April 1, 2014

The Honorable Kathleen Sebelius
Secretary
U.S. Department of Health & Human Services
200 Independence Avenue S.W.
Washington, DC 20201

Re: CMS-2345-P; Line Extension Drug (New Formulation)

Dear Secretary Sebelius,

We are deeply concerned that efforts by the Centers for Medicare & Medicaid Services ("CMS") to implement a new policy within the Medicaid Drug Rebate Program will significantly harm drug discovery and development in the United States. The CMS policy on line extension rebates[1] not only conflicts with initiatives being led by other operating divisions within the Department of Health and Human Services ("HHS"), but also creates an economic barrier to rare disease therapeutic innovation in conflict with the Orphan Drug Act.

Notwithstanding the plain statutory language[2] and legislative history[3] that make the CMS proposed implementation of the line extension rebate policy inherently unreasonable, we are not writing to debate the construction of a statute that we strongly oppose. We are, however, seeking more information on the rationale behind the CMS proposal to apply the line extension rebate policy to:

- drugs with "orphan" exclusive approval from the Food and Drug Administration ("FDA"),[4] and
- drugs that have more than one FDA-approved use .[5]

It is unclear to us how the inclusion of these types of oral solid form drugs fulfills the purported policy objective of preventing a "*slight alteration*" to a drug from insulating the

[1] *See* Medicaid Program; Covered Outpatient Drugs, 77 Fed. Reg. 5318, 5338-5341 (Feb. 2, 2012).
[2] *See* 42 U.S.C.S. § 1396r-8(c)(2)(C) (LexisNexis 2013).
[3] Congress demonstrated its clear intention to protect rare disease therapies when it excluded "orphan" designated drugs in its initial enactment of the line extension rebate policy. *See* the Patient Protection and Affordable Care Act § 2501(d), Pub. L. No. 111-148, 124 Stat. 119, 309.
[4] *See* 77 Fed. Reg. at 5340 (stating explicitly that "[it does] not plan to exclude drugs that have [received seven-year orphan exclusive approval from FDA] from the definition of line extension drugs.").
[5] *Id*. at 5360 (including such drugs in the definition of "line extension" in Proposed 42 C.F.R. § 447.502).

manufacturer from the inflationary rebate under section 1927 of the Social Security Act.[6] What is even more confounding are CMS efforts to apply this rebate policy in cases where the manufacturer of the "line extension" differs from the manufacturer of the initial brand.

For rare diseases, FDA views the Orphan Drug Act as providing a means to not only satisfy unmet medical need, but also encourage innovation necessary to make existing treatments safer and more effective, stating that "[t]he main purpose of the Orphan Drug Act is to stimulate innovation in developing treatments for patients with rare diseases and conditions *and to foster the prompt availability of therapeutically superior drugs*."[7] A "line extension" drug that has received "orphan" exclusive approval would have had to demonstrate it is "*clinically superior*" to the previously approved version of the drug,[8] which means FDA has determined it "provide[s] a significant therapeutic advantage over and above that provided by [the initial brand]" in terms of safety, efficacy, or by making a major contribution to patient care.[9] In terms of innovation, "clinically superior" certainly exceeds "slight alternation." Thus, the decision by CMS for the line extension rebate policy to include drugs with orphan exclusive approval demonstrates a fundamental lack of understanding of the current FDA regulations governing the Orphan Drug Act.

Additionally, with millions of Americans suffering from one of the nearly 7,000 rare diseases without an FDA-approved treatment, it is incomprehensible that CMS would attempt to penalize a manufacturer for developing a new use for a drug that has already received FDA approval. If CMS had engaged its colleagues at the National Institutes of Health ("NIH") and the FDA, the only reasonable conclusion would have been that applying the line extension rebate policy to a newly approved use for an already marketed drug will completely undercut valued drug repurposing programs – an initiative that you have helped spearhead, Madame Secretary.[10] Because of the unmet medical need, rare diseases are a major focus of drug repurposing. For example, the Office of Orphan Product Development within FDA has developed the Rare Disease Repurposing Database, while repurposing plays an important role in the Therapeutics for Rare and Neglected Disease program at NIH. Unless CMS revisits the line extension rebate policy, the resources dedicated to these programs will be wasted because the economic barrier for manufacturers will be too great.

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[6] *See* CONGRESSIONAL BUDGET OFFICE, BUDGET OPTIONS VOLUME 1: HEALTH CARE 143 (2008) (emphasis added) (demonstrating that orphan designated drugs, which provide incredible value to the rare disease patient community, do not fit within this narrow policy objective).

[7] Orphan Drug Regulations, 56 Fed. Reg. 3338 (Jan. 29, 1991) (emphasis added).

[8] *See* 21 C.F.R. § 316.20(a) (LexisNexis 2013) (emphasis added). Such a condition is required because FDA would view the reformulated drug as the "same" drug as the previously approved drug because both drugs consist of the same molecule and are intended for the same use. *Id*. at § 316.3(b)(14) (LexisNexis 2013).

[9] *Id*. at § 316.3(b)(3) (LexisNexis 2013).

[10] *See, e.g.*, *The National Institutes of Health – A Review of its Reforms, Priorities, and Progress: Hearing Before the Subcomm. On Health of the H. Comm. On Energy & Commerce*, 112th Cong (2012) (statement of Francis S. Collins, Dir., NIH) (describing the launch of the Discovering New Therapeutic Uses for Existing Molecules pilot program at the National Center for Advancing Translational Sciences).

The overreach by CMS is making a flawed statutory provision considerably worse through an arbitrary interpretation that demonstrates an unwillingness to work across HHS. We would like to know how HHS plans to (1) reconcile this inconsistent approach to innovation across its operating divisions and (2) ensure all of its operating divisions have procedures in place that will prevent the implementation of policies that have the unintended consequence of discouraging and undermining the development of therapies for rare diseases.

Sincerely,

CC: Margaret A. Hamburg, M.D., Commissioner of Food and Drugs
Francis S. Collins, M.D., PH.D., Director, NIH
Gaytari R. Rao, M.D., J.D., Director, Office of Orphan Product Development, FDA
Pamela McInnes, D.D.S., M.Sc., Acting Director, Office of Rare Diseases Research, NIH