February 10, 2022

The Honorable Xavier Becerra
Secretary, Department of Health and Human Services
200 Independence Ave, SW
Washington, DC 20201

Dear Secretary Becerra:

We, the undersigned, write out of great concern that a recent Centers for Medicare & Medicaid Services (CMS) proposed decision memo targeting certain products approved to treat Alzheimer's Disease (AD) will not only severely limit patient access to these novel therapeutics, but, if finalized as proposed, will also establish a dangerous precedent for coverage of future innovative therapeutics treating an array of unmet medical needs. We fear the consequences of this unprecedented overreach could delay patient access to novel therapeutics for years and create real disincentives to continue investments in certain therapeutic areas. We ask that you work with CMS to implement less destructive policies that allow continued collection of real-world evidence while simultaneously permitting patients to access novel therapeutics as deemed necessary by their physicians.

On January 11, 2022, CMS issued a proposed decision memo in its National Coverage Analysis (NCA) for Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease (Proposed National Coverage Determination (NCD)). Among other things, CMS's proposal would drastically restrict coverage of anti-amyloids for AD to trials supported by the National Institute of Health (NIH) and a small subset of randomized controlled trials (RCTs) that must be pre-approved by CMS. Even after such clinical trials are established and approved (which could take a year or more), this would effectively restrict Medicare coverage to a tiny fraction of beneficiaries with AD who are able to enroll in a CMS-approved clinical trial. What is more, is that CMS is harshly limiting patient access to a nascent class of drugs for a serious and life-threatening disease that lacks alternative treatments. Perhaps most concerning, in the long term to be sure, is that CMS is sending a strong signal to the biotech investment and innovation market that FDA scientific determinations are now subject to CMS second-guessing.

This proposal, from an investor and innovator standpoint, is profoundly anti-innovation and anti-patient. If finalized, the NCD would set a dangerous precedent that would restrict access to this promising class of new therapies, both current and future, and signals the same possibility for any cutting-edge therapeutic category yet to be advanced. In the near-term, this proposal will have life-altering implications for the over five million Americans struggling with AD. Longer-term, this decision would have far-reaching implications for other difficult to treat diseases, especially those approved by the Food and Drug Administration (FDA) under Accelerated Approval pathways. CMS's proposal to limit coverage only to patients enrolled in government-approved RCTs is even more troubling. It means that the vast majority of individuals suffering from AD will have no meaningful access to an approved medicine simply because of where they live and where they go for care. Such a decision also has implications beyond Medicare: Commercial insurers will follow what the agency does, so the decision will adversely impact patients with mild cognitive impairment and mild Alzheimer's who have private insurance.

Biotechnology innovation is fraught with uncertainty, but it is filled with promise. Producing a novel therapeutic is perhaps one of the riskiest business ventures an entrepreneur might face. More than 90% of clinical programs fail in our industry. For small start-ups that begin in the preclinical stages, the failure rate for programs can exceed 99%. The biotech sector alone represents over $188 billion in research and development annually.[1] Much of this research is undertaken by small and mid-sized biotech companies, often with backing from venture investors. In fact, in 2020 venture capital funding in emerging biotechnology companies totaled $17.9 billion, and small biotech companies are responsible for 80% of scientific research and development.[2]

These significant investments are predicated, in large part, on a heretofore stable and straightforward path to regulatory approval and to patient access. FDA evaluates the scientific evidence and balances the risks versus the benefits of a studied molecule. FDA maintains the ability, also, to require additional and ongoing reviews of products once they are approved to ensure study endpoints are consistent in broader application and larger populations. CMS, on the other hand, serves as the conduit to ensuring access to patients once FDA has made the scientific determinations. In order to promote research in difficult to treat conditions, like Alzheimer's, manufacturers and investors need the certainty that CMS will cover drugs for on-label indications after they have been determined by FDA to be safe and effective. CMS's Proposed NCD threatens to chill research and investment in new drugs targeting challenging disease states and to reduce reliance on a key mechanism that patients rely on to get faster access to desperately needed new therapies. Effectively, CMS is stating that past scientific determinations may no longer be definitive in its coverage decisions. Further, CMS is making such assertion at the class level, without any regulatory pronouncement and without any guidance or regulations in its own right as to how the Agency's own scientific determinations will supplant or overrule FDA's. This is untenable from an investment standpoint.

Moreover, CMS's proposal here threatens to negate the purpose of FDA's Accelerated Approval pathway more generally. CMS, in fact, criticizes FDA approvals based on studies of intermediate outcomes and surrogate endpoints. Going so far as to dispute the provenance of a specific endpoint in the particular drug at issue in the proposed coverage decision. FDA has used accelerated pathways for years to approve treatments for many severe diseases, such as a variety of cancers, HIV, Multiple Sclerosis, Sickle Cell Disease and others. The approval of the first HIV/AIDS drug, which was based on the use of surrogate endpoints, prolonged and saved the lives of millions of patients that did not have any other therapeutic options. Unfortunately, this current proposed policy is untenable, and portends a significant shift in the way investment dollars will be allocated towards new and novel disease areas. Patients, ultimately, will suffer the most drastic consequences, both in lack of access to certain products that do get approved but also in the inability to ever access products that never get developed.

CMS has myriad other avenues to ensure appropriate coverage and access short of a *de facto* disapproval of a particular drug and a denial of access to any future drug in that same class. There are registries, access restrictions based on clinical criteria, and multiple other avenues that would otherwise actually ensure physicians have the discretion to provide a therapeutic to their patients. This proposal,

[1] https://www.evaluate.com/thought-leadership/pharma/evaluatepharma-world-preview-2020-outlook-2026
[2] https://www.iqvia.com/insights/the-iqvia-institute/reports/emerging-biopharmas-contribution-to-innovation

however, sends a chilling signal to the entire biotech community. It indicates that accelerated approvals, novel science, and general innovation are all subject to disapproval based not on just scientific determinations by FDA, but also by CMS. We, as CEOs and investors of small and emerging biotechnology companies, urge CMS to take a more reasonable approach to this proposed NCD. Our future investments and research projects are all at risk in the currently proposed situation, and, again, patients will ultimately lose. Instead, we urge CMS to ensure access while also enabling long-term data collection to help the Alzheimer's community evaluate the practical advantages and disadvantages of any therapy that meets FDA's high bar for approval. This will ensure continued incentives to innovate both within this class and beyond.

Sincerely,

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