.

- The sponsor who redeems the PRV must notify FDA of its intent to submit an application with a PRV at least 90 days before submission of the application and must include the date the sponsor intends to submit the application. This notification should be prominently marked, **“Notification of Intent to Submit an Application with a Rare Pediatric Disease Priority Review Voucher.”**
- This PRV may be transferred, including by sale, by you to another sponsor of a human drug or biologic application. There is no limit on the number of times that the PRV may be transferred, but each person to whom the PRV is transferred must notify FDA of the change in ownership of the voucher not later than 30 days after the transfer. If you retain and redeem this PRV, you should refer to this letter as an official record of the voucher. If the PRV is transferred, the sponsor to whom the PRV has been transferred should include a copy of this letter (which will be posted on our website as are all approval letters) and proof that the PRV was transferred.
- FDA may revoke the PRV if the rare pediatric disease product for which the PRV was awarded is not marketed in the U.S. within 1 year following the date of approval.
- The sponsor of an approved rare pediatric disease product application who is awarded a PRV must submit a report to FDA no later than 5 years after approval that addresses, for each of the first 4 post-approval years:
 - the estimated population in the U.S. suffering from the rare pediatric disease for which the product was approved (both the entire population and the population aged 0 through 18 years),
 - the estimated demand in the U.S. for the product, and
 - the actual amount of product distributed in the U.S.

You may also review the requirements related to this program by visiting FDA's Rare Pediatric Disease PRV Program webpage available at <https://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/RarePediatricDiseasePriorityVoucherProgram/default.htm>.

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 commitments as described in your letter of September 15, 2026 as outlined below:

1. Conduct adequate analytical and clinical validation studies to support revisions to the labeling of FAYUVI to specify the use of an FDA-authorized *in vitro* companion diagnostic device to accurately and reliably identify patients who do not have anti-AAV9 Antibodies $\geq 1:100$ and for whom FAYUVI is indicated. The final study report should be accompanied by a revised labeling Prior Approval Supplement incorporating the authorized companion diagnostic device information.

Study Completion: December 31, 2028

Final Report Submission: June 30, 2029

Please submit clinical protocols to your IND 16850, and a cross-reference letter to this BLA, STN BL 125845/0 explaining that these protocols were 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 August 27, 2026 as outlined below:

2. Ultragenyx commits to re-evaluating the acceptance criteria for the (b) (4) QC release tests performed on the drug substance and drug product. Ultragenyx will submit the test results and, if applicable, revise the acceptance limits and justifications. The study report should be submitted within 60 days after the 15th commercial lot is released under the US license as a Postmarketing Study Commitment.

Final Report Submission: July 31, 2028

3. Ultragenyx commits to providing supplemental validation data for the (b) (4) analytical method used to (b) (4). This data is intended to (b) (4) while maintaining acceptable levels of precision, accuracy and linearity and submitted as a Postmarketing Commitment.

Final Report Submission: September 30, 2027

4. Ultragenyx commits to submit the 24-month stability data for PPQ1 and PPQ2 DP lots as soon as the data is available. This commitment is independent of any post-approval shelf-life extension requests, which must be submitted as a separate post-approval supplement (PAS), as a Postmarketing Commitment.

Final Report Submission: February 28, 2027

We request that you submit information concerning chemistry, manufacturing, and control postmarketing commitments and final reports to your BLA, STN 125845/0. 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,

Rosa Sherafat, MD
Acting Director
Office of Clinical Evaluation
Office of Therapeutic Products
Center for Biologics Evaluation and Research