Congress of the United States
Washington, DC 20515

March 4, 2014

The Honorable Margaret Hamburg
Commissioner
U.S. Food and Drug Administration
Rockville, MD 20687

Dear Commissioner Hamburg:

We write in recognition of the Food and Drug Administration's (FDA's) efforts to ensure public access to safe, innovative and novel therapeutics, particularly for rare diseases and where there are unmet medical needs, and to ask that you continue to commit to ensuring that potential new medicines are guided and reviewed consistently across the agency. Many families continue to struggle with too few options to manage serious and life-threatening diseases. The development of new and more effective medical treatments often comes too slow for the individuals and the families of those who are currently afflicted. Innovation of new and safe drugs is especially urgent for rare diseases, for which either no approved therapeutics or no cures currently exist.

Congress has acted to support the FDA's efforts, addressing the urgent need to move therapeutics for progressive, life-threatening, and often rare diseases to patients with its passage of the Food and Drug Administration Safety and Innovation Act (FDASIA) of 2012. In addition to creating a new breakthrough approval pathway at the FDA designed to expedite drug review, this act made additional revisions intended to create a larger and faster pipeline for new medicines to advance patient care and public health.

Since passage of FDASIA, the FDA has had multiple successes—approving 27 novel new medicines in 2013 alone, with nearly half utilizing at least one of the four expedited review pathways,[1] the first of which was formally established in 1988 and the latest which was provided for in FDASIA. These expedited pathways were especially important for approval of orphan drugs for rare diseases and first-in-class drugs that use unique mechanisms of treatment.[2] Furthermore, two of these review pathways allow for the submission and use of "preliminary clinical evidence" or "surrogate endpoints" that may be available earlier in drug development or from fewer patients than in conventional reviews. These pathways are especially important for drugs intended to treat rare diseases, and of course continues to require transparent post-approval review to ensure sustained safety and effectiveness.

---

[1] Number of 2013 new medicines using expedited review pathways: Fast Track (increased communication with FDA and rolling reviews), 10 drugs; Breakthrough (preliminary clinical evidence demonstrates at least one clinically significant endpoint over available therapy for serious or life-threatening illnesses), 3 drugs; Priority Review (time target for FDA review is 6 months), 10 drugs; Accelerated Approval (early approval based on surrogate endpoints or other clinical measure predictive of clinical benefit for serious or life-threatening illnesses), 2 drugs. Novel New Drugs 2013 Summary, FDA, January 2014.

[2] Six of nine orphan drugs and five of nine first-in-class drugs approved in 2013 utilized one out of the 4 expedited pathways.

We also agree with the FDA's conclusion that to markedly increase the number of new medicines approved, there must be an increase in the number of new medicines *submitted* for review[3]. FDA's pre-application guidance and communication with industry plays a critical role in the drug development pipeline. Given that some of these expedited pathways provide flexibility as compared to conventional clinical trial data requirements, it is important that all departments throughout the agency are familiar with guiding and utilizing the standards of 'preliminary clinical evidence' and 'surrogate endpoints' as the basis for approval, and that these terms are clearly defined.

Consistency in use of these concepts and predictable engagement on these standards across the agency serves as a way to encourage drug sponsors to pursue expedited approval designations. This in turn spurs the development of new drugs for rare diseases and for those with unmet medical needs, an often risky and expensive prospect for industry. Increased utilization of new pathways will move treatments more efficiently to the patients that need them most.

Additionally, FDASIA included a provision encouraging reviewers throughout the FDA to seek out input from external experts, including patients, researchers, and physicians, on rare diseases and subtypes of diseases of larger incidence. These consultations will provide FDA officials with a better understanding of the rapidly changing scientific landscape and ensure that they have the best, most complete information when making decisions about treatments under review. It is imperative that this guidance is implemented uniformly throughout the agency.

Predictability in engagement and review is important for the drug development pipeline and for patients awaiting novel treatments. In light of this, we ask that you prioritize efforts aimed at ensuring that potential new medicines are guided and reviewed consistently across the agency. We know FDA takes its mission very seriously, and is tremendously committed to working to chart a path forward for medicines showing early, unprecedented activity.

Sincerely,

Edward J. Markey
United States Senator

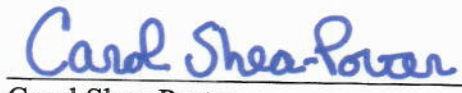
Kelly A. Ayotte
United States Senator

James P. McGovern
Member of Congress

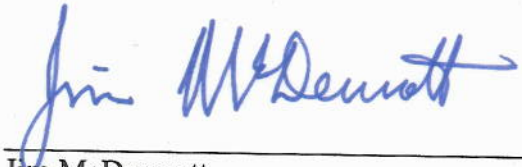
Tom Marino
Member of Congress

[3] Novel New Drugs 2013 Summary, FDA, January 2014.

Jeanne Shaheen
United States Senator

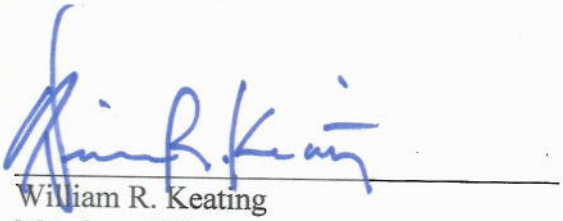


Carol Shea-Porter
Member of Congress

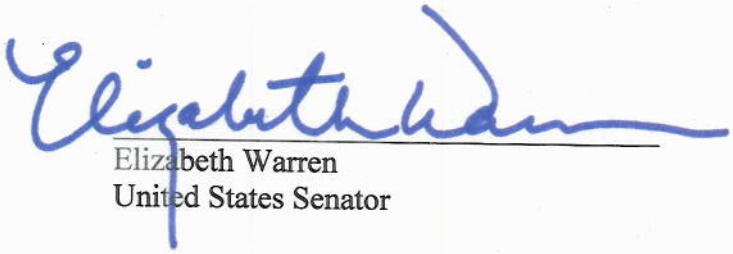


Jim McDermott
Member of Congress

Spencer Bachus
Member of Congress



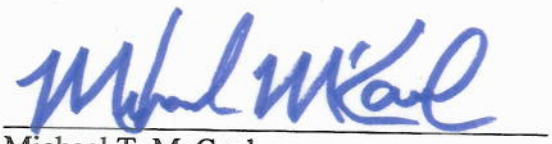
William R. Keating
Member of Congress



Elizabeth Warren
United States Senator

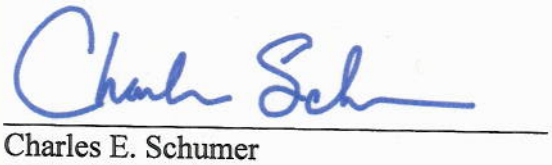
Louie Gohmert
Member of Congress

Yvette D. Clarke
Member of Congress

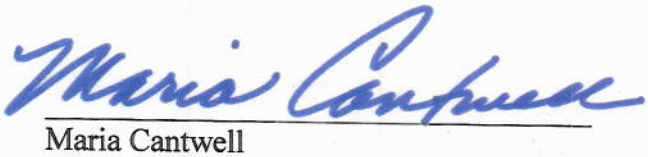


Michael T. McCaul
Member of Congress

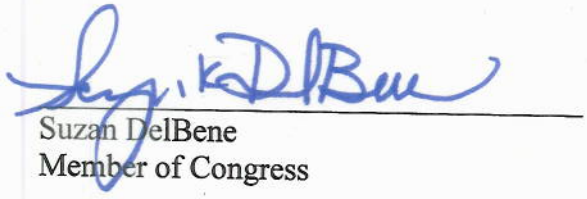
Adam Smith
Member of Congress



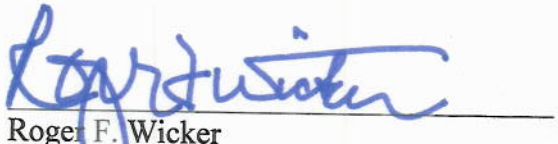
Charles E. Schumer
United States Senator



Maria Cantwell
United States Senator



Suzan DelBene
Member of Congress



Roger F. Wicker
United States Senator

Suzanne Bonamici
Member of Congress

Jared Polis
Member of Congress

Christopher H. Smith
Member of Congress

Katherine M. Clark
Member of Congress

James A. Himes
Member of Congress

Tammy Duckworth
Member of Congress

Sherrod Brown
United States Senator

Michael E. Capuano
Member of Congress

Mike Simpson
Member of Congress

Stephen F. Lynch
Member of Congress

Ron Johnson
United States Senator

Bob Goodlatte
Member of Congress

Richard E. Neal
Member of Congress

Niki Tsongas
Member of Congress

Sam Johnson
Member of Congress

Patrick J. Tiberi
Member of Congress

Mike Doyle
Member of Congress

Joseph P. Kennedy III
Member of Congress

John F. Tierney
Member of Congress

Jeff Sessions
United States Senator