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Companies Reveal Hurdles In Providing Drugs Via Expanded Access Programs

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Executive Summary

GSK, Stealth BioTherapeutics and Blueprint Medicines discuss the difficulties getting participation of physicians, the excessive cost of expanded access, and whether physicians should report research data.

BIOPHARMA COMPANIES DESCRIBE CHALLENGES IN EXPANDING ACCESS TO INVESTIGATIONAL DRUGS

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Experts in expanded access programs gave a glimpse of the difficulties in getting investigational drugs to patients, from helping physicians navigate the process to budgeting funds to pay for the programs.

They discussed their experiences at a meeting held recently by the New York University Grossman School of Medicine Working Group on Compassionate Use and Preapproval Access (CUPA).

Annmarie Galli, head of GlaxoSmithKline Pharmaceuticals Ltd.'s global managed access program for oncology, noted GSK's experience with its expanded access program for Blenrep (belantamab mafodotin-blmf) during a workshop on what clinicians need to know about expanded access.

The US Food and Drug Administration granted the antibody conjugate accelerated approval for the treatment of relapsed or refractory multiple myeloma in 2020. It was removed from the market in November 2022 after a confirmatory trial failed to meet its primary endpoint of progression-free survival. (Also see "GSK's Blenrep: 15 Days From Confirmatory Trial Failure To Withdrawal Announcement" - Pink Sheet, 28 Nov, 2022.)

The FDA was "incredibly helpful through the process of moving patients on commercial drugs back to investigational drugs to manage early access," Galli said. "And what we found is a real lack of understanding of especially community-based physicians about what the program is, how to access it. And even though we provided all of the support they needed, [they had] this real belief that this was an incredibly difficult process, that FDA demanded a lot of information."

At the same time, she said, academic medical centers only wanted to do a formal expanded access program (EAP), which involves a three-month delay going through the contracting process. She noted that it is much easier to run these programs in almost every other country than the US.

GSK announced topline results from a Phase III trial (DREAMM-7) of Blenrep in November. It showed that Blenrep significantly delayed disease progression or death compared with Johnson & Johnson's Darzalex (daratumumab) in their respective combinations with Takeda Pharmaceutical Co. Ltd.'s Velcade (bortezomib) and the steroid dexamethasone in multiple myeloma patients whose disease has relapsed after at least one prior treatment.

After some recent encouraging data, the company is awaiting results of a second Phase III study (DREAMM-8) expected later this year before contemplating a potential return to the market. (Also see "Encouraging Phase III Data For Blenrep But GSK Remains Cautious On Market Return" - Scrip, 6 Feb, 2024.)

Expanded Access v. Accelerated Approval

Expanded access is a potential pathway for a patient with a serious or immediately life-threatening disease or condition to gain access to an investigational medical product for treatment outside of clinical trials when no comparable or satisfactory alternative therapy options are available.

A licensed physician requests the product under the expanded access program and works with the company to submit, or has the company submit, the necessary paperwork to FDA and an institutional review board on the expanded access request.

Gregg Gonsalves, Yale School of Public Health, said he thinks there is "a perverse incentive" to not do expanded access programs because the goal of many patient advocacy groups is to have a product be granted accelerated approval.

"We have patient groups that are multi-million-dollar organizations, who could be the go-between between industry and clinicians. But they're much more interested in listening to companies who say 'we can't afford to do any of these, so get the accelerated approval pronto,'" he stated.

Richard Klein, director of expanded access programs & policy at GE2P2 Global Foundation and former director of FDA's patient liaison program, said he agreed with Gonsalves. He said another barrier is the financial burden that is put on clinicians.

"There are responsibilities that they have to take on that nobody is reimbursing them or monetizing for them," he said, and that raises the question of who should foot the bill for them, "should that be a societal burden or a corporate burden?"

Collecting Data From Expanded Access

Throughout the meeting there was discussion on whether clinicians participating in expanded access program should be collecting research data. At a workshop on who should pay for expanded access, company representatives emphasized that it is not realistic to expect them to do so.

Bethany Bearden, associate director of early access operations at Blueprint Medicines Corporation, said physicians want to do this but don't have the time or resources at their hospitals.

"They don't have five seconds in the day to enter anything beyond the AEs [adverse events] they are required to report," she said. "They want to help their patients, they want to advance the field, but they don't have time because the healthcare system itself is broken."

Another attendee at the workshop said it "should absolutely not be an option" that companies do not collect data from physicians or practitioners using their drugs. She said companies should be providing a cost supplement for their use of the data.

Bearden said it costs thousands of dollars per patient per month for Blueprint to operationalize expanded access, which excludes internal costs like the cost of the drug.

"We don't collect any data because that is more expensive. And we prioritize the greatest number of patients in our programs," she stated. "And so, what would you rather have? Do we need to pay out all this money for data that we don't know what we're going to do with? Or do we want to serve as many patients as possible?"

"Blueprint is a really access-positive company, they're very passionate about it," she added. We don't look for any sort of return on investment, "especially because for a lot of our indications, the patients are not going to live to commercial approval, so they're not converting."

Stealth's Ultra-Rare Disease Drug

Donna Cowan, associate director for expanded programs & registry at Stealth BioTherapeutics Inc. agreed with Bearden. She said Stealth spends a lot of its budget on maintaining an expanded access program for an investigational drug for Barth Syndrome, an ultra-rare disease.

"We've got probably close to a dozen patients in our expanded access program that have been on our drug for more than four years that has cost us a fortune," she said. She noted that the budget does not include her salary, her coordinator's salary, the time spent reviewing requests and moving forward, or the costs of safety and logistic vendors.

"We don't need more data, we need to treat these patients," Cowan stated. "I think this whole discussion around data and expanded access is problematic, because that's not what it was meant to be."

Barth Syndrome is a genetic disorder primarily affecting males that results in an inborn error of phospholipid metabolism, which is characterized by cardiomyopathy, neutropenia and muscle weakness. Cowen noted that most boys with the disease do not live past their teens.

Stealth submitted a new drug application for elamipretide for Barth Syndrome in August 2021 despite the FDA's advice to conduct a second trial before submission. The agency issued a refuse to file letter for the NDA and Stealth asked the agency to reconsider the totality of evidence already submitted for the drug, saying it is not feasible to conduct another trial. (Also see "Impasse At US FDA Could Mean Stealth Abandons Barth Syndrome Treatment" - Pink Sheet, 7 Sep, 2023.)

In an interview, Stealth BioTherapeutics CEO Reenie McCarthy said the company had another Type A meeting with the agency in December and resubmitted its NDA with two years of additional data that showed an improvement in six-minute walk, muscle strength and balance, and a 45% change in cardiac function. She said the agency remained skeptical of the approval pathway but there was a more collaborative discussion.

The agency has 60 days to respond to the submission and if it again refuses to file, McCarthy said the company will consider requesting an appeal to go through a formal dispute resolution process.

The Barth Syndrome Foundation, founded by parents who lost children to the disease, came to Stealth in 2014 and asked it to develop elamipretide. The group attended Stealth's December meeting with FDA and gave Norman Stockbridge, director of the Division of Cardiology and Nephrology, and Hylton Joffee, director of the Office of Cardiology, Hematology, Endocrinology and Nephrology, a citizen petition asking the agency to file an NDA for elamipretide and review it through the advisory committee hearing process. The petition has 19,374 signatories.

In a letter filed with the petition, foundation co-founder Valerie Bowen said the Barth Syndrome community is a prime example of an ultra-rare disease that is struggling over the lack of appropriate and consistent use of flexibility in reviewing clinical trial data for diseases that affect very few patients.

At the CUPA meeting, Cowan asked FDA Commissioner Robert Califf about the ramifications for patients if there is no regulatory pathway developed for ultra-rare diseases. Califf, who appeared virtually to give a keynote address, responded that the agency needs to think of some creative approaches to therapies for rare diseases. (*See sidebar.*)

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

By Brenda Sandburg

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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.

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