# Promising Pathway Act

## S. 1906 & H.R. 4408

## Summary

The Promising Pathway Act (PPA) calls for the U.S. Food and Drug Administration (FDA) to establish a rolling, real-time, priority review pathway to grant or deny provisional approval status for drugs intended to treat, prevent, or diagnose serious or life-threatening diseases or conditions. The granting of provisional approval requires demonstration of substantial evidence of safety (the same level as currently required for standard FDA approval) and relevant early evidence of positive therapeutic outcomes based on adequate and well controlled investigations. The PPA also allows for the use of real world evidence to support an application. The PPA provides for *provisional* approval only, for two year periods up to eight years. Patients must participate in an observational registry. The FDA must review the registry annually and shall withdraw provisional approval if a drug has serious side effects or is ineffective. Drugs must meet existing standards for full approval. In sum, the PPA provides a pragmatic pathway for the FDA to provisionally approve drugs for individuals with rapidly progressive terminal illnesses who will die of their diseases waiting for the usual FDA approval pathways to unfold. Provisional approval would be subject to fulsome FDA guardrails and oversight.

## Rationale

For individuals with rapidly progressive and 100% fatal diseases like ALS, timely access to promising therapies is essential and offers an opportunity for survival. Current FDA approval pathways take far too long to help those currently suffering from such diseases. Even its expedited pathways are insufficient. For example, the FDA's "accelerated approval" pathway allows for drug approval without evidence of direct clinical benefit In certain circumstances if a drug's effect on a biomarker (a biological measurement) is likely to predict clinical benefit. Over 95% of ALS cases do not have an accepted biomarker. Withholding promising and safe therapies until evidence of efficacy under current FDA standards Is met means certain death for those with ALS. The status quo can result in an unwarranted loss of life. The PPA affords patients access to safe therapies that have shown promise while the process of gathering additional evidence of efficacy proceeds. The PPA requires the FDA to withdraw provisional approval if such evidence is not provided. The PPA also preserves efficacy standards for final drug approval. We support efforts to bring safe, promising therapies to more people living with terminal diagnoses pending full FDA approval. The provisions in S. 1906 and H 4408 provide such a pathway.

## Key Contacts

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## Legislative Components

- Drugs qualifying to apply for provisional approval must be intended for the treatment, prevention, or medical diagnosis of serious or life-threatening diseases or conditions in which there is a reasonable likelihood that premature death will occur without early medical intervention. To receive provisional approval status, a drug must demonstrate substantial evidence of safety and relevant early evidence of positive therapeutic outcome(s).
- This pathway requires relevant early evidence of positive therapeutic outcome based on adequate and well-controlled investigations and also allows the use of real-world evidence and scientifically substantiated surrogates to predict the clinical benefits and ultimately support provisional approval.
- PPA requires the FDA to issue guidance that establishes clear protocols for enabling sponsors to submit rolling, real-time, mid-trial provisional approval applications. This provision preserves the integrity of ongoing clinical trial design, development, and enrollment, as well as prohibits sponsors from being penalized for utilizing this pathway mid-trial.
- Drugs and biological products granted provisional approval are limited to a 2-year approval period, renewable every 2 years, for up to 8 years.
- The sponsor of a provisionally approved drug must ensure that all patients who use the drug participate in an observational registry and consent to the collection of, and submission of, data related to the patient's use of the drug until the drug receives full approval. Importantly, the registries must be readily accessible to patients—as well as allow approved researchers and medical professionals to access the aggregated and de-identified data for public health research.
- The registries can be run by third party governmental, for-profit, or nonprofit entities—but must track the effect of provisionally approved drugs on patients, including patient treatments, uses, length of use, side effects, scan results, and adverse drug effects.
- Drug sponsors (often biopharmaceutical companies) may apply for full approval for a drug at any time under the pathway. The FDA shall withdraw provisional approval of a drug if a significant number of patients report serious adverse effects or if the drug is not efficacious compared to other FDA approved therapies.
- PPA prohibits any group health plans, health insurance coverage providers, and federal healthcare programs (e.g., Medicare) from denying coverage of a provisionally approved drug on the basis of it being experimental and mandates that provisionally approved drugs be treated in the same manner as drugs fully approved by the FDA under other review pathways.