	S. 1906	PROMISING PATHWAY ACT 2.0
PROVISIONAL VS. CONDITIONAL	The PPA is characterized as a "provisional" pathway.	The PPA is characterized as a "conditional" pathway – this change is aesthetic.
PRIORITY REVIEW	(a) requires the creation of a new priority review system for PPA-eligible drugs. Applications under this priority review system must be reviewed by FDA within 90 days	(a) routes eligible applications under PPA through FDA's existing priority review system, without a statutory mandate on review time.
ELIGIBILITY	(b) describes PPA-eligible drugs as "intended for the treatment, prevention, or medical diagnosis of a serious or life-threatening disease or condition for which there is a reasonable likelihood that premature death will occur without early medical intervention for an individual contracting or being diagnosed with such disease or condition.	(b) describes PPA-eligibility as either a drug intended to treat a disease that is rapidly progressive, is terminal, and has substantial unmet medical need, or an Orphan Drug Act rare disease (fewer than 200,000 cases in the U.S.) that results in a substantial reduction in quality of life.
STANDARD OF REVIEW	(c) describes the standard of review for PPA-eligible drugs as "[having] substantial evidence of safety for the drug, such that there is evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the safety of the drug involved, on the basis of which it could fairly and responsibly be concluded that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling…" and "relevant early evidence" demonstrating "positive therapeutic outcome"	(c) FDA must determine drugs to be safe and have shown early evidence of effectiveness from phase 2 to qualify for the initial 2 years of conditional approval under PPA 2.0. A sponsor must also submit a non-binding written affirmation of their intent to pursue traditional approval for the drug in question, including a plan for attaining such approval.

	S. 1906	PROMISING PATHWAY ACT 2.0
STANDARD OF REVIEW CONTINUED	(c) requires FDA to create a new process for accepting rolling applications for under PPA (c) allows for real world evidence to be used in support of provisional approval	(c) utilizes existing statutory language to allow FDA to receive a rolling application, as long as the applying drug qualifies for PPA (c) allows for sponsors to submit real world evidence to FDA in support of conditional approval as long as sponsor considers FDA's 2023 nonbinding guidance on RWE
SCIENTIFICALLY SUBSTANTIATED SURROGATES	(c) creates a new form of endpoint called "scientifically substantiated surrogates" that may be used in pursuit of provisional approval.	This provision has been struck in PPA 2.0
WITHDRAWAL AUTHORITIES	(e) permits FDA to withdraw provisionally approved drugs only if a significant number of patients experience serious adverse side effects.	(d) creates authorities for FDA to withdraw conditionally approved drugs for the purposes of safety, untrue statements in the original application that were not caught, or a lapse in eligibility. FDA must notice a withdrawal to sponsor 2 weeks in advance of the withdrawal. FDA must create an appeals process for sponsors to appeal a withdrawal. (d) gives FDA authority to examine sponsors and observational registry data for the purposes of instigating a withdrawal. (d) empowers FDA to require information from sponsors and levy fines should sponsor not comply. (d) mandates that, should a drug be withdrawn, it cannot be made available to new patients, but existing patients may continue taking it. Patients are not compelled to continue taking the drug, and sponsors are not compelled to continue making it. Sponsors will be subject to a CMP should they continue to make the drug available.

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AUTOMATIC WITHDRAWALS	N/A	Additionally, under (d), all drugs that are conditionally approved are subject to automatic withdrawal at the conclusion of the conditional approval period, unless sponsor attains renewal for conditional approval. Automatic withdrawal has the same effects as described above, but it cannot be stopped by FDA and cannot be appealed.
REQUIREMENT TO MARKET	Sponsor must bring conditionally approved drugs to the market within 180 days of receiving conditional approval.	Sponsor must bring conditionally approved drugs to the market within one year of receiving conditional approval.
LABELING	(h) requires all labeling and promotional materials to include a line indicating the provisional approval status of the product.	(e) mandates labeling requirements based heavily on existing LPAD labeling requirements.
REVIEW OF MARKETING MATERIALS	(h) requires that all promotional, educational and marketing materials for provisionally approved products be reviewed and approved by FDA before dissemination.	Sponsors must submit promotional materials to FDA for preliminary review 45 days prior to dissemination
LIST OF PPA DRUGS	N/A	FDA directed to host a public list of conditionally approved drugs on its website
RENEWAL OF CONDITIONAL APPROVAL	S. 1906 does not prescribe a process for renewal of provisional approval every 2 years	(f) creates a process wherein sponsors must present additional evidence of effectiveness to FDA to receive a renewal of conditional approval. Conditional approval may only be renewed by FDA in 2 year increments up to a maximum of 8 years.

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MANDATORY OBSERVATIONAL REGISTRIES	(d) mandates that sponsors establish an observational registry for each conditionally approved drug. Sponsors may use existing registries or create a new one. S. 1906 requires FDA to annually review all observational registries created under PPA and issue strong civil monetary penalties against sponsors that do not have 90% participation in a given registry. (d) allows approved researchers to access registry data- no process provided for FDA to approve researchers.	(g) mandates that sponsors establish an observational registry for each conditionally approved drug. Sponsors may use existing registries or create a new one. FDA may approve or deny an observational registry. Patients whom intend to access conditionally approved drugs must participate in the drug's observational registry. Patients must provide informed consent to participate in the registry. (g) FDA may approve certain researchers to access deidentified and aggregate registry data for the purposes of translational medicine to help advance breakthroughs in rare and progressive disease.
PURSUIT OF A DIFFERENT INDICATION	S. 1906 does not give sponsors the right to pursue a different indication	(h) gives sponsors the right to apply to FDA to pursue a different indication for a conditionally approved drug that has its approval withdrawn.
CLARIFYING ABILITY TO APPLY FOR TRADITIONAL/ ACCELERATED APPROVAL	N/A	(i) clarifies that a conditionally approved drug may apply for accelerated or traditional approval at any time during the conditional approval process. PPA 2.0 does not affect FDA full approval standards in any way.
INFORMED CONSENT	(g) requires a new process for informed consent from patients.	(j) requires patients to provide informed consent according to existing regulations.
LIMITATION ON LIABILITY	(j) limits sponsor liability for providing provisionally approved drugs	(k) limits sponsor and physician liability in providing conditionally approved drugs to patients.
ANNUAL REPORT	S.1906 requires an annual report from FDA on provisionally approved drugs	(l) PPA 2.0 requires a report to congress from FDA on conditionally approved drugs every 2 years.

	S. 1906	PROMISING PATHWAY ACT 2.0
INSURANCE COVERAGE	S. 1906 requires coverage from federal and private payers for provisionally approved drugs	PPA 2.0 requires coverage from federal and private payers without cost sharing of conditionally approved drugs.
RESEARCH RESTRICTIONS	(f) generally prohibits publishing research findings in an inaccessible medium for the public if the findings received government funding.	These provisions have been struck from PPA 2.0
ADVISORY COMMITTEES	(k) allows 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.	These provisions have been struck from PPA 2.0