SECTION-BY-SECTION FOR S. 1906
THE PROMISING PATHWAY ACT

Section 1. Short Title.
This section provides that the bill may be referred to as the "Promising Pathway Act."

Section 2. Provisional Approval of New Human Drugs.
Section 3 of the bill amends subchapter A of chapter 5 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 351) to add the following at the end:

Section 524C. Provisional Approval of New Human Drugs.

Subsection a—Priority Review and Evaluation of Applications.
This section requires FDA to establish a priority review system to accept provisional approval applications on a rolling basis and evaluate applications within 90 days of receiving a completed application. Drugs submitted for review under this pathway are eligible for FDA special designations and benefits, including any tax credits and fee waivers.

Subsection b—Eligibility.
This section defines the eligibility criteria for a drug to be granted provisional approval status. A drug may be eligible for provisional approval if it is intended for the treatment, prevention, or medical diagnosis of a serious or life-threatening disease or condition in which there is a reasonable likelihood that premature death will occur without early medical intervention.

Subsection c—Standard of Review for Provisional Approval.
This section allows FDA to approve applications for provisional approval that demonstrate substantial evidence of safety for the drug and relevant early evidence establishing that the drug provides positive therapeutic outcome(s) and that the outcome(s) of the drug are consistent with or greater than currently marketed on-label therapies, with equal or fewer side effects, if there are currently marketed on-label therapies. This section also requires FDA to establish protocols to enable sponsors to submit a rolling, real-time, mid-trial application for provisional approval while preserving the integrity of any ongoing trials. Importantly, this section requires FDA to allow for the use of real world evidence and scientifically-substantiated surrogates to support applications for provisional approval.

Subsection d—Transparency and Patient Monitoring Requirements.

1. ***Registries***
   This section requires drug sponsors of provisionally approved drugs to require patients to consent to participating in an observational registry and consent to the sponsor's collection and submission of patient provisional drug use data until the drug receives full approval. The registries can be run by a third-party (such as a government, for profit, or nonprofit) and must track all patients using provisionally approved drugs. The patient data must be transparent, easily accessible by patients, and accessible in an aggregated

and de-identified manner for approved researchers and medical professionals for public health research.

This section also requires drug sponsors and third parties to make reasonable efforts to limit protected health information to the minimum necessary to accomplish the intended purpose. Drug sponsors must safeguard the health information of a deceased individual for 50 years following the death of the individual, and any authority acting on behalf of the deceased individual shall be treated as a personal representative concerning protected health information. This section does not limit patients' access to their personal information collected during the research while receiving the provisionally approved drug.

2. ***Funding***
   The costs involved in running and maintaining the registry may be funded by drug sponsors, a third party, or a government.

3. ***Sponsor Requirements***
   This section requires FDA to conduct an annual review of any applicable registry. Drug sponsors that have fewer than 90 percent of patients participating in the registry and using a provisionally approved drug will receive a $100,000 penalty, if the violation is not corrected within 30 days then the sponsor will be issued a $10,000 penalty every day the violation is not corrected. If patient participation is not at or above 90 percent within six (6) months, provisional approval will be withdrawn.

4. ***Patient Privacy***
   This section requires drug sponsors to receive an explicit and affirmative informed consent form signed by each patient or the patient's representative, prior to the patient's use of a provisionally approved drug, that acknowledges the potential risks of taking a drug that has not yet received full FDA approval.

5. ***Annual Report to Congress***
   The Secretary is required to submit an annual report to Congress on drugs granted provisional approval status that includes a discussion of the minimum required amount of data required in the registry.

Subsection e—Withdrawal of Provisional Approval.
This section requires FDA to withdraw provisional approval of a drug if there are a significant number of patients who experience adverse effects compared to other available currently marketed on-label therapies for the disease or condition. If provisional approval is withdrawn, the drug sponsor may not give the drug to any new patients, but may continue to give the drug to patients, who started taking the drug before it was withdrawn, for a period of time based on patient need, as determined by the Secretary.

Subsection f—Transparency.
This section prohibits publishing research findings in an inaccessible medium for the public if the findings received government funding. Findings may only be published if they are made publicly available on the journal's website without a paywall or charge three months after the date in which it was first provided to subscribers of such journal (or first made available for purchase).

Subsection h—Postmarket Controls and Labeling.
This section requires FDA to annually review the data submitted to any patient registry related to a provisionally approved drug and rescind provisional approval for drugs in which the data shows the side effects do not outweigh the benefits provided by the drug, or that the drug is less beneficial than other drugs with full approval. This section also requires drug sponsors of a provisionally approved drug to ensure that all labeling and promotional materials for the drug include the statement, "provisionally approved by FDA pending a full demonstration of effectiveness under (the application number assigned by the Secretary)." All promotional, educational, and marketing materials for provisionally approved products must be reviewed and approved by the Secretary of HHS.

Subsection i—Duration of Provisional Approval; Requirement to Bring Drug to Market.
This section grants provisional approval for drugs for a two-year period. The sponsor may request renewal for provisional approval up to three subsequent two-year periods. Should a drug that is approved under PPA not be brought to market within 180 days of provisional approval, such provisional approval is rescinded.

Subsection j—Limitation on Liability.
This section prevents claims from being brought against drug sponsors or manufacturers of provisionally approved drugs alleging that a provisionally drug is unsafe or ineffective—unless the conduct constitutes reckless or willful misconduct, gross negligence, or an intentional tort under any state laws.

Subsection k— Right to Petition an Advisory Committee for Approval.
Drug companies that have received approval provisional approval for one of their products may request a meeting with the appropriate advisory committee within FDA for the purposes of receiving a recommendation from said committee pertaining to the full approval of a provisionally approved drug. This meeting must be granted by FDA within 90 days of FDA receiving a request.

This section also provides novel (though not statutorily new) authorities for FDA to waive requirements for "adequate and well controlled" studies for the purposes of approval under PPA.

Subparagraph c – Reimbursement.
Health insurance plans are prohibited from denying coverage for drugs approved under PPA *on the basis that such drugs are experimental*.