A Journey of **Building Global Scale**

SMALL MOLECULES

APIs and Generic Formulations

60+

As one of the largest makers of statins and immunosuppressants in the world, we supply these APIs to over 60 countries.

Biocon was among the early movers in developing a portfolio of fermentation derived statins, then referred to as 'the wonder drug of the 21st century' as they helped reduce blood cholesterol and prevent heart disease. Our scientists developed several non-infringing processes for manufacturing statins, which gave us a competitive edge in the global markets.

Most drugs on the market today are small molecules. These are compounds of low molecular weight (less than 900 daltons), which are usually taken orally in the form of a tablet, capsule, or liquid, or can be injected or infused.

India's patent laws in the 1980s had allowed local drug makers to build considerable competencies and offer a large number of small molecule generic drugs legally in the country at a fraction of the price of drugs sold in the Western world. A highly competitive domestic pharma industry ensured the country was self-sufficient in the production of both bulk drugs and finished dosages. Generic pharma producers in India were able to bring down the prices of life-saving drugs for tuberculosis, HIV, hepatitis etc. by as much as 90%. In doing so, India emerged as a vital manufacturer of affordable generic medicines for various acute and chronic conditions and became the world's largest supplier of generic drugs.

At that point in time, Indian vaccine producers were developing vaccines using fermentation which helped them disrupt the market through low-cost yet high quality, vaccines. Biocon, on the other hand, was using this technology to produce high quality bio-enzymes and supplying to the regulated markets of U.S. and Europe. This legacy gave us the confidence to take the unconventional path of producing biopharmaceuticals using fermentation technology. Thus we embarked on the next leg of our journey to develop a range of biopharmaceuticals to address chronic diseases. We set up a large-scale fermentation based manufacturing facility for APIs in Bengaluru and started work on statins and immunosuppressants.

Our move into biopharmaceuticals helped us accelerate revenue growth, from ₹318 million in 1999 to over ₹5 billion in 2004.

2004

Commercialized Lovastatin in the U.S. in 2004.

Statins Frontrunner

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We started developing Lovastatin in early 2000 using an innovative solid state fermentation technology. The submerged fermentation process used by the innovator was still under patent protection then. Our novel process helped us obtain our first approval from the U.S. Food & Drug Administration for manufacturing Lovastatin in 2001. We were the only company in the world to use this technology and were one among three players globally with approvals to supply the API to the U.S.

We simultaneously developed the submerged fermentation process for manufacturing Lovastatin for which we received U.S. approval in 2003. We commercialized Lovastatin in the U.S. in 2004, and successfully obtained Certificates of Suitability from the European Directorate for the Quality of Medicines (EDQM), qualifying our drug substances for use in EU member states. We were one of the largest APIs suppliers to leading Indian generics manufacturers for formulations they sold in the global markets.

2000

Biocon developed Mycophenolate Mofetil (MMF) using proprietary fermentation technology in 2000.

Statins went on to become a big growth engine for the company, fuelled by our early mover advantage in products like Lovastatin, Simvastatin, Pravastatin and Atorvastatin. We were among a handful of companies with U.S. and EU-approved APIs for these fermentation-derived statins, which helped lower the competitive intensity otherwise typical of chemistry-based APIs. This competitive edge led us to capture a significant market share for statin APIs in regulated markets by the mid-2000s.

We are now one of the largest statins manufacturers in the world supplying our drug substances to over 60 countries.

Seizing the Immunosuppressants Opportunity

As our expertise in microbial fermentation advanced, we recognized the potential advantages of combining our skills in solid state and submerged state fermentation technologies. Our R&D program to develop a novel hybrid bioreactor combining the two culminated in a patented invention, PlaFractor™. This unique bioreactor enabled solid state fermentation and extraction in the same vessel resulting in a unique containment feature that could be effectively utilised for the manufacture of highly contamination-sensitive products like immunosuppressants.

We quickly scaled up our novel PlaFractor™ technology to plant level and started a facility to manufacture Mycophenolate Mofetil (MMF). Our technology proved a commercial success as Biocon was one of the first companies to make MMF in 2000. We followed up with a full suite of generic immunosuppressants, including Tacrolimus and Mycophenolic Acid (MPA) Sodium using submerged fermentation technology.

Biocon is today one of the largest producers of immunosuppressant APIs globally, with a basket spanning MMF, MPA, Tacrolimus, Sirolimus and Everolimus. We are global suppliers of Tacrolimus and Sirolimus drug substances. Our immunosuppressant APIs are being supplied to leading international as well as Indian pharma companies.

50%

We are a leading producer of the Orlistat API with over 50% share of the global market.

Expanding our API Offerings

Having made an impact with statins and immunosuppressants, our R&D team kept working at new processes and produced more than a dozen difficult-to-make APIs through the 2000s. We developed Orlistat, an anti-obesity drug, using a combination of fermentation and synthetic chemistry techniques. Today, we are a leading producer of the Orlistat API with over 50% share of the global market.

In 2010, Biocon entered into a long-term supply agreement with Optimer Pharmaceuticals for the commercial manufacturing of the API, fidaxomicin, then the first in a new class of antibiotics for the treatment of a potentially life-threatening infection caused by the Clostridium difficile bacteria, which was a major threat in hospitals across the U.S.

Biocon's expertise in fermentation technology and synthetic chemistry gave us a key competitive edge, making us the sole supplier of the drug substance for this proprietary molecule to Optimer for global markets. Optimer is now a part of Merck (U.S.) through a sequence of M&As. Consequently, our supplies of fidaxomicin are now to Merck (U.S.).

Forward Integration Into Generic Formulations

Having built a strong Small Molecules business around a robust portfolio of APIs, which included statins, immunosuppressants and peptides, the natural progression of our technical competencies lay in forward integration to generic finished dosages. For over a decade we had built expertise in complex APIs. Our work in biosimilars had also led us to develop complex characterization, bio-analytical and strong manufacturing skills. We capitalized on these strengths to build a robust pipeline of difficult-to-make niche formulations especially for chronic conditions. We also built a portfolio of potent molecules and early entry opportunities through patent challenges or non-infringement.

Our existing cGMP compliant manufacturing facilities, including our injectable formulations and fill-finish facilities, worked to our advantage in this new endeavor.

In 2013, the Small Molecules business took a big step forward by creating a new Generic Formulations sub-business unit to vertically integrate into manufacturing finished dosage forms. This would help us address an important need in the market – continuity of supply for quality drug products. Our focus was chronic therapy areas, such as metabolics, oncology, immunology and autoimmune indications. We commenced multiple programs to build a robust pipeline of technology-intensive molecules for global markets, primarily the U.S.

We built commercial infrastructure to support this initiative in the U.S. Our brand equity as a reliable API supplier helped us, in a very short time, to build a good network of accounts that includes wholesalers, retailers, Pharmacy Benefit Managers (PBM), Health Management Organizations (HMO) and Group Purchasing Organizations (GPO).

In order to accelerate our entry into the U.S. generic formulations market, we decided to start with formulations for our statins portfolio as these are high volume products and our backward-integration into the API could help us deliver the volumes consistently. We introduced Rosuvastatin Calcium tablets under our own label in the U.S. in 2017. Since then, we have also launched formulations of Atorvastatin and Simvastatin. We also successfully debuted in Europe

by commercializing our Rosuvastatin formulations through a local partner in January 2018.

Biocon has successfully garnered a high-teens share of the market for Rosuvastatin tablets in the U.S. despite competing in a commoditized market with many other players.

Small Molecules Portfolio Holds Bright Prospects

Since the late 1990s, we have emerged as a preferred APIs partner for over 1,000 pharma companies in more than 100 countries and have long-term business relationships with many of them. We now want to leverage and expand upon the reliability we have built over the years to emerge as a key player with our Generic Formulations aimed at niche therapy areas. Potential customers who wish to secure their supply chain from a continuity of supply perspective appreciate our vertical integration across APIs and formulations and consistent track record in quality compliance.

To fuel future growth, we are developing newer fermentation and chemical synthesis-based APIs, which may have technical barriers for entry such as complexity in manufacturing, potent compounds or a mix of both. We are also working on a niche portfolio of finished dosage forms, which includes solid oral and parenteral products in both potent and non-potent categories of compounds.

To support our filings, we had commissioned our first oral solid dosage facility in Bengaluru in 2017. The facility successfully completed several regulatory audits subsequently following our various filings in the U.S. and Europe.

2017

Our first oral solid dosage manufacturing facility commissioned.

SMALL MOLECULES: FY19 at a Glance

Revenue

17,728

₹ Million

Growth 18%

The Small Molecules segment in FY19 recorded good growth on account of APIs as well as ramp up in the Generic Formulations sales. Higher volumes and pricing stability for Statins & Immunosuppressants led the growth in API sales while the Generic Formulations business recorded robust growth, albeit from a small base due to new product introductions in the U.S. market. We successfully commercialized Atorvastatin and Simvastatin formulations in the U.S. and recorded market share gains in the previously launched Rosuvastatin formulations. More launches are expected in the next 2-3 years, which cumulatively provide revenue growth visibility to this segment.

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