Congress of the United States
Washington, DC 20515

February 26, 2026

The Honorable Martin Makary, M.D.
Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Commissioner Makary,

Thank you for your continued leadership in building an America First Food and Drug Administration (FDA) that faithfully supports medical innovation and public health. As you know, Congress provided direction in the FY 2026 Agriculture, Rural Development, Food and Drug Administration, and Related Agencies Appropriations Joint Explanatory Statement regarding FDA's obligations under the Orphan Drug Act (ODA). The agreement underscores the need for strict adherence to section 527 of the Federal Food, Drug, and Cosmetic Act's (FFDCA) exclusive approval provision and directs FDA to apply determinations of clinical superiority in accordance with the statutory framework established by Congress.[1] With appreciation for your FDA's commitment to protecting the intellectual property of American innovators, we would be grateful for an update on the steps FDA is taking to apply the ODA as written.

Given that exclusive approval under section 527 of the FFDCA is a statutory prohibition, Congress believes FDA will exceed its authority if it approves the same molecule for the same rare disease indication during a seven-year period of orphan exclusivity, unless one of two narrowly defined exceptions apply.[2] The 2017 amendment to the ODA codified clinical superiority as a condition for follow-on products after exclusivity has expired, not a third exception to FDA enforcement of an orphan exclusivity period.[3] Thus, since 2017, FDA use of clinical superiority to break orphan exclusivity would be inconsistent with the statute. To take such action against the innovator orphan product's first rare disease indication would also be a departure from nearly 30 years of FDA precedent.[4]

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[1] *See* CONGRESSIONAL DIRECTIVES, AGRICULTURE, RURAL DEVELOPMENT, FDA AND RELATED AGENCY APPROPRIATIONS ACT, 2026 at 27, https://www.appropriations.senate.gov/imo/media/doc/ag_divbjes.pdf.
[2] *See* 21 U.S.C.S. § 360cc (LexisNexis 2026).
[3] *Compare* § 360cc(b) *with* § 360cc(c) (emphasis added).
[4] *Compare* FDA, HHS, NDA 50-740, Medical Officers' Review: AmBisome (liposomal amphotercin B) at 38-39 (Oct. 31, 1997) (demonstrating the last time FDA allowed the first follow-on product (AmBisome) to break orphan exclusivity of the innovator product's (Abelcet) first rare disease indication) *with* FDA, Clinical Superiority Findings, https://www.fda.gov/industry/designating-orphan-product-drugs-and-biological-products/clinical-superiority-findings (illustrating that Avadel's Lumryz, which is the *second* follow-on sodium oxybate product, never broke exclusivity for the *initial* rare disease indication for the *innovator* (Jazz's Xyrem), but did for the first follow-on (Jazz's Xywav)).

From our perspective, the plain language of section 527 of the FFDCA clearly articulates certain permissible and impermissible agency actions during a period of orphan exclusivity and clarifies when clinical superiority should be applied:

- **Permissible FDA Actions During an Orphan Drug Exclusivity Period**
  FDA may receive and review applications,[5] and it may issue "tentative approval" when an application is otherwise approvable, but its marketing authorization is blocked by orphan drug exclusivity.[6]

- **Prohibited FDA Actions During an Orphan Drug Exclusivity Period**
  The only two statutory exceptions to orphan drug exclusivity are exclusivity holder consent or a product shortage.[7] If neither of those exceptions apply, FDA would be unable to grant final approval to the same molecule for the same rare disease indication until exclusivity has expired.

- **Permissible Application of the Clinical Superiority Condition**
  FDA is not permitted to consider clinical superiority until exclusivity has expired. Clinical superiority is a criterion for a subsequent sponsor to obtain its own orphan exclusivity after approval becomes legally available (i.e., orphan exclusivity of the innovator is no longer blocking market entry of the follow-on).[8]

The ODA does not authorize FDA to break orphan exclusivity based on clinical superiority. During an active orphan exclusivity period, the appropriate resolution, consistent with both the law and precedent, is to complete scientific review of the follow-on product and, if applicable, issue a tentative approval letter, with final approval deferred until the exclusivity expires or one of the two statutory exceptions applies. Adhering to the statute will preserve the value of the most important incentive in the ODA.

Strict enforcement of orphan exclusivity is essential as American innovators continue to face threats from opportunistic, non-innovative foreign competitors seeking to exploit established rare disease markets through patent infringement and incremental changes at lower risk.[9] With only five percent of identified rare diseases having an FDA-approved therapy,[10] we appreciate the steps you are taking to align FDA's actions with Congress's directive to enforce orphan

[5] *See* Memorandum from Elizabeth Dickinson, Associate General Counsel for Drugs, FDA to Dr. James Bilstad, Dir., Office of Drug Evaluation II, FDA, Re: Refusal to File/ Orphan Exclusivity (May 28, 1996), https://www.accessdata.fda.gov/drugsatfda_docs/nda/98/20521_INFASURF%20INTRACHEAL%20SUSPENSION_corres_P1.pdf (reasoning that nothing in the ODA or the NDA filing regulations prohibit FDA from filing an NDA for review).

[6] *See* 21 C.F.R. § 314.105(a) (2026) (providing for a tentative approval letter from FDA for an NDA that otherwise meets the requirements for approval, but final approval is blocked by orphan drug exclusivity); *see, e.g.*, Memorandum from John Jenkins, FDA, to Janet Woodcock & Murray Lumpkin, FDA, Re: Addendum to April 22, 1997 Memorandum Regarding the Request by ONY for Dispute Resolution, at 2, fn. 1 (July 2, 1997), https://www.accessdata.fda.gov/drugsatfda_docs/nda/98/20521_INFASURF%20INTRACHEAL%20SUSPENSION_corres_P2.pdf

[7] *See* 21 U.S.C.S. § 360cc(b).

[8] *Id*. at § 360cc(c).

[9] *See* U.S. Int'l Trade Comm'n, In the Matter of Certain Drug Products Containing C-type Natriuretic Peptide Variants and Components Thereof, Notice of Institution of Investigation: Inv. No. 337-TA-1447 (May 2, 2025), https://www.usitc.gov/secretary/fed_reg_notices/337/337_1447_notice05022025sgl.pdf.

exclusivity as written in statute. Such enforcement protects American intellectual property and ensures continued investment in rare disease innovation.[11]

We look forward to your response and to continued collaboration in safeguarding the statute-based incentives that power America's rare disease innovation ecosystem.

Sincerely,

Cliff Bentz
Member of Congress

Rick W. Allen
Member of Congress

Mariannette J. Miller-Meeks, M.D.
Member of Congress

Vern Buchanan
Member of Congress

Claudia Tenney
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[10] *See* GOV'T ACCOUNTABILITY OFFICE, RARE DISEASE DRUGS, FDA HAS STEPS UNDERWAY TO STRENGTHEN COORDINATION OF ACTIVITIES SUPPORTING DRUG DEVELOPMENT, GAO-25-106774 at 1 (Nov. 18, 2024), https://www.gao.gov/assets/gao-25-106774.pdf

[11] *See* INCUBATE COALITION, 2026 SURVEY RESULTS, https://www.incubatecoalition.org/post/2026-investor-survey-one-pager (last visited Feb. 5, 2026) (revealing that more than 80% of investors surveyed indicated they would reduce biopharmaceutical investment if intellectual property protections were weakened).