Fair Medicine

Pharmaceutical R&D costs: the Fair Medicine point-of-view

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Executive summary

Recently, Gupta Strategists published an independent study on pharmaceutical R&D costs ('The cost of opportunity', 2019). The study provides a detailed and up-to-date insight into R&D costs of medicines using a novel, top-down model built on a single definition of pharmaceutical R&D costs and its principal drivers. In this whitepaper, we reflect on the findings and thoughts put forward in the Gupta study. In particular, we explore the lessons that can be drawn, relating to the role of authorities and governments, to improve the system from Fair Medicine's point-of-view.

Lessons learned from the Gupta study

The primary finding of the Gupta study is that costs of capital (53%) and cost of failures (40%) are the largest components of R&D costs. Based on the cost driver analysis, the study shows that costs differ substantially (> 10x) across therapeutic areas. The average development costs of a medicine for an orphan disease could be as low as 0.5 bln USD, while the costs of a medicine for an oncological disorder could be as high as 6.5 bln USD.

The study suggests several ways to increase the efficacy of R&D spending:

- Reduce the cost of capital, for example by reducing the time from preclinical phase to market
- Reduce the cost of failure, for example by relaxing the approval criteria for drugs in development

Our reflection on the findings of the study

We observe that R&D costs do not relate to the market price of new drugs and thus, lower R&D costs will not translate into lower market prices. In order to achieve a relationship between R&D costs and market price, a new pricing method is needed in combination with drug development models.

We believe that it is possible to reduce (cost of) failures by organizing coalitions in which multiple parties evaluate the product and make the decision to invest. Besides the reduction in failure, another benefit of coalitions is that the product is developed with input from all stakeholders, including patients and doctors. This ensures a diverse knowledge base with the focus on patient-centric product development.

Time of development is an important factor that drives the cost of capital. We believe that it is possible to reduce time to market by accepting early reimbursement with early (provisional) approval for specific categories of products; under the condition of transparency on development costs and product pricing.

We see an opportunity for investing public capital in drug development:

- at the same conditions as private money, and with influence on market entry conditions
- at better conditions than private money, but with strict conditions on pricing, and the primary focus on products for extreme small patient groups (ultra-orphans)

What does the Gupta study describe and analyse?

The study describes the R&D costs for the development of new molecular entities (small molecules and biologicals) from discovery and pre-clinical development up to and including product approval. It does not include post-marketing surveillance studies. An important notion to take into account is that there is great variance between types of products and indications. Therefore, when using the average R&D costs it is important to understand that the outcome is highly dependent on the type of products and indications included.

The primary drivers of R&D costs are trial size, trial duration, success rate and the weighted average costs of capital (WACC%). The study shows that there are three cost categories that make-up the total R&D costs: out-of-pocket cost of the successful product, out-of-pocket cost of the failed products and cost of capital calculated over the invested out-of-pocket costs. The understanding of what drives these costs gives insight on how to shape new initiatives and adapt rules and regulations to promote decreasing R&D costs.

- Out-of-Pocket success: the out-of-pocket costs in the study are divided into two parts: the success and failure out-of-pocket costs. The out-of-pocket costs directly related to the product that is successfully developed accounts for 7% of the total R&D costs.
- Out-of-Pocket failure: This accounts for 40% of the average R&D costs. The success rate is determined by the ratio between the products that make it to the market and products that do not. Failure of products can be caused by lacking proof of concept, safety problems, low efficacy or any other biological or medical reason. However, strategic decision-making by the company developing the product is also a factor that affects the ratio between successful and failed product.
- Cost of Capital: The largest part of R&D costs is the cost of capital, it accounts for 53% of total R&D costs and is driven by the WACC% and time. Capital costs are mostly driven by the financial market and therefore, is it difficult for the industry to influence this. As time is an important factor on cost of capital, the industry needs to develop products faster and bring products earlier to the patient in order to reduce these costs. For the latter, we should consider the role of the authorities as these have implemented strict regulation to which the industry needs to live up to. These regulations also add significantly to the time to market, new techniques to evaluate clinical data and to monitor real-life data may contribute to earlier access of products. This needs careful adaptation of the regulatory framework to register new products.

Fair Medicine point-of-view

The goal of the Fair Medicine foundation is to develop new models for pharmaceutical product development and put this into practice. The aim is to determine and describe changes the industry or authorities can make in order to decrease R&D costs and most important; relate the costs of drug development to the price of the product. From the Fair Medicine point-of-view, this study places the historic data in perspective. The prediction with its cost drivers can serve as an important basis of further adaptations and introduction of innovations or interventions to the current system of drug

development. Future research of Fair Medicine will answer these questions with focus on cost-based pricing and lowering the total R&D costs.

The role of authorities and governments

High prices of pharmaceutical products will always be paid by the consumer. Authorities and governments have the choice to wait until producers bring products to the market, and will only have the opportunity to accept or reject prices, with a limited scope to negotiate an acceptable price. Choosing a position earlier in the R&D process will give more opportunities to influence both the choice of products developed and the outcome of the market price. The study performed by Gupta strategists is a well-funded basis for the discussion on the future of healthcare, costs of drug development and pricing. The study can serve as a basis on which new rules and regulation can be tested and costs and pricing innovations can be assessed. The outcomes of this can be used in the discussion on drug pricing methods and the need for transparency.

In the opinion of Fair Medicine there is a need for an innovative and entrepreneurial position of governments, authorities and public institutions. Active participation of these stakeholders in segments of the pharmaceutic industry, where there is a need for accessibility and affordability, is key. Fair Medicine would like to see that there will be room for experiments for developing new drug development models. These experiments need to be carefully designed so they will not compromise safety nor efficacy of products but will deliver on reduced costs and pricing as well as earlier access for the patient.

The cost of capital is the primary cost category that the authorities can affect. In order to make an impact, there should be a trade-off on price or profit if authorities are becoming involved in this. The authorities can affect the cost of capital in two ways: shortening the time in which there is a need of capital by early reimbursement with early (provisional) approval and public investments in drug development. The two pictures shown below from the Gupta study show the distribution of the cost categories over time (figure 1) and the investments per phase and its contribution (%) to the total R&D costs (figure 2). These figures show the potential for early reimbursement and why pre-clinical investments from public institutions would be a viable and rewarding initiative.

Making early reimbursement possible for products where there is little added value from phase 3 clinical trials, rather than requesting a phase 3 study, perform increased post-marketing surveillance. This can be a tool to get products faster to the patient, especially for patients lacking adequate medicine at the moment.

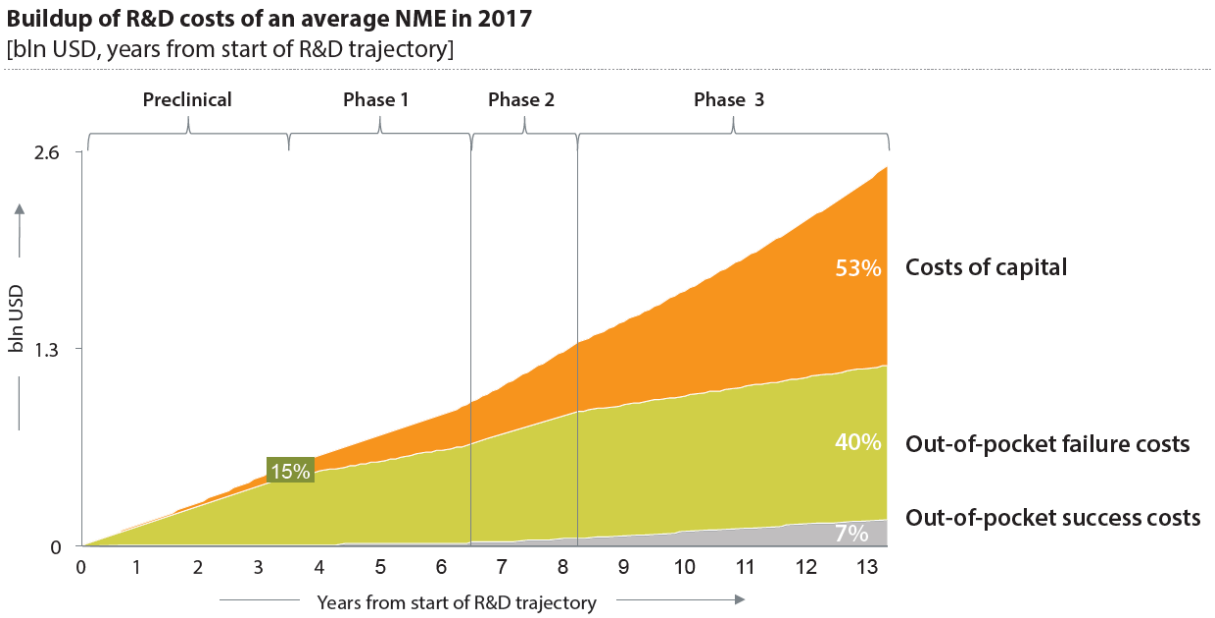

Figure 1: development of R&D costs during R&D trajectory (derived from the Gupta strategist study: The cost of opportunity, 2019).

Figure 1 shows the R&D cost distribution over time. The cost of capital rises up to 53% of the total R&D costs at the end of the clinical development. The cost of capital is time dependent meaning all costs will increase with the WACC% per year. As shown in figure 1, the contribution of cost of capital to the total R&D costs increases most in the later years of development. The registration of the product is the last hurdle before the product can generate revenue and all costs can be earned back. By implementing early reimbursement the accumulation of cost of capital after phase 3 can be significantly reduced.

The second option by which the authorities can affect the R&D costs is in the pre-clinical phase of development. In the current healthcare system, public capital is invested in basic medicine research. It is invested either in the early discovery through universities and hospitals or at the end with public capital when products are reimbursed. Therefore investing public capital should be a viable option under conditions predetermined by the government or public institutions, such as a linkage to future reimbursement price and transparency.

As shown in figure 2, the study by Gupta strategists shows that +/- 18% of the average R&D costs are allocated to out-of-pocket costs during the pre-clinical phase (e.g. 450 mln USD). This relates to 34% of the total R&D costs in pre-clinical cost of capital (e.g. 850 mln USD). Using a public source of funding or using public means in this phase of the development can drastically decrease the cost of capital accumulated at the end of the development. The effect is dependent on the amount invested, the required return on public capital and the agreement made on price. As Gupta strategists suggested, a public investment fund for drug development or a zero costs tech transfer of products developed at universities to the pharmaceutic industry, would be a suitable form of public investments in R&D.

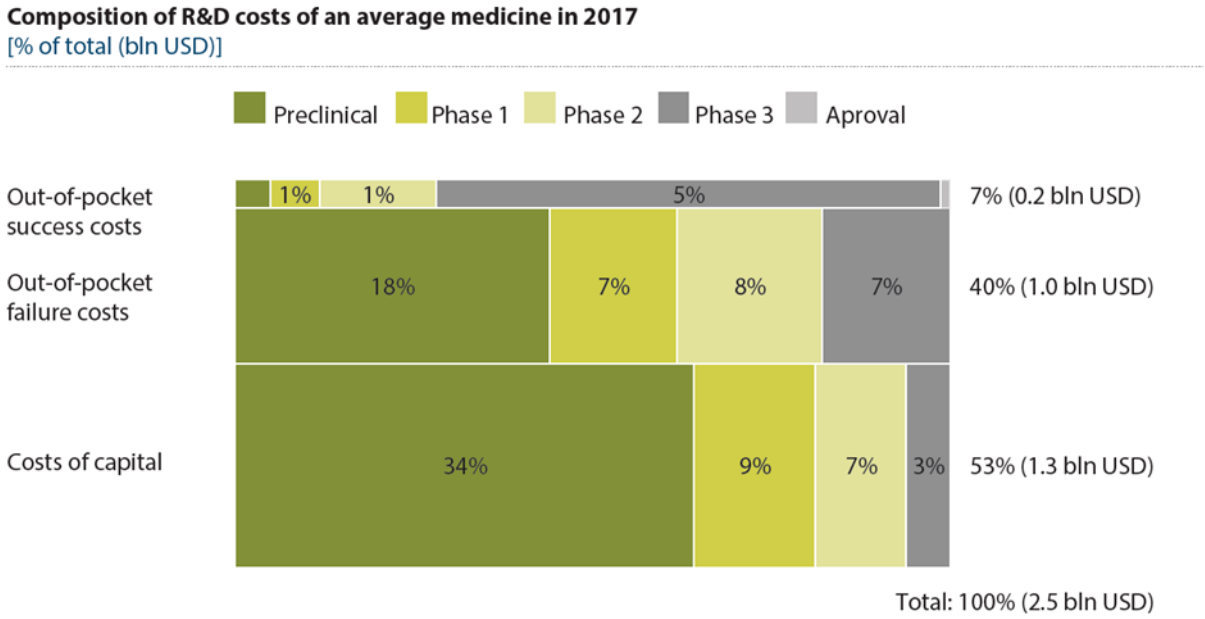

Figure 2: split of R&D costs across type of costs and type of phase (derived from the Gupta strategist study: The cost of opportunity, 2019).

According to Fair Medicine, public investments and tech transfer would be most suitable for (ultra) orphan drugs where development is often lacking and the price per patient is high. The average capital requirements to develop an orphan drug are 500 million dollar instead of the average costs of drug development; 2.5 billion dollar. The lower capital requirements and higher success rate make it more suitable for public investments.

When a government is able to positively affect the primary drivers of R&D cost or negotiate in order to reduce costs for the developing company, the government can get a return from this. The return is achieved through lower healthcare expenditures and pricing transparency by the predetermined conditions of public investments and development advantages.

Fair Medicine's future goals; use of the report findings

The primary goal of Fair Medicine is to develop a new business model for drug development. The model is based on collaboration and transparency. An important part in this is the next step after the cost determination; Transparent price determination related to the costs of drug development. In order to achieve this, it is important to map all costs. The study by Gupta strategists showed the methods for cost determination of drug development. This aids in future validation of the Fair Medicine model and methods.

One of the drivers of R&D costs is the failure of products. Within the Fair Medicine model, the failure costs are reduced through the lower failure rate as a result of co-development. The innovative structure of the Fair Medicine model reduces the profit margin on top of the total R&D costs through cost based investments by the coalition partners in the projects and sharing in risk by all stakeholders.

The secondary goal of Fair Medicine is to determine and describe changes which the industry or authorities can make in order to decrease R&D costs and most important; relate this to the price of the product. From the Fair Medicine point-of-view, this study places the historic data in the right perspective. The prediction with its cost drivers can serve as an important basis of further adaptations and introduction of innovations or interventions to the current system of drug development. Future research by Fair Medicine will describe the effect on the total R&D costs and the potential effect on price.

An important conclusion from the Gupta analysis is that the costs can differ significantly between indications and types of product. Therefore the use of the average costs of drug development is not sufficient in the discussion on development costs. Instead, product type or indication specific data should be used. In the discussion of pricing of medicine, the focus should be on pricing method and not the costs of drug development because this has no direct relationship to the market price of the product.

We observe that there is an industry shift towards orphan drugs. This has an advantage compared to non-orphan drugs; its lower R&D costs. Fair Medicine sees the shift towards orphan drugs as a predecessor for personalized medicine due to its comparable characteristics. Both the positive and negative examples of orphan drugs can serve as a basis of improvement with the focus on the development, registration and pricing of personalized medicine products.

The two cost categories, not included in the Gupta study, that are of importance for Fair Medicine and the translation from costs to price are production costs and post-marketing costs. Product development according to the Fair Medicine model will aid in gaining insight in these costs. Fair Medicine will look for collaboration with companies marketing orphan products and are willing to work together to determine the effects of such post-marketing costs on the market price of a product. Fair Medicine aims at mapping all relevant costs in a transparent manner.

In order to achieve the goal of a viable and sustainable, but also affordable and accessible, pharmaceutic industry and healthcare system, we propose facilitating the development of a pricing algorithm developed in collaboration with both the industry and authorities. This should relate the costs of drug development to the price of the product and be transparent to the payer and consumer.