Alone we are rare. Together we are strong.®

NORD Position on S. 4426, the Promising Pathway Act 2.0

NORD is opposed to the Promising Pathway Act 2.0 (PPA 2.0) as it could put patient safety at risk and make it harder to develop and access safe and effective treatments for rare diseases.

NORD recognizes the urgency for more treatments for all rare diseases. Finding solutions to address the lack of treatment options available to those living with rare disease is complex and NORD remains committed to working with all stakeholders to pursue policy and regulatory solutions that foster more innovation and can bring faster patient access to safe and effective FDA-approved treatments.

Primary Reasons NORD Does NOT Support PPA 2.0

- **PPA 2.0's conditional approval pathway jeopardizes patient safety as early clinical data is very often a poor predictor of safety or whether a drug will work as intended.**
  - Treatments for some children could be conditionally approved after being tested only on animals, yet up to 90% of drugs tested successfully on animals fail in human trials, mostly due to safety issues not detected in animal models.[i,ii] In fact, previously unknown toxic side effects are responsible for 50% of failures in phase II trials and ineffectiveness is responsible for another 30% of failures.[iii]
  - Drugs for adults could earn conditional approval after being tested in healthy adults (phase I trials) and demonstrating some evidence from people living with complex medical conditions (phase II). However, data consistently show that on average, fewer than half of all drug development programs successfully progress from phase II to phase III.[iv,v]
- **PPA 2.0 endangers future drug development.**
  - Conducting clinical trials to bring a second drug to market requires fundamentally different trial designs that rely on data from the first approval. The lack of robust data required for conditional approval could compromise subsequent drug development programs with promising therapies.
  - Patient identification and recruitment for subsequent clinical trials in diseases with already small patient populations become more difficult, as do the financial challenges of raising R&D funding for an orphan disease with an approved treatment already on the market. These problems could be worsened if products not yet proven to be safe and effective are on the market.
- **Rare disease patients may not be able to access or afford conditionally approved drugs, compounding an already complex health coverage process and creating health equity issues for those who cannot afford the high costs of noncovered treatments.**
  - While PPA 2.0 attempts to mandate coverage for conditionally approved therapies, many rare disease patients face coverage delays and denials for treatments proven to be safe, effective and FDA-approved for their condition.[vi,vii]
  - A conditional approval pathway based on very limited evidence of safety or effectiveness would do little to support payor confidence in FDA approval. This will likely leave patients to shoulder high out-of-pocket costs to obtain a therapy that may not be safe or effective when their health insurer denies coverage.[viii]
  - A conditional approval pathway may also be inappropriately conflated with the FDA's accelerated approval pathway, and this could undermine patient access to products that utilize accelerated approval, potentially further contributing to health inequities.

NORD Urges Congress to Strengthen Clinical Trials and Expanded Access Programs

- **Make clinical trials work better for the rare disease community:** Many people are left out of clinical trials who could benefit from them or should be able to participate. This is a largely solvable problem through

decentralization, appropriately easing eligibility criteria, and using alternative trial designs, such as real-world data for external study controls.

- **Strengthen the FDA's expanded access program:** Expanded access offers several protections for patients, as the cost of treatment is covered by manufacturers and individuals receive experimental therapies under the consultation of a medical provider. Applying lessons learned from the FDA's Oncology Center of Excellence's Project Facilitate, expanding this program within and beyond oncology could make it easier for more people to navigate the expanded access process when clinical trial participation is not feasible.

NORD invites you to join our efforts to find solutions to help people living with rare diseases by following our public policy positions and statements, becoming a patient advocacy member organization, and joining our Rare Action Network.

Contact: policy@rarediseases.org | rarediseases.org

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[viii] Id.