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Non-profit drug research and development: the case study of Genethon

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ABSTRACT

Non-profit drug research and development (R&D) has the potential to deliver innovative treatments at affordable prices. Using the case study methodology, we discuss some ethical and economic issues, including the possible impact of non-profit companies on innovation efforts from for-profit firms. Like other non-profits, Genethon is willing to adopt an ethical attitude toward their donors by pricing their products affordably. It remains to be seen if the approach to internalize the marketing authorization, manufacturing and distribution activities prove to be efficient and sustainable. Also, the firm faces an ethical dilemma because lower prices of innovative drugs can dry the for-profit R&D in the area and prevent patient access to future innovations.

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Introduction

Non-profit drug research and development (R&D) is of growing attention worldwide [1–3]. In affluent societies, the exorbitant cost of advanced treatments, particularly in the segment of rare diseases, has placed increasing strain on the budgets of health care insurers and patients [2,4–10]. Even in European healthcare markets where national payers employ value-based frameworks to assist drug pricing decisions, orphan drugs achieve prices which fall much above typically used cost-utility thresholds [11]. Further, orphan drugs in Europe are purchased at a higher relative cost in lower income countries, due to differences in gross domestic product per capita [12]. Particularly, the for-profit sector has little interest in developing treatments for the so-called ultra-rare diseases which affect less than 150 patients across Europe due to small market size. Non-profit drug R&D has the potential to deliver innovative treatments for rare diseases at affordable prices [4,5].

Further, non-profits have been pioneers in the fields of gene therapies and rare diseases. From 1990 to 2010, the field of gene therapy was investigated almost exclusively by non-profit organizations. In Europe, the two major companies were established: Genethon in France and the San Raffaele Telethon Institute for Gene Therapy (SR-Tiget) in Italy. The development of the field was largely supported by donations from the society and patient organizations. The first sign of interest in the field from the for-profit sector was marked by a 2010 deal between SR-Tiget and GlaxoSmithKline PLC [13].

Today, many gene therapy products in pipelines of major biotech and pharmaceutical companies can be traced back to non-profit organizations. For example, GlaxoSmithKline's Strimvellis was initially developed by SR-Tiget. Further, AveXis' spinal muscular atrophy AAV9 vector, Audentes' AT132 for X-linked myotubular myopathy, Gensight Biologics' GS010 for Leber Hereditary Optic Neuropathy (LHON), Bluebird bio's childhood cerebral adrenoleukodystrophy and beta-thalassemia, sickle cell anemia programs and Orchard Therapeutics' X-linked chronic granulomatous disease program are fruits of the collaboration between the companies and Genethon.

Here we analyze Genethon, a French non-profit biotherapy R&D organization established in 1990. Genethon's mission is to 'design gene therapy products for rare diseases and to ensure their pre-clinical and clinical development in order to provide patients with access to these innovative treatments.' [14] Genethon is conducting four Phase I/II clinical trials as a sponsor or partner and is leading a dozen projects at various stages of preclinical development.

Using the case study methodology, we discuss some ethical and economic issues, including the possible impact of non-profit companies on innovation efforts of for-profit firms.

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Origins and current challenges of genethon

Genethon was founded by the French patient support organization called Association Against Myopathies (Association Française contre les Myopathies, AFM-Telethon) [15]. Genethon's roots stem from its successful efforts to map the human genome in early 1990 and identify genes involved in several hundred genetic disorders [16–19]. In 2015, Genethon had a budget of €42 million, and in 2016, of €38 million; of wich, nearly 60% was collected during fundraising events organized by AFM-Telethon. Currently, the company has 6,000 m^2 of laboratories and the largest Eropean bank of DNA and cell lines from humans with genetic disorders [14].

However, like many other non-profit R&D organizations, Genethon may face important challenges [1,4]. For instance, small ventures which are often established around a focused R&D program may not have the expertise or resources that are needed to develop medicines from discovery to commercialization. Even if the clinical development program for one of Genethon's products is successful, the company may struggle to obtain the necessary marketing authorization (MA) or to subsequently manufacture and distribute the product, because of funding and human resource shortages [1]. In the following section, we discuss how Genethon has tackled these issues.

Securing resources for the entire value creation chain

The owner of Genethon has decided, at least for some of its inventions, to manage internally the regulatory activities, as well as manufacturing and distribution of its innovative products so that it can maintain the control over the supply and a 'fair and controlled price' for the products.

In 2016, AFM-Téléthon and the SPI fund (supported by the French government investment program), founded a firm called YposKesi [15]. The mission of the company is to obtain MA for Genethon's products and to ensure their manufacturing and distribution. AFM-Téléthon contributed to R&D assets by investmenting €37.5 million; the SPI fund invested €84 million. Because AFM-Téléthon has the majority holding in the venture, and thus, it can control prices of the marketed products.

However, even if YposKesi hires experienced talent from the largest pharmaceutical companies, it takes time to build effective teams in new functional areas. This may translate into delays or even limitations of patient access to Genethon's innovative therapies, as compared to more established organizations.

Possible alternatives to internalization of all activities while still avoiding monopoly that can lead to high prices include outsourcing activities to contract organizations or licensing the new product to multiple for-profit companies in order to encourage price competition [4]. While these approaches have proven useful in the developing world context, it remains to be seen if they can be effective in wealthy markets.

Issues with affordable pricing

Various non-profit R&D programs have adopted two general approaches to pricing their products: a) setting an affordable price that ensures sustainability of the drug supply by the company and b) forgoing price control by licensing products to for-profit entities, likely leading to a very high price [4]. The affordable pricing model would result in prices that fall significantly below the typical price range in the orphan drug segment. Therefore, the affordable price is lower than prices typically accepted by health care payers for such therapies.

The former approach to pricing is exemplified by Genethon through its affiliate YposKesi. Whereas the company has not marketed any drugs so far, it is strongly committed to affordable pricing, at least for some of its products.

The latter approach is exemplified by the US Cystic Fibrosis Foundation (CFF), which spent $150 million to develop ivacaftor – a cystic fibrosis medication – and subsequently sold the sales rights to a private company for $3.3 billion. Ivacaftor was one of the most expensive drugs available at that time, priced at $300,000 per year. Although CFF expressed concerns regarding the drug's price, it could not affect it once the deal was accomplished [20]. More recent examples of costly drugs whose discovery was funded by public funds at academia include voretigene neparvovec for the treatment of Leber's congenital amaurosis and tisagenlecleucel for the treatment of B-cell acute lymphoblastic leukemia priced at $850,000 per patient and $475,000 per treatment, respectively [4]. Further, Genethon has entered into exclusive licensing agreements for two of its products for an undisclosed genetic target and spinal muscular atrophy with Spark Therapeutics and AveXis, Inc for unrevealed amounts of money [21,22]. Consequently, it is likely that the company will not be able to influence the price of the licensed products and that their prices will be very high.

Whereas these prices may seem unethically high, the substantial royalties obtained by the non-profits from the transaction could be re-invested into research on novel drugs or used to support patients, depending on the profile of the organization. Because the royalties exceed by far the sums donated, more money will be invested back into R&D than the donors had provided

[4]. However, such high prices bring about a risk related to delaying patient access due to possible unfavorable reimbursement decisions of insurers.

The 'affordable pricing' model and internalization of the value creation chain adopted by Genethon for some of its products have some ethical issues. Firstly, public donations collected for R&D are spent on commercial sale activities, but with a return on investment potential below that of the for-profit sector [4]. Secondly, building new infrastructure instead of using resources of established companies can delay or jeopardize patient access to products [4]. Thirdly, it remains to be seen if lower drug price tags will ensure commercial sustainably for the company, given the small sizes of target patient populations and high manufacturing costs for the innovative therapies.

Another possibility would be to price drugs differentially so that they are cheaper in low-income countries [23]. This approach has a limited value in the case of advanced treatments because they are deemed costly even in the wealthiest nations. Further, differential pricing in Europe or Africa could result in parallel import of the drugs from countries where they are cheaper to countries where they are more expensive, possibly leading to stock outages in the source countries [24,25].

Incentives for future innovation

The absence of R&D on unprofitable diseases and the increase in R&D on selected rare diseases was observed after the US Orphan Drug Acts suggested that high drug prices create an actual incentive for R&D investment by the for-profit sector [4,26]. Therefore, the 'profit-maximizing pricing' of innovative products seems to maintain the traditional incentive for the pharmaceutical industry, because of the high potential for large revenues from the sales of expensive novel treatments.

However, this incentive could be compromised if a non-profit organization sells an innovative product at a relatively low price. Since innovative drugs are typically priced above previously used treatments in the same therapeutic area, the revenue prospects for a new product in the same pharmaceutical segment would be relatively low. This means that R&D on future products in the same area, which may be significantly better than the existing ones developed by non-profits, could be abandoned by the for-profit organizations for commercial reasons. This backlash in innovation may potentially limit the range of therapeutic options available to patients.

Conclusion

Like other non-profits, Genethon is willing to adopt an ethical attitude toward their donors by pricing their products affordably. However, the antitrust law does not permit them to impose prices on potential licensees. Possibly, the company chose to diversify their revenue by licensing certain products to for-profit firms and losing price control over the inventions and preserving exclusive rights to other products that are commercialized at affordable prices internally. The licensing route will likely accelerate and optimize market access for the products, but it will lead to very high prices. It remains to be seen if the approach to internalize the MA, manufacturing and distribution activities for other gene and cell therapy products prove to be efficient and sustainable. Although it will allow maintaining price control, it may delay access and induce collateral damage. Indeed, the firm faces an ethical dilemma because the lower prices of innovative drugs can dry the for-profit R&D in the area and prevent patient access to future innovations.

Disclosure statement

No potential conflict of interest was reported by the authors.

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