Article

The R&D Marketing Interface in Biopharma and MedTech

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ABSTRACT

This article highlights the importance of building a marketing led cross-functional team that integrates the R&D, and commercialization process in an early stage Biopharma and MedTech company. Marketing should play a prominent role in the cross-functional team at the earliest stages of company formation and product development to identify unmet need, design the development plan, shape the product life cycle, position the product in the competitive set, and understand all market drivers and competitive factors that are essential to ensure commercial success. In particular, in this paper, the focus is on the importance of creating an appealing target product profile (TPP) and describe the rational and methodology for creating the TPP. Drug development is a high risk, high cost, high reward undertaking, and the TPP provides a market-guided approach to development of drugs more quickly, inexpensively, and with a higher rate of success.

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INTRODUCTION

Earlier in this Monograph, Boni has discussed emerging trends in Biopharma, MedTech and digital medicine (see Chapter One of Part Two titled "Innovation Principles in the Pharma 3.0 Business Model Paradigm: User-Centric Applications to Biopharma, MedTech and Digital Medicine with Cross-Sector Convergence). Differentiated product, patient centricity, access, cost control, and price transparency are important factors for commercial success as the Pharma 3.0 business model emerges and is being implemented by the industry. With increasing sensitivity to the cost of medicines, power is shifting to patients and payers, so the importance of value and outcomes is increasing. Alternative delivery models and partnerships are emerging, and digital transformation is enhancing patient engagement in the health care ecosystem. All of these factors are centered in the domain of marketing, the focus of this Chapter. First, we discuss briefly the life sciences drug development environment followed by the role of marketing in shaping the Target Product Profile and how TPP can improve commercial success of a product.

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LIFE SCIENCES ENVIRONMENT

When a life sciences product (pharmaceutical, biotech, MedTech) is discovered, invented or conceived major commercialization challenges include the cost risk, and time to develop the product for the market. For example, in the case of pharmaceutical and biotechnology products, the cost and time required to develop the product for FDA approval is a very expensive and lengthy process. According to the research from the Tuft's Center for the Study of Drug Development, it is estimated that the cost to develop a pharmaceutical drug is $2.558 billion (2013 dollars)[1]. The $2.558 billion figure per approved compound is based on estimated average out-of-pocket costs of $1.395 billion and time value of money (expected returns that investors forego while a drug is in development) of $1.163 billion. The average length to develop a drug is about 12-15 years (Pre-IND 5-7 years, Post IND 6-7 years and approval 10 months).[1] For every 10,000 drug candidates developed about 250 enter clinical trials and one gets approved. These very low approval rates highlight the risk involved in drug development. Then the drug, upon commercialization, has to recoup the cost of all the failed projects to be reinvested to support further drug development. To minimize these risky drug development projects, pharmaceutical companies have created an options model of drug development that includes partnership(s) with early stage companies thereby investing simultaneously in a multitude of technologies, monitoring the

research outcomes over time, and also partnering or acquiring technologies that are promising for the market at later stages of development, e. g. Phase II a, b, or Phase III in the FDA schema. Also with the advent of biologic drugs the cost of investment capital and manufacturing are both high. So, it is imperative that the company should have a good understanding of the market potential, timeline and cost of development before investing significant resources in developing the drug.

Even after the FDA approval, only a third of the drug launches meet the forecasted sales[2]. One of the reasons for lack of market adoption is the lack of clarity of differentiation of the products vs. current standard of care alternative treatments. For example, a recent study classified the pharmaceutical products into three categories: 37% of the market falls into the commodity category; 35% would be consider as differentiated products; and, the remaining 28% would be "transitional", i. e. between commodity and differentiated products[3]. In another study, only 24% of the total number of products launched are considered strongly differentiated in the market.[4] Because of the increasing cost of healthcare, the payers are increasingly focusing on the value and outcome of products in their reimbursement strategy. Rajkumar et al have identified four categories of the CMS (Center for the Medicare and Medicaid Services) framework for payment or reimbursement to providers.[5]

- Category 1 – Fee for Service – no link to value
- Category 2 – Fee for Service – link to value
- Category 3 – Alternative Payment Models Built on Fee-for-Service Architecture
- Category 4 – Population-based Payment – where physicians and organizations are responsible for the care of individuals for an extended period of time.

By 2018, 50% of payments are expected to be alternative payment models (Categories 3, 4), and 90% are Fee for Service linked to value (Categories 2,3, 4). So, a measurement of value created and delivered is becoming an increasingly important component of the commercial success of biomedical products, i. e. the value captured. CMS indicated in early 2016 that they have already achieved the goal of 30% of payments based on alternative payment models set for 2016 and are on track to achieve the 2018 goals. The message is that the value-based reimbursement models will increase the need for pharmaceutical companies to show evidence of value for their newly launched products.

An additional trend that is stressing the importance of marketing is the loss of exclusivity for pharma products with the emergence of generics and biosimilars in recent years

The patent expirations are expected to be 50% more in the next five years[6]. An estimated $140 billion dollars of branded products are going to losing patent exclusivity between 2017-2021[6]

Therefore, there is increasing need to bring to market high value products to replace the loss of revenue due to the patent expirations.

In summary, the medical product development process is a high-risk model. Given the changing life sciences industry landscape both startup and established companies alike have to create innovative products to serve markets with high unmet need and deliver value to those markets. The start-up companies, being resource constrained, have to be especially prudent in their choices of products to develop for the market. In this context, the role of marketing within the companies can assist in identification and development of high value products.

MARKETING

By definition, marketing comprises the activity and processes for creating (Product), communicating (Promotion), delivering (Place or distribution), and exchanging offerings that have value (right Price) for customers, clients, partners, and society at large[7]. Marketing facilitates developing an acceptable product that satisfies an unmet need, creates awareness of the product by communicating the value of the product to the stakeholders such as physicians, patient and payers via promotion, makes the product accessible by executing a distribution strategy also called place, and finally offer the product to the customers capturing the value created using appropriate pricing strategy (See Table1 below).

High-performance marketing in an organization can create the ability to leverage customer insights, demonstrate superior cross-functional collaboration, and achieve strategic focus. Accordingly, marketing needs to be empowered to generate and share its knowledge of customers (and of the overall constituents/competitive set outside of the organization) with all other functional aspects of the innovation team in the life sciences company: from research, preclinical, clinical, regulatory, manufacturing, finance, health economics & outcomes research (HEOR), analytics, and sales, so that the knowledge can be reflected and incorporated into everything the company does (c. f. Fig. 1). In this Chapter, we discuss how marketing can help to create, commercialize, and offer an innovative product with high potential to obtain a significant market share.

An innovative Product is by definition a differentiated product (solution) that offers a meaningful

Table 1: 4 Ps, A's and Objectives of Marketing

4 Ps	4 As	Objectives
Product	Acceptability	Address unmet needs
Promotion	Awareness	Communication of value
Place	Accessibility	Create convenience
Price	Affordability	Value to payers

Figure 1: Marketing facilitate cross-functional decisions

advantage (value) over existing treatments for a given condition. Marketing can shape (or frame) a differentiated product using the target product profile (TPP) developed for the purpose of creating a competitive advantage for the product.

TARGET PRODUCT PROFILE

In 2007, FDA developed a target product profile (TPP) guidance document as a strategic tool to facilitate effective constructive dialogue between the FDA review staff and the sponsors (companies), thus potentially reducing the drug development timeline and minimizing the risk of late stage failures of the drug

for a targeted indication.[8] Three common reasons for pharmaceutical failures in phase III trials are efficacy (failure to meet the primary endpoint), safety (unexpected adverse or serious adverse events) and commercial/financial (failure to demonstrate value compared to existing therapies) value of the products.[9] TPPs can improve the probability of optimal safety and efficacy data in a timely manner, thus enhancing the commercial value of the product. The sponsor would begin developing the TPP with the end goal of creating the best possible label in mind, and to specify the drug development program and specific studies to support the proposed label; and, to guide the design, conduct and analysis of the clinical trials. Ultimately, the TPP should allow for an improved label, decrease the total amount of time spent on the entire drug development process, and reduce the cost as well.

ATTRIBUTES OF A TPP

A Target Product profile (TPP) is an important strategic document that provides a detailed summary of the product being developed, product's desired characteristics and features, developmental plan that demonstrate the product performance and the features that would provide competitive advantage. Sponsors should start with the TPP with the commercial objectives of the product in mind. How should the final label describe the product that will meet customer needs? Here the customer includes (patient, payer, pharmacist, and provider). It is important to conduct market research thru questioning to gain insights and to understand the needs of all these constituencies. The TPP would include: indication, dosage form and frequency, and differentiation (efficacy safety, economics). The attributes shaped by marketing would include (indication and usage, dosage and administration, dosage forms and strengths, contraindications, warning and precautions, adverse reactions, drug interactions, use in specific population, drug abuse and dependence, clinical pharmacology, nonclinical toxicology formulation, trade dress, efficacy/superiority, safety, pediatric dose and pharmacoeconomic data). All parties (research, development, marketing, regulatory, and clinical testing are required to work together to develop and execute a strong development plan that demonstrates superior clinical performance, patient benefit, and health economic value. Note that in startup companies and in companies practicing open innovation, some of these parties may be obtained from outside sources obtained by contract and/or partnership.

The resulting document should contain an optimized realistic view of the objectives of drug development. This document ideally contains a synopsis of what will end up on the drug label, listed for each of three scenarios: the ideal product description ("best-case"), a minimally acceptable product description ("worst-case"), and a realistic description that falls in between these best- and worst-case scenarios that will likely resemble the actual commercial product label after approval (Target or "likely-case"). The best case should be the goal: what the sponsor hopes to claim on the final label, which will be used to guide the design, conduct, and analyses of clinical trials to provide maximum efficiency to the overall development program (see Table 2). An annotations or comments section can be added to provide information on proposed, planned or completed studies that will support the target, including protocol numbers and relevant dates. A TTP is a dynamic living document which can be updated as the drug development program progresses and knowledge of the drug increases. Thus, TPP provides a structure for the scientific, technical, clinical, and market information that is required to achieve a desired commercial outcome. It provides all stakeholders with a clear vision of the product objectives and helps guide research and development decisions. It is a dynamic strategic document that should be reviewed and updated throughout the development process.

As noted earlier, significant sunk costs during R&D, and poor market acceptance upon launch does not lead to a favorable financial outcome for the developer. We posit that early stage and continuous marketing input can change this equation. Recall in the lean startup model where continuous feedback from all constituents during the development process is needed for successful demonstration of product/market fit upon the product launch and growth stages. In the biomedical arena market feedback is required from all of these (multiple) constituencies: patients, physicians, providers, payers, partners, regulators, (and investors)! Close collaboration of all these constituencies is required to achieve an integrated commercial model, i. e. product/market fit in lean startup jargon. In addition, we note that marketing is too important to be left to marketers alone, all cross functional team members should be engaged in creating the marketing message and TPP.

STRATEGIC FRAMEWORK

Tebbey and Rink[10] have provided the following strategic framework in three levels:

1. **Target Market Profile (TMP)** – to delineate the unmet needs of the market for which

Table 2: Sample TPP

	Description	Example		
Product Description	Brief description and/or current product name.	CTSI-001		
Mechanism of Action (MOA)	The mechanism by which the product produces an effect on a living organism.	Blocks the interaction between		
Clinical Pharmacology	Pharmacokinetic information, distribution and pathways for transformation.	• Intravenous (IV) administration of CTSI-001 to subjects was well tolerated in the ascending single-dose (0.002-10 mg/kg) and multiple-dose (0.5-5 mg/kg) studies. • The pharmacokinetic profile is roughly linear at doses above 2 mg/kg and the mean half-life is around 28 days. • Safety and PK profiles from the subcutaneous tolerability study are expected to be comparable to that seen in IV studies and PK/PD profile in treatment population will be supportive of monthly closing regimen.		
Indication	Target disease or manifestation of a disease and/or population.	Moderate to severe patients inadequately controlled on inhaled corticosteroids (ICS).		
Primary Efficacy Endpoints	The most important clinical outcome measure. Ideally should be easy to interpret and sensitive to treatment differences.	***Optimistic***: >50% exacerbation rate reduction vs. inhaled corticosteroids.	***Target***: 50% exacerbation rate reduction vs. inhaled corticosteroids.	***Minimal***: 35% exacerbation rate redution vs. inhaled corticosteroids.
Secondary Efficacy Endpoints	Additional criteria that may be met during a clinical trial, but that are not required to obtain a successful positive clinical trial result.	***Optimistic***: Four (4) months asthma control measured by Asthma Control Questionnaire (ACQ)	***Target***: Three (3) months asthma control measured by ACQ	***Minimal***: Two (2) months asthma control measured by ACQ

Source: Launchpad.ucsf.com

Table 3: Strategic Framework

	Target Market Profile (TMP)	Strategic Target Profile (STP)	Target Product Profile (TPP)
Purpose	Captures all the key information about the market	A vision for a product that will meet the needs of the market	A record of the drug that is most likely to launch
Content	Therapeutic areas/diseases • Unmet Need • Patient Populations • Drivers of use • Competitive assessment • Economic cost of disease	Target attributes (desired profile) • Value drivers • Global • Pricing/Reimbursement • Patient Share • Revenue – Profitability • Pharmacoeconomics • Investments (R&D, COGS, SGA) • Cost of goods • Licenses, Royalties	Indications and usage (label) • Dosing and administration • Contraindications • Warnings and precautions • Adverse reactions • Description • Clinical Pharmacology • Clinical Studies • Storage and handling
Rigidity	Create before the STP or TPP Details are updated as findings emerge, but core facts change only in response to major market events	Set at the beginning of clinical development and updated only when necessitated by changes in the TMP	Updated as clinical and pharmacologic findings emerge and in response to guidance from regulatory authorities

Source: Tebbey, P. W. and Rink, C. (2009) "TPP: A Renaissance for its Definition and Use, Journal of Medical Marketing, Vol. 9 (4), 301–307

the product is viable. The TMP will capture information regarding the therapeutic areas/diseases including unmet need, patient populations, drivers of use, competitive assessment and the economic cost of the disease.

2. **Strategic Target Profile (STP)** – a vision of how the product should meet the needs of the market. The STP includes the target attributes (desired profile) along with value drivers/positioning, global reach, pricing/reimbursement, revenue/profitability, investment, cost of goods, and any licenses/royalties that may be required. This material is developed prior to clinical testing and then would be updated as needed as the clinical trials advance.
3. **Target Product Profile (TPP)** – a dynamic summary of the drug that is most likely to launch. This would include indications and usage (label) including: dosing and administration, contraindications, warnings, adverse reactions, description, clinical pharmacology, storage and handling. This information is updated as clinical trials advance and with the guidance of the regulatory authorities.

This strategic framework (TMP, STP) is used to shape the TPP and to define the clinical and commercial value of the product (see Table 3). Application of the framework encourages the right dialogue within the company and with the FDA to optimize label and commercial success. The framework enables the identification of key development milestones, critical times to assess the achievement of TPP and success criteria. Marketing is key for creating a "beyond the pill" solution, and shaping the label for the product.

VALUE OF TPP

TPP can help the inventor to understand how the drug can be valuable to the customers' (patients, physicians and payers), differentiate from other competitive offerings and identify the critical value drivers and improve internal communication for product development. Specifically, TPP helps to identify the indications to pursue, obtain additional intellectual property (IP), develop publications and presentations to validate the technology, design clinical trials to get optimistic outcomes such as efficacy, specificity, reduce adverse events, decrease cost of goods sold, and explore novel mechanism of action (MOAs). TPP can potentially develop the label and the drug product insert from the global perspective. TPP can provide varying labeling scenarios and also estimate each scenario from the perspective of probability of success for regulatory approval, personnel needed, manufacturing, competitors and market penetration thus guiding the strategy development and decision making of the inventor. Investors have potentially many different alternatives to invest. Effective use of TPP can make the investors understand the importance of your technology.

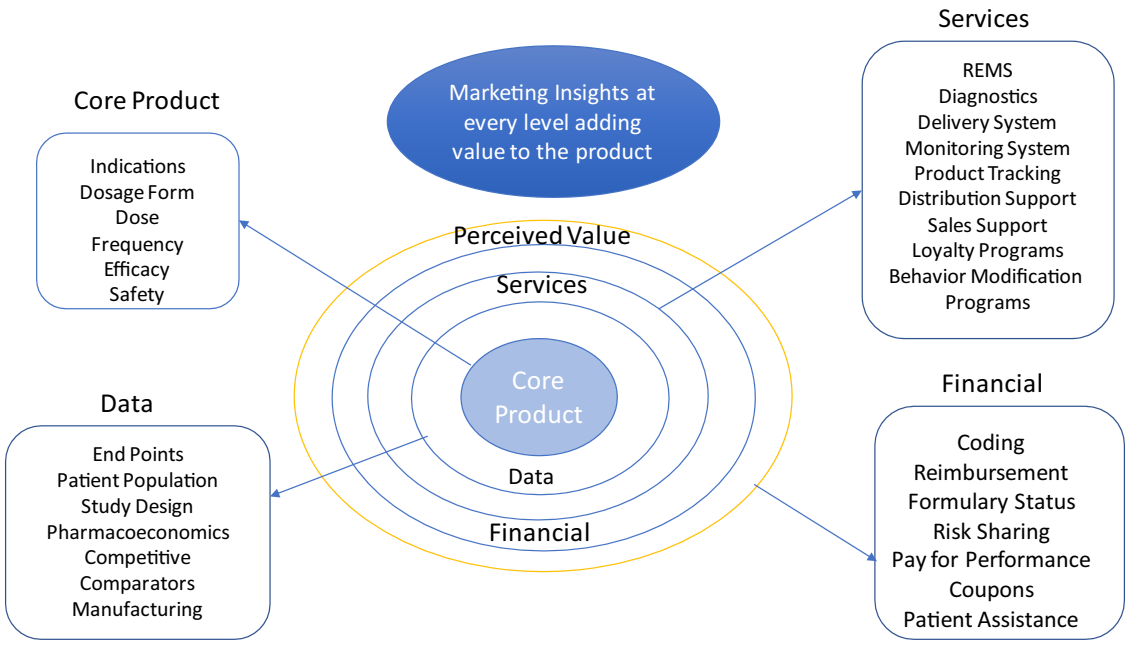

Figure 2: Marketing insights shaping the value of products

However, recent research published in Nature has shown that while TPP is valuable, it is underused.[11] Our goal is to stress the importance and power of TPP as an influence to successful outcomes, and how it can lead to more efficient and successful drug development.

When used properly, the Target Product Profile can be an invaluable strategic planning tool. TPPs can assess potential pitfalls and create mitigation plans at all stages of the clinical development process. They can aid in planning through distribution to clinical and nonclinical research organizations in order to solicit advice and modify existing study plans to be more time- and cost-efficient. These documents also promote a team-based approach to drug development, by raising awareness of the marketing goals and the clinical programs among team members and promoting collaboration within the project.

The TPP can also be used to estimate the market potential and establish the net present value of a given product. By taking into consideration the optimal (best-case) scenario, the target (likely-case) scenario, and the minimal (worst-case scenario), a sponsor can provide develop the competitive strategies required to make a successful product; keeping in mind that a successful product is not only an approved product, but also one that is optimally profitable.

ROLE OF MARKETING -"BEYOND THE PILL SOLUTIONS"

Marketing shapes the core value of the product using TPP. But designing a differentiated value-based product require appropriate planning in shaping the data, service and financial dimensions of value in addition to the core product. These additional dimensions can provide "beyond the pill solutions" (see Fig. 2)

CONCLUDING REMARKS

Our message is that inclusion of marketing as an integral part of the R&D team is a critical component of ultimate commercial success. Market research and competitive intelligence is essential in clinical trial planning and label development. Cross functional teams work best to provide interdisciplinary perspective required to gather and incorporate all data and factors that will be important to ultimate commercial success of the intended product, and to understand the users (patients), payers, physicians, regulators, providers, partners.

So, start with the end in mind. That is to develop the ideal TPP and label that will win in the market. Then incrementally develop the drug to meet that TPP (which may evolve as more information and data are developed). A detailed Target Product Profile, when created early in the development program and updated as new information becomes available throughout the

drug development process can be extremely helpful in mapping out the strategic marketing and scientific pathway. The TPP can not only facilitate interactions with the FDA, but also help in the strategic planning of the clinical and nonclinical programs and provide a valuable tool in the assessment of the market value of the product. TPP can also enable effective interaction with the payers to get valuable input on the commercial value of the product. It defines the goals of the drug development early in the process, focusing team efforts and streamlining program implementation. All of these advantages contribute to the ultimate goal of driving greater efficiencies and shorter timelines to the approval of an optimally marketable and profitable product. The success is when the final version of TPP is similar to the annotated draft labeling!

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