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Current Pathways For Rare Disease Drugs Are Not Optimal, US FDA's Califf Says

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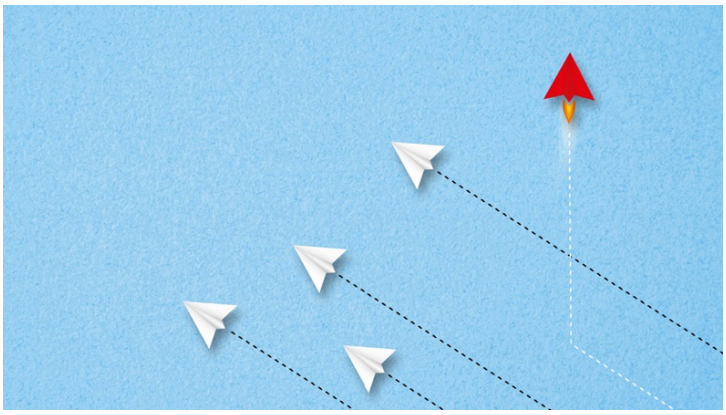
Executive Summary

Anticipating a 'tsunami of therapies' for rare diseases, commissioner says the agency will have to think of creative approaches and employ regulatory flexibility for them. FDA considers copying the oncology center's Project Facilitate for expanded access to other diseases.



CREATIVE APPROACH IS NEEDED FOR APPROVAL OF RARE DISEASE TREATMENTS

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The US Food and Drug Administration is aware of the difficulties of getting approval of rare disease treatments, Commissioner Robert Califf said, and the agency needs stakeholders help to develop creative approaches to overcome them.

Califf gave a closing keynote address at a recent conference sponsored by the New York University Grossman School of Medicine Working Group on Compassionate Use and Preapproval Access (CUPA). Appearing virtually, he was asked about the ramifications for patients being treated with unapproved drugs if there is no regulatory pathway for an ultra-rare disease.

Califf noted that the day before he had a conversation with former NIH director Francis Collins about this issue.

“We're about to see a tsunami of therapies for a rare and ultra-rare disease and I don't think any of us think the current pathways are optimal,” he said. “This is a time where we’ve really got to get creative. And I'd say some of it has to do with regulatory pathways that can sustain the necessary fundraising that's needed to generate high quality evidence, even if the trials are different because they're small patient populations.”

Califf said that of the 10,000 rare diseases, many hundreds are likely to have effective treatments in the not-too-distant future and there will also be questions about how to pay for them.

“I wish I could tell you I had a magic formula for it. I don’t. But you should know that we're very aware of the issue,” he added.

The question about an ultra-disease pathway was posed by Donna Cowan, associate director of expanded access programs and registry at Stealth BioTherapeutics. The FDA had refused to file Stealth's new drug application for elamipretide for Barth Syndrome in 2021. The company resubmitted the NDA last month with additional data and is hoping the FDA will change its position that the company needs to conduct another clinical trial.

Focus On Rare Diseases

The agency has taken steps to help with the development and review of rare disease treatments. FDA issued a final guidance, “Rare Diseases: Considerations for the Development of Drugs and Biological Products,” in December.

That month, it also announced the establishment of the Genetic Metabolic Disease Advisory Committee to provide independent advice and recommendations on technical, scientific, and policy issues related to medical products for genetic metabolic diseases. There are hundreds of genetic metabolic diseases, most of which are rare and carry significant morbidity and mortality. (Also see "Genetic Metabolic Diseases Get Their Own US FDA Advisory Committee" - Pink Sheet, 12 Dec, 2023.)

And in January, an FDA biostatistician said at an FDA-Duke Margolis Center for Health Policy meeting that the agency is open to innovative statistical approaches to address challenges in rare disease drug development. (Also see "US FDA Open To Innovative Statistical Approaches For Rare Disease" - Pink Sheet, 3 Jan, 2024.)

Possible Expansion Of Project Facilitate

Califf was also asked whether the Oncology Center of Excellence's Project Facilitate could be developed for other disease areas, such as neurological and rare diseases. The OCE established Project Facilitate, a call center to help physicians and patients navigate the expanded access pathway for cancer treatments, in 2019. (Also see "US FDA Expanded Access Pilot Launching Soon With Staffing Questions Unanswered" - Pink Sheet, 20 May, 2019.)

Califf said Project Facilitate has made expanded access more equitable, and the agency will be looking at what it can do to extend the project.

"Needless to say, this does involve considerable work. And so we have to have the personnel that can be allocated to it, which is a different issue that we're grappling with in the current budget environment, which is not very favorable for the Health and Human Services agencies," he said.

Tamy Kim, director of regulatory affairs at OCE, noted that the center has two full time staff and that OCE is in the process of hiring a third clinical analyst to intake, review and process IND requests. She said they provide guidance to oncologists and their healthcare teams on how to submit an expanded access request.

Many times healthcare providers call in "and they just cannot believe that they're talking to a live person," Kim said.

She noted that part of Project Facilitate's mission is to provide more equitable access to patients. She said single patient IND requests were coming from the major cancer centers, typically in Texas, New York, Massachusetts and California, and less so in the Midwest or non-coastal states. In addition to handling requests, the call center also does outreach to academic centers and oncology practices.

Asked about Project Facilitate's approach to data collection, Kim said that when the project started, the center wasn't getting many end-of treatment summaries that are required to be submitted, or getting annual reports for single-patient INDs.

"So probably about a couple of years ago, we started to make a concerted effort to contact health care providers if they did not submit their annual reports or end of treatment summaries and encourage them to submit this information," she stated. "So whereas previously we weren't getting much information in terms of outcomes data or annual reports or any information, we're now getting about 50% of a return when we're asking for these data."

Kim also noted that the call center has cut down the response time from submission of single patient IND request from four to five days to less than 24 hours for both regular single-patient INDs and emergency INDs.