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Why's BioPharma Breaking R&D Shackles?

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The Indian industry bore witness to biotech companies collaborating with vaccine manufacturers, vaccine technologies being transferred, licenses to manufacture several drugs granted to pharma companies, among other notable developments. These collaborations and partnerships have furthered R&D, commercialisation and distribution of several critical drugs throughout 2021. However, key barriers to R&D-based innovation still persist in the Indian pharma market that needs to be sorted out soon. We shall take a closer look at the industry' quest to realise even more, swift innovations and fewer hindrances.

2021 has been an action-packed year for the pharma and the biopharma sector. Several vaccines have been approved for COVID-19 globally as well as in India. First-ever mRNA, DNA and nanoparticle protein-based COVID-19 vaccines have been approved. The year has witnessed partnerships and collaborations between major pharma/biopharma companies for the development of newer drugs for the treatment of chronic diseases and COVID-19.

Notably, the Indian industry bore witness to biotech companies collaborating with vaccine manufacturers, vaccine technologies being transferred, license to manufacture several drugs granted to pharma companies, these collaborations and partnerships have furthered R&D, development, commercialisation and distribution of several critical drugs.

Since the onset of the global COVID-19 pandemic, there has been ongoing research and development for COVID-19 vaccines and drugs to halt the spread of the dreaded infection that has had a global impact on the economy and the health of the human population.

Sharing his views Dr Rajesh S Gokhale, Secretary, Department of Biotechnology (DBT), New Delhi said, “DBT has been shifting, adapting and mirroring the innovative nature of the biotech industry quite rapidly. The challenges clearly are to mitigate the development costs so that it becomes beneficial to all and the safety of all stakeholders are in place.”

“COVID-19 has been a good learning phase, clearly we can speed up approvals, we have realised that we can work in teams

and deliver which is very important as we have worked in silos and then we have tried to connect with one another. DBT BIRAC seed grants have changed the biotech startup ecosystem, this has been the game changer that has played a tremendous role," concluded Gokhale.

Collaborations & tech transfer

Serum Institute Life Sciences Private Limited (SILS), a subsidiary of Serum Institute of India collaborated with Biocon Biologics Limited (BBL), a subsidiary of Biocon Ltd for a 15-year pact, that covers vaccines and various biological products. According to the agreement, BBL will be offloading a 15 per cent stake to SILS with a valuation of $4.9 billion, BBL will have access to 100 million vaccines annually for 15 years and Adar Poonawalla, CEO, Serum Institute of India got a seat on the board of Biocon Biologics Limited.

Commenting on the strategic alliance, Adar Poonawalla, CEO, SII, Pune mentioned, "We look forward to complementing each other's capabilities and capacities in vaccines and biologics, with the objective of addressing inequitable access both in emerging and developed markets for life-saving vaccines and biologics."

SII has also collaborated with Novavax Inc, US-based biotechnology to contract manufacture the nanoparticle protein-based COVID-19 in India. SII has announced that the companies have filed regulatory submissions for emergency use authorisation of Novavax' recombinant nanoparticle protein-based COVID-19 vaccine candidate with Matrix-M adjuvant. The submission was made to the Drugs Controller General of India (DCGI) and is awaiting approval.

SII is in an existing partnership with AstraZeneca to produce COVID-19 vaccines, which has been the frontrunner in India's fight against COVID-19. Covishield manufactured by the SII through the technology transfer from AstraZeneca is the most used vaccine in India.

Covaxin being another indigenous vaccine manufactured by Bharat Biotech on November 3 has received World Health Organisation's (WHO) emergency use authorisation. The approval has helped India in its quest to beat the pandemic. The WHO approval has been a boost in the arm for India against the coronavirus disease.

Speaking on the sidelines of the approval by WHO, Dr Krishna Ella, Chairman and Managing Director, Bharat Biotech, Hyderabad said, "Validation by WHO is a very significant step towards ensuring global access to India's widely administered, safe, and efficacious Covaxin. As an organisation, we have focussed on maintaining stringent quality and safety standards that meet rigorous assessment, and scientific standards established by WHO, as a result, many of our vaccines have received WHO prequalification. The EUL authorisation for Covaxin will enable us to contribute to accelerating the equitable access of COVID-19 vaccine, and the access to our vaccine globally thereby addressing the current public health emergency."

To increase the manufacturing capacity of Covaxin, Bharat Biotech has transferred the technology to several Indian biopharma companies. Hyderabad-based Indian Immunologicals Limited (IIL), the market leader of veterinary and human biologicals with a strong focus on paediatric and rabies vaccines and Uttar Pradesh-based biotechnology company Bharat Immunologicals, manufacturer of oral polio vaccines (OPV vaccine), diarrhoea management kit and zinc tablet have entered into technology transfer agreements. Mumbai-based Haffkine Bio-Pharmaceutical Corporation Limited is likely to start production of Covaxin in November 2021.

Speaking on this achievement Dr Renu Swarup, the then Secretary, Department of Biotechnology (DBT) and Chairperson, BIRAC, New Delhi said, "The government has worked relentlessly to provide all possible support for ramping up Covaxin production in the country and speed up Covaxin inoculation drive. The loan license agreement by Central Drugs Standard Control Organisation (CDSCO) for Indian Immunologicals to produce Covaxin Drug Substance is a major milestone, achieved in a very short span of time. The DBT-BIRAC support under Mission Covid Suraksha aims to meet the COVID-19 vaccine requirement of our country. I congratulate the team for the efforts put in for this achievement."

With emergency use authorisation granted by DCGI to the Russian made Sputnik V COVID-19 vaccine, Russian Direct Investment Fund (RDIF), Russia's sovereign wealth fund with reserved capital of $10 billion under management, has inked agreements with Gland Pharma, Hetero Biopharma, Panacea Biotec, Stelis Biopharma, Virchow Biotech, Morepen and Dr. Reddy's for the distribution and manufacture of the vaccine.

Hyderabad-based firm Biological E. has inked an agreement with Johnson & Johnson for the manufacturing of their Janssen,

single-dose COVID-19 vaccine. EUA has been granted by the DCGI.

Development and approval of COVID-19 vaccines

Biological E. is in the late stages of clinical trials of their COVID-19 vaccine candidate, Corbevax. The company is getting ready with 100 million doses for the launch. The studies are expected to be completed by the end of November, following which approval is expected by the DCGI. Biological E. is developing a COVID-19 vaccine for children, the study of the vaccine is currently ongoing, post which approvals are expected by the company for manufacturing and distribution of the vaccines. The US International Development Finance Corporation (DFC) has finalised a financing arrangement formalising $50 million to expand the company's capacity to produce COVID-19 vaccines.

"We are pleased with the financial support from the US government, especially DFC, which was announced at the Quad Summit in March 2021," said Mahima Datla, Managing Director, Biological E. Limited, Hyderabad. "This investment will not only help us augment our capacity to produce more COVID-19 vaccines, but also help the global community that has been relentlessly fighting against the spread of the COVID-19 pandemic," addec Mahima Datla.

On another front Bharat Biotech has made steady progress in the development of BBV154, an intranasal COVID-19 vaccine. The company has completed Phase II trials of the vaccine and the results have been good in preventing the spread of COVID-19. Post the completion of Phase III and submissions to regulatory authorities, approvals will be granted. The Hyderabad-based company in association with the DBT has also developed a COVID-19 vaccine for the 2-18 age group. Further regulatory approvals are awaited from the Central Drugs Standard Control Organisation (CDSCO) before product launch and market availability of Covaxin for children.

On the other hand, Zydus-Cadilla has developed ZyCoV-D, a DNA-based vaccine for the prevention of COVID-19 infection. The DCGI, Government of India has approved the vaccine for emergency use which will be soon available in the Indian market. This is a first-of-its-kind vaccine using the plug and play technology to upgrade the vaccine to newer variants of the virus.

Pankaj R Patel, Chairman, Cadila Healthcare Ltd, Ahmedabad, said, "This is a historic milestone with ZyCoV-D, a product of Indian innovation becoming the world's first DNA vaccine being offered for human use and supporting the world's largest immunisation drive. Our vaccine will contribute to this fight against COVID-19 and enable the country to vaccinate a larger population especially in the age group of 12-18 years."

Gennova Biopharmaceuticals, a subsidiary of Pune-based Emcure Pharmaceuticals, is in the final stages of clinical trials of its mRNA COVID-19 vaccine. The results from the clinical trials have been promising. Once the Phase III trials are completed, Genova will be applying for approval of the vaccine.

Sharing his views on the development of the mRNA COVID-19 vaccine, Sanjay Singh, Chief Executive Officer, Gennova Biopharmaceuticals, Pune remarked, "We have completed Phase II and are in Phase III with our mRNA COVID-19 vaccine. Let's see how the results come in. Based on the results, the DCGI approves it. But we are very positive about it."

"All the 39 raw materials required for the mRNA vaccine are imported. We cannot afford the timeline. We do not have the kind of money power in pursuit of the raw materials. We need to do backward integration and for this policymakers should look at this through a different lens. Innovative products should be seen from a different lens and backward integration should be listed differently," he added.

Drug development

The onset of the pandemic brought about various challenges. The most prominent was the treatment of patients that had contracted the SARS-Cov-2 virus. Pharma majors have been working round the clock in developing drugs to treat COVID-19. Initially, experimental drugs were repurposed for the treatment of COVID-19 as researchers and scientists worked on understating the virus better and decided on the course of treatment.

Swiss multinational healthcare company Roche collaborated with Regeneron Pharmaceuticals, an American biotechnology company to manufacture and distribute REGN-COV2. In India Roche collaborated with Cipla to market the antibody cocktail (Casirivimab and Imdevimab).

Zydus Cadila has been developing an antibody cocktail for the treatment of COVID-19. The monoclonal antibody cocktail has been a promising candidate for therapy in early COVID-19 cases. Clinical trials are ongoing. Once the clinical trials are complete, the company will be applying for the distribution and commercialisation of the COVID-19 drug.

Another drug that was approved under the emergency use authorisation in India was developed by the Institute of Nuclear Medicine and Allied Sciences (INMAS), a lab of Defence Research and Development Organisation (DRDO) and Dr Reddy's Laboratories, Hyderabad. The drug 2-deoxy-D-glucose (2-DG) is available in sachets in the form of a powder that is administered orally. It prevents virus growth by stopping virus synthesis and energy production by accumulating in virus-infected cells. DRDO has granted the licence to manufacture 2-DG to several pharma companies, namely Mankind Pharma, BDR Pharma, Granules India, Laurus Labs and MSN Laboratories.

A drug that may soon be available in the Indian market for the treatment of COVID-19 is currently under the review of DCGI. Molnupiravir pill, the drug developed by Merck, known as MSD outside the US and Canada, and Ridgeback Biotherapeutics. Sun Pharma is gearing up to launch Merck's Covid pill under the brand name Molxvir in India. The United Kingdom Medicines and Healthcare products Regulatory Agency (MHRA) has granted authorisation in the United Kingdom (UK) for Molnupiravir (MK-4482, EIDD-2801), the first oral antiviral medicine authorised for the treatment of mild-to-moderate COVID-19 in adults with a positive SARS-CoV-2 diagnostic test and who have at least one risk factor for developing severe illness.

Biocon Biologics has received an exclusive licence from US-based Adagio Therapeutics to manufacture and commercialise an antibody treatment based on ADG20 for India and select emerging markets. ADG20, a novel monoclonal antibody targeting the spike protein of SARS-CoV-2 and related coronaviruses, is in global clinical development by Adagio as a single agent for both the treatment and prevention of COVID-19, the disease caused by the SARS-CoV-2 virus, its variants, as well as future variants that may emerge.

Speaking about the development, Dr Kiran Mazumdar-Shaw, Executive Chairperson, Biocon Biologics Ltd, Bengaluru said, "This partnership with Adagio aligns our joint vision of bringing superior biologic therapies to millions of patients in low and middle-income countries. Vaccines alone will not protect and make the world safer. Biologic therapies that arrest the virus in its path of devastation are a necessity for sustainable protection and safety."

Strengthening 2022 with 2021 developments

2021 could be the precursor to more developments, approvals, partnerships and technology transfers in 2022. The pandemic has unravelled the huge demand-supply gap for essential drugs and vaccines. Partnerships and agreements forged have helped bridge the gap between the demand and supply of essential drugs and vaccines.

With the shortage of drugs and vaccines for the treatment of COVID-19, pharma majors could consider furthering their technology transfers and partnerships for the development of novel drugs and technologies with other organisations. As the world prepares for the post-pandemic era the sector is poised to witness major headways in the development and distribution of various critical drugs for various diseases.

In addition, while India has been a powerhouse in the manufacturing of generics and Active Pharmaceutical Ingredients (API)s there is room for growth in terms of R&D that is gradually being attended to. Key barriers to R&D-based innovation include a weak patent environment, volatile pricing policies that hinder long-term investment decisions, and a lack of a venture capital sector in the Indian pharma market that needs to be sorted out soon.

Putting forth his views on similar lines, Dilip Shanghvi, MD, Sun Pharma, Mumbai says, "Innovation for a new product is an important milestone for Indian companies to succeed. The research led incentive scheme is a very good effort towards recognising the challenges of the industry in terms of making this long term investment and it is essentially talking about engaging in dialogue with all the stakeholders with a view to form a policy which would be a long term policy because I think there is a recognition that innovative new products take a long time to come to the market.

Shanghvi further says, "The important challenge that we have is the collaboration between industry and academia and collaboration between various capable organisations, so that missing skill sets in companies can be overcome. Historically it was easier for us to do Phase I-II studies outside of India."

"The key goal of the Indian pharmaceutical industry has always been to improve the access and availability of affordable

medicines not just in India but across the globe. This is the appropriate time to move ahead of the short-term goals and focus on the long-term value chain adjustments. The aim should be to streamline the regulatory system in India that will improve the value of competition and enforce growth in quality and encourage innovation," remarked Sudarshan Jain, Secretary-General, Indian Pharmaceutical Alliance, Mumbai.

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