Expert Opinion

Pharmaceutical technology management – profitable business avenue

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Growing research expenditure, regulatory framework and generic erosion have forced pharmaceutical companies globally to resort to pharmaceutical technology management (PTM). Indeed, the pharmaceutical industry has witnessed the impact of innovative drug delivery and device technologies and their influence on business. PTM has given a new business insight with greater profits and enhancement of product franchise. Promising breakthrough technologies have not been able to reach a commercial platform largely owing to lack of capital at the preliminary stages of the product development program. Intellectual property plays a considerable role in protecting innovative technologies. Joint ventures and strategic alliances also become important for commercializing a new technology. The synergy of PTM with options of in-licensing is expected to infuse newer opportunities to the pharmaceutical business.

Keywords: business, drug delivery, innovation, pharmaceutical technology management

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1. Introduction

Over the past few years, the pharmaceutical industry has witnessed unprecedented changes. Conventionally, pharmaceutical research organizations have focused their attention on the discovery of new chemical or biological moieties. The industry is confronted with escalating costs involved in R&D, the imminent fact of patent expiry of blockbuster molecules, mergers and acquisitions, and increasing demands of the consumer for better efficacy and therapy compliance. The success rate of new molecular entities (NMEs) in the clinical phase of development has also seen drastic decline. The NMEs approved in the year 1996 were 56 as compared with just 16 in 2007, resulting in high investment cost-to-output ratio [1]. It has been reported that ~ 36 drugs from the top 50 pharmaceutical companies face a patent expiration threat worth $115 billion from 2007 to 2012 [2]. These aspects have created tremendous pressure on pharmaceutical firms to seek new business opportunity in the market product portfolio. In view of all these factors, industrial business development teams are now turning to pharmaceutical technology management (PTM). This has led to the growth of several technology-based drug delivery systems and devices, including platform technologies. Platform technologies are fundamental innovations in dosage forms, which can be utilized for the delivery of a large variety of molecules for different therapeutic applications. Such technology serves as the basic formulation in which active pharmaceutical ingredients can be replaced without much alteration in the core formula to achieve the same intended objective or performance of the product. Some of these approaches have solved unmet medical needs for chronic drug therapies. They not only infuse business competitive edge over the forerunner, but also afford improved therapeutic benefit. The key to PTM is innovation. The degree of innovation is the differentiator factor among various research teams. A significant means to a sound investment is protectable intellectual property. Any innovative technology needds to have intellectual property protection to avoid duplication of the

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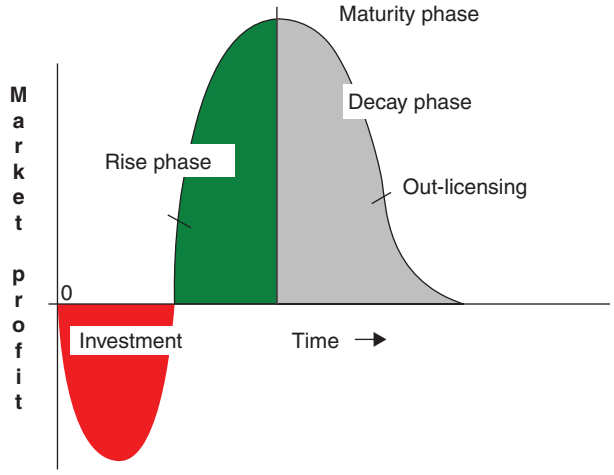

Figure 1. Pharmaceutical technology management.

technology and to maximize profits. A patent on innovative technology would give you the right to prevent others from making, using, importing or selling your invention without your permission. A granted patent can remain in force for a period of 20 years and is a valuable asset to the company. The patentable technology should be able to demonstrate novelty, non-obviousness, and it should be a useful technology. Another advantage of patenting is that it allows the inventor to license others to use the technology. The licensing agreement can be exclusive wherein sole rights are bestowed on the license holder or it can be non-exclusive where more than one license holder has the right to exploit the patent. In the graph of PTM, strong patents can extend the slope and duration of the rise phase. It is thus very critical for the companies engaged in PTM to have an appropriate intellectual property cell (preferably in-house) to carry out patent-related activities. This paper discusses some basic aspects of PTM and its relevance in the present pharmaceutical business scenario.

2. Pharmaceutical technology management

The concept of PTM can be elucidated by a typical business profit–time graph, as shown in **Figure 1**. The *x*-axis is business profit of a corporate organization and the *y*-axis of the graph denotes time period. There is a difference between product life cycle management and pharmaceutical technology management. The product life cycle management basically deals with the life of a pharmaceutical product in the market with respect to time of introduction of the product, marketing measures taken for gaining success and overall business costs. Pharmaceutical technology management is related to time and investment involved in developing a particular technology to be adapted in a pharmaceutical product. This would also include the period of recovery of the costs involved as well as the methods of gaining profit out of the product in the marketplace.

PTM can be elucidated in four phases. The first phase is the 'investment phase'. Here the pharmaceutical company invests in the development of a particular technology or innovation. The technology conceptualization takes place at this point. The product is in R&D and at this point of time the cash-flows are negative and the failure rate is also unpredictable or at times high. Once the product has demonstrated its proof-of-concept in clinic it is ready to enter the market, and enters the 'rise phase' of the graph. This phase can be considered as the strongest region, wherein the technology can command premium profits. In this phase basic investment costs start to recover and the technology starts to gain momentum in the market. After a few years, the product reaches 'maturity stage' where profits gained are highest. The saturation level of business revenue is attained. The flat curve at this point may be attributed to other competitive challenging technologies that begin to penetrate the market. Later the utility of the technology starts to decline, the phase being termed the 'decay phase'. As a result, influx of profits starts to decrease. The attractive value of the technology also slowly diminishes. It should be noted that technology can be licensed at any point of the PTM graph, but most companies opt for it at the maturity phase period. Many firms also select what are called straight licenses, which are basically free from the control of the technology owner. The viability and price of such straight licenses often depend on estimated 'residual life' of the particular technology. If the principal patent on technology has a very short expiry or has expired, the balance viability of technology may be narrowed, although residual life may be managed by technology knowhow, which could have an extended life if appropriately protected.

A pharmaceutical technology initially undergoes a conceptualization process (**Figure 2**). Technical evaluation is done for a particular technology. The concept may or may not be patented at this point of time. Once this is in place the prototypes of delivery systems or devices are created. Depending on the technology, research groups undergo the 'modify–test–modify' cycle until success is achieved. *In silico* approaches are also important tools used for technology assessment. To demonstrate the performance of the system, proof-of-concept needs to be established either in animals or in humans. Pharmacodynamic, pharmacokinetic or scintigraphy studies play a crucial role at this stage in the process. Scale-up of the product from bench scale to production is then undertaken. The technology product then enters the clinic to show its safety and efficacy. After regulatory approval is obtained, the product is launched on the market.

Many promising research findings have not been able to reach the commercial platform basically because of a lack of proper funds at the initial stages of development. Small and medium-sized business firms may encounter financial constraints at R&D levels after completion of research and in the early phases of technology development. A growing number of companies have collaborative research with universities, but this does not exclude venture capitalists from playing a major

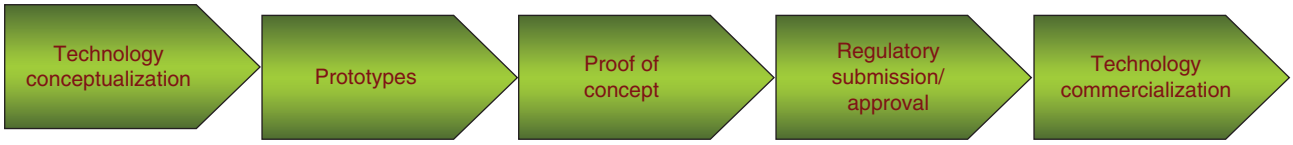

Figure 2. Critical developmental stages in pharmaceutical technology management.

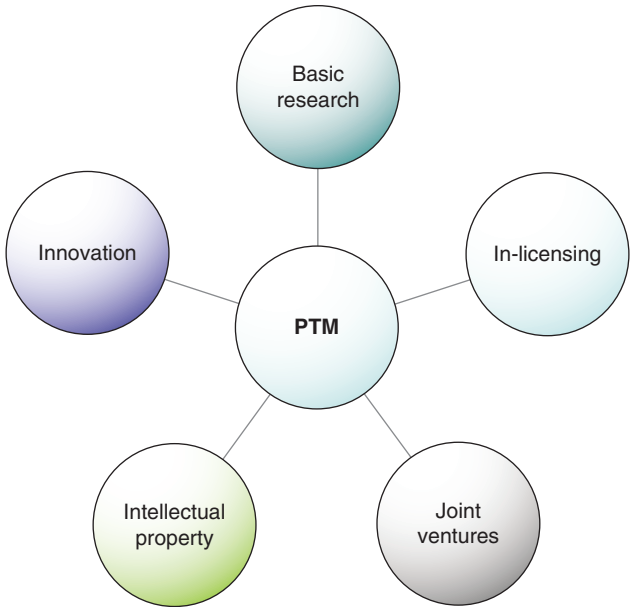

Figure 3. Key elements of pharmaceutical technology management.

role [3,4]. In these cases, venture capitalists play a significant role. The venture business capitalists essentially finance the critical phases of technology development and in return gain a share of the profits in terms of royalty payments. Joint ventures and strategic alliances are some of the other available options.

2.1 Drug delivery systems and devices of PTM

Pharmaceutical technology and its role in improving the delivery of molecules to the target site with improved benefits has been the core area of research for product development scientists [5]. Drug delivery systems and devices play a significant role in PTM. Technology development in the case of devices has been seen mostly in the respiratory segment. Innovative pulmonary delivery devices have demonstrated superior delivery of molecules. In recent years, reformulation of existing molecules has accounted for a large percentage of newly approved drugs [6-8]. It has been reported that ~ 39% of the products launched by the major Pharma companies from 2002 to 2005 were reformulations [9]. Further, reformulation has been more in the areas of the CNS and 'alimentary and metabolic' therapies, indicating the large number of patient populations in these disease segments and higher commercial market values. The reformulated product is successful when it demonstrates clear therapeutic benefit over its predecessor [10]. The critical factors that are to be considered during selection of a product for reformulation include the pharmacokinetics of the molecule, its safety and toxicity profile, the disease being treated, the targeted indications, and the innovator product's treatment regimen [11]. However, only a small percentage of the reformulations are governed by technology platforms. Technology platforms are delivery systems or devices that use a particular technology (generally a patented technology) that serves as a prototype base for different molecules. PTM has been extended to change the route of administration. The switch from the pulmonary route to nasal delivery is an example of this change. This would call mainly for modifications in the container closure system and delivery unit (such as a change from the respiratory add-on mouthpiece of a pressurized metered dose inhaler to a nasal adapter). The advantage of this changeover is that certain studies such as toxicology and extractable studies may not be needed. This would speed up the regulatory submission and approval process. There are examples where drug delivery science has brought about enormous change in the product characteristics; few have been cited here as reference. Drug delivery sales of fast dissolving products have increased rapidly over the last few years. The market potential, patient need and clinical requirement are the key factors that need to be considered when selecting a particular technology [12]. The oral drug delivery segment, which is the preferred route, has seen rapid development and technological advancements [13,14]. Oral disintegrating tablet technology has offered the considerable benefit of reducing product development times as a result of faster launch of products [15]. The clinical, technical and business challenges of product management have been discussed in the literature [16,17]. Melt extrusion technology is now used in pharmaceutical research for the manufacture of a variety of dosage forms and formulations, such as tablets, suppositories, granules, pellets, implants, transdermal systems, stents and ophthalmic inserts [18]. The respiratory segment has also seen various technological advancements for improved targeted delivery as compared with conventional methods [19]. Many of the technological platforms derived from technology management have made a breakthrough in business, yielding high profits for the pharmaceutical companies. These

representative examples are a testimony for the fact that technology management is the mantra for the future.

2.2 Technology selection attributes and key elements

When selecting a particular innovative technology one should keep in mind the important attributes, such as stage of technology development, focus on innovation, development timelines, manufacturing capability *vis-à-vis* in-house capabilities, predicted sales and business profitability, scientific understanding, similarity of compounds or problems addressed, realistic assessment of success, freedom to operate (therapeutic area, route of delivery, etc.), scope for intellectual property, estimated costs, investments and skilled technical manpower.

The product developed through PTM should be competitively priced with careful consideration of the cost–benefit ratio of the new product. The buying capacity of the consumer with regard to a medical insurance program needs to be assessed carefully. Another important question to be answered is whether unmet therapeutic needs are addressed in a proper and convincing manner to the physician and medical experts. The convenience and comfort factor of the consumer – for example, size of inhaler in Exubera® (Pfizer Inc.) – was a key issue [20]. With the size of a hairspray can, it was very inconvenient from the point of view of the patient. Improvement of pharmaco-economics by reducing adverse effects, identifying new indications and improving therapeutic safety, efficacy and convenience along with user compliance should be the target. Further, the developed technology should offer a competitive business edge over others. Key elements of PTM (depicted in **Figure 3**) basically comprise in-licensing opportunity, joint ventures and intellectual property, including a strong foundation of basic research with innovation.

3. Expert opinion

The concept of PTM has been used successfully by many pharmaceutical companies to 'rejuvenate' their product range. The benefits of PTM are multifarious. Research-based pharmaceutical companies can expand their business by utilizing an innovative technology in their portfolio or alternatively can partner with interested firms to enter markets of strategic significance. From the commercial perspective, it is welcome for extending the life of existing successful products. The new technology can essentially provide added benefits, such as improved patient compliance, safety and/or efficacy, improvement in dosing regimens and therapeutic outcome, improved bioavailability, and so on. PTM has opened new avenues for better commercial opportunity in the marketplace. This has given a new business insight, with greater profits and enhancement of product franchise. There will be more demand for technology science that would have the answer to some of the significant challenges of the global pharmaceutical industry. Further, technology in-licensing opportunities will impart a newer dimension to pharmaceutical business.

Declaration of interest

SP Puthli is an employee of Panacea Biotec Ltd.

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