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Review

'Project Launch': From research finding to therapeutic product

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ABSTRACT

Only 0.1–0.5% of new therapy candidates gains marketing approval; just 10–20% of the approved ones ultimately recoup the ~0.6–0.9 $USbn invested into their R&D until marketing authorisation. One reason is the high inherent risk of new therapeutic products development. Further reasons are suboptimal decisions during R&D and, too often, lack of adequate experience. To bridge the latter gap, this article succinctly reviews identification of new product opportunities and their patent protection, the resulting commercial opportunity and portfolio valuation, planning and conduct of the ensuing preclinical and clinical tests, as well as therapeutic product registration and price reimbursement, covering risk management as an aside. The article also clarifies the key terms, identifies the main pit falls, highlights the essential requirements for and the goals of different product development steps, to facilitate communication between researchers and developers. By combining public information with personal experience and recommendations the article aims at informing more broadly those who are familiar mainly with some of the (strictly regulated) activities involved in design, development and launch of new therapeutic products, be it that they are medicinal products or medical devices. Taken together, this should support initiation and evolution of new therapeutic products and assist researchers in finding—and better and more smoothly co-operating with—consultants or partners in development and marketing.

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1. Introduction

Many scientists dream about and many research grant applications project a bright future resulting from scientific finding translated into therapeutic product. The reality is bleaker: less than one half of a percent of all preclinical product candidates ever gets to be tested in humans (Preziosi, 2004) and out of the clinically tested product candidates only between a third and a fifth reaches marketing authorisation (Downing et al., 2012); ~30% of discontinuations are due to commercial reasons and ~30% to lack of efficacy

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Table 1
Survey of the main initial cost ($US) associated with an US (USPTO) and European (EPO) patent applications in the year 2013.

Service/task	USPTO	EPO	
	$US	$US	EUR
Provisional application (PA) filing fee	130		
PA Size Fee/for each additional 50 sheets that exceeds 100 sheets	200		
Basic filing fee – Utility (electronic filing for small entities)	70	150	115
Independent claims in excess of three	210		
Claims in excess of 20	40		
Each claim in excess of 50		293	225
Each claim in excess of 50		722	555
Multiple dependent claim	390		
Utility Application Size Fee: each additional 50 sheets>100 sheets	200		
Additional printing fee for 36th and each subsequent page		18	14
Utility Search Fee/Eurepean search or a supplementary European search	300	1515	1165
International search or a supplementary European search		2438	1875
Request for prioritized examination/Fee for preliminary examination of international application	2000	2405	1850
Request for continued examination (RCE) (see 37 CFR 1.114)	600		
Examination fee		2022	1555
Basic National Stage Fee	140		
US Application fee (non-refundable)	40		
Designation fee for one or more contracting states 13		722	555

All official EPO-defined cost re-calculated into $US using $US/EUR = 1.30.

(DiMasi, 2001). Moreover, out of the approved therapeutics only some are sold at the price and in quantity needed to recover the cost of development, and then make money for the product originator. (Among several new products approved for a similar indication treatment, typically, only the first one or two yield profits.) Too few scientists know these facts and even fewer have sufficiently clear picture of the various steps involved in therapeutic products development, registration and launch. Having recently taken all the steps 'from bench to registration', I wish to help fellow scientists to gauge better the odds of *their* product development and to differentiate better between the stepping and the stumbling stones in such. I therefore review herein the key steps from discovery to the potentially resulting product approval,[1] combining information from the relevant official sources and pertinent publications with personal experience and recommendations. I supplement these advices with illustrative cost and timing data. This should offer to the interested readers enough information for picking up the thread, and then either gain further clarity from independent sources or else involve appropriate professional advisors and supporters.

2. Transforming discoveries into therapeutic product ideas

An open-minded scientist should always ask her/himself whether a newly found substance, procedure or fact—i.e. a discovery—has any value beyond the better understanding of nature and its laws. On the other hand, a person seeking commercial value in a discovery should moreover not hide the latter from public too long, aiming to secure intellectual protection before publication, as this may render the discovery obsolete. In turn, the discoverer should not hasten into practical application before properly understanding the new concept, drug, procedure, or mechanism of action; otherwise, she/he will have spent too much time and money on it. Indeed, any timing error ultimately costs dearly, and false timing can destroy an interesting scientific lead or kill an otherwise viable project.

Any *academic* research project should therefore be worth doing in its own right, as a generator/accumulator of fundamental knowledge. If it yields something practical as an aside: good news! It is naïve to target an invention, however, as only, first, unexpected and, second, non-obvious findings are patentable and only the patented inventions have a tangible *commercial* value.

A new and non-obvious finding with a prospect of usefulness fulfils the third criterion for patent ability. A provisional or a full-fledged patent application describing such an invention then can, and for a sufficiently valuable discovery should, be filed. To be defendable, some unambiguous evidence of the invention priority should back the application. An acceptable proof can be a hard bound, paginated and signed laboratory journal, for example, containing the claim-supporting, witnessed,[2] information. A timely, written disclosure to an official, a patent counsel, or a lawyer serves the purpose as well.

It is paramount to file any provisional or patent application prior to disclosing the discovery to any third party,[3] as even a single non-confidential disclosure brings the novelty into public domain and destroys its patentability! As the Table 1 shows, the expense for this is tolerable: a US provisional patent application costs in 2013 just 130 $US/100 EUR for a small entity, excluding professional advisor fees, and does not even need to have an explicit claim. Such an application secures the filing party's priority right for at least 12 months, if nobody else has filed an earlier related invention before. During the year following the provisional patent application, its inventor can gather further data and study scientific background in more detail. Up to the day 365 after the filing, the inventor can then decide between letting the filing lapse and transforming it into an official patent application. This costs 2020 $US/1554 EUR for a US (see http://www.uspto.gov/web/offices/ac/qs/ope/fee031913.htm for more information) and 3581 $US/2755 EUR for an international PCT (see http://www.epoline.org/portal/portal/default/epoline. Scheduleoffees for more details) application with 50 pages, 5 independent and 10 dependent claims,[4] excluding lawyers fees. The legal advisors fees can be substantial, however, in the 1500–15,000 $US range for an application, depending on its complexity and maturity.

[1] Where necessary, I differentiate between medical products and medical devices but not between chemical and biological drugs, or nanotechnological products, as most guidance and rules apply to all of them.

[2] To confirm its credibility, one should sign any essential piece of information entered into a lab-book. If such an information is glued into a lab-book, one should sign the glued-in part over its edge.

[3] Even a verbal disclosure in a private conversation is harmful, in the extreme. Notable exceptions are third parties that have signed a non-disclosure agreement with the inventor *in spe*, and lawyers.

[4] All specified prices apply to an electronic filing by a small entity, which pays only 50% of the standard cost. The US filing cost for a "micro-entity" is by another factor of 2 lower.