UNDERSTANDING THE BUSINESS OF VACCINES: COVID-19

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Abstract:
Both the first vaccine produced to combat COVID-19, and the country of its production would not only have the financial edge over other countries, but also geopolitical supremacy. The current statistics of COVID-19 reported around hundreds of thousands of deaths in the world and counting. This article deals with the vaccine development process and costs related to COVID-19 and also highlights the significance of open alliances in the biotech sector in a post-COVID regime. This article focuses on ways in which the challenging worldwide health crises of the current pandemic can be overcome in distinctly local ways through open, transparent, and collaborative practices.

Keywords: COVID-19, vaccine, open alliances, biotech sector, pandemic

INTRODUCTION

Most infectious diseases are of three types: endemic, epidemic and pandemic. Endemic diseases are linked with a particular country and have a constant presence e.g., malaria which is endemic to parts of Africa. Epidemics affect a large number of people within a community, region, or population while pandemics are epidemics spread over multiple countries or continents, an instance being the current COVID-19 pandemic. China suffered from SARS in 2002 caused by the SARS-CoV-virus. It was an epidemic that affected 26 countries with a global death toll of ~8000 individuals. This stands in no comparison to the current statistics of COVID-19, which has reported around hundreds of thousands of deaths in the world and counting. SARS and COVID-19, both have demonstrated similar signs and symptoms. Hence, a major question arises – why did COVID-19 turn into a pandemic in 2020 while SARS had a local effect in 2002?

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The economic prosperity of China has increased several-fold from 2002 to 2019, for which the chief indicator has been GDP per capita, according to the World Bank. With an increase in work and tourism-related mobility across countries and continents, the economy has played a key role in converting an epidemic into a pandemic. Hence in a globalised flat world, chances of the pandemic are more frequent; COVID-19 is just the beginning! After COVID-19 turned into a pandemic, every media story has been discussing the on-going vaccine development processes, costs, and related scientific and societal issues.

In this article, we try to fathom the costs and procedures of vaccine development, collaboration among pharma giants for the same, its global market and strategic implications in the context of COVID-19.

VACCINES: COST AND THEIR DEVELOPMENT PROCESS

The science behind vaccine development is based on the dictum that 'better prevent the disease before its infection, if not possible, make the causative organism ineffective inside the human body'. Vaccines are ineffective or dead, fully or partly bacteria or viruses. According to the Centre for Disease and Prevention, there are at least 26 vaccines used in the USA for humans which are administered at recommended age-groups, while a few are needed before travelling. According to a marketing consultancy firm, the global vaccine market was valued at approximately 31 thousand million USD in 2016 and it will reach up to 65 thousand million USD in 2023.

Two major constraints for vaccine development are: (i) longer time-frame from the preclinical phase to FDA registration and (ii) productivity gap or invested resources not matching the expected product turn over. Thus longer time frame and productivity gaps are associated with the pharmaceutical and biotech industries and are common features in vaccine development. Vaccine development undergoes several stages as illustrated in Figure 1.

1. *Exploratory stage* (research phase; where scientists identify antigens, synthetic or natural to treat the disease), 2. *Preclinical stage* (whether the candidate vaccine will produce immunity or not is determined at this stage using cell or tissue culture or through animal testing), 3. *Clinical development* (here the candidate vaccine goes through three stages of human testing: Phase I, II, III), 4. *Regulatory review and approval* (once all the clinical trial phases are cleared, a license application is submitted to the regulatory authorities for approval), 5. *Manufacturing and quality control* (mass quantities of vaccines are manufactured after the regulatory review and safety; performance and effectiveness of an approved vaccine are monitored for quality control).

The clinical development phase is a three-phase process. In Phase I, one or two dozen recruited patients receive the trial vaccine, which upon validation goes up to a thousand during phase III of the trial. In general, an average vaccine from its pre-clinical phase takes over 10.7 years to complete the entire development tenure and has an average 94 % chance of failure (Pronker et al., 2013). Therefore, there is uncertainty and little agreement on R&D outcomes across global vaccine development institutions. New vaccine development requires a capital investment ranging from 500 million USD for the least complex one to a billion USD for the most sophisticated ones (Pronker et al., 2011). A published report based on a portfolio of 11 epidemic infectious diseases that also includes the MERS coronavirus and SARS would cost a minimum of 2.8-3.7 billion USD until the phase II trial (Peeri et al., 2020). This implies that the cost of a single epidemic infectious disease vaccine from preclinical trials through the end of Phase II is 31-68 million USD (14 -159 million USD range), assuming no risk of failure (Gouglas et al, 2018). Post-covid, **in silicon, automation, & artificial intelligence** (scientific experiments or research conducted or produced using computer modelling or computer simulation) can facilitate recruitment and monitoring of trial patients remotely, but so far radical shifts in trial designs have not taken place.

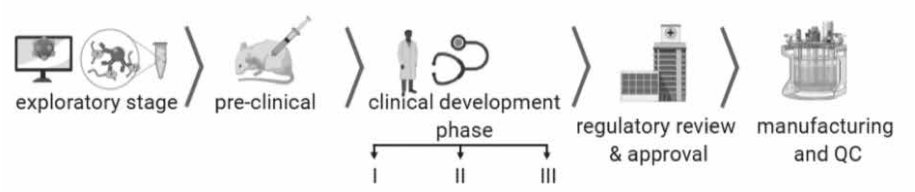

Figure 1. Development of a Vaccine

COVID-19 being a pandemic, its first vaccine and its country of origin would not only have the financial edge but also geopolitical supremacy. As per the COVID-19 vaccine and therapy tracker, *BioRender* there are a total of 103 vaccines in development, out of which 88 are in preclinical development and 15 are in human trials. Globally, the COVID-19 vaccine market is segmented based on several categories: infection type, vaccine type, product type, administration type, patient type and lastly, firm type and the region. Therefore, plenty of big pharma companies such as Roche, Gilead, GSK, Pfizer to name a few are actively involved in the development of vaccines by partnering with governments agencies and large and small organisations across continents and communities. Massachusetts-based Arrakis Therapeutics and Roche are bundled in a co-development deal on RNA-targeting small molecules worth 190 million USD.

The Coalition for Epidemic Preparedness Innovations was formally launched at the 2017 World Economic Forum in Davos with an initial investment of 460 mil-

lion USD. The governments of Norway, Japan, Germany, The Wellcome Trust, Gates Foundation, and India's Department of Biotechnology are a part of the consortium and working towards advancing affordable vaccines to help contain the outbreak. MERS-CoV and SARS-CoV-2 (causative agent of COVID-19) are very similar in structure and symptoms (Ehreth, 2003). According to *Nature, a* USA-based biotechnology company *Moderna* has exhibited positive results tentatively to an expectant world but the firm has adopted a very different approach for the production of the vaccine. Similarly, the University of Oxford is working in collaboration with the Serum Institute of India for a promising under-trial COVID-19 vaccine to be ready by late Fall 2020. The Israel Institute for Biological Research, Ness Ziona, has completed a round of tests of its vaccine on rodents and hope to finish in a year or even earlier. Mimicking a public-private partnership collaboration that happened 30 years ago to combat the HIV/AIDS crisis, a similar consortium is currently led by the National Institute of Health (NIH) and the Foundation for the NIH. It is formally known as "Accelerating COVID-19 Therapeutic Interventions and Vaccines" or ACTIV and involves global health regulatory agencies, philanthropic organizations, non-profits, leading biotech companies and renowned academic researchers. The ACTIV initiative of the NIH provides a platform for infrastructure, subject matter expertise and/or funding to identify, prioritize and facilitate some of the most promising candidates into clinical trials.

PHARMA AND BIOTECH FIRM ALLIANCES IN A POST-COVID-19 WORLD

The biotech industry should be studied from a dynamic capabilities perspective as it paves the way for theoretical frameworks to comprehend the diffusion of technology at an international level. The two aspects of dynamic capabilities are: geographical and organizational (Madhok & Osegowitsch, 2000). The former deals with locational embeddedness of technology development and commercialization. The latter deals with individual firm's boundary choices and their collective impact on technological flows between countries in the aggregate. Both aspects help firms to seek, build, and exploit the technological and competitive advantage. Dynamic capabilities have evolved from a resource-based view (RBV) and suggest that the firm needs to develop new capabilities to identify opportunities and to respond quickly to them, in contrast to RBV which suggests that firms in the same industry perform differently as they differ in resources and capabilities and exhibit competitive advantage.

The dynamic capabilities lens provides insights into the "capability development and diffusion process within the firm as well as across firms and countries" (Madhok & Osegowitsch, 2000). There are enormous internal complexity and perceived coordination challenges in managing biotech alliances, especially if the partner interdependence is present to a greater degree. Both upstream and down-

stream aspects of the value chain have noteworthy, although different, implications in the context of biotechnology (Rothaermel & Deeds, 2004).

R & Dalliances with established pharmaceutical firms and new biotechnology firms (NBFs) are common phenomena in the health industry. These alliances are conducted to produce a U.S. Food and Drug Administration-approved drug so that it eventually enters the market. In these alliances, the research component of the drug is provided by the new biotechnology firm (NBF) and the development component of the drug is provided by the established pharmaceutical firm. Established firms acquire novel technologies from the NBF (Rothaermel & Deeds, 2004) and the disease-specific development skills of the experienced pharma are accessed by the NBFs (Macher & Boerner, 2006). The development and regulatory experience needed to transform a novel technology into a fool-proof drug are generally lacking in NBFs (Diestre & Rajagopalan, 2012). The pharmaceutical company has the required set of complementary skills such as development, manufacturing and marketing needed to exploit any appropriated novel discovery. Then there is a dilemma of 'value creation vs. value appropriation' in these R&D alliances. Within an R&D alliance, when the big pharma provides resources to the NBF (biotech firm) instead of NBF's knowledge, then two probabilities exist: (a) furthering NBF's value resulting in value creation and (b) furthering risk to the NBF resulting in value appropriation. NBFs always face a dilemma in selecting the right alliance of whether the selected pharma company will help create value or appropriate value. For an alliance to happen, both parties need to mutually select each other, even though NBFs might practice some discretion on their part and not select pharmaceutical firms unilaterally. On the contrary, pharmaceutical firms can be quite heterogeneous in their alliance preferences, preferring one NBF over the other (Adegbesan & Higgins, 2011). There is a huge risk of appropriation as the development process calls for sharing proprietary knowledge owned by the NBF with the big pharma. Asymmetry in the partnerships and the risk of appropriation is higher for the NBFs as compared to the pharmaceutical firms. Even patents are not enough to protect the tacit and difficult to codify internal know-how of the NBFs, and in most cases, they are not even able to enforce their patent rights in an infringement suit. Value can be easily created if the pharma company shares the technological similarity and development experience needed to transform the research into a marketable drug with the NBF. Technology relatedness enhances the absorptive capacity (Cohen & Levinthal, 1990) which helps assimilate and understand the discovery of NBFs, thus enhancing the incentives for value creation in R&D partnerships. The opportunities in these alliances are dyad specific, which implies that opportunities are contingent on the unique characteristics or attributes of pharmaceutical firms and NBFs (Diestre & Rajagopalan, 2012).

Big pharmaceutical firms have enhanced alliance-management capabilities as they deal with different types of partners thus engaging in different types of

alliances. Different types of partners transfer different types of knowledge in these alliances. The big pharma allies with the NBF, provided both of them share dominant logics, knowledge repository and organizational logics (Rothaermel & Deeds, 2006). According to Baum et al., (2000) NBFs look forward to three types of alliances: *Upstream* alliances involving universities, research institutes, government labs, and industry associations, *Horizontal* alliances involving other biotechnology firms, and *Downstream* alliances involving big and established pharmaceutical, chemical and marketing firms.

Most alliances between NBFs and established pharma are initiated when the candidate molecule has moved past the pre-clinical testing and is ready for clinical trials. In other words, when the new drug candidate has undergone substantial development, then the tacitness, ambiguity and complexity aspects of the alliance is well-taken care of. Repeated engagements with NBFs facilitate the alliance management capabilities of big pharma. The entire range of alliance management, right from partner selection to alliance termination, is a build-up of accrued alliance experience effects. Repeated partnering and the ability to effectively manage multiple alliances over time foster performance in subsequent alliances, thus creating and sustaining competitive advantage. For example, Gilead has an established alliance-management process which can be simultaneously both defined and flexible. The team responsible for managing and optimizing several drug development alliances and commercialization (as illustrated in Figure 2.) comprises the Associate Director (responsible for integration between the two alliance partners), the Director (responsible for day-to-day alliance management) & the Senior Director (responsible for high-end support and insights).

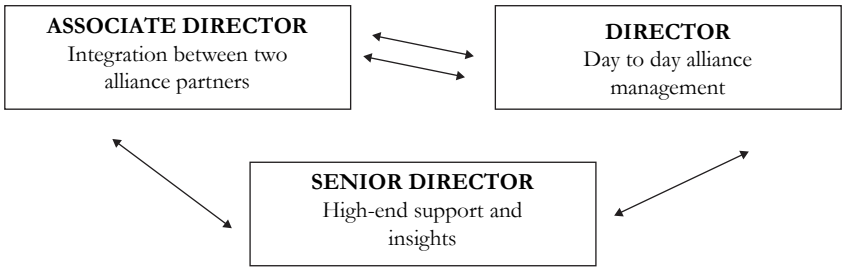

Figure 2. Typical Alliance Management Process and Team in a pharmaceutical company.

There are a lot of variables that contribute to the development and maintenance of alliance-management capabilities for big pharma, such as selecting the right NBF, absorbing the discovery, developing trust, codified routines (Dyer & Singh, 1998) and so on. Alliance management capability is a multi-dimensional construct which builds over time, is very difficult to measure.

Post-Covid, there will be more open alliances in the biotech sector and hence the process of alliance management may depart greatly from the traditional route. There will be a need for novel strategic alliances focused on pandemic management and underlying social needs in the new normal. The heterogeneity of partners in novel strategic alliances would range from commercial organizations, governments, universities, research institutes, and NGOs to industry associations and would be referred to as "systems integrators", bringing together expertise from many different stakeholders. Managing these stakeholders would require meeting power, trust, governance and risk-related challenges. The pharmaceutical industry is simply not incentivized to develop new drugs and vaccines for pandemic diseases, despite regular calls from supranational organizations. Hence, there will be a break down in some of the traditional boundaries and silos that normally exist in the way pharma companies conduct their business.

CONCLUSION

The origin of COVID-19 raises an umpteen number of questions and is still a global health crisis. Therefore, its vaccine development is not merely financially lucrative, but its strategic implications are of paramount importance. During the pandemic, we have witnessed the role of hydroxychloroquine in foreign policy. Sooner or later the COVID-19 vaccine is going to play a role in diplomacy, foreign trade, and international relations owing to its strategic implications.

In the years to come, globalization will be more relevant in the biotech sector and the exploration-exploitation alliance framework (Rothaermal & Deeds, 2004) will be revisited once again in the International Business literature. There will be a rise in new biotechnology firms (NBFs) with narrower knowledge applicability. The biotech sector has its confident reasons for future growth due to its monetary wealth. It has weathered previous recessions, witnessed decades of scientific team experience, and possesses a wide investor base. According to PitchBook, US venture funding for the biotechnology or bio-pharmaceutical sector reached a peak of 5.5 billion USD, adding four new private biotech funds in the first quarter of 2020. NBFs need to examine different alternatives when collaborating with the "sharks" — in other words, established pharmaceutical firms. The future research in a post-COVID-19 world needs to explore how NBFs deal with the "value creation vs. value appropriation" dilemma (Diestre & Rajagopalan, 2012) with the pharmaceutical firms when it comes to partner selection decisions. Future research should also attempt to sketch the evolution of an established pharmaceutical firm's alliance management capabilities in the domain of vaccines.

With hardly any part of the globe remaining unscathed from this calamity, the post-COVID-19 world is not going to be the same. This demands serious reflection on our part so that we remain prepared for the very real possibility of similar epidemics. The challenge is to overcome a worldwide health crisis in distinctly

local ways through open, transparent and collaborative practices. There is a pressing need for reducing tariffs especially in the context of the on-going COVID-19 pandemic. As new pharmaceuticals and vaccines will need to be moved across the borders to be made available globally at a mass scale, governments should be legally obliged via international action (updating the WTO Pharmaceutical Agreement) to reduce the tariffs. Any trade barrier regarding the distribution of the emerging COVID-19 vaccine, thus driving up the price, should be identified and rejected at the very first hint. Ideally, the vaccine should be promoted as a global, public, or social good.

The simple goal is to prioritise the best drug candidates, streamline regulatory processes, share knowledge among all partners as quickly as possible and reduce pharmaceutical tariffs to respond to COVID-19 and future pandemics. Battling the COVID-19 pandemic is far too great a challenge for anyone firm or institution. Together, we can be stronger than COVID-19.

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