ALEON®

Fast Track Designation:

How Aleon Can Help Sponsors Speed up Their Drug Development to Serve the Underserved

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Dedicated for Approval ®

Introduction

From bench to bedside, drug development takes an average of more than ten years. Traditionally, drug development exposes thousands of patients in clinical trials to establish safety and efficacy before reaching the market. In recent years, advancements in drug development, such as targeted therapies in oncology, have shown exceptional and significant efficacy at the early stage of drug testing. Fortunately, health authorities' have adopted expedited programs to help shorten drug development and review timelines for especially promising drugs and biologics. This provides the opportunity for patients with severe and life-threatening diseases to access effective and safe treatment sooner. This position paper discusses one such FDA program known as fast track.

The Food and Drug Administration Modernization Act of 1997 (FDAMA) introduced fast track designation in the U.S. to expedite the development and review time for promising drugs for serious conditions. This became part of the Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA). It is one of four FDA programs to help expedite promising and urgently needed products. The others are breakthrough therapy designation established by FDASIA of 2012, accelerated approval established under Subpart H of FDA's New Drug, Antibiotic, and Biological Products regulation in 1992, and priority review created via the passage of the Prescription Drug User Fee Act in 1992. Table 1 summarizes the general criteria and benefits for each FDA expedited development and review program.

Table 1. FDA Expedited Development and Review Programs[1]

	Fast Track Designation	**Breakthrough Therapy Designation**	**Accelerated Approval**	**Priority Review Designation**
Year Established	1997	2012	1992	1992
Qualifying Criteria	• A drug that is intended to treat a serious condition, And • Clinical or nonclinical data demonstrate potential to address an unmet medical need	• A drug that is intended to treat a serious condition, AND • Preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapies on a clinically	• A drug that treats a serious condition, AND • Generally provides meaningful advantage over available therapies AND • Demonstrates an effect over a surrogate endpoint that is reasonable	• An application (original or efficacy supplement) for a drug that treats a serious condition, AND • If approved, would provide a significant improvement in safety

		significant endpoint(s)	likely to predict patient benefit	and/or effectiveness
Timeline for FDA Response	• Within 60 days of request receipt	• Within 60 days of request receipt	• No specified timeline	• Within 60 days of receipt of original BLA, NDA or efficacy supplement
Programs Features	• Actions to expedite development and review, such as opportunities for frequent interactions with the review team • Rolling Review	• Intensive guidance on efficient drug development • Organizational commitment from FDA, involving senior managers • Rolling Review • Other actions to expedite review	• Approval based on an effect on a surrogate endpoint or an intermediate clinical endpoint that is reasonably likely to predict a drug's clinical benefit • Drug sponsor must conduct post-approval studies to confirm clinical benefit	• Reduces FDA review period from 10 months to 6

Sponsors may request fast track designation as early as the Investigational New Drug (IND) application stage of development. However, the agency recommends the request be submitted no later than the pre-Biologics License Application (BLA) or pre-NDA meeting.

Fast track and breakthrough therapy designations offer similar benefits. However, unlike breakthrough therapy designation, which requires substantial preliminary clinical data, fast track designation may be granted if either the clinical or nonclinical results have shown the potential to address an unmet medical need. Also, breakthrough therapy designation includes all features and benefits of fast track designation. It is not uncommon therefore to see a drug which has been

granted early fast track designation, to be at some later time also granted breakthrough therapy designation.

From fiscal year 2013 to 2018, among the 634 requests for breakthrough therapy designation, 39 percent were granted, 48 percent were denied, and the drug sponsors withdrew 13 percent of the requests before FDA reached a decision. In contrast, during the same period, of the 965 fast track designation requests, 71 percent were granted, 24 percent were denied, and 5 percent was withdrawn by the sponsors before FDA reached a decision[2]. Another review showed that between January 2012 and December 2016, the clinical development time (from IND to marketing approval) was reduced by 0.9 years for drugs granted for at least one of the expedited programs than those developed under none of these expedited programs[3].

Aleon's process and tips for creating a high-quality fast track designation request

Aleon streamlines the request preparation process. We can also coordinate application preparation for both fast track designation (FTD) and breakthrough therapy designation (BTD) in parallel, if the product's data package meets the criteria.

Table 2 is a simplified overview of Aleon's preparation process for fast track designation requests.

Table 2. Fast Track Designation (FTD) Request – Aleon Preparation Timeline

<table>
<tr><th>Project Initiation
Week 0</th><th>Week 0 to 4/6</th><th>Week 5/7</th><th rowspan="2">Health Authority(s) Decision

e.g. FDA 60-Day Review</th></tr>
<tr><td>• Provide sponsors preliminary information request sheet
• Gap analysis
• Clinical trial design consultation</td><td>• FTD request preparation
• Conduct literature search
• (BTD request preparation)*</td><td>• FTD request submission on the sponsors' behalf to the FDA
• (BTD request submission on sponsors' behalf to the FDA)*</td></tr>
<tr><td colspan="3">Aleon helps develop regulatory strategies during the process, with up-to-date regulatory affairs knowledge and experience demonstrated by years of professional relationships with health authorities.

*On sponsors' behalf, Aleon can in parallel prepare both fast track and breakthrough therapy designation requests if the investigational drugs meet the criteria.</td></tr>
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Following best practice communicated by authorities, Aleon develops a thorough internal review checklist to capture key items during the request preparation and review periods to ensure high-quality submissions.	

Each case is different. If you are interested in requesting fast track designation for your valued products, contact Aleon at info@aleonpharma.com or call us at 973-850-5300. With our years of regulatory affairs experience, we help our sponsors avoid common pitfalls and prepare high-quality requests to serve the underserved patient populations sooner.

References

1. U.S. Food and Drug Administration. (2014). Guidance for Industry: Expedited Programs for Serious Conditions - Drugs and Biologics. Silver Spring: U.S. Food and Drug Administration. https://www.fda.gov/media/86377/download. Accessed July 2020.
2. FDA DRUG APPROVAL. Application Review Times Largely Reflect Agency Goals. United States Accountability Office Report to Congressional Requesters March 2020. https://www.gao.gov/assets/710/705193.pdf. Accessed July 2020.
3. Hwang TJ, Darrow JJ, Kesselheim AS. The FDA's Expedited Programs and Clinical Development Times for Novel Therapeutics, 2012-2016. *JAMA.* 2017;318(21):2137-2138.