Vaccines, Biologics: Indian Pharma's New Temptations

API, diagnostics, New Chemical Entity — Covid has thrown up new opportunities, and domestic pharma biggies are are charging in with renewed focus.

By **Gina Krishnan**
Photo Illustrations by **Amit Sharma**

THERE COMES A TIME when work becomes a mission — more than money, power or fame. For Indian pharma, the moment came in 2020, when the pandemic hit the country. As the world closely watched the actions of a nation accounting for a little over a sixth of humanity in anticipation, the pharmaceutical industry put its best foot forward. Vaccine companies, drug makers and suppliers took on an unknown disease and delivered to an anxious nation — and the world — new business models and new ways of drug development and research.

"2021 has been pharma's Y2K," says Sudarshan Jain, secretary-general, Indian Pharmaceutical Alliance [IPA]. New de-cluttered strategies picked up pace as the pandemic became the defining moment for the $44-billion domestic pharma industry, which is targetting $130 billion in annual revenues by 2030.

Antecedents

In the early 2000s, Indian pharmaceutical companies rode the tailwind of Para IV filings [before the patent on a drug expires, a generic company can file an application showing their version does not infringe the innovator's patent] and earned in dollars like never before. Two decades later, the industry is seeing a different kind of traction, having learnt to navigate the business and challenges of innovation.

The Para IV filing earnings fed the growth of big companies. Driven by the vision of Dr. Parvinder Singh and Dr. Anji Reddy, the industry began investing in original research in the quest for a new chemical entity over a decade ago. But despite small successes, out-licensing agreements and partnerships, India failed to make a mark as a drug innovator. Instead, domestic firms mastered the art of generics, spawning a global industry.

Today, the companies are seeking new paths to growth, including biologics, active pharmaceutical ingredients (APIs), contract research, or the quest to offer innovative products in the U.S., the world's biggest pharma market.

"Currently there is no other Indian company with global scale in bio-pharmaceuticals. The future of pharma is bio-pharma."

Kiran Mazumdar-Shaw, executive chairperson, Biocon

"We are committed to research & development. Sun will be make a play in Biologics coming off patent in the third wave."

Dilip Shanghvi, MD, Sun Pharma

The Biologics Market

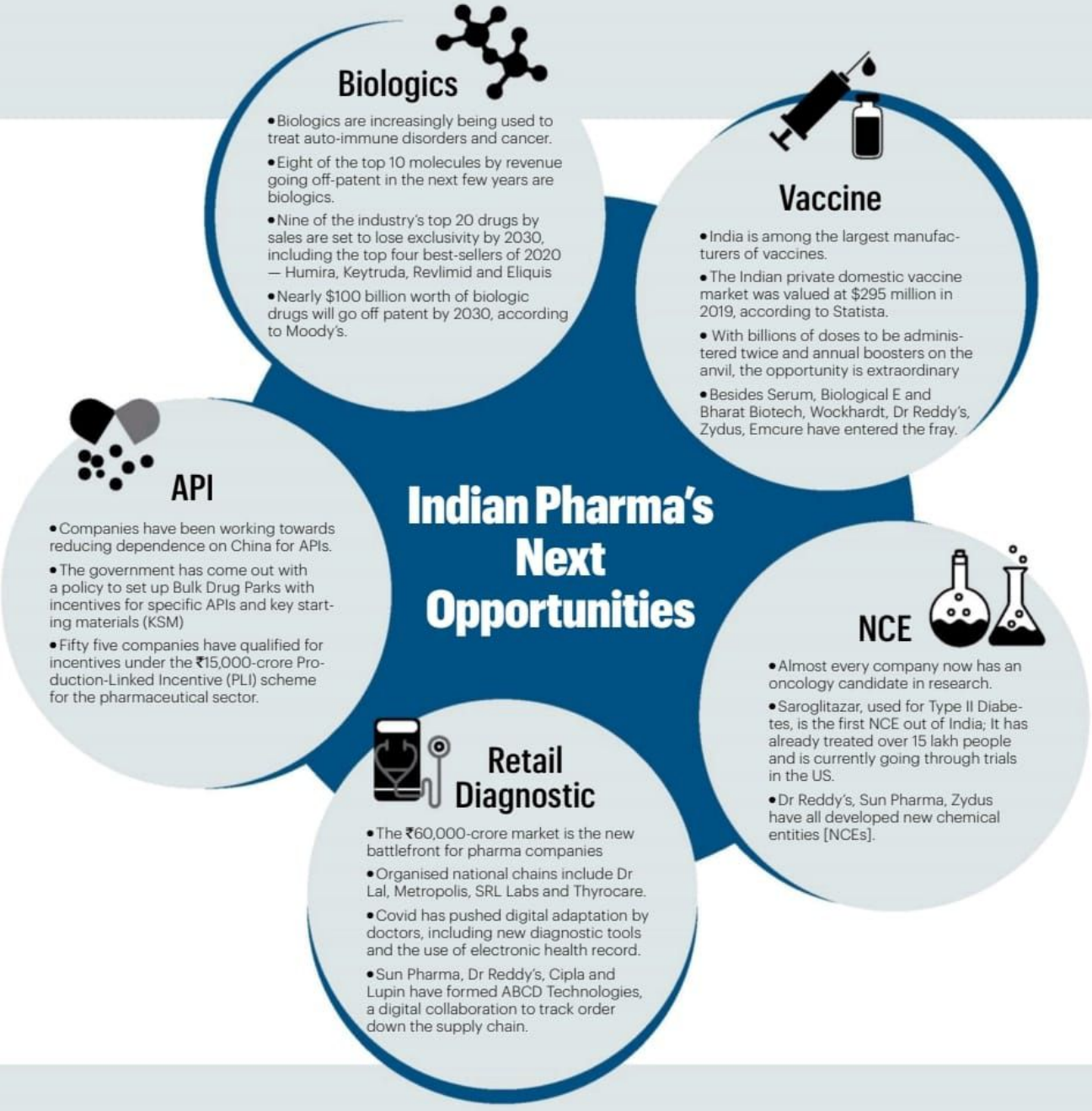
Biologics is the path-breaking industry, despite high barriers. Biologics are increasingly being used for treatment of auto-immune disorders and cancer, and with eight of the top 10 molecules by revenue going off-patent in the next few years being biologics, it is the business to tap. The biggest names set to face generic pressure include the top four best-selling drugs of 2020 — Humira, Keytruda, Revlimid and Eliquis. Nine of the industry's top 20 drugs by sales set to lose exclusivity by 2030, says Moody's in a recent report, will be biologics. In all, nearly $100 billion worth of biologic drugs will go off patent by 2030.

US-based AbbVie's Humira — used to treat rheumatoid arthritis — the world's top drug with $20 billion in sales in 2020 will start facing US generics in 2023. Humira accounted for 43% of AbbVie's 2020 revenues, while Keytruda pulled in about 30% for Merck. Bristol Myers Squibb is set to lose exclusivity over Revlimid, Eliquis

The Covid Driver

TWO DAYS AFTER THE national lockdown was declared in 2021, Sun Pharma's Dilip Shanghvi asked IPA's Sudarshan Jain to convene a meeting of pharma leaders. Cipla's Samina Hamied, Lupin's Nilesh Gupta, Zydus' Sharvil Patel and Torrent's Samir Mehta along with Shanghvi and Satish Reddy agreed to meet virtually daily. The pharma industry was not on the initial essential services list in 2020 and factories were shut. "The industry could not be closed down. If the supply chain was squeezed, how could we deal with the pandemic," says Jain. "We learnt a lot in the first wave and could deal with the second because we had more information," says Nilesh Gupta. The industry came together to ensure medicine supply continued uninterrupted. Now, most companies are growing at double digits and anticipate a good run in the foreseeable future.

PHOTOGRAPH OF DILIP SHANGHVI BY **PADMINI B**



and Opdivo this decade.

"The early 2000 saw progression towards biologics and we invested in bio-similars and biology based products," says Sharvil Patel, managing director, Zydus Cadila. "It is more expensive to do bio-similars than developing novel biologics. When you do a bio-similar, you have to deal with the innovator, which is half the cost. When you are doing a novel molecule, you focus on the studies," adds Patel.

Biocon, the Indian biologics leader, along with partner Viatris (Mylan) in end-July 2021 received the U.S. Food and Drug Administration's (USFDA's) approval for Semglee (an insulin injection) as the first interchangeable bio-similar. It allows substitution at pharmacy counters across the U.S. Biocon has already developed and launched six bio-similars. "Currently there is no other Indian company with global scale in bio-pharmaceuticals. The future of pharma is bio-pharma," says Kiran Mazumdar-Shaw, executive chairperson, Biocon.

"One ANDA (abbreviated new drug application) filing takes about $2-3 million. It will cost you $100 million to develop one bio-similar, so the ratio is many times more," says Mazumdar-Shaw. Biocon invested close to $1 billion for just bringing these molecules to the market. Meanwhile, Sun Pharma announced its intent to ride

"We are very interested in research driven by mRNA technology for the future."

G.V. Prasad, co-chairman and MD, Dr Reddy's

"We would be interested in offering healthcare-related services for products we sell, in respiratory or even insulin-education, which is a direct-to-consumer business"

Nilesh Gupta, MD, Lupin

the third wave of bio-pharmaceuticals going off patent in 2026-27. Lupin, too, has throw its hat in the ring.

Emcure Pharmaceuticals set up Gennova Biopharmaceuticals to start biologics research under Dr. Sanjay Singh, a senior scientist recruited from the National Institute of Health. He put together a team and zeroed into mRNA as a technology platform for future biologics products. "The idea was to develop expertise in mRNA and come out with products," says Singh. After the pandemic hit, the Department of Biotechnology (DBT) gave a ₹125-crore grant to Emcure to research and develop the Covid vaccine. "The vaccine is on track to go into Phase III clinical trials and will be the first mRNA-based product to enter the Indian market," says Samit Mehta, president, R&D, Emcure.

Hyderabad-based Dr Reddy's is betting on biologics as well. Morepen, one of the companies likely to manufacture the Russian Sputnik V vaccine, has announced its intent for setting up biotech manufacturing facilities.

Mazumdar-Shaw believes the industry is still not investing enough in biotechnology. Performance-linked schemes are favouring generic pharma as incentives are based on ANDA filings. In the global market, to pass muster with the USFDA or the EMEA to make a compliant plant, investments increase 50% unlike small molecules. Mazumdar-Shaw feels with focus on generics, the country is missing a huge opportunity in biologics.

NCE: Research In New Technology

The holy grail of a pharma company is a New Chemical Entity (NCE). Earlier, companies looked at incremental innovation, picked up a successful molecule and found a 'me too' product. Now almost every company has an oncology candidate in research.

Dr Reddy's research has consolidated into a subsidiary — Aurigene Discovery Technologies — that has a services and collaborative drug discovery model working with many innovators. It also has its own NCE pipeline. In the last 18 months its work has been separated into discovery technologies and services components. Oncology NCE is its quest now. "Our focus is oncology," says G.V. Prasad, co-chairman and managing director, Dr Reddy's.

It has developed competence in immune oncology. "We have four assets in the clinic which belong to us and 10 with partners. We work with partners on drug target exclusively. If we give it to them, it belongs to them and we absorb some risk, they take some risk. The burden of clinical development is with the partner. We do early stage discovery work," explains Prasad.

Sun Pharma Advanced Research Company (SPARC) has developed two NCEs, which have been registered for clinical studies. "I wanted to reach where we have much faster but that does not mean it is a delay. We continue to invest in new research," says Dilip Shanghvi, managing director, Sun Pharma. Cipla has earmarked ₹264 crore for research with focus on oncology and lung leadership.

Zydus spends 8% of its revenue on R&D. "We are a research-based company and have invested in talent, machines, R&D infrastructure, clinical research infrastructure and regulatory and legal teams to guide us through," says Patel. Saroglitazar, used for Type II Diabetes, is the first NCE out of India, after Phase III trials in the country and Mexico. It has already treated over 15 lakh people and is currently going through trials in the US.

The Vaccine Opportunity

Vaccine manufacturing is the new opportunity for domestic pharma. Though India is among the largest manufacturers of vaccines, it was restricted to the likes of Serum Industries, Biological E and Bharat Biotech. Wockhardt received a fill and finish opportunity for the AstraZeneca vaccine, Dr Reddy's received a vaccine marketing opportunity with Sputnik

PHOTOGRAPH OF G.V. PRASAD BY **VIKAS CHANDRA PURETI**

Getting Innovation Right

INDIA DOES NOT have the innovation ecosystem which China got right, including risk funding by venture capitalists, simpler regulations and industry academia-research partnership. "India needs to start rewarding companies for innovating. Once Indian firms register products globally, it will encourage others to invest in that kind of research," says Dilip Shanghvi. One big miss is lack of academia-industry partnerships. There is no pathway for government labs, universities to work with the industry.

V and by then Zydus and Emcure through Gennova was also in the fray.

"We had no plans for a vaccine or a vaccine platform. But an employee decided the vaccine could make a difference to Indian patients and he went to find it on his own. He had to convince the management for a buy-in. He said we exist to do this," says Prasad. Marketing of Sputnik V opened an opportunity and Dr Reddy's is seriously considering entering the vaccine business using mRNA as a platform in biologics for its R&D.

The Indian private vaccine market was valued at $295 million in 2019 according to research firm Statista. Now with billions of doses to be administered twice and annual boosters on the anvil, the opportunity is extraordinary.

Zydus' first DNA vaccine is a needle-free application. "With our tetravalent vaccine earlier and now the imminent roll-out of India's first DNA vaccine for children 12 years and above, we want to double up on the vaccine opportunity," says Sharvil Patel.

Biocon has entered into a strategic alliance with Serum Institute. It gets committed access to 100 million doses of vaccines annually for 15 years with commercialisation rights of the vaccine portfolio (including Covid-19 vaccines) for global markets. The company recently announced a partnership with Boston-based Adagio Therapeutics for ADG20, a novel Covid-19 antibody therapy, in select emerging markets.

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Retail Diagnostic Push

The ₹60,000-crore highly fragmented Indian diagnostics market is the new battlefront for pharma companies. There are only a handful of organised national chains — Dr Lal's, Metropolis, SRL Labs and Thyrocare. Lupin recently announced setting up of Lupin Diagnostics as a separate line of business with a five-year plan to cover the country. "We would be interested in offering healthcare-related services for products we sell, in respiratory or even insulin-education, which is a direct-to-consumer business," says Nilesh Gupta, managing director, Lupin. "We have leadership in many therapeutic categories and have to add services related to the product."

Every new opportunity has a tipping point. Telemedicine has been around for over 20 years, but Covid pushed everyone to the digital platform. Doctors reluctant to adopt technology embraced it. New diagnostic tools, marketing, and the use of EHR catapulted it to a different level.

Lupin is drawing up a scalable business model with a clear revenue stream. "We have conversations on

telemedicine, diagnostics, digital tools, but they have to be at scale," says Gupta. Medical education is one way the digital platform was used to engage with global opinion leaders.

Sun Pharma and Dr Reddy's invited global leaders in therapeutic areas to conduct medical education. Worldwide doctors connected to look for information on latest developments and for treating Covid. "We could call global doctors to talk to local doctors and that is likely to continue," says Shanghvi.

The big change was the use the digital platform to bring in efficiency into the supply chain. Top pharma companies joined hands after working with Pharmarack, a B2B healthcare platform with over 7,000 distributors and companies who can order medicine online. Sun Pharma, Dr Reddy's, Cipla and Lupin have formed ABCD Technologies, a digital collaboration to track order down the supply chain.

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Sharvil Patel, MD, Zydus Cadila

Owning The API Space

Every country is reconsidering dependence on China for APIs. The government came out with a policy to set up Bulk Drug Parks with incentives for specific APIs and key starting materials [KSMs]. "At the core we are generic manufacturers, and not just of complex generics. There is alignment between the government and the industry to get capability back into the country," says Lupin's Gupta.

Fifty five companies have qualified for the ₹15,000-crore Production-Linked Incentive [PLI] scheme for the pharmaceutical sector. It includes all the big names. The first category includes biopharmaceuticals; complex generic drugs; patented drugs or drugs nearing patent expiry; cell-based or gene therapy drugs; orphan drugs; special empty capsules; and complex excipients. The second category includes APIs; KSMs; Drug Intermediates [DIs], products of strategic importance. The third category comprises manufacturing repurposed drugs; auto-immune, anti-cancer, anti-diabetic, anti-infective, cardiovascular, psychotropic and antiretroviral drugs.

Marketing Partnerships

The $2.3-billion Cipla led by vice chairperson Samina Hamied is driving the partnership agenda. As the pandemic hit the country and the world, Cipla entered into partnerships to offer a comprehensive portfolio of Covid-19 products in India, from diagnostic kits to repurposed medicine. Lupin has partnered with US-based ForDoz Pharma to distribute two complex injectables in the development stage. It has also entered into an agreement with UK-based TTP plc to acquire the exclusive worldwide rights to develop, manufacture and commercialise inhalation products using TTP's soft-mist inhalation technology platform.

The Road Ahead

The pandemic bolstered the growth path for domestic pharma companies. "But the industry also realises that it is a changing time," says Sujay Shetty, global health industries advisory leader, PwC. According to him, there are three challenges — domestic pharma companies need to innovate with new class of drugs based on biology, recombinant technology like mRNA or DNA and get into API manufacturing; factor in digital disruption; judiciously use the funding that has come into the sector since last April from PE/VCs.

All said, after close to two years of the pandemic, the industry is at the crossroads with multiple opportunities in a fast-changing world. ■

The $2.3-billion Cipla has entered into various partnerships to offer a portfolio of Covid-19 products in India.