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Breakthrough Therapy Designation

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Why is a breakthrough therapy designation important and challenging?

Breakthrough therapy designation is a US Food and Drug Administration (FDA) program to expedite the development and review of urgently needed investigational products (including biologics) for serious or life-threatening conditions. To receive a breakthrough therapy designation grant, the preliminary clinical evidence must suggest substantial improvement over available therapy on a clinically significant endpoint.[1] Drugs so designated receive the following benefits: [2]

- All Fast Track designation features
- Intensive guidance on an efficient drug development program, beginning as early as Phase 1
- Organizational commitment involving senior FDA managers

The breakthrough therapy designation has significantly shortened drug development time. A comparison of development time for recent oncology drugs reveals that the time from submission of an investigational new drug application (IND) to submission of a new drug application (NDA) or biologics license application (BLA) for non-breakthrough designated drugs is median 7.4 years, compared to only 5.2 years for breakthrough designated drugs. This is an average savings of over two years for breakthrough.[3]

While the designation program expedites drug development significantly, the granting ratio is relatively low. From July 2012 to September 2019, the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) received 939 requests for breakthrough therapy designation in total.[4,5] Of those requests, 365 were granted, 464 were denied, and 110 were withdrawn,[4,5] which indicates less than 40% of the designation requests were successfully awarded by the FDA.

As it is highly beneficial as well as challenging to be successfully awarded a breakthrough therapy designation, Aleon is here to help. With our experience and dedicated team, valuable advice and effective strategy will be provided to our clients to help them optimize their efforts to achieve success in the breakthrough therapy designation and reach the goal of final drug approval.

What will happen to your development project if you receive a breakthrough therapy designation?

Once an investigational product is designated as a breakthrough therapy, the sponsor will have more and better opportunities to obtain feedback from and collaborate with FDA. Benefits[6] to the sponsor include the following:

- FDA will hold meetings with the sponsor and the review team throughout the development of the drug.
- FDA will provide timely advice to, and interactive communication with, the sponsor regarding the development of the drug to ensure that the development program to gather the nonclinical and clinical data necessary for approval is as efficient as possible.

- FDA will take steps to ensure that the design of the clinical trials is as efficient as practicable, such as by minimizing the number of patients exposed to a potentially less efficacious treatment.
- FDA will assign a cross-disciplinary project lead for the FDA review team to facilitate an efficient review of the development program and to serve as a scientific liaison between the cross-discipline members of the review team (i.e., clinical, pharmacology-toxicology, chemistry, manufacturing and control, compliance) for coordinated internal interactions and communications with the sponsor through the review division's Regulatory Health Project Manager.
- FDA will involve senior managers and experienced review staff, as appropriate, in a collaborative, cross-disciplinary review.

When is the best time to submit a breakthrough therapy designation request?

- **Standard submission time**

The sponsor may submit a request for a breakthrough therapy designation concurrently with an IND application or at any time after the submission of the IND application. However, the sponsor should not submit the breakthrough therapy designation request until they have preliminary clinical evidence indicating that the drug may demonstrate substantial improvement over available therapy.[7]

- **FDA suggested submission time**

Ideally, FDA encourages the sponsor to submit a breakthrough therapy designation request no later than at the time of the end-of-phase-2 meeting (i.e. before initiation of the clinical trials that are intended to serve as the primary basis for demonstration of efficacy.)[1]

The sponsor is encouraged to consider submitting a request for breakthrough therapy designation in either of 2 scenarios[1]:

(1) When FDA reviews the sponsor's data and information, including preliminary clinical evidence, and FDA believes the drug development program may meet the criteria for breakthrough therapy designation;
(2) When the remaining drug development program can benefit from the designation.

What is the FDA timeline for review of a breakthrough therapy designation request?

FDA will respond within 60 days after their receipt of the request.[6]

How can Aleon help the sponsor achieve a successful breakthrough therapy designation request?

Achieving breakthrough designation therapy is a demanding and challenging exercise in most cases, requiring planning, analysis, and the preparation of a high-quality formal request. An experienced professional Regulatory Affairs vendor could be very beneficial for the sponsor. At

Aleon we will provide our best knowledge and expertise to support the sponsor to achieve breakthrough designation success. An exclusive end-to-end service, including gap analysis, planning, document preparation, and communication with the FDA will be provided to our clients. Our team will work closely with you and give our best effort to prepare a high-quality breakthrough therapy designation request in a timely manner. With extensive experience in communication with the FDA, we can help the sponsor build up a strong relationship with the FDA throughout the breakthrough therapy cycle.

When to submit preliminary breakthrough therapy designation advice? How can Aleon help the sponsor achieve a successful preliminary breakthrough therapy designation advice prior to the breakthrough therapy designation request?

Before requesting a breakthrough therapy designation, the sponsor can submit a preliminary breakthrough therapy designation advice to the FDA. This is an opportunity to receive the agency's recommendation on a breakthrough therapy candidate via teleconference.[8] Sponsors are encouraged to take advantage of this opportunity as a means to advance urgently needed therapies.

To achieve a successful preliminary breakthrough therapy designation advice, Aleon can guide and work with the sponsor to prepare and submit the necessary documentation. Aleon has arranged many successful teleconferences between sponsors and FDA. As such, we have helped our sponsors gain valuable inputs from the FDA.

References

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