Terns Pharmaceuticals, Inc.
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Via E-mail

Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
U.S. Department of Health & Human Services
7500 Security Boulevard
Baltimore, MD 21244

Re: Medicare Drug Price Negotiation Program Guidance

Dear Deputy Administrator Seshamani:

Terns Pharmaceuticals, Inc. (Terns) is a clinical-stage biopharmaceutical company with a mission of advancing transformative small molecule medicines that address serious diseases. Our pipeline portfolio includes four clinical stage development programs that will address the unmet needs of patients suffering from chronic myelogenous leukemia (CML), obesity, and non-alcoholic steatohepatitis (NASH). For example, one pipeline product is an allosteric BCR-ABL inhibitor for the treatment of CML, an orphan disease indication that affects 110,000 people in the U.S. today.

Terns appreciates the opportunity to submit comments to the Centers for Medicare & Medicaid Services (CMS or the Agency) in regards to its Initial Memorandum on the Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026 (hereinafter, Guidance).[1] As a patient with a rare form of peritoneal cancer, I, Senthil Sundaram, have benefitted from treatment with older cancer drugs being studied for new purposes. As such, it pains me to have to forsake my fellow cancer fighters in the United States because of economic policies that stifle medical innovation. I worry that many treatments, such as those that have temporarily extended my own life, could also be abandoned in the United States and may only wind up being approved in other countries. In the fight against rare cancers and other rare diseases, every day matters. Policies should be developed in a manner that does not hinder the development of new therapies.

As a threshold matter, Terns respectfully disagrees with CMS's position that Congress exempted CMS from the Administrative Procedure Act (APA) and notice-and-comment rulemaking

[1] *See* Medicare Drug Price Negotiation Program Guidance, available at https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf.

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obligations because Congress authorized implementation "by program instruction or other forms of program guidance."[2] CMS presumably is referencing that language in an effort to qualify under an exception to notice and comment rulemaking for "interpretive rules, general statements of policy, or rules of agency organization, procedure or practice."[3] However, interpretive rules and general statements of policy generally are exempt from notice and comment requirements only so long as they do not alter substantive rights. Here, the Guidance adopts substantive legal standards set forth in the IRA and, therefore, plainly qualifies as a substantive rule under the APA that is presumptively subject to notice and comment rulemaking. As discussed below, the Guidance includes provisions that would change the rights and obligations of manufacturers. Accordingly, notice and comment is required.

CMS further asserts that if "this guidance establishes or changes any substantive legal standard, CMS finds that notice and public procedure on this guidance would be impracticable, unnecessary, and contrary to the public interest, in light of . . . the complexity of the preparation that must be undertaken in advance of the publication of the selected drug list by September 1, 2023."[4] Thus, CMS is also seeking to invoke the APA's "good cause" exemption to notice and comment rulemaking for substantive rules.[5] However, the good cause exception is narrow. "The [good cause] exception excuses notice and comment in emergency situations, where delay could result in serious harm, or when the very announcement of a proposed rule itself could be expected to precipitate activity by affected parties that would harm the public welfare."[6] Accordingly, the mere fact that Congress set a deadline for implementation of certain provisions does not constitute good cause to exempt the agency from notice and comment rulemaking.[7]

The substantive complexity of the IRA's Medicare Drug Price Negotiation Program—rather than being an excuse or basis for skipping the notice and comment process—is, in fact, a strong reason why notice and comment requirements exist, and why stakeholder input should be sought and considered here. Accordingly, rather than finalizing the Guidance without the notice and comment process – an approach that will invite stakeholder litigation and further delay IRA implementation – CMS should permit notice and comment as required under the APA before finalizing the Guidance.

Notwithstanding the foregoing concerns, we submit the following comments:

Sec. 30.1.1 - Exclusion of Orphan Drugs

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[2] *Id*. at 1.
[3] 5 U.S.C. § 553(b)(A).
[4] Guidance at 2.
[5] *See* 5 U.S.C. § 553(b)(B).
[6] *Chamber of Commerce v. SEC*, 443 F.3d 890, 908 (D.C. Cir. 2006) (citations omitted).
[7] *Am. Fed'n of Gov't Emp., AFL-CIO v. Block*, 655 F.2d 1153, 1158 (D.C. Cir. 1981); *United States Steel Corp. v. EPA*, 595 F.2d 207, 213 (5th Cir. 1979).

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Our mission to address serious diseases includes orphan diseases, such as CML. Terns is the only U.S. company currently developing n investigational novel type of tyrosine kinase inhibitor (TKI) for chronic myeloid leukemia (TERN-701), called a STAMP inhibitor, which is an oral drug that has the potential to help people with CML, which affects about 150,000 individuals in the U.S.,[8] and Ph+ acute lymphocytic leukemia (ALL), which is a genetic subtype affecting approximately 25,000 people in the U.S.[9]

Clinical studies showed that STAMP inhibitors are about twice as effective as the older generation of drugs used to treat CML, with less than half the side effects[10]. There is currently one STAMP inhibitor on the market for CML and Tern's goal with TERN-701 is to match or beat the efficacy and tolerability profile of the currently marketed product. STAMP inhibitors have also been studied in PH+ ALL [11] and we believe they have the potential to be effective for that population.

However, due to the innovation-limiting price controls for orphan drugs approved for more than one indication, Terns does not plan to pursue regulatory approval of TERN-701 for Ph+ ALL in the United States, but may pursue approval in countries outside of the United States.[12] We understand that other companies may be taking similar positions.

As such, Terns strongly supports the exclusion of orphan drugs from the IRA's Medicare Drug Price Negotiation Program and thanks CMS for its consideration of how to "best support orphan drug development," which appears to acknowledge the critically important goals of orphan disease development programs.[13] Currently, however, only orphan drugs that are "designated for only one rare disease or condition under section 526 of the Federal Food, Drug, and Cosmetic Act and for which the only approved indication (or indications) is for such disease or condition" are excluded.[14] This restriction is incredibly harmful to innovation and will result in fewer orphan therapies on the market.

In order to encourage the development of orphan drugs, we encourage CMS to do all it can to exclude orphan drugs from the negotiation and minimize the impact of the law on these drugs,

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[8] Elias Jabbour & Hagop Kantarjian, *Chronic myeloid leukemia: 2020 update on diagnosis, therapy and monitoring*, 95 AM. J. HEMATOLOGY 691, 692 (Apr. 2, 2020).
[9] *PH-Positive All Therapy*, Leukemia & Lymphoma Society, https://www.lls.org/leukemia/acute-lymphoblastic-leukemia/treatment/ph-positive-all-therapy.
[10] Delphine Réa et al., *A phase 3, open-label, randomized study of asciminib, a STAMP inhibitor, vs bosutinib in CML after 2 or more prior TKIs*, 138 BLOOD 2031-2041 (Aug. 20, 2021), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9728405/.
[11] Jérémie Zerbit, *Asciminib and ponatinib combination in Philadelphia chromosome-positive acute lymphoblastic leukemia*, 62 Leukemia & Lymphoma 3558, 33560 (July 8, 2021).
[12] *See* Press Release, Terns Pharmaceuticals, Terns Pharmaceuticals to Highlight 2023 Priorities and Clinical Milestones at the 41st Annual J.P. Morgan Healthcare Conference (Jan. 5, 2023), https://ir.ternspharma.com/news-releases/news-release-details/terns-pharmaceuticals-highlight-2023-priorities-and-clinical.
[13] Guidance at 11.
[14] *Id*. at 10.

including going to Congress to explain the feedback it will undoubtedly receive across the healthcare industry and from patient groups about the chilling effect of this unduly narrow exclusion. Indeed, Tern urges CMS to consider working with lawmakers to expand the definition of orphan drugs to include drugs designated for *multiple* rare diseases or conditions.

Sec. 30.1 – Disparity Between Small and Large Molecule Drugs

We are very concerned by the disparity in treatment between small and large molecule drugs under the IRA. Developers of small molecules, such as Terns, are subject to potential price negotiation after only 9 years, instead of the 13 years afforded to large molecule drugs. This distinction is arbitrary and we urge CMS to work with Congress to provide parity of 13 years between small and large molecule drugs.

We note that this change would also help limit the harms from IRA's treatment of orphan drugs that treat multiple orphan diseases. This would encourage cancer companies to develop its novel small molecule cancer drugs to benefit as many people in the U.S. as possible.

Sec. 30.1 – New Formulations & Fixed Combination Drugs

CMS must revise the Guidance to adopt the IRA's plain language definition of "qualifying single source drugs." Under the Guidance, CMS states that it will "use data aggregated across dosage forms and strengths of the drug, including new formulations of the drug, such as an extended release formulation, and not based on the specific formulation, package size, or package type" to identify "qualifying single source drugs."[15] This means that drugs approved under different NDAs or BLAs could be considered new formulations, rather than distinct, qualifying single source drugs. This is contrary to the IRA's definition of "qualifying single source drugs", which the IRA defines as drugs approved under a new NDA or BLA.[16] It would be arbitrary and capricious and inconsistent with the statute to expand the definition of new formulation to include multiple, distinct qualifying single source drugs.

In addition, we support CMS treating fixed combination drugs with two or more active moieties/ingredients as distinct from a drug containing only one of the active moieties/ingredients that is offered by the same NDA or BLA holder for the purpose of identifying qualifying single source drugs. We further agree with CMS utilizing FDA's definition of a fixed combination drug and encourages CMS to leverage FDA's determination of active ingredients or moieties in order to identify fixed combination drugs.[17]

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[15] *Id*. at 7-8.
[16] Inflation Reduction Act of 2022, Pub. L. No. 117-169, SSA § 1192(e)(1)(A)-(B) (defined as "A drug—(i) that is approved under section 505(c) of the Federal Food, Drug, and Cosmetic Act and is marketed pursuant to such approval" or "[a] biological product—''(i) that is licensed under section 351(a) of the Public Health Service Act and is marketed under section 351 of such Act").
[17] Guidance at 9.

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Sec. 40.2.1 – Data Use and Confidentiality

In the Guidance, the Agency proposes to implement a confidentiality policy within the negotiation process and to treat information provided by manufacturers as proprietary if it constitutes commercial or financial information that is publicly unavailable.[18] Terns supports the implementation of a confidentiality policy as it aligns with the industry's treatment of any commercial or financial information that is not publicly available. We believe it is critical that CMS swiftly implement a proposed confidentiality policy and permit stakeholders to provide comment before finalizing.

Sec. 40.4 – Access to the Maximum Fair Price

We support and appreciate the flexibility given to manufacturers of selected drugs in the Guidance to determine the method in which to provide access to the maximum fair price.[19] The Guidance provides that manufacturers can provide access to the maximum fair price by either ensuring that the price paid by the dispensing entity when acquiring the drug is no greater than the maximum fair price, or providing retrospective reimbursement for the difference between the dispensing entity's acquisition cost and the maximum fair price.[20] We appreciate the flexibility to allow manufacturers to ensure they comply with their obligations under the IRA and permit them the tools needed to prevent duplicate discounts.

Sec. 60.5 - Scaling WAC in Pricing Methodology

CMS has solicited comments for its proposed approach under the Guidance to scale the use the wholesale acquisition cost (WAC) of a selected drug to calculate the maximum fair price per unit for each dosage form and strength to identify a single price for the selected drug.[21] We disagree with the proposed approach. Pricing for different dosage forms and strengths of a drug is intentional and such decisions take into account factors such as costs of research and development, setting of care, patient access, and dosing variations. The proposed approach will cause a severe discrepancy in charges for formulations that are intentionally priced to accurately encompass their costs, and thus is inherently arbitrary and capricious. Therefore, we urge CMS to identify individual maximum fair prices for each dosage form and strength with different prices per unit.

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[18] *Id*. 29-30.
[19] *Id*. at 31.
[20] *Id*.
[21] *Id*. at 58.

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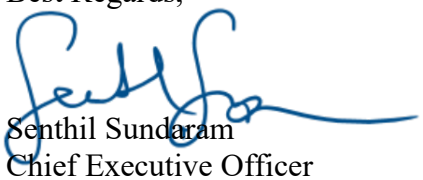
We appreciate your consideration of our comments as you develop the Medicare Drug Price Negotiation Program policy. Please let us know if you have any questions.

Best Regards,



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