Syngene COO On Delivering Cost Gains For mRNA Products

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Executive Summary

Syngene's COO, Mahesh Bhalgat, tells Scrip the firm is better placed than some peers to serve clients for biologics-based advanced therapies and address the cost element for new modalities like mRNA. He also outlines the research, development and manufacturing services company's capabilities in oligonucleotide-based therapeutics, an area that's seeing growing interest.

SYNGENE COO DR MAHESH BHALGAT

The Indian contract research, development and manufacturing services firm Syngene International Ltd. says it has what it takes to rein in the cost element to make therapeutics based on the new star modality, messenger RNA (mRNA), "more dominant" across markets.

Syngene's chief operating officer, Dr Mahesh Bhalgat, said that while the company's facilities for biologics are also set up to do mRNA manufacturing, providing a cost advantage by not having to build new sites, it is alongside geared to address aspects of thermostability, as well as other components of cost on the raw materials front. (Also see "The Emergence Of A New Medicinal Platform: mRNA" - In Vivo, 11 Aug, 2022.)

"We are set up to make some of the raw materials that are the most limiting for the supplies of what the Pfizer Inc.-BioNTech, Moderna, Inc. vaccines actually use. So that is the component which we can do to bring the cost down," Bhalgat said in an interview with *Scrip*.

The COO emphasized that having that vertical integration of raw materials and mRNA manufacturing all set up within a Syngene site is where the firm believes it is "better prepared" to serve clients with advanced therapies, which are more biologics-based.

"We do have clients who are looking at mRNA-based approaches through Syngene. mRNA for the most part is currently most prevalent for looking at vaccines and that's what our programs are," said Bhalgat, a former COO of Shantha Biotechnics Ltd., part of the Sanofi group.

Last year, executives from EY-Parthenon said that mRNA technology offers a multitude of opportunities to develop therapies beyond vaccines and that, relative to traditional approaches, mRNA therapeutics can provide a quick development-manufacturing-scaling-up cycle. Fast scaling of the manufacturing process had triggered cooperation between biotechnology and pharmaceutical giants, as well as multiple contract development and manufacturing organizations (CDMOs) and technology providers, they noted in an article.

Although the COVID-19 vaccine landscape remains fluid, mRNA platforms will likely "continue to solidify as a therapeutic concept" and capture a tangible share of the preventive vaccines market, authors Isabelle Heiber, Elias Eckert, Miroslav Iacovlev, and Joey Wilson, all of EY-Parthenon, predicted at the time.

Oligonucleotide-Based Therapeutics

Bengaluru-based Syngene, which is a publicly listed arm of Biocon, Ltd., is also set up to serve biopharma in areas like small interfering RNA (siRNA) and guide RNA (gRNA).

Bhalgat indicated that Syngene is seeing significant interest from clients in oligonucleotide-based therapeutics and maintained that the firm "stands out" since it has a cGMP oligonucleotide manufacturing facility, "because of which we can provide oligos of this nature that can go into clinical trials."

Syngene deploys advanced technology platforms to provide a comprehensive set of oligonucleotide synthesis services, ranging from development to the manufacture of chemically synthesized oligonucleotides.

There's been significant activity in the oligonucleotide therapeutics segment over the recent past. For instance, last month Biogen, Inc. said that its investigational antisense oligonucleotide tofersen is undergoing a priority review at the US Food and Drug Administration for superoxide dismutase 1 (SOD1) amyotrophic lateral sclerosis.

July also saw the Shanghai-based biotech Rona Therapeutics seal a deal with Sanofi, getting worldwide exclusive rights to the French group's siRNA platform of chemical modification and delivery moiety, as well as rights to four preclinical candidates for undisclosed targets.

Sanofi retains the exclusive option to acquire neuro and muscular disease candidates for ex-China territories under the deal. (Also see "Here We Go Again: US FDA Weighing Accelerated Approval For Biogen's ALS Drug Tofersen" - Pink Sheet, 26 Jul, 2022.) (Also see "Asia Deal Watch: Rona Takes On Sanofi's siRNA Platform" - Scrip, 25 Jul, 2022.) (Also see "RNA-Based Therapies Back In Spotlight As Chinese Biotechs Raise $366m" - Scrip, 8 Apr, 2022.)

On the discovery services front, Syngene's capabilities also include gene editing platforms that support multiple modalities, including CAR-T research. While it is not into the manufacturing part yet, Bhalgat sees that as a "natural progression" of the firm's collaboration with clients who are in discovery. (Also see "India Trials And Tribulations: J&J, IQVIA Execs Offer Potential Solutions" - Pink Sheet, 7 Jul, 2022.) (Also see "It's Coming Home: ImmunoACT Advances Plans For Cut-Price CAR-T In India" - Scrip, 30 Jun, 2022.)

"Once clients progress their molecules from discovery to development to manufacturing, that's where we will be ready with what the needs of the clients are at the time," Bhalgat explained.

Syngene's roster currently has over 420 active clients and also includes collaborations with the top 20 global pharma companies.

Earlier Mover In Biologics

Syngene also appears unfazed by growing competition in biologics contract manufacturing, both on the home front as well as globally, including signs of rising South Korean interest.

Bhalgat maintained that the sheer increase in the CDMO volumes for biologics is a good thing for the industry, because it is indicative of innovators getting "comfortable" with working with CDMOs in this complex manufacturing area, opening up more opportunities generally.

"Overall growth of the industry therefore is also showing up in the number of players that are entering that space. I see that as healthy competition, which is supported by healthy growth volumes," the COO said.

The large molecules CDMO market was valued at $11bn in 2020 and is expected to reach $20bn by 2026, a Frost & Sullivan report predicted. This is also against the backdrop of a growing industry pipeline of biologic drugs.

Data from *Pharmaprojects' Pharma R&D Annual Review 2022* published earlier this year indicated that the percentage of the industry's pipeline that can be apportioned to biotech origin over the 1995-2022 period continues to creep up – it currently stands at about 44.7%, up by 1.8% from last year. (Also see "Industry Flying High With Record-Breaking First Novel Launch Tally in 2021" - Scrip, 28 Apr, 2022.)

Bhalgat underscored that Syngene is significantly differentiated and has been one of the "early movers" in biologics, initiating investments in the segment almost 10 years ago. The firm offers not just biologics manufacturing but also integrated work – discovery, development and manufacturing services.

"We've not just been a pure-play manufacturer, but we've been a manufacturer that is well versed in handling microbial, mammalian, yeast and other expression systems. So therefore, our range of knowledge, diversity, experience positions us more as a preferred player," the executive emphasized.

Moreover, biologics supporting services, he explained, are more complicated given the need for a lot more analytical/process characterization and a "lot more work in terms of putting a dossier together."

Syngene is set up to do all of that in-house and also boasts the only facility in India which is a GLP-certified laboratory to do work such as viral clearance tests. These aspects, he said, make the firm "more of a one-stop shop," along with the knowledge base that it brings.

"A key advantage for Syngene is because we're able to offer drug discovery, all the way to manufacturing and everything that is needed in between and specifically for biologics. These are things that make us clearly head and shoulders above our competition. For us, we look at biologics as a key driver of growth," he asserted.

Syngene has dedicated research facilities for Amgen.,Baxter. and Bristol-Myers Squibb – how did the sites cope with pandemic-related turbulence? Any new operating models that are now here to stay?

Dr Bhalgat: Thanks to the right decisions made by the local authorities and the overall pandemic management team from the [Indian] government, we were classified as an essential facility because we produce and support research of drugs and were also doing testing.

Given all of that, we didn't really have to shut down our facilities for more than a couple of weeks, which we were able to cope with by making sure that there isn't any loss of actual time that is needed for productivity.

We came up with many changes not just for the dedicated centers but for essentially serving all of our clients.

This includes a key change, which is we started operating in shifts. That shift operation gave us the opportunity to make sure that people are working and working almost around the clock and with their full level of safety, because you don't have as much density in the labs and in our manufacturing facilities.

All of that literally helped in terms of making sure that we were now operating in a completely different model, because working in shifts in a research environment is not very common in any part of the world. We were able to make that operational and deliver through that model.

We continue to operate in a certain number of areas with the shift model because it is a more efficient approach and I don't believe that we should yet say that we are completely out of the pandemic.

Additionally, we did a lot of work with regard to making sure that there is speed delivered through some of the staff that had to do data analysis, for example, doing that more remotely. Again, that kept things working around the clock.

Normally, what data review may have happened in a certain time or a zone now could happen in a different time or a different zone because of the fact that we were working around the clock in shifts.

In addition, there were a number of things we had to do to make this actually a success. We went from two cafeterias to 20, effected a 10-fold increase in the number of buses that we were using to bring our staff and a dramatically different model that we were able to put in place on contact tracing, sanitization, and both on-site and remote reporting of [workers'] temperature to make sure that we are proactively not having infected staff come on site.

We were one of the few companies that was continuously testing their staff to make sure that you are limiting and catching early, anybody who's infected coming onto the site and therefore, acting as a focal point for additional spread, along with many other components of visitor management.

More Competition Building Up

Syngene, though, will likely be keeping a close eye on Korean firms getting into the fray and also developments in Europe.

For instance, following the success of the Samsung. and SK groups, Lotte Corp. had indicated it is buying Bristol Myers Squibb Company's US manufacturing facility in East Syracuse, NY, which will serve as the Korean conglomerate's center for its North American biologics CDMO operations.

Lotte had earlier hired an executive from Samsung BioLogics, set up a new affiliate, Lotte Biologics, and launched a CDMO business. (Also see "Korean Firms Hunt For Overseas Biologics Manufacturers To Support Growth" - Scrip, 6 Jun, 2022.)

Ambitious plans in the sector are also underway in Europe. In May this year, eureKING, the first European special purpose acquisition company in healthcare dedicated to biomanufacturing, was launched with hopes of becoming a leading CDMO in the region. It was co-founded by a group of industry experts including ex-Sanofi-Aventis. CEO Gérard Le Fur and eureKARE, an investment firm focused on financing and developing synthetic biology and microbiome innovation across Europe. (Also see "European Biomanufacturing SPAC Launched, Backed By Former Sanofi-Aventis CEO Le Fur" - Scrip, 9 May, 2022.)

Large Indian firms such as Dr. Reddy's Laboratories Ltd. have also recently indicated an intent to double down on CDMO activities, with plans for a play in the biologics space. (Also see "What's Next At Dr Reddy's: Biologics CDMO, Cell And Gene Therapy Push" - Scrip, 27 Jun, 2022.) (Also see "Cipla Resets Biosimilars Interest, Readies Respiratory-Focused JV" - Scrip, 27 Aug, 2021.)

Syngene, though, has had some important recent wins in the biologics space. Last month, it struck a 10-year manufacturing agreement with animal health company Zoetis, under which Syngene will manufacture the drug substance for Librela (bedinvetmab), a first-in-class monoclonal antibody used for treating osteoarthritis in dogs.

"We've been partnering on this particular mAb for quite some time. Now this mAb will actually get commercialized in the US - it's already commercial in Europe," Bhalgat noted.

Syngene and Zoetis have a long-running alliance initiated way back in 2011, under which the Indian firm has undertaken work on several animal health mAbs, including developing and manufacturing clinical supplies of a treatment for allergic or atopic dermatitis, now widely used, and Librela.

The latest agreement, though initially focused on Librela, could open up opportunities for other molecules as well in future and is estimated to be worth up to $500m over 10 years, subject to regulatory approvals and market demand, the company said at the time of the announcement.

Geopolitical Issues, Supply Chain Turbulence

Meanwhile, Bhalgat also weighed in on evolving market dynamics amid geopolitical tensions, first as a result of the war in Ukraine and now the simmering issues around Taiwan, and also ongoing global supply chain turbulence. Biopharma has been keen to de-risk its supply chain and onshoring to the extent feasible and a "China plus one" strategy have been some of the more prominent approaches widely being evaluated. (Also see "India FY22 Earnings: Everyone's Talking Of Big Spikes In Input, Logistics Costs" - Scrip, 27 May, 2022.) (Also see "USP Exec On Onshoring, Impact Of War-Fueled Metals Turbulence On Pharma" - Scrip, 28 Apr, 2022.)

Bhalgat said that on the CRO front, the most immediate aspect that's come to the fore is clients reconsidering whether they need to have as many full-time equivalents in certain regions, versus moving them into a different environment like potentially India.

"That's something that we are seeing, which is of course a benefit for us, and our competitors that are based in the India region. This a trend that has started and I expect it to only get further accentuated through the whole Taiwan issue," he noted.

On the CMO side, things are likely to play out over a longer term, since it is not so easy to dramatically change the supplier base, because facilities need to go through GMP processes, site qualification, regulatory approvals and so on.

Syngene's COO believes that India's Production Linked Incentive (PLI) schemes could also contribute and help bring more active pharmaceutical ingredients (APIs), key starting materials and raw material manufacturing into the country over the next few years.

India had earlier put into action some medium- to long-term measures to shrink its overall dependence on China for starting materials. In 2020, the country outlined details of a large-scale PLI scheme for manufacturers of certain critical APIs and drug intermediates, as it sought to galvanize the domestic industry and with an eye on longer-term medicines security. (Also see "India APIs Incentive Scheme: Will It Galvanize Local Firms, Bridle The Dragon?" - Pink Sheet, 8 Jun, 2020.)

In 2021, India notified another large PLI scheme intended to enhance its broader manufacturing capabilities and facilitate "product diversification to high value goods" in the pharmaceutical sector. (Also see "Will The $3bn Stimulus Amid COVID-19 Place Indian Cos Among Goliaths?" - Scrip, 12 Mar, 2021.)

In addition to APIs and key starting materials, the second scheme covered a range of segments including complex generics, orphan drugs, repurposed therapies and even cell-based and gene therapy products.