BREAKING THROUGH LAUNCH BARRIERS:

Critical Success Factors for Launching Products With Breakthrough Therapy Designation

While the FDA's Breakthrough Therapy Designation (BTD) expedites patient access to innovative new treatments, limited clinical evidence at launch and a compressed launch timeline present stumbling blocks and uncertainties for commercialization teams tackling launch strategy, planning and execution. This white paper provides an overview of the implications of launching BTD products and some critical success factors from EVERSANA commercialization experts.

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The FDA's evaluation process for new therapeutics has historically been criticized for being inefficient and slow to approve therapies that patients need. To address these criticisms, over the last 30 years the FDA has launched four expedited programs aimed at drugs with the potential to provide significant advantages for patients lacking treatment options.

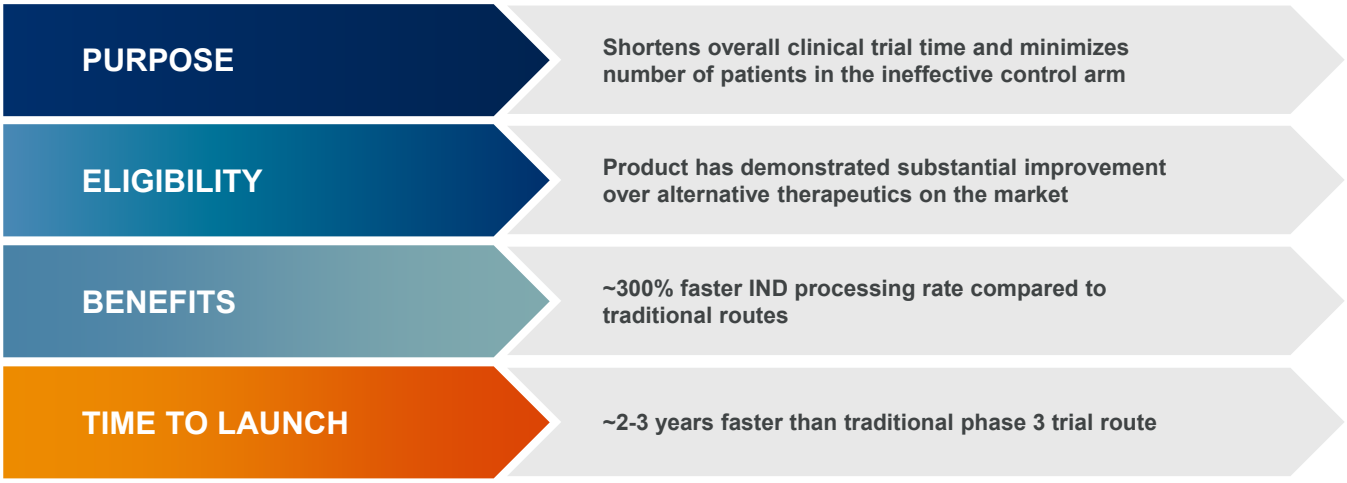

Figure 1: Overview of Key FDA Breakthrough Therapy Designation Components for Manufacturer Consideration (Adopted from US FDA Guidance for Industry and Kwok et al. 2015)[1,2]

EXPEDITED PATHWAY	Accelerated Approval	Fast-Track Designation	Priority Review	Breakthrough Therapy Designation
PROGRAM TYPE	Approval Pathway	Designation	Designation	Designation
QUALIFYING CRITERIA	• For life-threatening or other serious diseases • Yields benefits over existing treatments • Surrogate endpoints may predict clinical benefit	• For life-threatening or other serious diseases • Yields benefits over existing treatments • Surrogate endpoints may predict clinical benefit	• For life-threatening or other serious diseases • Yields benefits over existing treatments • Surrogate endpoints may predict clinical benefit	• For life-threatening or other serious diseases • Preliminary clinical data demonstrates significant improvement compared to available treatments
Review Process	Marketing application (MA) submitted when complete; MA reviewed within 10 months	Option for a rolling review of MA	Submitted when complete; review of MA within 6 months	Rolling review optional; may qualify for "expedited review" of MA within 5 months
Other Features	Conditional approval; confirmatory trials executed to verify suggested clinical benefits	More frequent communication occurs earlier	Decided at the same time as MA submission	"Expedited Review"; intensive guidance and organizational commitment with senior leadership

Table 1: FDA Expedited Programs for Serious Conditions (Adopted from: Kwok et al. 2015)[2]

As shown in Table 1, of four expedited pathways, Breakthrough Therapy Designation most effectively shortens the time necessary to conduct major pivotal trials or minimize the number of patients treated in a comparatively ineffective standard-of-care arm.[2,3] We expect that use of these pathways will continue to grow, particularly for small-cap companies (<$10M USD) developing targeted therapies and personalized medicines.[4] While accelerated approval pathways are frequently leveraged by manufacturers using conditional phase 3 data, the scope of this paper will address only companies concerned with BTD.

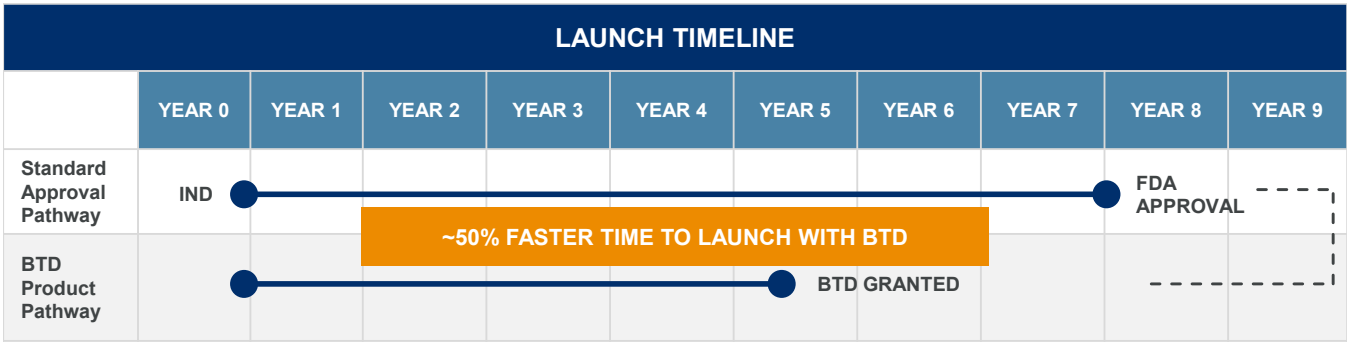

Figure 2: Overview of potential temporal benefits for manufacturers based on historical oncology products initiating either standard or BTD regulatory review pathways. (Timeline adopted from Dimasi, Hansen and Grabowski, 2003)[5]

BTD is granted to drugs with preliminary clinical evidence demonstrating substantial improvement over existing therapies in one or more clinically significant endpoints.[1,6] Therefore, the majority of marketing application authorizations for BTD products are supported by early-stage trials; our analysis of more than 400 drugs granted BTD since 2013 showed that 40% of BTD drugs' FDA marketing authorizations were supported only by phase 2 data, and another 30% of the marketing authorizations were supported by phase 1 or phase 1 and 2 data.[7] While the compressed timeline of approximately 50%,[5] as shown in Figure 2, offers an early revenue opportunity for manufacturers, early-stage limited data also pose challenges to launch strategy. Our analysis also revealed that oncology makes up 60% of BTDs granted (Figure 3), and smaller firms with limited or no revenue have garnered the greatest share of BTDs (Figure 4).

Breaking Through Launch Barriers

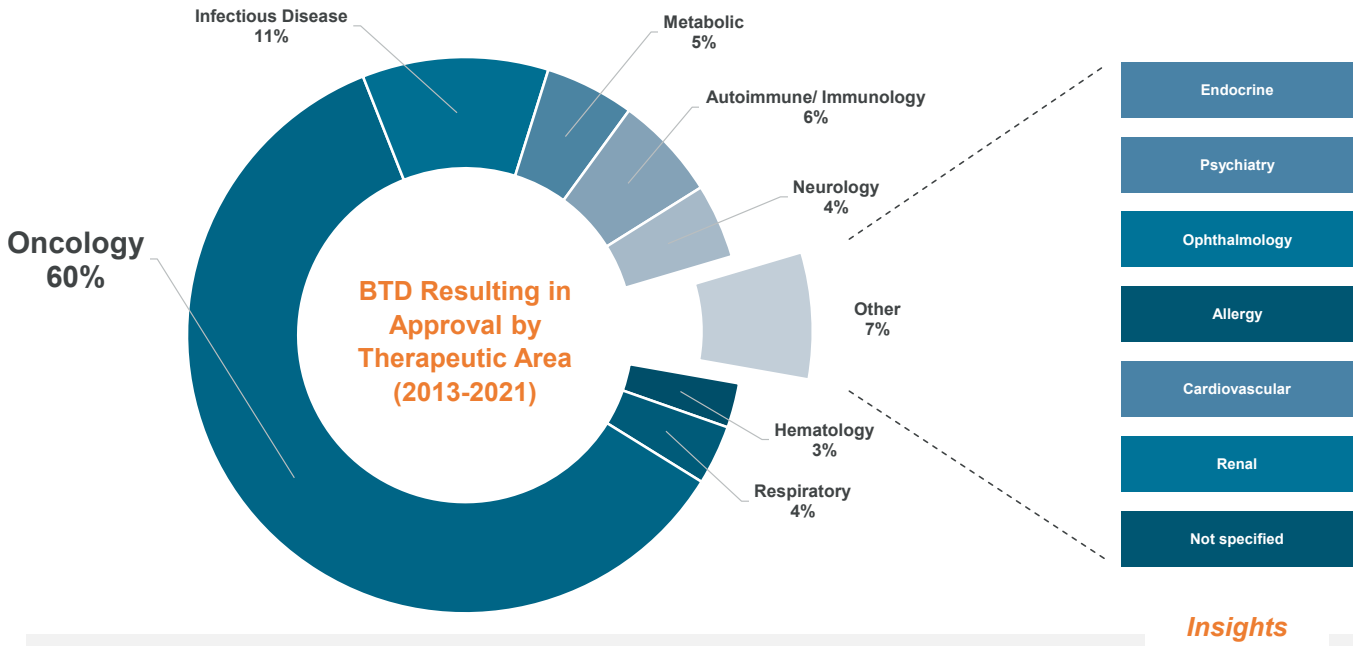

Figure 3: Breakthrough therapy designations approved in the United States from 2013 through 2021 by therapeutic area

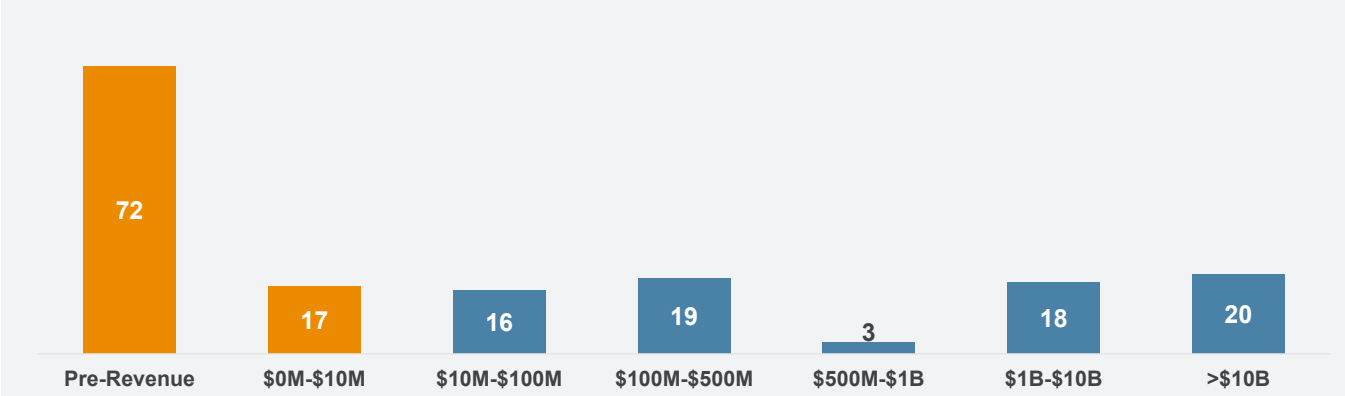

Figure 4: Company size—based on revenue—at time of BTD drug launch. Approximately 54% of all BTD launches were by companies with revenue not exceeding $10M USD (highlighted in orange)

IMPLICATIONS FOR LAUNCH STRATEGY, PLANNING AND EXECUTION

Launch Strategy

OPPORTUNITY ASSESSMENT

Very early on, the launch team is tasked to identify the product's key value drivers and differentiators, total addressable market size, and likely patient numbers for multiple TPP (target product profile) scenarios. These can be difficult to address, as the clinical data supporting the drug may be based on limited data in a smaller number of patients and using multiple product profile scenarios. These uncertainties are compounded in therapeutic areas that are highly competitive—such as oncology—and pose a greater risk for small market cap companies with limited or no revenue. Forecasting must include carefully selected assumptions and include how expected and unexpected events would impact the BTD drug's commercial forecast.[8]

PATIENT JOURNEY AND ARCHETYPING

The early-stage clinical data that support marketing authorization for a BTD drug are at the core of many launch strategy challenges. During clinical development, several interim analyses are planned. Typically for BTD drugs, efficacy and safety data in a broad heterogenous patient population is lacking, as the pivotal trial may be small, it may have stringent inclusion/exclusion criteria, or the length of follow-up may be short. Therefore, patient journey research must be conducted early, appropriately encompassing patient archetypes who are correlated with the product's clinical data.

EVERSANA's approach to patient journeys includes considerations of various product profile scenarios that may address the unmet needs of various patient archetypes, and the approach seeks to understand various leakage and pain points in a therapeutic area in which very few treatment options existed previously. The insights from the patient journey are then used to develop a robust positioning, customer engagement model, and support services that account for the unique needs of the target patient population.

MARKET SEGMENTATION AND TARGETING

BTD is often granted based on surrogate endpoints. For example, data on more well-accepted survival endpoints may be lacking, but such data can be critical to the value proposition of oncology drugs. Based on clinical data alone, it may not be clear whether patients with certain comorbidities, differing degrees of disease severity or various treatment histories will benefit from the BTD product. Market segmentation studies must focus on identifying physicians who are comfortable with ambiguity in data, who are able to discern how data from surrogate endpoints support their treatment goals, and who have experience in treating a diverse patient population.

PRODUCT POSITIONING

Developing compelling product messaging can be a major challenge with a BTD product, given the limited clinical data available and lack of familiarity about clinical options among stakeholders. Product positioning must be refined when greater clarity emerges around the most likely product profile scenario. It is often most effective to focus on a niche patient population that is ideally suited for the drug and generate positive initial experiences with early adopters.

EVERSANA's brand strategy team of experts reviews all the critical uncertainties based on market insights and balances risk with opportunities to create a positioning strategy that gives the brand the best chance to succeed. Insights from the patient journey are also used to develop a customer engagement model and support services that consider the nuanced and unique needs of the ideal patient population and the providers who treat them.

COMPETITIVE READINESS

After a BTD drug is authorized and launched, the possibility exists of a competing drug eventually entering the market with more robust clinical data. It is crucial for the launch team to create a robust competitive intelligence monitoring program to stay apprised of competitors' progress and conduct timely, well-informed competitive readiness workshops to align the functional teams on key risks and opportunities and proactively implement planned responses.

EVERSANA's launch execution team implements a highly structured intelligence monitoring program to foresee competitive threats, recognize early warning signals, avoid blind spots, and enable firms to address key challenges to their assets with well-designed competitive simulation workshops. These initiatives assess various risk scenarios with competitive entry, align on implications, determine the best course of action to mitigate such threats, and capitalize on opportunities.

Launch Planning

LAUNCH PROJECT MANAGEMENT

In addition to the expedited development associated with BTD drugs, the FDA also expedites the review and attempts to respond within 60 days of submission.[1,6] While this expedited process opens up the possibility for a faster time to market entry, it also compresses the launch preparation timeline by up to three years. Judicious trade-offs must be made to ensure that the most critical activities are identified early on and are prioritized. Rigorous cross-functional program management is needed to ensure the various functions are not siloed to avoid working plans based on misaligned TPP and market entry scenarios. EVERSANA's launch project management team works with manufacturers to identify operational bottlenecks and critical interdependencies.

PATIENT SUPPORT AND MEDICAL INFORMATION

Given the fact that limited treatment options existed in the space prior to the launch of the BTD product, often an elevated need exists for robust wrap-around services to address coverage challenges and medical information support. EVERSANA's patient support and medical information support teams have a nuanced understanding of these challenges and create a custom suite of services to provide a white-glove service for patients and HCPs.

PROVIDER, PATIENT AND PAYER ENGAGEMENT

BTDs are typically granted in indications with high unmet need and a lack of treatment options. Key opinion leaders and thought leaders in the field may be scarce or may not have much experience with new therapies. While comprehensive scientific and medical education will be critical to condition the market prior to launch, educating prescribers may require more investment due to limited prior pharma-sponsored medical education activities. EVERSANA's key influencer mapping engagement approach is based on a brand's strategic objectives and blends strategy, data analytics and technology to deliver value. We leverage multiple public and private data sets to identify and rank influencers.

In these situations, the EVERSANA team has implemented medical education activities to cast a broader net and has often included PCPs who play a critical role in screening, diagnosing and referring patients to specialists for

confirmatory diagnoses . EVERSANA ENGAGE's medical education activities are aimed at the differential diagnosis of the target indication and assisting physicians in remaining alert for targeted patients.

Medical education also includes nurses and nurse practitioners—who are likely to be in close contact with the patients more frequently—to facilitate early recognition of side effects and pre-emptive measures to prevent treatment dropouts. The medical information team must be right-sized and trained rigorously to handle a barrage of queries on dose titration, adverse events, side effects, contraindications and drug interactions in the broader patient population. In many cases, EVERSANA's Medical Information and Pharmacovigilance experts have worked with the sponsors to create nurse educator teams that are highly trained on legally compliant answers to address anticipated queries from the HCPs and patients.

FORMULARY INCLUSION

Even an excellent product that satisfies the needs of thought leaders can be held back if pharmacy benefit managers and P&T committees do not add the product to often conservative formularies. From the outset of launch, commercial teams should be cognizant of the fact that certain health plans are more likely to bring on products as early adopters, while more conservative organizations will wait until additional data indicate the drug is favored and offers benefits at justifiable costs. For health plans and organizations to align on the benefits of adding a BTD drug, the product must have a clear story of the true value that it will offer patients, and clarity is needed on the ideal patient sub-population. EVERSANA combines traditional healthcare provider segmentation with innovative analytic tactics to accurately identify the providers who tend to be early adopters and are more likely to function as early product champions.

VALUE AND EVIDENCE FOR MARKET ACCESS

Market access is often the greatest challenge for BTD drugs. Working in the product's favor is that current treatments are likely ineffective; however, with the new treatment, the lack of data in a broad patient population and data with surrogate endpoints present significant risk and uncertainty for payers. Limitations in the trial for the patient population, comparator drug, study design and health outcomes cause payers to be concerned about how efficacy in the trial translates into effectiveness, efficiency and budget impact in the real world. A need may also exist for payer education to bring awareness of the indication of the BTD drug.

In order to overcome the risk and uncertainty in cost effectiveness and budget impact of the BTD product, EVERSANA's Value and Evidence experts recommend starting planning early with specific studies aimed at understanding the evidence gaps encompassing unmet needs, efficacy and safety, comparative effectiveness and value for money to address these evidence gaps with rigorous cost-effectiveness, comparative effectiveness and budget impact models.

SCENARIO/CONTINGENCY PLANNING

The outcome of the FDA review process depends on additional data being submitted on a rolling basis, and multiple rounds of discussion with the agency are common. Therefore, the FDA review time frame is uncertain, requiring the launch planning team to be flexible and prepared for a range of potential launch dates and product profiles.

EVERSANA's launch planning team considers multiple factors, such as potential scenarios for final indication language, dosing information and setting of care recommendations, which can all be subject to change during the FDA review process.

Additionally, if it is not the manufacturer's first launch, an internal assessment must be performed to consider reorganizing the commercial teams. EVERSANA can help to assess the headcount needs of all commercial functions, ensure that they are well-trained on the therapeutic area and the details of the BTD product, and plan for multiple contingencies to be launch-ready for a moving target.

Launch Execution

LIMITED OPPORTUNITY FOR PRE-LAUNCH MARKET SHAPING

The successful execution of a BTD drug launch can be thought of in two phases: pre-launch and post-launch. In the pre-launch phase, an opportunity exists for market shaping and disease education for patients and prescribers. However, such engagements must be carefully evaluated to maximize impact while minimizing risk, as time is much more limited compared to traditional launches.

BALANCING FLEXIBILITY WITH CONSISTENCY

Post-launch, the commercial teams must balance flexibility with consistency. Flexibility will be imperative—in adjusting to customers and the market as the landscape inevitably changes due to the impact of the BTD product launch—while remaining consistent with the key strategies and value proposition of the drug. Active monitoring of the commercial teams' performance and meeting their needs as hurdles arise will be critical for success. With EVERSANA's COMPLETE Commercialization solution, commercial functions are in close communication with each other, allowing for new directions and insights nearly immediately across all integrated commercial functions.

Best Practices to Launch BTD Therapies Successfully

While a differentiated product will contribute to broader adoption in the marketplace, that is not the sole factor determining its success. Launch teams must understand that they can control and shape the product's trajectory. Below are some of the key critical success factors for a successful BTD product launch:

- Start planning early; develop a sense of urgency across cross-functional teams; and create a launch plan with clear accountability, dependencies and timelines, as there is effectively no margin for error in a BTD drug launch.
- Develop insights from the patient journey to understand key leakage points and potential challenges to develop a robust customer engagement model, which includes manufacturer support services that take into account the nuanced and unique needs of the ideal patient population and providers that treat these patients.
- Conduct customer segmentation, including patients, providers, and payers. The ideal target patient population most likely to benefit from the BTD product must be determined, which can help with identifying providers who might be early adopters and product champions treating those patients. Payer segmentation should be based on willingness and ability to control BTD product usage.
- Conduct scenario/contingency planning for multiple product profiles and launch time frames, including competitive readiness planning for potential competitors that may emerge with a more robust data set in the future.
- Develop a robust health economic outcome research strategy based on unmet needs, comparative effectiveness, cost effectiveness, clinical data and value for money assessment to overcome potential access barriers.
- Perform pre-launch market shaping through a scientific communication plan and disease education to elevate the awareness of unmet need, disease pathophysiology, the drug's mechanism of action and clinical evidence supporting the BTD drug.

Build for Success

EVERSANA has built an integrated operation model for each full-scale launch that is predicated on repeatable processes that ensure pitfalls and risks are identified and resolved in an expedited manner. Our ability to ensure this outcome is centered within a "contained commercial operating model" that functions within the dedicated hierarchy overseeing these programs. This team presents detailed program updates on a monthly basis to the CEO and broader leadership team across EVERSANA. In addition, in-person leadership meetings are conducted twice per month to assess program status, lessons learned and broadscale applicability for other programs. All programs are guided by a "COMPLETE Commercialization Playbook" that functions as written operating procedures that are followed by all CCOs.

In summary, EVERSANA will launch 10 programs per year compared to an average of two launches per year within large pharma. We believe that this level of oversight, documented processes, contained commercial model and lessons learned across a large volume of launches ensures better opportunity for success.

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