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Reinventing or get back to basics: the necessary change(s) in the Pharma industry

Since 2019, the House Committee on Oversight and Reform launched a comprehensive investigation into pharmaceutical pricing and business practices; 7 staff reports were released until now, the 7th report analyzes financial data of the 14 largest drug companies in the world[1]. This report highlights the imbalance between research investments and the remuneration attributed to shareholders. The commission's work on pharmaceutical industry practices clearly demonstrates the existence of a drift away from the industry's mission of research and development by favoring profit maximization. Unfortunately, these practices seem to be common to all the companies studied[2].
A classic explanation for this drift lies in the need for pharmaceutical companies to satisfy their shareholders. Indeed, the Corporate law makes shareholder primacy, *i.e.* that corporations exist principally to serve shareholders, a foundation to the current business model. This argument is often used to absolve companies of their duty to the rest of their stakeholders. However, since a few years, a clear call to action[3] emerged: the societal impact of the registered companies has to be considered. Hence, a greater focus upon economic growth that is sustainable and inclusive for the majority of people[4] rather than a purely financial approach could become a key component of the new corporate behavior. This evolution will embrace a broad stakeholder approach larger than the pure shareholder focus that has driven corporate executive strategy in the past years, Indeed it is now widely accepted that shareholder value should be a goal, but also a result of a company serving its customers, serving its employees, and serving its communities[5].

> *"Shareholders do not own corporations. Contrary to the popular understanding, public companies have legal personhood and are not owned by their investors. The position of shareholders is like that of bondholders, creditors, and employees, all of whom have contractual relationships with companies but do not own them" (Tunjic, 2017)*

In the situation of the Pharma industry, in addition to this dimension of the corporate culture, the common belief that Health is a human right and does not belong to the consumer world has a major impact on the acceptable corporate attitude for this industry. One major consequence is that the Pharma has a societal duty to advance health trough developing innovative and efficient drugs, the best financial indicator of this commitment being represented by the resource dedicated to fund research & development. In the current work, we have found that an average of 20% of sales are allocated to fund R&D *versus* 25% to SG&A. This unbalanced allocation is triggering concerns and questions from many stakeholders regarding the ability of the classical marketing and sales model to really support innovation well. In other terms, how much should a company allocate to sales and marketing versus medical or research ? A model based on promoting products through a consumer lens seems to generate undue costs as it will not discriminate on the real value of the drug but on the capability of the company to trigger sales through marketing techniques. This approach does not differentiate between innovative companies and followers and introduces a bias in the market as investors are solely focusing on top line: "cash is king" may become a deadly moto for the Pharma industry. Furthermore, we can see than most of the Pharma companies are slowly switching their model to build strong partnership with patient associations, medical societies and are trying to build partnerships with the governments.

This new typology of business models emerges for biotechnology[6] to answer to this fast-evolving research environment: from closed or stand-alone business models, to open or networked business models. Open

[1] Drug Pricing Investigation. Industry Spending on Buybacks, Dividends, and Executive Compensation. Staff Report, Committee on Oversight and Reform, U.S. House of Representatives, July 2021, oversight.house.gov
[2] 116th COngress. Drug Pricing investigation, individual company analysis - report 1 to 6
[3] Business Roundtable, 2019b
[4] Fink, 2018;Grove & Lockhart, 2019
[5] McGregor, 2019b
[6] Towards a Typology of Business Models in the Biotechnology Industry. Preprint. January 2018. DOI: 10.13140/RG.2.2.14753.51046/1

innovation is the innovation paradigm shift that opens the way to this open business model by using partnership both on the research side and on the commercial side in order to mitigate costs. Open-innovation R&D model and network business models are seen to become the new standard in biotechnology. Last but not least, patient-centricity is a critical element of these new approaches. Similarly, the technology-driven ability to leverage data is supporting more informed treatment decision accelerating the shift from old drug to new generation treatment choices: "old" in these days can be counted in months, the adoption of the RNAm technology may be a good example of this new paradigm. Innovative patient-centred models[7] involves a shift from a product-driven approach towards a connected patient-centred healthcare system approach with a new continuum of patient engagement: crowd research, research partnerships, co-design programs, patient communities and focus groups. Diseases such as Alzheimer are a perfect example of this state of intricacy: the patient (with his family) is not a consumer anymore but a co-developer and an actor of his own health.

A model based on sharing information and partnering with stakeholders needs investments; supporting both the classical promotion model and this partneurial model is both ethically questionable and too restrictive on the bottom line with a dropping profitability. Analysts and Investors could ask for more clarity on the allocation of SG&A as well as defining a threshold for SG&A spent in order to maintain a healthy profitability. In the same spirit, the socially responsible investing (ESG) impacts the investing behavior by creating a mission-related investing approach to balance interests of shareholders with concerns of stakeholders. ESG investors tend to be more activist investors, moving to ESG-focused exchange-traded funds (ETFs) and looking at specific indicators as described above. Critics of the trend toward socially responsible investing consider that the latter detracts from profitable investments and makes both businesses and the financial markets operate less efficiently. For example, Friedman[8] argued that evaluating a stock should focus on the company's financial value and bottom-line profits and that socially responsible corporate expenditures are nearly always "non-essential expenses" that erode corporate and shareholder profits. However, when it comes to the Pharma industry, we could consider that investment in R&D and building this partnership model is an "essential expense" supporting both innovation and the social contract between the Pharma industry and its stakeholders. This should be seen as "the right thing to do" and over the long-term the best possible risk-adjusted return on investment.

How well do executive management and the board of directors attend to the interests of the company's various stakeholders: employees, shareholders, and customers ? Does the company give back to the community where it is located ? These two questions are central to any transformation of the Pharma industry and the balance between the investor's interest and the medical innovation transforming the community well-being is the foundation of this sustainable, ESR-friendly approach of the Pharma business. As soon as the market rewards a non-innovative company or a company with mercantile practices dedicated solely to creating profit in a purely commercial logic, the moral and social contract between the Pharma companies and the society is broken. Medicines and health cannot be considered solely as market goods insofar as they also have a common goods dimension due to their potential to transform the health of humanity as a global community. Investors should acknowledge this dimension and support companies with clear sustainable goals.

1 The new world: leveraging ESG to maintain the innovative edge of the Pharma industry

Investors and shareholders have a clear moral responsibility towards society to support, encourage and drive the evolution of the current Pharma business model. By allowing a clear cut between efficient research-based Pharma companies and consumer-based Pharma companies through an advantage on the financial market, investors will initiate this change. The moto "cash is king" could evolve to "innovation is king": capital should be redirected towards companies with a clear innovative signature, a differentiated pipeline and a strong reinvestment in R&D.

Various mechanisms could help to implement this change:

1. By having a detailed analysis on the SG&A spent, shareholders could optimise the overall return for all stakeholders; Indeed, a strong push towards non-related marketing & sales spent will accelerate the evolution of the Pharma model towards a medical & partnership-based model. The unknown behind this evolution is the impact on the top line; However, one could argue that this "new" model could at the same time:

[7] Saias and Kapadia, 2016

[8] The Social Responsibility of Business is to Increase its Profits. Milton Friedman. The New York Times Magazine. September 13,1970

(a) protect the overall profitability of the company and maintain both Dividends and SBB return by decreasing costs and optimising P&L,

(b) increase the relative spent in R&D to maintain the absolute spent in R&D or even increase it,

(c) decrease the budget impact on the health system by delivering more value to the society trough the partnership with all stakeholders.

Currently, marketing and sales have the lion share of the overall spent in most companies, as highlighted in the present work. However, pure players *i.e.* focusing on Pharma, could definitely maintain a competitive advantage by bringing on the market innovative drugs that could be priced accordingly to their added value to the health system and their potential to cure more and more diseases. These drugs will not need a heavy lift through marketing and aggressive sales techniques as they will bring the medical innovation expected by health professionals, patients and healthcare managers. The recent debate on Alzheimer *i.e.* the beta-amyloid hypothesis, clearly demonstrated that understanding the true clinical value of a drug is central to stakeholder's acceptance and could not be compensated by any marketing or sales approaches. Poor development leads to poor evaluation which then jeopardize access making commercialisation nothing more than a dream. On the opposite, a clear medical narrative based on robust clinical data supports the claim of innovation without the needs of heavy commercial investment but with a clear contribution to science and medical knowledge: shaping medical practice is always needed when facing true innovation.

2. The ESR approach has helped to steer the market towards sustainable investment. Simple changes of the current ESR evaluation criteria could accelerate this evolution:

   - A greater focus on SG&A with the concern to differentiate between investment in medical or in partnership with health authorities *versus* investment in sales & marketing techniques,
   - An important weight given to rNPV in order to value the pipeline and innovation more than short-term financial performance,
   - The definition of a basket of companies emphasising innovation when peer comparisons are made. This will help to distinguish between true innovative companies and consumer-oriented companies.
   - Last but not least, boosting the access to non-patent drugs through mechanisms like the non-profit Medicines Patent Pool[9] should be rewarded and included in the ESR criteria.

By shifting the weight given to short-term financial performance to a more sustainable approach for all stakeholders, the market will support the development of a sustainable Pharma business model. Governments could work alongside investors by implementing new legal and regulatory measures to enable the medical and patient-centric model to emerge.

An overarching financial issue is the need for the industry to raise enormous amounts of money to finance its research and develop drugs. But beyond this issue, scientific breakthroughs will play a major role in shaping the industry's business model: money should finance transforming science, there is no place for me-too. Broadly, the message from stakeholders is that the pharmaceutical sector needs to rediscover its true values and the sense of scientific and social purpose if the sector is to continue to thrive.

On the flip side, pharma companies who are at the top of their reputational game have shown that good governance can be a key driver of profitability and success. Analysts who measure reputation across numerous industries, have continued to find a strong link between reputation and a company's bottom line.

Six unique reputational issues that can vex a company's good name: ethics, innovation, safety, sustainability, quality and security. If a company isn't living up to their promises in these areas, its reputation will take a hit, which could anger stakeholders and lead to economic, and importantly for pharma, political losses. As a matter of fact, the pharma industry has grown increasingly interested in the issue of reputation in recent years — but companies often confuse it with marketing and public relations.

Companies that discuss global health issues at board level, and systematically work to improve the affordability and accessibility of their products for people living in lower-income countries as well as companies that develop breakthrough innovations are companies who will survive this paradigm shift:

> *"The general perception is that pharma creates just a win for the companies and not society,... We see that many investors and stakeholders now frame the conversation around the license to operate and the importance of pharma maintaining that societal contract so that their business is a win-win for both." (Access to Medicines Foundation)*

[9] https://medicinespatentpool.org/

2 Pricing effectively: combining a market approach favouring competition between innovative drugs with a "common good" perspective on non-innovative drugs

What issues will shape the immediate future of the pharmaceutical industry ? Stakeholders predict that financial pressures will dominate in the next three to five years. Fair pricing policies will be crucial, both for the people needing the drugs and for the sustainability of the companies.

However, the Pharma market is known for a high price volatility for innovative drugs. This is the consequence of a complex economic landscape in which supply and demand factors, financial incentives and legislation play a role. The firm commitment to reinvest cash in R&D, selling and marketing over distributing it to shareholders has direct implications to the willingness for external stakeholders to accept such price volatility and/or high price. When it comes to health, a pure competitive approach of market price seems to be leading to a common narrative that prices are too high due to a form of monopoly exercised by Pharma companies. Outside the US and now in the US, the concept that price controls improve social welfare and should overshadow business considerations leading to a more inclusive and humanistic process for determining prices, becomes the mainstream concept. However, this shouldn't threaten the industry to earn or premium prices for breakthrough drugs. The question of the "appropriate" or "fair" price is central to this debate, a common understanding among all stakeholders is that this price should support the right investment in research to develop breakthrough innovations and the adequate return to shareholders. A remaining problem is related to the fair business model supporting this growth: sales are supporting reinvestment in research for the next generation of innovations; but how can a Pharma company support sales'growth ? Is the Pharma model a consumer model and as such a model for which sales are being driven through promotion ? Currently, drug promotion plays a key role in maximising sales and the Pharma industry has faced much criticism for its promotional practices. Creating awareness among healthcare professionals and updating their knowledge on recent advances in treatment options are two important consequences of the right promotion approach. However, many stakeholders were concerned that drug promotion had gradually evolved to embrace aggressive marketing strategies and sometimes unethical business and scientific practices where the need for profit-making eclipses commitment to patient care and scientific exploration. This evolution is largely responsible for the poor reputation of the Pharma industry in the past few years and has definitely impacted drug costs by raising the average wholesale price with the evidence that aggressive marketing techniques induce overuse and overtreatment creating an artificial market expansion.
This period is now behind and it has clearly been understood that the Pharma industry will have to shift its promotion model with a greater support for the medical education programs run by academic institutes, the management of a network of external alliances and a better understanding of governments and health insurers. The connection to secondary-care specialists and patients' association will help to drastically change the promotion model. A process in which information is continuously disseminated in a series of non-controversial interactions will be the key to change the reputation of Pharma in order to ensure that all stakeholders are truly supporting its business model. This shift in the model will have direct impact on how investors could evaluate the main Pharma groups and reward them on the market.
A common theme[10] emerges: the new business model will connect in a triangle, "the academic world, the government and the industry". Governments can no longer merely be financing bodies, research centers should gather together to focus their effort, the industry should channel its effort into trajectories of long-term development. The time of competition derived from the classical consumer market ideology is over, due to the increased needs in health. The booming discoveries in research leading to new paths which are very capital-intensive increase the pressure on health systems making the economic pressure unbearable. At the same time, global trends towards open innovation, fast growing emerging markets and patent cliffs, provide a favorable environment for special medicinal products developed on highly specific technological platforms allowing to share innovation efficiently and with fair returns to all parts.

Having all parties around the table will definitely impact how drugs are priced: the concept of value-based pricing (VBP) is then becoming central. VBP implies that prices are mainly driven by a drug's value (value for money) and that the impact on budget (sustainability) is considered secondary to this value. VBP has been applied according to two models:

- direct models in which cost-effectiveness is a driver,
- indirect models or multi-attribute models characterized by greater discretion on the integration between

[10]Biopharmaceutical Entrepreneurship, Open Innovation, and the Knowledge Economy.James J. Gillespie, Gregory J. Privitera, Joseph Gaspero Journal of Innovation Management 7, 2(2019) 59-77

the different value domains and the evaluation of consistency between costs and value. In these models, cost-effectiveness is not a driver.

There are clear features to VBP:

- clear predefined link between added value and the premium price,
- transparency in the way added value is converted into a premium price,
- Measurable outcomes: value can only be calculated where there are measurable outcomes for the population being treated with a significant correlation with the product use.
- No generic alternatives available: if there are generic versions of the product already on the market – or soon to be available – the drug is competing with other products on costs rather than outcomes, reducing the relevance of the concept of value.

Other 'Nice to have' conditions have been described to enable the use of VBP:

- When clinicians and/or payers have concerns over the effectiveness and/or appropriate use of the product: in such circumstances, VBP enables pharmaceutical companies to show their commitment by demonstrating their confidence in the drug's efficacy in a real-world setting. This is also an excellent opportunity to gather clinical evidence and address potential efficacy concerns,
- When the market for the drug is highly competitive: VBP gives pharmaceutical companies an opportunity to differentiate their therapies and gain market share, through preferred or exclusive status on the formulary,
- When actual or potential sales volumes are significant: the substantial cost of administering VBP effectively can only be justified where the product can generate a high total sales revenue.

VBP is essentially an approach that reward companies based on their promises and make them true to their commitment to the society. Maintaining high prices for innovative drugs helps to fulfil the commitment made by companies to the market that high risks will be met by high rewards.

As described in this work, few countries are adopting this approach and even doing so most of the early adopters are facing methodological issues:

- lack of appropriate data,
- difficulties in agreeing on a common definition of value: clinical, societal, patient-centered,
- fear to increase budget deficit when moving from a pure commercial perspective to a more holistic value definition,
- necessity to overcome regulatory and legal limitations.

One other burning discussion concerns the "temporary monopoly" on sales granted to Pharma companies under their patent rights to help pay for drug development. In a paper published in 2020[11], researchers established that, in the U.S., the market exclusivity period was on average 12.5 years with a a fast market share erosion as soon as generics are made available on the market. Savings related to generic entry in the US have been estimated to be $313 billion in 2019; over the period 2010 - 2019, the U.S. saved $2200 billion through generic drugs. In Europe, the situation is more contrasted with a lower penetration of generic in most European countries when compared to the U.S. It is commonly accepted that there are opportunities for cost savings in off-patent drug markets in Europe and the United States through reduced delays in generic availability, stimulation of price competition, and increase generic drug use[12]. However, the current system is showing its limitations with some tools used by the Pharma industry such as secondary and divisional patents, patents thickets and patent linkage to delay the entry on the market of new generic and biosimilar drugs[13].
This calls for a new era of collaboration between Pharma companies and governments, one example of such collaboration around patents is the non-profit Medicines Patent Pool (MPP)[14]. The MPP is a Unitaid-backed international organisation founded in July 2010, it has been created to lower the prices of HIV, tuberculosis and hepatitis C medicines through voluntary licensing and patent pooling: the MPP negotiates public-health driven licenses with patent holders, and sub-licenses to generic manufacturers. This initiative was directed to support a more inclusive approach to fight HIV, tuberculosis and hepatitis C in the world and has been expanded to support the fight against COVID19. It worked well with many Pharma companies in these fields granted deals on their products to the MPP. It definitely demonstrated that in times of need, a consensus can

[11]Updated trends in US brand-name and generic drug competition Henry Grabowski, Genia Long, Richard Mortimer, Ani Boyo.J Med Econ. 2016 Sep;19(9):836-44. doi: 10.1080/13696998.2016.1176578. Epub 2016 Apr 20

[12]Comparing Generic Drug Markets in Europe and the United States: Prices, Volumes, and Spending. Olivier J. Wouters, Panos G. Kanavos and Martin McKee. Milbank Q. 2017 Sep; 95(3): 554–601.Published online 2017 Sep 12. doi: 10.1111/1468-0009.12279 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5594322/

[13]https://www.pharmaworldmagazine.com/barriers-to-generic-and-biosimilar-entry-on-the-market/

[14]https://medicinespatentpool.org/news-publications-post/covid-19-generic-pledge-press-release/

be found preserving both the business while balancing the cost for the health systems.
Another interesting debate occurred at the end of 2021 when Novartis reported that it was seeking to divest its generics subsidiary Sandoz. Following the announcement, the vice-president of the Swiss Socialist Party, Samuel Bendahan, tabled a motion for the Swiss government to acquire Sandoz. He argued that acquiring Sandoz will be both a question of critical importance to redesign the health strategy of the Swiss government as well as securing a safe and trustable source. Indeed the perspective of a public institution on profitability is rather different from the requirement of the pharmaceutical industry. Funding could be done through partnerships, and multiple financing strategies could be envisioned. The core belief behind this proposal was that the question of generics is above all a question of security of supply and quality of care; the proposal was not accepted.
These two examples could be seen as an attempt to consider drugs, when the patents are no longer in place or in an emergency situation, as "global public goods". The concept of global public goods refers to "programmes, policies, and services that have a truly global impact on health"[15]; we could argue that drugs fall under this category after their initial innovative phase if a common agreement was found to define non-patented drugs as non-rivalrous and nonexclusive. This will definitely lead to a debate as drugs will be seen as clear private goods at start (*i.e.* at the patent stage) but in the post patent stage could become impure public goods[16] or merit goods[17] trough the creation of new drug policies. An example of this approach was the idea proposed by Suerie Moon and al. when they proposed a R&D treaty as an effective tool to generate medical R&D as a global public good arguing that such an approach will institute a fair benefit-sharing for all[18]. The current proposal is less ambitious but will definitely be a good step towards a more collaborative area. We can hope, then, that the dream of a new social contract between pharmaceutical companies and each and every stakeholder will become a reality.

[15]Global Public Goods for Health, The Report of Working Group 2 of the Commission on Macroeconomics and Health, August 2002, WHO

[16]Global Public Goods for Health, The Report of Working Group 2 of the Commission on Macroeconomics and Health, August 2002, WHO

[17]merit goods are goods to which people should have access, regardless of their ability or willingness to pay, because the goods display important externalities of public concern (such as health in our situation)

[18]Innovation and Access to Medicines for Neglected Populations: Could a Treaty Address a Broken Pharmaceutical R&D System? Suerie Moon, Jorge Bermudez, Ellen't Hoen, PLoS Medicine — www.plosmedicine.org 1 May 2012 — Volume 9 — Issue 5 — e1001218