MASSBIO

700 Technology Square, 5th Floor
Cambridge, MA 02139
617.674.5100 | massbio.org

August 13, 2026

Submitted Via Electronic Submission

The Honorable Robert F. Kennedy, Jr.
Secretary
U.S. Department of Health & Human Services
200 Independence Avenue, S.W.
Washington, DC 20201

The Honorable Dr. Mehmet Oz
Administrator
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244

RE: Medicare Drug Price Negotiation Program and Medicare Prescription Drug Benefit Program Proposed Rule, CMS-4215-P

Dear Secretary Kennedy and Administrator Oz:

The Massachusetts Biotechnology Council ("MassBio") appreciates the opportunity to comment on the Centers for Medicare & Medicaid Services' ("CMS's") proposed rule to codify the Medicare Drug Price Negotiation Program (the "Negotiation Program") and related requirements of the Medicare Prescription Drug Benefit Program (the "Proposed Rule").[1]

MassBio represents the premier global life sciences and healthcare hub of Massachusetts, a vibrant biomedical research and development community that is a global leader in medical discovery and innovation. MassBio's 1,800+ member organizations are dedicated to preventing, treating, and curing disease through transformative science and technology that brings value and hope to patients. MassBio's mission is to advance Massachusetts' leadership in the life sciences to grow the industry, add value to the healthcare system, and improve patient lives.

MassBio remains concerned about the impact the Negotiation Program will have on the future development of innovative and life-saving therapies, and on the world-leading small and emerging biotech companies based in Massachusetts. We continue to urge CMS to adopt a "do

[1] 91 Fed. Reg. 36,236 (June 16, 2026) (to be codified at 42 C.F.R. pts. 423, 429) ("Proposed Rule").

no harm" approach that errs on the side of mitigating the disincentives created by the program's framework and that preserves the agency's ability to make corrections as needed to protect innovation.

I. CMS Should Use This First Rulemaking to Take a Fresh Look at Policies Developed Through Guidance.

For initial price applicability years ("IPAYs") 2026 through 2028, CMS implemented the Negotiation Program exclusively through program instruction and other sub-regulatory guidance, as the IRA directed for that transitional period.[2] MassBio and its members submitted extensive comments on that guidance, including with respect to the orphan drug exclusion, the treatment of small biotech companies, MFP effectuation, and the transparency of CMS's negotiation methodology. The Proposed Rule marks the first time CMS has sought to establish binding, notice-and-comment regulations governing the Negotiation Program, generally applicable beginning with IPAY 2029 and subsequent years.

Because CMS is no longer restating program instruction but is instead promulgating legislative rules with the force of law, ***MassBio urges CMS to treat this rulemaking as an occasion for genuine reconsideration of the policy choices reflected in prior guidance, not a ministerial re-codification of them***. The Administrative Procedure Act requires reasoned decision-making and meaningful engagement with significant comments.[3] This includes a consideration of comments that were previously raised in the guidance process but have not, to date, been tested through notice-and-comment rulemaking. MassBio's members have raised many of the concerns below in prior comment cycles; we ask that CMS use this rulemaking to substantively address them on this fuller record, rather than carrying forward prior positions without renewed analysis.

With that overarching principle in mind, MassBio urges CMS to:

- Finish the job of clarifying the orphan drug clock-start rule proposed at § 429.125(c)(3)(i) in a manner that preserves incentives for rare disease innovation;
- Ensure the new Temporary Floor for Small Biotech Drugs provides meaningful protection for emerging Massachusetts biotech companies in a manner consistent with statute;
- Provide greater transparency and predictability regarding the identification of therapeutic alternatives and the application of statutory negotiation factors;
- Preserve incentives for meaningful post-approval innovation by maintaining predictable treatment of separately approved fixed-dose combination products; and

---

[2] See 91 Fed. Reg. at 36,237 (explaining that for IPAYs 2026 through 2028, sections 11001(c) and 11002(c) of the IRA directed CMS to implement the Negotiation Program through program instruction and other guidance, rather than notice-and-comment rulemaking).

[3] 5 U.S.C. § 706(2)(A), (C). *See also* Perez v. Mortgage Bankers Ass'n, 575 U.S. 92, 96 (2015); Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto. Ins. Co., 463 U.S. 29, 43 (1983).

- Ensure that Part B MFP effectuation and 340B non-duplication policies are developed thoughtfully, with robust stakeholder engagement, before being codified.

II. CMS Should Adopt an Orphan Drug Clock-Start Policy That Preserves Incentives for Rare Disease Innovation.

MassBio has historically expressed deep concerns that the narrow scope of the orphan drug exclusion creates a strong disincentive for developers to continue to develop new indications and formulations for existing orphan therapies. Fortunately, Congress enacted the ORPHAN Cures Act as part of the Working Families Tax Cut legislation,[4] which broadened the scope of the orphan drug exclusion to include drugs with multiple orphan drug designations and added a new provision addressing the treatment of former orphan drugs. Specifically, consistent with MassBio's previous comments, Congress clarified that the pre-negotiation period for a drug that loses the orphan drug exclusion (i.e., a former orphan drug that obtains approval for a new non-rare indication) begins only upon the loss of that exclusion, rather than upon the drug's original approval date. MassBio appreciates that this statutory change addresses, at least in part, the concerns MassBio and other stakeholders have raised.

Consistent with this statutory change, the Proposed Rule would now clarify that the 7- and 11-year pre-negotiation periods for drugs that formerly qualified for the orphan drug exclusion begin upon the loss of the exclusion.[5] This is directly responsive to MassBio's longstanding request, and MassBio supports the proposed approach.

We are concerned, however, that CMS has proposed that the pre-negotiation "clock" for such drugs would continue to run, even if approval for the non-orphan indication that triggered loss of the exclusion eligibility is subsequently withdrawn. Not only is this policy not contemplated in statute, it directly contravenes the intent of ORPHAN Cures. Indeed, ORPHAN Cures was clearly designed to toll the pre-negotiation "clock" for the entire period an orphan drug qualifies for the orphan drug exclusion, thereby preserving incentives for orphan drug development that were initially curtailed by the IRA, as enacted.

The continued need for incentives for orphan drug development is well-understood. Since the enactment of the Orphan Drug Act (ODA) 40 years ago, there has been a surge in the development of drugs for rare disease populations,[6] with much of this development occurring in

---

[4] Pub. L. No. 119-21, § 71203(a)(2)-(3) (July 4, 2025) (amending SSA § 1192(e)(1)(3)(A) and adding SSA § 1192(e)(4)).

[5] Proposed 42 C.F.R. § 429.125(c)(3)(i); 91 Fed. Reg. at 36,236 (describing this proposal as intended to "clarify how CMS would identify the day from which to measure the 7- and 11-year time since approval and licensure periods for drugs that formerly qualified for the Orphan Drug Exclusion").

[6] L. J. Fermaglich & K. L. Miller, A comprehensive study of the rare diseases and conditions targeted by orphan drug designations and approvals over the forty years of the Orphan Drug Act. Orphanet J Rare Dis. (June 2023), https://pmc.ncbi.nlm.nih.gov/articles/PMC10290406/.

Massachusetts.[7] However, over 90 percent of known rare diseases still do not have therapies or treatments.

This scarcity in therapies for the vast majority of rare diseases is due to a variety of reasons, including the resource and time investment generally needed to design, develop, and bring a drug to market,[8] as well as the low success rate of this process.[9] There are also a plethora of challenges specific to developing drugs for rare diseases, as the low number of actual patient numbers for certain diseases makes it difficult to establish an adequately sized and diverse patient population for a clinical trial, as well as obtain the high-quality patient data necessary to evaluate clinical trial outcomes.

To give full effect to the incentives restored by ORPHAN Cures, CMS should revise its proposed policy such that the pre-negotiation "clock" is tolled for the entire period a drug qualifies for the orphan drug exclusion—even if there is an intervening period during which the drug is temporarily ineligible due to the approval of a non-orphan indication that is subsequently withdrawn.

MassBio also urges CMS to clarify that, when determining eligibility for the orphan drug exclusion, CMS looks only at the *active* indications as of the drug selection date. While not directly addressed in the Proposed Rule, we note that this is the only possible read of the statute. The orphan drug exclusion is stated in the present tense; accordingly, any drug that currently has at least one orphan drug exclusion, and for which all of its indications are for designated rare diseases or conditions, must qualify, even if the drug historically had approval for non-orphan indications. We note that this approach is also consistent with prior CMS policy—before ORPHAN Cures removed the requirement that a drug have only one orphan drug designation, in order to qualify for the exclusion, CMS similarly clarified that the agency would look only at *active* designations in determining whether that requirement was met.

Finally, as noted in prior comments, MassBio reiterates that, for orphan drugs and former orphan drugs alike, CMS should ensure that the agency's consideration of the statutory negotiation factors adequately values the clinical benefit these therapies bring to rare disease patient populations, who, by definition, have limited or no therapeutic alternatives.

---

[7] D. Seiffert, Massachusetts owns the orphan drug market. Here's the proof, Boston Business Journal (Nov. 9, 2015), https://www.bizjournals.com/boston/blog/bioflash/2015/11/massachusetts-owns-the-orphan-drug-market-here-s.html.

[8] It can take 10 to 15 years and $1-2B for a drug to be designed, developed and approved for use in patients. I.V. Hinkson, B. Madej, E.A. Stahlberg, Accelerating therapeutics for opportunities in medicine: a paradigm shift in drug discovery, Front Pharmacol, 11 (2020), p. 770.

[9] 90 percent of developed drugs are unsuccessful. H. Dowden & J. Munro, Trends in clinical success rates and therapeutic focus, Nat Rev Drug Discov, 18 (2019), pp. 495-496.

III. CMS Should Ensure the Temporary Floor for Small Biotech Drugs Provides Meaningful Protection for Emerging Companies.

Per statute, the full exclusion of small biotech drugs from negotiation eligibility ended after IPAY 2028.[10] In its place, the Proposed Rule would implement the statute's Temporary Floor for Small Biotech Drugs for IPAYs 2029 and 2030, establishing a floor on the maximum fair price for eligible small biotech drugs rather than excluding them from selection altogether.[11] Given Massachusetts' outsized concentration of small and emerging biotech companies, this transition is a matter of direct and significant interest to MassBio's membership.

MassBio urges CMS to ensure that the Temporary Floor is implemented in a manner that provides meaningful, predictable protection for small biotech companies during this transition period, including by providing clear, workable criteria and processes for a manufacturer to seek and obtain a determination of eligibility, and by publishing sufficient detail regarding how the floor will be calculated so that companies and their investors can reliably factor it into long-term R&D planning. To these ends, MassBio expresses deep concern regarding CMS's proposal to calculate an alternative floor in circumstances in which the Temporary Floor is above the statutory ceiling. This proposal has no clear basis in statute and directly contravenes the longstanding canon of statutory construction that "the specific governs the general."[12] CMS's proposal would also arbitrarily undermine Congress' clear intent to protect small biotech companies—the engine of biotechnology innovation—through the creation of a Temporary Floor for these products. We therefore urge CMS to instead clarify that, where the Temporary Floor is above the ceiling, the floor controls.

MassBio further urges CMS to begin, now, to evaluate whether a floor limited to IPAYs 2029 and 2030 is sufficient to protect the incentives Congress intended to preserve for small biotech innovators and to identify, through the data-tracking recommendations discussed in Section VIII below, whether an extension or enhancement of the Temporary Floor is warranted in future legislation.

IV. CMS Should Provide Greater Transparency and Predictability in the Negotiation Factors and Therapeutic Alternative Determination Process.

MassBio has consistently urged CMS to adopt a predictable, transparent methodology for applying the statutory negotiation factors.[13] That need remains as CMS moves from guidance to

---

[10] See SSA § 1192(d)(2); 91 Fed. Reg. at 36,238 (noting that "the exclusion for small biotech drugs from what is otherwise a negotiation-eligible drug under section 1192(d)(2) of the Act ended in initial price applicability year 2028").

[11] Proposed 42 C.F.R. § 429.440; 91 Fed. Reg. at 36,238 (describing the Temporary Floor for Small Biotech Drugs applicable for IPAYs 2029 and 2030).

[12] *See RadLAX Gateway Hotel, LLC v. Amalgamated Bank*, 566 U.S. 639, 645 (2012); *Morales v. TWA*, 504 U.S. 374, 384 (1992).

[13] Proposed 42 C.F.R. § 429.510.

binding regulation. Because CMS's identification of therapeutic alternatives plays an outsized role in determining the initial offer, it is critical that the process for selecting therapeutic alternatives be both predictable and consistent with the statutory directive to compare a selected drug to true therapeutic alternatives. MassBio urges CMS to limit its selection of therapeutic alternatives to products in the same category and class that share a common clinical use, and to clarify how CMS will weigh net prices across multiple indications and therapeutic alternatives, where applicable, in developing the starting point for the initial offer.

MassBio also continues to urge CMS to provide greater detail regarding how the extensive data manufacturers submit during negotiation is actually applied to adjust the starting point and preliminary price. Manufacturers of selected drugs invest substantial resources in these submissions; codifying the negotiation process without corresponding transparency into how submitted information is weighed will leave manufacturers unable to meaningfully anticipate outcomes, undermining the predictability that this rulemaking is intended to provide.

V. CMS Should Preserve Distinct Treatment for Separately Approved Fixed-Dose Combination Products.

The Proposed Rule would modify CMS's existing policy for identifying qualifying single-source drugs ("QSSDs") by treating certain fixed-dose combination products as the same QSSD as a previously approved product where an additional active ingredient or moiety primarily facilitates a different route of administration. Under this proposal, for example, an intravenous ("IV") biologic and a separately approved subcutaneous ("SC") product containing an additional ingredient that enables SC administration could be treated as the same QSSD and subject to the same MFP. MassBio is concerned that this change departs from CMS's prior approach and could have unintended consequences for patient access and continued post-approval innovation. MassBio urges CMS not to finalize this proposed modification. The statutory framework for identifying negotiation-eligible drugs is closely tied to FDA approval and licensure. Where FDA has separately reviewed and approved a product pursuant to its own NDA or BLA, following a distinct clinical and regulatory development program, CMS should give substantial weight to that determination rather than treating the products as indistinguishable based on CMS's assessment of the pharmacological role served by an additional active ingredient or moiety. Maintaining an approach anchored in FDA approval decisions would also provide manufacturers with greater predictability regarding how subsequent product development will be treated under the Negotiation Program.

CMS should also consider the meaningful clinical and patient-centered benefits that can result from a new route of administration. SC therapies can reduce infusion time, decrease or eliminate the need for venous access and surgically implanted ports, and reduce the time and burden associated with receiving treatment in an infusion setting. These improvements may materially affect treatment choice, patient and caregiver burden, and the setting in which care can be

delivered. A policy that automatically subjects a separately approved SC product to the same MFP as an earlier IV product risks failing to account for the value of these differences. The proposed policy could also weaken incentives for post-approval research and development. Developing a new formulation or route of administration can require substantial additional scientific, clinical, manufacturing, and regulatory investment. These investments are an important part of the innovation lifecycle and can result in products that are easier to administer, less burdensome for patients, or more efficient for the healthcare system. MassBio is concerned that treating separately developed and approved products as economically indistinguishable from an earlier formulation could discourage investment in these types of patient-centered improvements.

Before finalizing any change, CMS should also evaluate the proposal's potential effects on healthcare utilization and Medicare spending. In appropriate circumstances, SC administration may reduce preparation and administration time, provider resource use, and reliance on more resource-intensive infusion settings. Conversely, a policy that discourages development or adoption of SC products could create incentives to continue treatment in higher-cost settings. CMS should therefore conduct a thorough economic analysis that considers not only negotiated drug spending, but also site-of-care effects, provider costs and capacity, future competition, and the longer-term consequences for investment in improved formulations and delivery technologies.

For these reasons, MassBio urges CMS to retain its existing approach to separately approved fixed-dose combination products while the agency further evaluates the legal, clinical, and economic implications of the proposed modification. CMS should also engage FDA, patients, clinicians, manufacturers, and healthcare providers before reshaping this policy. If CMS nevertheless elects to finalize a modified approach, MassBio urges the agency to establish clear criteria under which separately approved products will continue to be treated as distinct QSSDs where there are meaningful differences in formulation, route of administration, clinical development, treatment burden, setting of care, or other patient-centered characteristics.

VI. CMS Should Develop Part B MFP Effectuation and 340B Nonduplication Policies Thoughtfully Before They Are Codified.

MassBio appreciates that the Proposed Rule does not attempt to fully codify MFP effectuation policy for IPAY 2029 and subsequent years, and that CMS instead intends to issue further program guidance on effectuation, including for drugs payable under Part B, before addressing effectuation through future rulemaking.[14] Given the substantial operational differences between Part B and Part D, including differences in dispensing entities, buy-and-bill acquisition, and

[14] 91 Fed. Reg. at 36,238 (noting CMS's intent to issue guidance on manufacturer effectuation of the MFP for 2028, including for drugs payable under Part B, and to codify effectuation requirements for 2029 and subsequent years in future rulemaking).

claims and reimbursement systems, MassBio agrees that these issues warrant continued guidance development and stakeholder engagement rather than premature codification and looks forward to submitting comments as that process unfolds.

MassBio also reiterates its longstanding concern that manufacturers cannot, on their own, reliably prevent duplicate discounts between the Negotiation Program and the 340B drug discount program, notwithstanding the statutory requirement that the MFP be provided to 340B covered entities only in a "nonduplicated amount."[15] MassBio continues to urge CMS to take an active role in preventing duplicate discounts when it addresses effectuation policy in future guidance and rulemaking, rather than leaving manufacturers to resolve deduplication bilaterally with covered entities, and looks forward to continued engagement with both CMS and the Health Resources and Services Administration (HRSA) on this issue.

VII. CMS Should Continue to Evaluate and Publicly Report on the Negotiation Program's Impact on the Innovation Ecosystem, Particularly in Massachusetts.

MassBio continues to urge CMS to carefully examine the Negotiation Program's impact, including in Massachusetts. Given Massachusetts' unique concentration of companies engaged in the research, development, and manufacturing of innovative therapies, Massachusetts will be a leading indicator of how implementation of the Negotiation Program, including the policies addressed in this rulemaking, affects the broader biotech industry.

MassBio urges CMS to build the infrastructure necessary to track IRA's impact on the innovation ecosystem over time, using CMS's own data together with data available from the FDA, including metrics such as:

- Number of new technology add-on payment applications for drugs and biologicals;
- Requests for pass-through status under the Hospital Outpatient Prospective Payment System;
- Number of new NDCs in average sales price (ASP) reporting data;
- Number of NDA/BLA submissions, tracking the proportion of small-molecule versus large-molecule products over time;
- Number of supplemental NDA/BLA submissions;
- Number of applications for, and approval rates of, orphan drug designation;
- Number of applications for breakthrough therapy, fast-track, and regenerative medicine advanced therapy designations; and
- Utilization of the Temporary Floor for Small Biotech Drugs, including the number of manufacturers seeking and obtaining eligibility determinations.

[15] SSA § 1193(d)(1)-(2).

MassBio urges CMS to publicly report these metrics to inform both the public and policymakers in Congress and to establish a framework under which significant adverse trends in these metrics trigger reconsideration of the policies implemented through this rulemaking.

VIII. Conclusion

MassBio appreciates CMS's continued efforts to implement the Negotiation Program and the opportunity to comment on this Proposed Rule. Please don't hesitate to contact me if you have any questions or would like any additional information to consider our comments.

Best regards,

Kendalle Burlin O'Connell
CEO & President
Massachusetts Biotechnology Council (MassBio)