

Pre-Commercial Marketing and Planning

Securing Future Success through Meaningful Differentiation

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Executive Summary

Early marketing and planning efforts can significantly increase the future success of a product. The delayed initiation of these activities significantly decreases the benefits and options available to marketers and may slow market acceptance and adoption for the product at launch.

Marketing executives within pharmaceutical, biotech, and medical device companies face daunting challenges each day. They are challenged to deliver exceptional financial results for marketed products, while having little control over market dynamics, such as the product's label, reimbursement challenges and hurdles, competitive threats, and slowing physician adoption for new therapies, all of which impact a product's sales. The secret solution is that marketing efforts should begin when the product is in pre-commercial development, ideally at the initiation of Phase II studies. This is the best opportunity to impact a product's benefits and minimize its inherent challenges when it is on the market. Early marketing and planning efforts can significantly increase the future success of a product. The delayed initiation of these activities significantly decreases the benefits and options available to marketers and may slow market acceptance and adoption for the product at launch.

Marketing activities for pre-commercial products differ significantly from traditional brand and product marketing tactics. Pre-commercial marketing requires the collaboration of multiple brand stakeholders, including clinical affairs, pre-clinical, regulatory, legal, medical affairs, and marketing. Everyone involved should have an understanding of the broad commercial issues that will or are likely to affect the product when it reaches the market, as well as the elements that create value for a product.

Achieving meaningful differentiation focuses on creating value, which will ultimately secure future success for a product. Achieving meaningful differentiation requires **action, collaboration, and boldness**. Creating value for physicians, patients, and payers will greatly enhance the future success of the product.

New Era Emerging

The industry is changing dramatically. Our assumptions about how the industry operates need to undergo a major shift as well.

The pharmaceutical/biotechnology and medical device industry is changing dramatically. Our assumptions about how the industry operates need to undergo a major shift as well. Trends that require our attention include:

- Slower physician adoption of new therapies. In 2007 total US sales of new innovative medicines were \$441M, or approximately 20% of the total \$286.5B in US prescription sales in 2007, reflecting fewer product launches and slower adoption by physicians¹.
- US sales for pharmaceutical/biotech products will continue to moderate in the next five years. Forecasts predict 3% to 6% growth annually through 2012, continuing the trend that began in 2001¹. Factors impacting slowed growth include fewer new drug applications being submitted to the FDA and patent expirations that, in turn, create growth opportunities for generic products.
- Closer scrutiny of safety issues, which may bring added caution to the industry¹.
- Growth in specialty drugs will continue². These products tend to be more expensive than drugs used by primary care physicians; managed care organizations and pharmacy benefit managers will continue to control utilization through tiers and increased patient co-pays.

These, and other, trends have a profound impact on the future success of a product. Two of the four key trends outlined above, specifically slowing physician adoption of new therapies and growth of specialty drugs, can be directly impacted through marketing efforts. In order to minimize risk and maximize the future success of a product, marketing efforts must begin early in the development life cycle, ideally at the initiation of Phase II studies. Although there will be little certainty about a product's safety and efficacy profiles at this early stage, marketers must weigh the risk of delaying these activities against the financial investment of initiating these tactics this early in a product's development.

Defining Meaningful Differentiation

The key to achieving meaningful differentiation is to demonstrate a product's value in a scientifically rigorous and compelling manner.

For a pharmaceutical, biotechnology, or medical device product creating meaningful differentiation goes beyond claims of efficacy and safety to demonstrating a product's value in treating an acute condition or managing a chronic disease. The key to achieving meaningful differentiation is to demonstrate a product's value in a scientifically rigorous and compelling manner. Value is demonstrated in several ways, including data, services, and products. In pre-commercial phases marketers must focus on demonstrating value through data. Health-related quality-of-life instruments and patient outcomes data can provide insights into a product's ability to improve patients' daily lives or demonstrate a product's overall benefit. As a product gets closer to FDA approval and market availability, efforts should include initiatives that demonstrate value through services and products.

Creating Meaningful Differentiation: Action, Collaboration, and Boldness

To effectively demonstrate a product's value, it is critical to implement actionable tactics and to collaborate with team members and external experts on the design and implementation of bold and innovative programs.

In the pre-commercial setting, achieving meaningful differentiation requires a broad view and understanding of all factors that impact the future success of a product. Begin with understanding what is valuable and compelling for physicians, patients, and payers within a specific therapeutic area. What physicians, patients, and payers consider valuable will vary depending on the disease/condition. Once "value" is understood, it is essential to collaborate with internal team members and external experts to design programs that demonstrate value and meet the needs of physicians, patients, and payers.

A Three-Pronged Plan for Success

- Successful pre-commercial marketing and planning involves two key components: an understanding of all the elements that will impact a product's success and developing programs to achieve meaningful differentiation and demonstrate value.
- Pre-commercial marketing and planning requires collaboration with multiple stakeholders in order to maximize the product's success in the marketplace.
- Marketers have to be bold and challenge traditional assumptions about how the industry operates, understand the broader commercial issues impacting a product, and invest in pre-commercial marketing and planning while little is known about a potential product and its eventual success.

Taking Action: Understand What Customers Value

To understand what physicians, patients, and payers value begin by developing an informed view of the market; this process evaluates all of the elements that can impact the future success of a product.

Tactical Research Areas

- Patient population, incidence, and prevalence
- How the condition is currently treated
- What unmet needs exist
- Who treats patients and what are the referral patterns
- Current reimbursement standards

Creating Meaningful Differentiation (continued)

- How will treatments likely evolve
- How will reimbursement likely evolve

Understanding these areas will provide insights into key drivers and potential challenges/hurdles for the product. These insights guide development plans and also provide insights into what is most valuable and compelling to physicians, patients, and payers. Marketers need to leverage these insights to develop programs that will achieve meaningful differentiation.

Collaborate with Team Members and External Consultants

To effectively demonstrate a product's value, it is critical to collaborate with internal teams, such as clinical affairs, health economics/outcomes, medical affairs, and regulatory affairs on the design and implementation of these programs. For these activities to be successful, they should be completed in the pre-commercial phases. It takes time to incorporate these initiatives into development plans, obtain management approval and funding, and to discuss initiatives with regulatory authorities.

Tactical Steps for a Collaborative and Meaningful Program

- Engage the pre-commercial team
 - Discuss the need to demonstrate value
- Review findings from informed view of the market research
 - Competitors (current and future)
 - Treatment evolution scenarios
 - Reimbursement evolution scenarios
 - Seek to understand dynamics, key drivers, potential hurdles/challenges
- Outline the needs of customers (ie, physicians, patients, and payers) in the target therapeutic area
 - Understand what is most meaningful to them (may need to confirm with advisors or key opinion leaders)
- Develop options for demonstrating value
 - Brainstorm options

Creating Meaningful Differentiation (continued)

- Review and revise each option based on ability to meet regulatory requirements and guidance
 - Anticipate regulatory agency concerns
 - Understand how the data will impact future marketing programs
- Review and revise each option based on ability to alleviate concerns of managed care organizations and pharmacy benefit managers
 - Anticipate payer concerns
 - Understand how compelling additional data may be in alleviating payers' concerns

The quality of the recommendations and, ultimately, the plan's implementation depend to a great deal on the quality of the pre-commercial team's collaborations. A few recommendations to ensure successful collaborations are:

- Share information openly
- Provide clear objectives
- Identify and clearly assign responsibilities

Be Bold: Develop Innovative and Impactful Recommendations

Achieving meaningful differentiation requires bold actions. In the pre-commercial phase little is known with certainty about a product's safety and efficacy, but this is the opportune time to impact a product's future success. Successful marketing solves a customer's problem. To maximize future success, marketers must objectively understand what is valuable and meaningful to physicians, patients, and payers, and seek expert consultation through a multi-disciplinary team of internal team members and external consultants to contribute to the development of options for demonstrating value. The final step is to leverage the learnings to formulate bold recommendations that challenge traditional assumptions about how the industry operates and to act on them. It seems simple, but often the most challenging aspect of innovative and effective marketing initiatives is taking action.

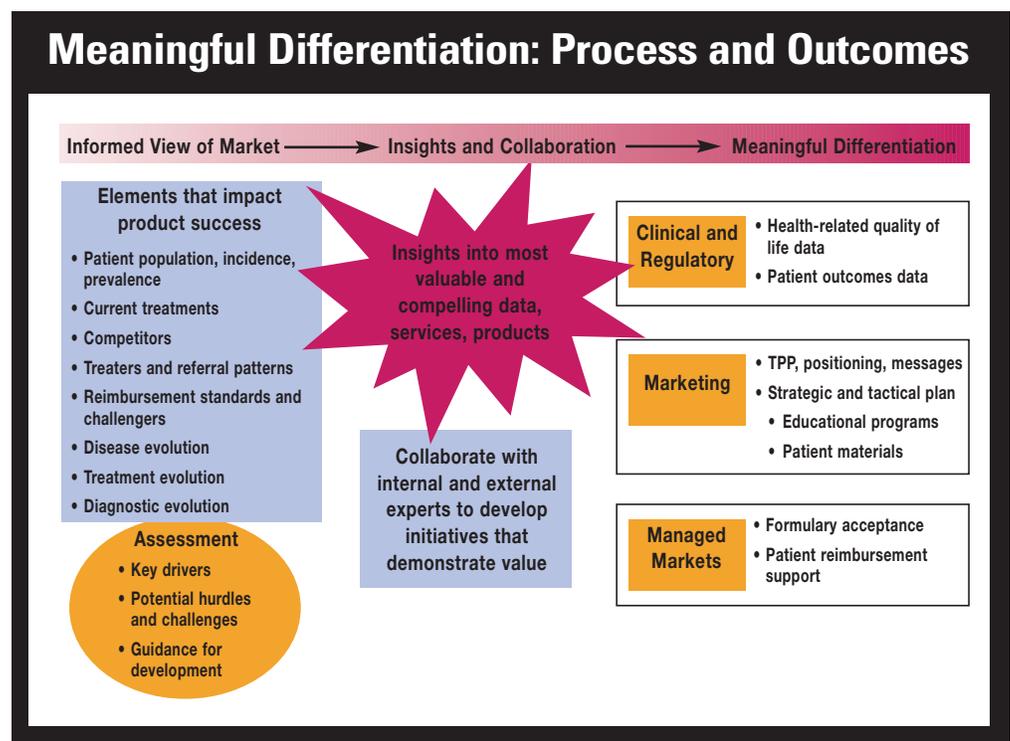
Tactical Steps for Developing a Bold Program

- Outline needs and concerns of physicians, patients, and payers
 - Articulate what is meaningful and valuable

Creating Meaningful Differentiation (continued)

- Articulate corporate objectives
- Aim to align customer needs with corporate strategies and goals
- Analyze options and formulate recommendations
 - Evaluate each option, rank based on degree it meets needs of physicians, patients, and payers, as well as corporate objectives and goals
 - For top initiatives, identify implementation challenges (ie, time, funding, staff resources, etc.)
 - Evaluate challenges and discuss potential solutions
- Formulate recommendations and act on them
 - Obtain buy-in and approvals (if needed)
 - Incorporate into development plans
 - Champion initiatives that will support achievement of meaningful differentiation

The figure below depicts the process of creating meaningful differentiation through action, collaboration, and boldness.



Products that demonstrate their value are much more likely to have preferred formulary placement and fewer hurdles for physicians and patients to clear in using the product.

Benefits of Achieving Meaningful Differentiation

Achieving meaningful differentiation will clearly articulate how a treatment will fit into clinical practice and identify which patients will benefit thus aiding physicians in determining when and how to use the product. These data also make it easier for payers to evaluate the product and determine reimbursement levels and requirements. As therapeutic categories have more treatment options, a key advantage in negotiating with managed care organizations will be the quality of the clinical data and demonstrating a product's value. Compelling value propositions, to physicians and payers alike, demonstrate a change in the natural course of disease; provide data that show the transition of a life-threatening condition to a chronic, but, manageable condition; or outline information that shows a significant decrease in the likelihood of surgery. Products that demonstrate their value are much more likely to have preferred formulary placement and fewer hurdles for physicians and patients to clear in using the product.

By creating critical differentiators pre- and post-launch and aggressively developing meaningful differentiation, marketers can enhance physician desire for and formulary acceptance of the product at launch. The risk in not developing meaningful differentiation in the pre-commercial phase can result in undesirable reimbursement levels and practices, suboptimal placement in the treatment paradigm, and ultimately a product that is underutilized and underperforms. In an industry that is more competitive and growing more slowly, these realities can have a detrimental effect on the financial success of a product and company.

The process of achieving meaningful differentiation can be a large undertaking, but its benefits provide an opportunity to maximize the success of the product once it is on the market.

Tactical Steps to Maximize Efficiency and Timeliness to Achieve Meaningful Differentiation

- Assign pre-commercial team members to lead specific sections within their expertise
- Use a smaller working group to formulate recommendations

Benefits of Achieving Meaningful Differentiation (continued)

- Engage the services of a strategic marketing consultant who can:
 - Provide a thorough understanding of the process, guides the team on next steps, and provides solutions to overcome hurdles
 - Support research, analysis, and assessment, which allows the team to focus on other internal responsibilities
 - Provide expertise in identifying key drivers and hurdles and helps develop strategies and tactical programs
 - Communicate broad-based therapeutic and product development (ie, clinical, regulatory, marketing, etc.) knowledge

Case Study: Macugen® (pegaptanib sodium injection) for Treatment of Neovascular (Wet) Age-related Macular Degeneration

Since 2004 there have been significant advances in the treatment of neovascular (ie, wet) age-related macular degeneration (AMD). In December 2004, the FDA approved Macugen® (pegaptanib sodium injection), which represented a significant advance in how wet AMD is treated. Macugen inhibits vascular endothelial growth factor (VEGF), which promotes angiogenesis and increases vascular permeability and inflammation ultimately leading to debilitating central vision loss. Phase III clinical trial results showed that Macugen injections slowed vision loss, and in some cases stopped it, versus placebo³. Macugen was the first VEGF inhibitor to be approved for wet AMD, and it entered the market approximately 18 months ahead of Lucentis® (ranibizumab), its nearest competitor.

As the first to market, it is likely to be assumed that Macugen would have a significant advantage over later entrants. The US sales performance for Macugen and Lucentis are shown in the table on the next page.

Benefits of Achieving Meaningful Differentiation (continued)

US Sales Performance: Macugen and Lucentis

Anti-angiogenesis			
Inhibitor Product	2005 Year Total	2006 Year Total	2007 Year Total
Macugen	\$175M - \$190M ⁴	\$103M ⁵	N/A
Lucentis	—	\$380M* ⁶	\$815M ⁶

Note: * Results for seven months, available as of June 2006

Macugen had a strong start with total estimated US sales of \$175M to \$190M in 2005⁴. There was a great deal of excitement among retina specialists for Macugen. One investment fund estimated that 2006 sales of Macugen would reach \$400M⁷. However, actual sales of \$103M⁵ are far below expectations. 2007 US sales results are not available for Macugen.

There have been a number of factors that have impacted Macugen sales and its lackluster performance in the wet AMD market:

- Phase III clinical trial results for Lucentis showed that the product stopped, and in some cases reversed, vision loss in wet AMD patients⁸.
- In 2006, Genentech received FDA approval for Lucentis.
- The use of Avastin[®] (bevacizumab) (a drug closely related to Lucentis and used in an off-label manner) as a highly effective and much cheaper alternative to Macugen and Lucentis⁸.
- In mid-2005, Eyetech Pharmaceuticals, the company that developed and marketed Macugen, was acquired by OSI Pharmaceuticals.

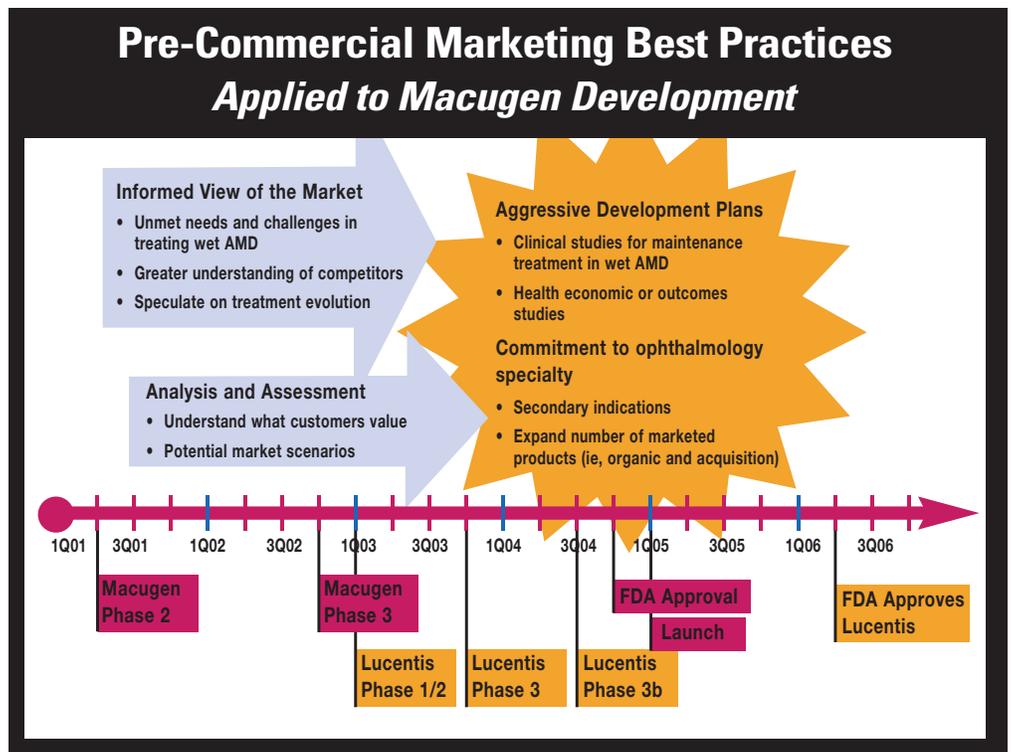
It is difficult to speculate the impact each of these factors had on Macugen’s performance, but collectively they have been detrimental to the product achieving market success.

This case study emphasizes the importance of beginning marketing efforts in pre-commercial stages of development, as well as the need to continually evaluate market dynamics throughout a product’s development. Had a systematic process of

Benefits of Achieving Meaningful Differentiation (continued)

obtaining an informed view of the market and analyzing market dynamics been implemented in Macugen’s pre-commercial phases different decisions may have been made and its market performance may have been significantly better.

The figure below applies Best Practices in pre-commercial marketing and planning, including taking action to develop an informed view of the market; collaborating to analyze and assess information and enhance understanding; and developing plans and strategies from these insights to maximize the future success of Macugen.



About L3 Healthcare Marketing

L3 Healthcare Marketing is a strategic healthcare communications and marketing company specializing in market conditioning for novel products and technologies. Our ideas are grounded in market insight, vast pharmaceutical and biotech experience, and a pragmatic approach that delivers comprehensive and timely results. Leverage our market knowledge, business planning, and strategic development services to maximize your product's potential.

To access a Podcast on this topic featuring Laurie Lucas, Principal, L3 Healthcare Marketing, please visit <http://www.pharmavoices.com/podcasts>.

For more information on Achieving Meaningful Differentiation for your product, contact Laurie Lucas, L3 Healthcare Marketing, at 630.547.8154, e-mail laurie.lucas@L3HM.com, or visit www.L3HM.com.

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