Evaluating Social Pharmaceutical Innovation as a Means of Reducing High Therapeutic Costs

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On my honor as a University Student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments

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Introduction

Merck, the now multinational pharmaceutical giant, first began as a quaint apothecary shop in Darmstadt, Germany during the late 17th century. Selling little more than morphine, quinine, and strychnine, the drug discovery and production pipeline was simple and left much room for experimentation and very little for safety (*Fundamentals of Drug Development*, n.d.). It was not until nearly 300 years later when Congress passed the U.S. Food, Drug, and Cosmetic Act, that the first form of regulatory framework in the U.S. for conducting pre-market safety evaluations for new drugs would be created. This act, as well as its amendments, helped lay the groundwork for the pharmaceutical research and development (R&D) process scientists adhere to today, establishing the need for proof of safety and "substantial evidence" of efficacy (Commissioner, 2023). Nowadays, for Merck to bring a new drug to market, it would cost around an estimated $2.6 billion and take around 10-15 years to complete the R&D phase (Morgan et al., 2011; O'Donnell, 2019).

Within the R&D pipeline, clinical trials are the most laborious and costly stage, accounting for around 80% of the total expenses (Parker-Lue et al., 2015). It is an expensive investment to establish the trial infrastructure, gather materials and participants, and ultimately conduct these trials, and in the case of developing treatments for rare diseases, these costs can become exponentially greater. To elaborate, a primary reason for these increased expenses is because of the inherent rarity of the illness, there is a much smaller patient population as compared to more prevailing aliments. More resources must be invested into recruiting participants and gathering data for the trials, consequently driving up R&D costs (Fellows & Hollis, 2013).

Since the participants of the pharmaceutical sphere operate as for-profit businesses, they naturally have a duty to their shareholders to generate a return on their investment in the R&D of new therapies. But as the cost of drug development continues to rise, financial studies suggest that it has reached a point where companies may no longer be monetarily incentivized to invest in new drug discovery since their rate of return is approaching nearly 0% (O'Donnell, 2019). To compensate, many firms have resulted to simply increasing drug prices. This becomes an alarming issue when specifically considering therapies for the treatment of rare diseases. Since there is a limited market size, the heightened costs of drug development is spread across such fewer patients, causing pharmaceutical companies to charge even higher prices to patients and insurance companies in order to make a return on investment. In fact, these therapies can cost over $100,000 per patient per year (Fellows & Hollis, 2013). With these prices continuing to rise, it threatens the affordability and accessibility of these medications that dramatically improve a patient's quality of life.

Thus, it becomes apparent there must be another way to approach the issue of diminishing returns in order to maintain innovation incentives besides merely raising drug prices. The aforementioned U.S. Food & Drug Administration (FDA) regulations were created with the intention to protect consumer safety and ensure a standardized approval process, however this rigid framework has divided the pharmaceutical industry into distinct sectors. This division of the industry discourages collaboration between fellow pharmaceutical firms and as well with the public sector. Disrupting the current innovation practices of the pharmaceutical industry to promote collaboration will help to create harmonization between the various public and private sides of the industry (Siddiqui & Rajkumar, 2012). This increased sense of congruity will

promote research for rare disease therapies through pooling resources together, streamlining R&D efforts, and ultimately streamlining regulatory processes.

Promoting open collaboration and public-private partnership is one of the main pillars of the science, technology, and society (STS) concept of Social Pharmaceutical Innovation (SPIN). The purpose of SPIN is to reframe the already firmly established innovation pathways of the pharmaceutical industry (Douglas et al., 2022). This deviation from traditional practices will drive the creation of safe, efficient, and readily available therapies, catering to unmet needs of rare disease patients, prioritizing social impact over market-driven motives. Thus, in this paper I will formally define SPIN, elaborate on the main strategies of the framework, and propose methods for assessing the strategies' effectiveness.

Current Practices

There are five stages to the FDA drug approval process. First is drug discovery and development, where initial research is done to discover the target therapies that are worth investing in bringing to market. This primary phase typically lasts around two to five years. Followed by one to two years of pre-clinical testing, and once basic safety requirements are met, about five to seven years of clinical trials. Once all the pre-clinical and clinical data is gathered, the findings are presented to the FDA in the form of several hundred paged reports for potential approval. Now out of the hands of the pharmaceutical company, the final decision from the FDA can take anywhere from six months to two full years. Even after a drug has been fully approved and is on the market, the FDA will continue to monitor the safety and efficacy of the therapy to ensure pharmacovigilance (Commissioner, 2020).

Within the clinical research step there are four sub-phases that progressively require more time and more participants. By phase four, several thousand participants with the disease the

drug is intended to treat are needed (Commissioner, 2020). A disease is only designated as rare by the FDA if the condition affects less than 200,000 people in the U.S., thus one can see the logical limitations that may arise when conducting clinical research for the treatment of rare diseases (Commissioner, 2022b). With the increased complications for rare disease therapy R&D and limited market size, a tradeoff is generated between increased pharmaceutical pricing and innovation in the industry. To elaborate, these pharmaceutical companies are incentivized to innovate and invest in finding novel therapies in the treatment of rare diseases only if they can sell the resulting product for a price that will generate a return on investment (Parker-Lue et al., 2015).

Previous attempts to balance innovation and drug prices include the Orphan Drugs Act of 1983. This legislation includes incentives for the development of rare disease therapies, or orphan drugs, such as 7 year market exclusivity agreements, tax credits of up to 50% of R&D costs, and access to R&D grants (Commissioner, 2022a). Although this act has been successful in stimulating research in the rare disease area, there are limitations to its impact. A pharmaceutical company may see the 7 year market exclusivity and be motivated at the prospect of being the sole supplier of an orphan drug and thus invest in its development. However, this market exclusivity inherently leads to a lack of competition, allowing the company to practically set the price at whatever level will generate a return on investment. Monopolizing the market for the treatment of a specific rare disease not only leads to increased prices, it also strips away any future incentive for the company to continue to innovate and increase the quality and efficacy of the drug (Siddiqui & Rajkumar, 2012). The desire to be the lone firm manufacturing an orphan drug and the intellectual property rights that stem from it limits a culture of collaboration between pharmaceutical companies. Information sharing and synergizing research abilities

would help streamline the R&D process and bring rare disease therapies to market faster and at a more affordable price. Yet this growing sense of pre-market competition is placing importance on profit-generating motives over the well-being of patients and is unsustainable for the healthcare industry (Douglas et al., 2022).

Formally Defining SPIN

SPIN is defined as the use of novel forms of collaborative approaches, initiatives, policies, methods, and/or designs engaging various stakeholders that diverge from traditional pharmaceutical innovation practices (Douglas et al., 2022). The various stakeholders include pharmaceutical companies, researchers, healthcare providers, patients, advocacy groups, and the federal government. The ultimate goal of the SPIN framework is to disrupt the current innovation pipeline such that these groups can all work together to address unmet medical needs and improve access to safe, effective, and affordable medications for the treatment of rare diseases. For the purpose of this paper I specifically explore three avenues of disruption: promoting collaboration and harmonization between pharmaceutical companies and regulatory agencies, modifying the economic incentive schemes for developing rare disease therapies, and developing new models of affordably pricing these therapies. These three strategies are considered a part of the SPIN framework as they are decidedly not part of the status quo in current pharmaceutical operations and, importantly, take an approach that will help balance the needs of patients with the innovation incentives that are necessary to spark successful R&D efforts.

Introduced as an STS concept in 2022, SPIN is adapted from the social innovation (SI) framework through the combined efforts of researchers in the areas of social sciences, law, and public health (Douglas et al., 2022). SI itself is defined by scholars as "...a complex process of

introducing new products, processes or programs that profoundly change the basic routines, resource and authority flows, or beliefs of the social system in which the innovation occurs. Such successful social innovations have durability and broad impact (Westley & Antadze, 2010)." These innovation frameworks are built upon the phenomenon observed in STS research that there is an innate inseparability between the social and technological aspects of the world we live in. These two aspects continually co-develop and mutually shape one another. Technological change is not brought on by a simple linear progression. Instead, this evolution is multi-directional and takes place over many iterations (Douglas et al., 2022). With this, it is clear to see where the rigidity of the current practices of pharmaceutical innovation misalign with STS practice and how the application of SPIN can be used to correct this issue and promote well-being in both an economic and medical sense.

Using SPIN to emphasize the need for collaboration, transparency, and a strong commitment to improving the health of patients will help to create a more sustainable and equitable healthcare system, especially in cases of rare disease treatment. With this being a newly fashioned way of approaching pharmaceutical innovation, it is important to conduct research such as this and determine appropriate metrics to quantify the predicted success of SPIN. By outlining the distinct strategies and providing explicit quantifiers of success, the relevant stakeholders will then be encouraged to adopt SPIN practices and positively impact the pharmaceutical industry.

Applications of SPIN

Collaboration and Harmonization

As previously mentioned, cultivating a standard of collaboration between the various stakeholders of the healthcare industry is a crucial aspect of SPIN. Research on drugs that were

approved for market by the European Medicines Agency (EMA), the European equivalent to the FDA, from the years 1995-2007 revealed that company size and developmental experience are critical factors in determining whether a pharmaceutical will successfully be approved for the market (Regnstrom et al., 2010). Following this logic, combining the infrastructure, resources, and knowledge of several firms will positively impact the research efforts of investigating rare disease treatment, streamlining the lengthy R&D. Additionally, complying with guidance from regulatory agencies was also a strong indicator of eventual market approval. This accentuates the importance of collaboration between the both the public and private sectors, further helping to streamline the approval process and reduce developmental expenses. Furthermore, harmonizing regulatory processes across various countries and their respective regulatory bodies can also help to increase the agility of the pharmaceutical industry by allowing faster approval to many areas of the world all at one time. In summary, current literature shows the promising outlook of promoting alliances between pharmaceutical companies, between these companies and regulatory agencies, and also between various regulatory agencies for increasing the likelihood of an orphan drug being approved for market while decreasing the necessary time and effort (Rollet et al., 2013).

Prize Funds

A patent is the traditional innovation incentive, giving exclusive rights to the inventor to manufacture and sell their invention in the market for a specified time period. The reasoning behind this is to allow the inventor to make back the money invested in the R&D of the product and any further profits will then go on to finance the development of future innovations. In other words, the patent rewards an inventor for their creativity, society is rewarded with a new product that adds value, subsequent inventions will be financed, and the economy as a whole is

benefitted. Although this incentive scheme works in most industries, the pharmaceutical industry is unique in that, since drug R&D can take up to the entire lifetime of a patent (20 years), there are certain inefficiencies in the market that inhibit patents from providing the previously mentioned benefits. There then becomes an incentive to innovate based on the potential of profit as a prime motivator as to fulfill fiduciary responsibilities. The consequence of this is that it shifts the focus of pharmaceutical R&D on innovations that have the greatest market potential, regardless of their potential in increasing social welfare (Kim & Schwartz, 2006). An approach outlined by SPIN would be to shift the incentive model away from the historical mode of awarding patents and instead promote innovation through the awarding of prizes or granting compulsory licensing (Douglas et al., 2022).

To begin, the prospect of awarding prize funds for the successful development of orphan drugs can be combined with the current practices of the FDA to award research grants. These prize funds would help to further incentivize rare disease treatment development by, similar to the grants, helping to offset the costs of the R&D (Douglas et al., 2022). A proposed mechanism for determining the amount of prize to be awarded would be based on calculating the incremental therapeutic value of the newly developed drug in relation to the next best alternative treatment for the same condition. Specific therapeutic value can be quantitatively measured by the drug's impact on a patient's health outcomes. Objective measures of health outcomes include quality-adjusted life-years (QALYs) or disability-adjusted life-years (DALYs) (Kim & Schwartz, 2006). The first, QALYs, refers to the number of years that would be added to a patient's lifespan by a medical intervention then adjusted for quality of life. Thus the metric takes into account both the gained life expectancy and the quality of life. QALY is computed by multiplying the number of additional years by the quality of life value, Q. The value of Q ranges from 0.0 to 1.0

where 1.0 represents perfect health and 0.5 represents a quality of life that is 50% of normal (Siddiqui & Rajkumar, 2012). The second metric, DALYs, is computed by summing up the years of the patient's life lost due to premature mortality (YLLs) and the years lived with a disability (YLDs). So, one DALY signifies the loss of one year of full health and can be used to compare the impact of burdens of diseases with varying degrees of mortality and disability. (*Indicator Metadata Registry Details*, n.d.). These metrics are already used by the World Health Organization (WHO) and insurance companies to analyze and draw comparisons on the impact of diseases and the cost-effectiveness of current medical treatments and innovations.

The QALY metric is particularly helpful in calculating the incremental cost-effectiveness ratio (ICER) which can be subsequently used in calculating the exact amount that should be awarded as a prize. ICER can be calculated by finding the difference between the cost of the new therapy and the standard/next best therapy and dividing this value by the difference in QALY associated with each therapy (Siddiqui & Rajkumar, 2012). Ideally, the amount that should be awarded as a prize will be between 10 to 20 percent of the predicted cost savings or societal benefit of the new therapy. This will result in a reward that is less than the return that would be theoretically realized from having patent exclusivity of the market, but yet still suitable for properly incentivizing drug R&D. Circumventing the lengthy patent approval process will also help further stimulate innovation in the industry as the scientific knowledge gained from the development of the product will enter the public domain more quickly, facilitating the faster discovery of ensuing innovations. The prize award creates a more immediate return on R&D investment and reduces the financial risk and opportunity cost of the market exclusivity model. To elaborate, typically when a patent is awarded for a new therapy, the pharmaceutical company then must invest even more money into advertising and market campaigns for the drug, further

extending the timeline of when a possible return on investment may be seen. The money earned from the prize in that moment will be innately worth more than any money generated in the future from said campaigns simply based on the principle of the time-value of money (Kim & Schwartz, 2006).

Compulsory Licensing

Similarly, the granting of compulsory licenses to pharmaceutical companies is another promising SPIN strategy for driving down the prices of these rare disease therapies while still promoting innovation in the industry. Compulsory licensing in the pharmaceutical industry refers to the practice of the federal government authorizing a company to produce an already patented drug. This essentially enables the creation of a generic before the 20 year market exclusivity of the patent expires (Qunaj et al., 2022). Allowing for the development of generic versions of expensive drugs prompts innovation as it may result in a drug that has increased clinical outcomes, safety, and overall efficacy as compared to the original version. Furthermore, introducing generic versions of the existing therapies helps to increase competition in the market, naturally causing a decrease in prices with consumer choice being greatly increased (Dranove et al., 2014). In summary, addressing the role of intellectual property rights in the pharmaceutical industry through the SPIN approaches of awarding prize funds or compulsory licenses is a worthwhile strategy for balancing the need for incentivizing and exciting innovation in drug development with creating affordable prices for rare disease treatments.

Valued-Based Pricing

The final avenue of disrupting the current practices of the pharmaceutical industry that this paper will explore is the alteration of how specific orphan drugs are priced. The value-based pricing model uses the value drugs bring in terms of improved health outcomes and quality of

life. Computing the value-based price of an orphan drug and comparing this to the current industry prices will give valuable insight into how this SPIN strategy can disrupt the conventional pharmaceutical pricing models, meeting patient needs at more affordable rates (Douglas et al., 2022).

In order to make these value-based calculations, researchers must first conduct cost-of-illness (COI) studies. These studies take into account both economic and epidemiologic data, considering the volume of data resources, the quality of the resources, direct costs (medical and non-medical), indirect costs, intangible costs, prevalence and incidence of the disease. The ultimate takeaways of COI research is the identification of primary cost drivers and identification of the relevant stakeholders that bear the most economic burden of a disease, a consideration often neglected by alternative economic evaluation methods. The spread of burden of the disease revealed by these studies can then be used in the decision-making of how pharmaceuticals are priced (Armeni et al., 2021).

A 2021 literature review performed COI research on hemophilia, fragile X syndrome (FXS), cystic fibrosis (CF), and juvenile idiopathic arthritis (JIA) to assess each diseases' burden had shifted over the previous 15 years through the introduction of novel treatments. In the case of hemophilia, it was revealed that clotting factors accounted for about 90% of the direct costs of managing the disease. The overall cost of treating hemophilia remains high because as novel therapies become increasingly available, direct costs of the disease have become the main cost driver, typically ranging from 77-97% of the total costs. The COI reveals that FXS is a disease where the burden of disease lies not just with the patient, but also with the patient's caregivers. In fact, a study revealed that 60% of parents with a child who has FXS have had to change work hours or quit jobs entirely due to their child's disease. Since FXS leads to intellectual disability,

learning and behavioral challenges, additional treatments beyond just medical are needed. Speech and language therapy, occupational therapy, special education, behavioral interventions, and genetic counseling add to the cost and burden of the disease. The COI of JIA is similar to FXS in that a large burden of the disease falls upon the patient's caregivers. Lastly, as causative treatments for CF have been developed, the prices of the resulting drugs have increased dramatically. In addition to the higher prices of these novel therapies, it has also led to increased indirect costs of the disease as life expectancy of CF patients increases. Although life expectancy for the patients is extended by these therapies, as the patient ages the disease severity intensifies leading to these higher direct and indirect costs (Armeni et al., 2021).

This literature review helps reveal the importance of conducting COI in the case of rare diseases as main cost drivers can vary greatly across various diseases. Thus, basing the pricing of orphan drugs to follow the model of pricing for more prevalent ailments with many forms of treatment ignores these differences in cost drivers. Understanding the main cost drivers can show where the burden of disease primarily lies and thus pharmaceutical companies can use it to inform drug pricing through a value-based approach to help drugs become more affordable for patients. Instead of a uniform pricing model for diseases of varying prevalence, using value-based pricing will help to tailor pricing schemes to a specific therapy's market segment and clearly demonstrate the resulting health and economic benefits of the developed treatment.

Evaluating the Effectiveness of SPIN

As previously mentioned, SPIN is still a novel concept in the pharmaceutical industry and thus not yet enforced or widely adopted as a standard of operation for firms. Therefore, determining metrics that will quantify the effectiveness of SPIN strategies is important for making this framework the status quo and holistically understanding the impact. First, no

changes to the pharmaceutical industry will be entirely successful without heavily involving patients and advocacy groups in the drug R&D process. Asserting their insights, priorities can be set for research to ensure that their immediate needs are valued and addressed by these companies. Thus, the use of patient surveys is a direct mode of evaluating the effectiveness of SPIN as data on how mortality rates, life expectancy, quality of life, and patient reported outcomes (PROs) can be comparatively analyzed from before and after the adoption of SPIN. This information from patients can also give an insight into the economic impact through the calculation of previously mentioned empirical metrics such as QALYs and ICER.

On the industry side, the effect of SPIN on the innovation pipeline can be quantitatively assessed through R&D innovation metrics such as an increased rate of production of patents and the discovery of new molecules. These key performance indicators (KPIs) will help to demonstrate how SPIN has improved the robustness, infrastructure, and diversity of the R&D efforts (Fellows & Hollis, 2013). In the same vein of using patient surveys for collecting data on the economic and health impacts of SPIN, surveys could also be conducted by pharmaceutical companies to gauge how embracing this novel framework has been received by their scientists and R&D departments. Using SPIN to reshift the corporation's interests to emphasize delivering results to patients over simply maximizing the returns on investments will also help to improve company morale (Douglas et al., 2022). Employees will feel a sense of professional fulfillment for contributing to the operations of a mission-driven firm. Scientists are intrinsically motivated to solve complex problems in their field of study. Enabling them to focus more on creating these meaningful contributions to patients will further foster this motivation and thus improve efficiency and innovation within the company. In summary, administering employee surveys can

be valuable for understanding how SPIN has influenced changes in the internal culture of pharmaceutical companies and has disrupted their existing innovation pipelines.

Conclusion

The drug development pipeline in the U.S. is an expensive, rigid, and lengthy process. The current atmosphere of innovation and operations in the industry is unsustainable for both the producers and the consumers. Drug prices are exponentially increasing while, simultaneously, returns on R&D are nearing closer and closer to zero (O'Donnell, 2019). This is exacerbated in the case of the development of orphan drugs due to complications in gathering data for clinical trials, further escalating the investment needed for successful R&D. Furthermore, the current lack of harmonization between the various regulatory bodies and the pharmaceutical firms producing these therapies poses a blockade in the R&D process (Parker-Lue et al., 2015).

It is essential for the industry to find a new approach to balancing the needs of pharmaceutical industry stakeholders, regulatory agencies, and patients. Finding an equilibrium between the economic incentives for pharmaceutical innovation and development of orphan drugs and ensuring these life-saving drugs are not financially inaccessible to their intended market. The prospect of companies and regulatory agencies adopting SPIN strategies, primarily adopting a culture of collaboration with fellow firms, awarding prize funds or compulsory licenses, and taking a value-based pricing approach is a promising avenue towards improving transparency and decreasing the high drug prices that patients face while still allowing pharmaceutical companies to fulfill their fiduciary duties.

The performance in the application of these specific SPIN strategies can be then assessed through various empirical metrics with data gathered from regularly conducted patient surveys. This can provide powerful insights into how mortality rates, life expectancy, quality of life and

PROs have changed over time with the implementation of SPIN. Economically, the impact can be understood by calculating QALYs and the ICER of newly developed therapies. And from the perspective of company operations, determining the change in the rate of production of patents and the discovery of new molecules can also be a powerful metric and KPI in understanding the effect SPIN has on the innovation pipeline of rare disease therapy R&D.

In conclusion, in this paper I have outlined how employing SPIN as a standard framework in the operations of pharmaceutical companies and regulatory bodies will successfully shift the motives of the industry away from primarily profit-driven to focusing more on improving patient's lives.

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