Opening Doors to Developed Markets

Biocon has meticulously scripted a differentiated story through its biologics business, from novels to biosimilars, demonstrating endurance and commitment to traverse a long and arduous journey.

BIOLOGICS

Biosimilars

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- Trastuzumab
- Bevacizumab

RECOMBINANT HUMAN PEG - GCSF
- Pegfilgrastim

INSULINS
- Insulin Glargine
- Other Programs

Novel Biologics
- Insulin Tregopil
- Itolizumab
- Nimotuzumab
- QPI-1007 (siRNA)
- FmAb2

We are driven by our commitment to pursue high science to develop cutting edge, high quality biotherapeutics in order to provide affordable access to patients across the globe. We have thus built differentiated R&D capabilities and acquired expertise across the value chain from cloning, cell line development, CMC to large-scale manufacturing and commercialization. Our structured approach to incorporate advanced science and technology in order to build a wide portfolio of biologics has brought us the reliability and credibility of an innovation-led organization. Today, we are among the first wave of global biosimilars players to successfully gain regulatory approvals for some key biosimilars in several jurisdictions, including the U.S. and EU.

Biocon's proprietary technology using *Pichia pastoris* platform for expressing recombinant protein is used in the recombinant human insulin and insulin analog product lines. Our consistent and scalable mammalian CHO and NSO cell-based expression platforms are helping us deliver novel and biosimilar monoclonal antibodies. Our highly robust process sciences significantly augment our ability to develop world-class biotherapeutics. The upstream and downstream processes continually incorporate latest innovations in cell culture and purification. Our advanced analytical capability, which is anchored in cutting-edge tools and latest orthogonal approaches, guarantees the high quality and consistency of our products. The production of drug substance in the state-of-the-art bio-manufacturing facilities ensures cost effective production. Our expertise in Formulation & Product Science enables us to convert drug substances into formulations for transfer into vials, cartridges and pre-filled syringes at our biologics drug product facilities. Partnerships with key global and strong local players allow us to take our products to patients worldwide.

Our capabilities and technologies have given us the 'enduring edge' and helped us emerge as an end-to-end player with a strong pipeline of approved and in-development biosimilars and novel molecules.

Biosimilars

Biocon has one of the largest global biosimilars portfolios, spanning recombinant human Insulin (rh-Insulin), insulin analogs, monoclonal antibodies and other biologics for diabetes, oncology and immunology. We have successfully commercialized several of our biosimilars in various markets across the globe.

MONOCLONAL ANTIBODIES

Biocon has been developing a high-value portfolio of biosimilar mAbs and recombinant proteins in partnership with Mylan since 2009. During FY18, we made significant progress with milestone approvals in key developed and emerging markets.

Trastuzumab

December 2017 was a defining moment in our biosimilars journey when Biocon and partner Mylan became the first companies globally to receive U.S. Food and Drug Administration (FDA) approval for biosimilar Trastuzumab. Ogivri™ (trastuzumab-dkst) was the first biosimilar from Mylan and Biocon's joint portfolio approved in the U.S., and it made us the first Indian company to receive a U.S. FDA approval for a biosimilar.

This approval, ahead of major global biotechnology competitors, demonstrates our scientific depth, quality of the teams and our ability to execute on difficult-to-develop and manufacture, complex products like biosimilars. Placing us in an exclusive league of global biosimilar players, this approval has established Biocon as a credible biologics player from India that can compete with the best in the world.

The data package presented to the FDA included results from structural and functional characterization of the biosimilar molecule, non-clinical studies and pharmacokinetic (PK) evaluation in healthy volunteers. Data also included results from India Phase III and multi-centric global HERITAGE studies, which compared the biosimilar to the reference product in terms of safety, efficacy and immunogenicity in nearly 600 patients. Biocon and Mylan submitted extensive analytical, non-clinical and clinical study data to the FDA as a part of the Biologics License Application (BLA) for biosimilar Trastuzumab.

The data demonstrated that Ogivri™ is highly similar to Herceptin® and no clinically meaningful differences exist between the two in terms of safety, purity and potency.

The U.S. FDA's Oncologic Drugs Advisory Committee (ODAC) unanimously voted (16-0) endorsing the approval of our biosimilar Trastuzumab in July 2017, and in December 2017 the FDA granted final approval for our product.

Ogivri™ will enable Biocon and Mylan to provide an affordable, high quality alternative for eligible cancer patients in the U.S., where it has been approved for all indications included in the label of the reference product, Herceptin®, including for the treatment of HER2-overexpressing breast cancer and metastatic gastric cancer. In the U.S., an estimated 2,50,000 new cases of female breast cancer and 28,000 new cases of stomach cancer were diagnosed in 2017 alone. Approximately 25% of primary breast cancers are HER2-positive. Herceptin® had U.S. sales of USD 2.7 billion in 2017, according to IMS.

Our partner Mylan anticipates potentially being the first company to be able to offer this biosimilar to patients in the U.S., as a result of its ability to secure global licenses for our Trastuzumab product from Genentech and Roche earlier in 2017. The settlement gives Mylan a global license to commercialize biosimilar Trastuzumab product in various markets around the world.

HIGHLIGHTS

Trastuzumab

Type: mAb

Indications: HER2-overexpressing breast cancer and metastatic stomach cancer (gastric or gastroesophageal junction adenocarcinoma)

GLOBAL SALES:

USD 7.1 billion*

**Source: Company reports*

We also received regulatory approvals for biosimilar Trastuzumab in Brazil and Turkey, two of the Top 4 emerging markets for this key breast cancer drug. Our product, sold as Zedora through our partner Libbs Farmaceutica, has been well received in Brazil.

Our biosimilar Trastuzumab is currently under review by regulatory authorities in Australia, Canada, EU and several additional markets.

Biocon's introduction of CANMAb™ in India in 2014 as the world's first biosimilar Trastuzumab had opened the doors for the patients to access an affordable therapy, which is now the No. 1 brand of Trastuzumab in the country, has garnered a volume market share of over 30% in India. *(Source: IMS TSA February 2018).*

CANMAb™ has helped treat ~12,700 HER2-positive metastatic breast cancer patients in India since its launch in 2014. *(Source: IPSOS 2017).*

The results of the HERITAGE study were published in the Journal of the American Medical Association (JAMA) in 2016, as well as, presented at the American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago, U.S. and the European Society for Medical Oncology (ESMO) Congress in Copenhagen, Denmark. Recently, Mylan and Biocon presented new 48-week data from the HERITAGE study at the 2018 ASCO Annual meeting reinforcing the efficacy, safety and immunogenicity of Ogivri™, the first biosimilar for Herceptin® to be approved.

HIGHLIGHTS

Bevacizumab

Type: mAb

Indications: First-line treatment of patients with metastatic colorectal cancer, and is accepted as a standard treatment option in combination with chemotherapy for patients with non small-cell lung cancer, glioblastoma, cervical cancer, metastatic renal cell carcinoma and recurrent ovarian cancer.

GLOBAL SALES:

USD 6.8 billion*

**Source: Company reports*

Bevacizumab

We successfully launched our biosimilar Bevacizumab in India as KRABEVA® for patients of various types of cancer in November 2017. KRABEVA®, our second oncology biosimilar in India after Trastuzumab, is prescribed for metastatic colorectal cancer (mCRC) and several other types of lung, kidney, cervical, ovarian and brain cancers. This high quality, world-class biosimilar Bevacizumab has benefited a large number of patients in India within a few months of its launch.

Bevacizumab was one of Biocon's first endeavors in the biologics (biosimilar) sphere. The journey of developing a biosimilar Bevacizumab, which blocks blood and oxygen supply to cancerous cells arresting their growth, began in 2008 with a very extensive analysis of the protein sequence. The analysis helped us identify the sequence that encodes the DNA for the Bevacizumab antibody. This DNA sequence, inserted into the Chinese Hamster Ovary (CHO) cells, transcribed the Bevacizumab protein. Once the protein was transcribed it was purified and formulated in a liquid to stabilize it. The expressed protein was extensively characterized using a battery of highly sophisticated techniques at various stages of development, which helped determine the analytical similarity to the reference product in terms of its structure, purity and functionality.

We conducted a three-way Phase I PK study in healthy volunteers in Europe using EU and U.S. sourced reference products, and the study met its primary endpoints.

Subsequently, our biosimilar Bevacizumab underwent a Phase III study in mCRC patients in India, which met its PK, safety and efficacy endpoints.

The Drug Controller General of India (DCGI) approved our biosimilar Bevacizumab in 2017 on the basis of our data package, which included results from the Phase I study and the Phase III India study.

The global development of our biosimilar Bevacizumab is on track. A Phase III trial in non-small-cell lung cancer patients is progressing well at more than 100 sites across multiple countries.

RECOMBINANT HUMAN PEG - GCSF

Biocon and Mylan have successfully developed a biosimilar Pegfilgrastim, a long-acting pegylated granulocyte colony-stimulating factor, to enable enhanced access to a cost-effective alternative to reduce the duration of neutropenia (low count of neutrophils, a type of white blood cells) and the incidence of fever associated with neutropenia in adult patients treated with chemotherapy in certain types of cancer.

Pegfilgrastim

In June 2018, Biocon and its partner Mylan became the first to receive approval for a biosimilar Pegfilgrastim from the U.S. FDA. We were able to cross the finishing line ahead of a pack of strong competitors who are also developing this product.

Once launched, Fulphila™ (pegfilgrastim-jmbd) will give cancer patients in the U.S. the first alternative and affordable treatment option to branded Pegfilgrastim. It is the second biosimilar from Mylan and Biocon's joint portfolio to be approved in the U.S. after biosimilar Trastuzumab.

Fulphila™ will help patients with nonmyeloid cancers reduce the risk of infection following myelosuppressive chemotherapy.

The approval for Fulphila™ was based on a comprehensive package of analytical, non-clinical and clinical data, which demonstrated that there were no clinically meaningful differences between the biosimilar and the reference product in terms of safety, purity and potency. It represents a further endorsement of the Biocon-Mylan partnership's ability to successfully develop complex molecules to exacting quality and regulatory standards.

The approval of biosimilar Pegfilgrastim expands our oncology portfolio for the benefit of cancer patients and supports our mission to improve access to high quality, affordable biopharmaceuticals globally.

Regulatory reviews of our biosimilar Pegfilgrastim dossier in EU, Australia and Canada are progressing well.

HIGHLIGHTS

Pegfilgrastim

Type: Granulocyte growth factor

Indications: Reducing the duration of neutropenia (low count of neutrophils, a type of white blood cells) and the incidence of fever associated with neutropenia in adult patients treated with chemotherapy in certain types of cancer.

GLOBAL SALES:

USD 4.7 billion*

**Source: Company reports*

INSULINS

We made sure-footed progress towards our aspiration of providing our insulins to 'one in five' insulin-dependent people with diabetes globally.

During the year, we received approvals in key developed and emerging markets for our rh-Insulin and Insulin Glargine. Insulin and analogs present a huge global opportunity for us with a volume growth of over 20% between 2013 and 2017. *(Source: IMS MAT June 2017).*

Insulin Glargine

As a credible, global insulins player, we are committed to addressing the growing healthcare challenges associated with diabetes. To deliver on this commitment, we have made significant investments in developing and manufacturing a leading portfolio of insulin analogs, including Insulin Glargine.

Semglee™ 100 units/mL 3 mL prefilled disposable pen, our biosimilar Insulin Glargine co-developed with Mylan, was approved by the European Commission for sale in all 28 European Union (EU) member states and the European Economic Area (EEA) member states of Norway, Iceland and Liechtenstein. The approval followed a positive opinion issued by European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) recommending approval of our Insulin Glargine in EU. The first biosimilar approval in EU from our joint portfolio, it is yet another validation of our development, regulatory and manufacturing capabilities.

Semglee™ 100 IU/mL 3 mL prefilled pen was also approved by the Therapeutic Goods Administration (TGA), Australia.

Semglee™ is expected to be launched by our partner Mylan in Australia and Europe in the second half of 2018.

Additionally, Biocon received regulatory approvals for its biosimilar Insulin Glargine in Russia and South Korea. Russia is among the Top 3 emerging markets for Glargine.

During FY18, Biocon launched Glaricon™ (Insulin Glargine) its first biosimilar product in the UAE market.

In the U.S., Mylan's application for Insulin Glargine under the NDA pathway is under review by the U.S. FDA. A 30-month stay was triggered on Insulin Glargine approval due to expected patent litigation initiated by the innovator, which implies a potential launch timing in 2020.

HIGHLIGHTS

Insulin Glargine

Type: Long-acting insulin analog

Indications: Control of high blood sugar in adults with Type 2 diabetes; adults and pediatric patients with Type 1 diabetes.

GLOBAL SALES:

USD 5.2 billion*

**Source: Company reports*

Following the submission of our Insulin Glargine application, we had agreed with the U.S. FDA to provide additional clinical data in support of the manufacturing site change from Bengaluru to Malaysia. Hence, the Complete Response Letter (CRL) was anticipated and built into our plan. Together, Mylan and Biocon are executing on all required activities as agreed upon with FDA, and they are progressing according to plan. We do not anticipate any impact on the expected timing of the approval and the anticipated launch by our partner Mylan.

Other Programs

Work on our recombinant human insulin product targeted at the U.S. market and two other global programs for insulin analogs (Insulin Aspart, Insulin Lispro) continues.

For Insulin Aspart, we have just successfully completed our Phase I study.

Our insulins manufacturing facilities in Bengaluru and Malaysia underwent several key inspections during FY18, which would enable regulatory approvals in some emerging markets going forward.

We expect that our near-term growth in biosimilars will be driven by expanding our footprint in key emerging markets through strong local partnerships. Product approvals and commercial success in the developed markets of the U.S. and Europe would be significant milestones that can help the Company lay a strong foundation to stay ahead of the game in biosimilars in the next decade. These will be supported by capacity expansions in a phased manner and additions to our product portfolio to cater to the next wave of opportunities.

Status of Biocon's Global Biosimilars Portfolio

Partner	Therapeutic Area	Molecule	Status
Mylan	Oncology	Trastuzumab	Approved in U.S. Under review in EU, Canada and Australia. Launched in emerging markets.
	Diabetes	Insulin Glargine	Approved in EU & Australia. Under review in U.S. and Canada. Launched in Japan* through partner FUJIFILM Pharma. Launched in emerging markets.
	Oncology	Pegfilgrastim	Approved in U.S. Under review in EU, Canada and Australia.
	Diabetes	Insulin Aspart	Global Phase I study completed.
	Diabetes	Insulin Lispro	Preclinical.
	Autoimmune	Adalimumab	Global Phase III completed.
	Oncology	Bevacizumab	Global Phase III ongoing. Launched in India.
	Oncology	Filgrastim	Preclinical.
	Autoimmune	Etanercept	Preclinical.
Lab Pisa	Diabetes	Recombinant Human Insulin	Preclinical.
Sandoz	Oncology & Immunology	Various	Early Stage / Preclinical.

**Japan launch is outside of Mylan partnership.*

Expanding Our Biosimilars Pipeline

After successfully collaborating with Mylan for near-term biosimilars opportunities, we have partnered with Sandoz, a Novartis division and a global player in biosimilars.

This collaboration is targeted at developing a next-generation biosimilars portfolio which will help patients worldwide gain access to a range of high quality, affordable immunology and oncology biologics. Biocon and Sandoz will strategically leverage their combined strengths to address the next wave of the global biosimilars opportunities.

Under the terms of the agreement, both companies will share the responsibility for end-to-end development, manufacturing and global regulatory approvals for a number of products and will have a cost and profit share arrangement globally. Worldwide commercialization responsibilities will be divided and each company's strengths tapped within specific geographies. While Sandoz will lead commercialization in North America (U.S. & Canada) and the EU, Biocon will lead commercialization in Rest of the World including India, Russia and the CIS.

We have agreed to extend the Mylan partnership to include two new assets.

Through both these collaborations, we are targeting opportunities that are expected to open up in the middle of next decade.

Novel Biologics

As practitioners of frontier science, we have built a pipeline of novel biologics that can address the unmet medical needs in diabetes, cancer and autoimmune conditions. Our basket of novel assets under development, representing an interesting combination of early and advanced stage programs, progressed in the clinics in FY18.

Insulin Tregopil

Our quest for a game changing delivery method for insulin led Biocon to endure an arduous journey to clinically validate Insulin Tregopil, a first-in-class oral insulin molecule for post-prandial glycaemic control. As a novel insulin molecule it mimics the physiological benefits of direct delivery into the portal vein and promises to offer better patient compliance. Biocon has endured and invested in this long development phase driven by its strong belief in the attributes of this asset.

Our conviction that our success would enable us to make a very significant change in diabetes management continues to push us forward. Studies conducted in people with Type 1 diabetes, Type 2 diabetes as well as normal healthy volunteers have demonstrated an excellent safety profile for Tregopil, with evidence of significant post-prandial glucose excursion control in Type 2 diabetes patients.

During the fiscal, we initiated a pivotal Phase II/III study in Type 2 diabetes patients in India with Tregopil. We also tied up with JDRF, a leading U.S. organization funding Type 1 diabetes research and advocacy worldwide, for a multiple ascending dose study in Type 1 diabetes patient population. These combined studies in different diabetic populations will form the foundation of a broad global program envisioned for Insulin Tregopil.

Itolizumab

Itolizumab is a novel first-in-class humanized anti-CD6 monoclonal antibody approved in India for treating psoriasis. Itolizumab binds to a specific molecule (CD6) on the surface of white blood cells, known as T cells. The binding of Itolizumab to CD6 on T cells blocks the autoimmune activation of these cells, which would otherwise have resulted in the formation of skin rashes, known as plaques in patients with psoriasis.

After receiving approval from the DCGI, we launched our Itolizumab under the brand name ALZUMAb™ in 2013, offering dermatologists the option of prescribing a biologic to treat acute psoriasis and ensuring a better quality of life for patients. This novel product has been well received by doctors and patients alike, benefiting several hundred patients in India.

Our global development of Itolizumab continues to progress. We completed a Phase I clinical trial in Australia, in which the intravenous route of administration was compared to the subcutaneous route in normal healthy volunteers. Using this data, along with the toxicology data and extensive characterization of the product quality attributes, Biocon

is preparing to submit a request for an investigational new drug application to initiate clinical trials in various other diseases.

Nimotuzumab

Nimotuzumab is India's first indigenously produced novel biologic developed by Biocon and launched in the country as BIOMAb EGFR® for head and neck cancer in 2006.

Nimotuzumab is a targeted therapy that specifically blocks the EGFR protein and impedes cancer cell growth. EGFR (Epidermal Growth Factor Receptor) is overexpressed in about 80-100% of head and neck cancers.

Through the introduction of this molecule, Biocon has enhanced the treatment outcome as well as quality of life of cancer patients in India.

With an excellent safety and efficacy profile, BIOMAb EGFR® remains one of the most preferred targeted therapies in the treatment of head and neck

cancers. BIOMAb EGFR® has helped treat thousands of patients since launch. It has seen nearly 1,200 new patient enrollments in FY18.

Recently, the results of a randomized controlled clinical study conducted in 536 patients with our Nimotuzumab at the Tata Memorial Hospital (TMH), Mumbai were presented at the 2018 American Society of Clinical Oncology (ASCO) Annual Meeting held in Chicago.

The investigator-initiated study, one of the largest randomized clinical studies on head and neck cancer patients in India, evaluated the efficacy and safety of administering Nimotuzumab during concurrent chemo-radiation in locally advanced head and neck squamous cell carcinoma (LAHNSCC). Adult patients of LAHNSCC were randomized 1:1 into either radical radiotherapy with weekly cisplatin (CRT arm) or the same schedule of chemo-radiation with weekly Nimotuzumab (NCRT arm). The primary endpoint of the study was 'progression free survival', while other key secondary endpoints were 'disease free survival', 'duration of loco-regional control' and overall survival. The study successfully met the primary endpoint Median progression free survival of 60.3 months in NCRT arm as compared to 21 months in CRT arm which was statistically significant.

Dr Kumar Prabhash, Head, Solid Unit, Medical Oncology, TMH and his team has conducted this large patient study over a period of six years to establish the superior profile of Nimotuzumab and the difference it can make to patients. The results also showed that the addition of Nimotuzumab to chemo-radiotherapy improved the locoregional control rate, disease free survival and had a trend towards improvement in overall survival.

The positive results from this study are a significant milestone in Biocon's ongoing efforts to establish Nimotuzumab's 'best-in-class' status for the treatment of one of the most common forms of cancer in India.

QPI-1007 (siRNA)

Our partnered program with Quark Pharma, QPI-1007, a novel siRNA molecule to treat non-arteritic ischemic optic neuropathy (NAION), continued to make good progress in pivotal global Phase II/III studies during the year, with patients randomized in India. Biocon is the first biopharma organization in India to have forayed into the exciting space of (small interfering RNA) siRNA-based therapeutics.

FmAb2

In Immuno-Oncology, Biocon's lead program, FmAb2, is a fusion protein of EFGR mAb and TGFß RII ECD. This fusion antibody works on the concept of preferentially delivering immune modulators to the tumor site, providing a potentially broad clinical opportunity in multiple tumor types. With this molecule, we have already established Pharmacology and Mechanism of Action (MoA) via in-vitro and in-vivo tumor models. This fusion antibody progressed in pre-clinical development during FY18.

Biocon recognized the importance of developing the technology, critical mass and skillsets required for biologics at a time when few international players existed with almost no Indian player in this space. Today, we have developed a robust biosimilars pipeline, perhaps one of the largest in the world. As a result, we are now attractively positioned to capitalize on the unfolding global opportunity for these advanced therapies.