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BY ELECTRONIC SUBMISSION

Re: Drug Repurposing: Considerations for Selection Criteria and Prioritization

Hyman, Phelps & McNamara, P.C. submits these comments based on our experience counseling industry sponsors who are developing repurposed therapies for serious and, often, rare diseases. We commend the U.S. Food and Drug Administration ("FDA" or "the Agency") and the Reagan-Udall Foundation for convening the August 5, 2026 public meeting on drug repurposing and for the Agency's broader initiative to expand treatment options by identifying new uses for approved drugs. These comments respectfully urge FDA to ensure that, as it develops its candidate selection and prioritization framework, the framework's emphasis on drugs with "no commercial interest" does not inadvertently create misaligned incentives that discourage rather than encourage commercially-sponsored repurposing. Industry-sponsored drug development is often the most reliable route to a consistently manufactured and systematically evaluated product. Sponsors are prepared to undertake this work to meet the applicable evidentiary standards for approval. FDA can facilitate industry participation by better defining an appropriately streamlined regulatory pathway for repurposing development.

FDA's proposed repurposing framework is expressly scoped to "FDA approved drugs for which there currently appears to be no commercial interest in adding a new use through a supplemental application." Bringing attention to genuinely orphaned generics is laudable. However, we believe that through clearer articulation, and more consistent application, of streamlined development approaches deemed capable of meeting Agency expectations for safety and effectiveness, there will be greater commercial interest in repurposing.

We respectfully urge FDA to keep non-commercial and commercial tracks in balance. Much of the public discussion on August 5th centered on the former, but the corollary should not be that industry-sponsored programs face a higher regulatory bar. As public commenters observed, a commercial sponsor's development is frequently what converts fragmented off-label or compounded use into a consistently manufactured, FDA-approved therapy supported by product-specific labeling, pharmacovigilance, and reliable patient access.

While FDA participants in the meeting were clear that the standard for safety and effectiveness is not different for repurposed drugs, the Agency has an opportunity to put forward guidance on repurposed drug development that articulates opportunities to streamline development taking into account that these drugs often already have significant clinical trial and real world safety characterization, as well as extensive off-label and compounded experience for the new use, oftentimes as standard of care. For example, much of the meeting explored opportunities to leverage non-traditional evidence for orphaned generics, including published literature, real-world evidence ("RWE"), natural

history, and mechanistic and pharmacologic data. FDA confirmed streamlined approaches have been used in practice, even if not widely. For example, in approving leucovorin for cerebral folate deficiency, the Agency determined there was substantial evidence of effectiveness based on a systematic review of the published literature with patient-level data, treated as an adequate and well-controlled investigation, with confirmatory support from the drug's mechanism. FDA shared how it leveraged RWE in substantial evidence of effectiveness determinations for new indications, including as an external control arm and as confirmatory evidence for label expansions. If the defining advantage of repurposing is that much of the foundational work has already been done, more than sparce examples are needed to give industry confidence.

The MODERN Labeling Act authorizes label updates only where the new use is "supported by data that meets FDA's approval standards". MODERN thus incorporates, rather than lowers, the substantial evidence standard. This places a burden on FDA to provide a repurposing framework for how this class of drugs can meet its standards. FDA should be careful not to inadvertently create a framework that applies only in the absence of commercial interest and, instead, use this framework as an opportunity to address industry stakeholders to incentivize their participation in repurposing.

To facilitate commercially-sponsored repurposing a part of the public-health strategy, we respectfully recommend that FDA:

1. **Publish a clear evidentiary roadmap for relying on existing evidence.** Articulate, in guidance, how the standards for safety and efficacy can be met using evidence that already exists. This includes use of published literature, RWE, natural history, prior FDA findings, and pharmacologic bridging, including when such evidence can support approval without a new efficacy study or how non-traditional study designs and statistical approaches can be leveraged when additional information is needed to fill evidentiary gaps. Predictability about how existing evidence will be weighed is what will allow sponsors to confidently invest in drug repurposing.

2. **Define the submission and review mechanics.** Clarify the vehicle (e.g., 505(b)(2) applications and labeling supplements), opportunities to expedite review, and early-engagement options so sponsors know how and to whom to bring a drug repurposing program.

3. **Explicitly leverage regulatory programs.** Because generic entry and patent expiration erode the incentive to invest in repurposing, FDA should prioritize using regulatory programs as incentives. For example, FDA could establish standards for how existing information on repurposed drugs can meet criteria for Breakthrough Therapy Designation. The Agency could also consider new administrative programs (e.g., similar to the START Pilot) that could ease the administrative burden on, and speed the timing for, sponsors to receive feedback.

The ongoing work towards a drug repurposing framework is an opportunity for FDA to advance both non-commercial and commercial repurposing at once. Solving for repurposing that no company will pursue is a worthy goal, but the Agency should not miss the opportunity to facilitate commercial interest. We appreciate the opportunity to comment and welcome the chance to work with the Agency as this initiative progresses.