BIOCON'S
TRASTUZUMAB JOURNEY

Making Quality Cancer Care Affordable

We created history in December 2017 when biosimilar Trastuzumab co-developed with our partner Mylan won approval from the U.S. Food and Drug Administration (FDA). Ogivri™, a drug for treating aggressive forms of breast and gastric cancers, is the first biosimilar Trastuzumab to be approved in the U.S. It defines an inflection point in Biocon's biosimilars story as Ogivri™ is not only the first biosimilar from our joint portfolio with Mylan to get a regulatory approval from the U.S. FDA but has also made us the first Indian company to have a biosimilar approved in the U.S.

Trastuzumab is a targeted therapy indicated for the treatment of certain HER2-positive early stage and metastatic breast cancers, as well as, metastatic gastric cancer. HER2-positive cancers are those that test positive for the human epidermal growth factor receptor 2 (HER2), which promotes cancer cell growth. About 25% of the nearly 2 million women diagnosed with breast cancer each year worldwide have HER2-positive tumors. Trastuzumab is a monoclonal antibody that binds to the HER2 protein in tumor cells and flags it for destruction by the body's immune system. It has been included in the World Health Organization's list of essential cancer medicines.

Initial Development

Our Trastuzumab development journey began in 2008 with the cloning of the antibody. The DNA sequence that encodes Trastuzumab antibody was engineered from a very extensive analysis of the protein sequence. This DNA sequence, inserted into the Chinese Hamster Ovary (CHO) cells, helped transcribe the Trastuzumab protein. The protein was purified from the cell culture and formulated. Subsequently, extensive physicochemical and biological characterization involving highly sensitive and orthogonal comparative analytics across a wide range of product attributes and iterative process development were conducted on the expressed protein to ensure that the characteristics of the biosimilar drug and the reference product fell within the same ranges.

India Launch

In 2011, we initiated a multi-centric Phase III clinical trial in India, administering either the biosimilar or the reference product in patients in a blinded manner. The clinical studies conclusively established the similarity of our Trastuzumab to the reference product in terms of pharmacokinetics (PK), safety, efficacy and immunogenicity. On completion of clinical trials in July 2013, the regulatory submission for biosimilar Trastuzumab was made to the Drug Controller General of India. In November 2013, our product became the first biosimilar Trastuzumab to be approved anywhere in the world and in 2014 it was launched in India as CANMAb™.

Global Clinical Studies

In 2013, we started the global HERITAGE study, a double-blind, randomized clinical trial designed to evaluate comparative efficacy and safety of our biosimilar Trastuzumab versus the reference product. Eligible patients had centrally confirmed, measurable HER2-positive metastatic breast cancer without prior chemotherapy or Trastuzumab for metastatic disease. Patients were randomized to receive either the biosimilar or the reference product with taxanes (docetaxel or paclitaxel) for a minimum of eight cycles. Subsequently, patients with at least stable disease were continued with the biosimilar or reference product until disease progression. The primary endpoint was overall response at week 24 by blinded central evaluation using RECIST 1.1. Secondary endpoints included progression free survival, safety and overall survival at 48 weeks. A sample size of 456 patients was calculated to demonstrate equivalence in overall response at week 24 for biosimilar versus the reference product. This HERITAGE study was the last major step of a multi-phased program to demonstrate that our biosimilar Trastuzumab met the criteria for equivalence in comparison to the reference product. Published study results showed an overall response rate of 69.6% for biosimilar Trastuzumab compared to 64% for the reference product. There was no statistical difference between the biosimilar and the reference product at week 48 for tumor progression, progression free survival and overall survival.

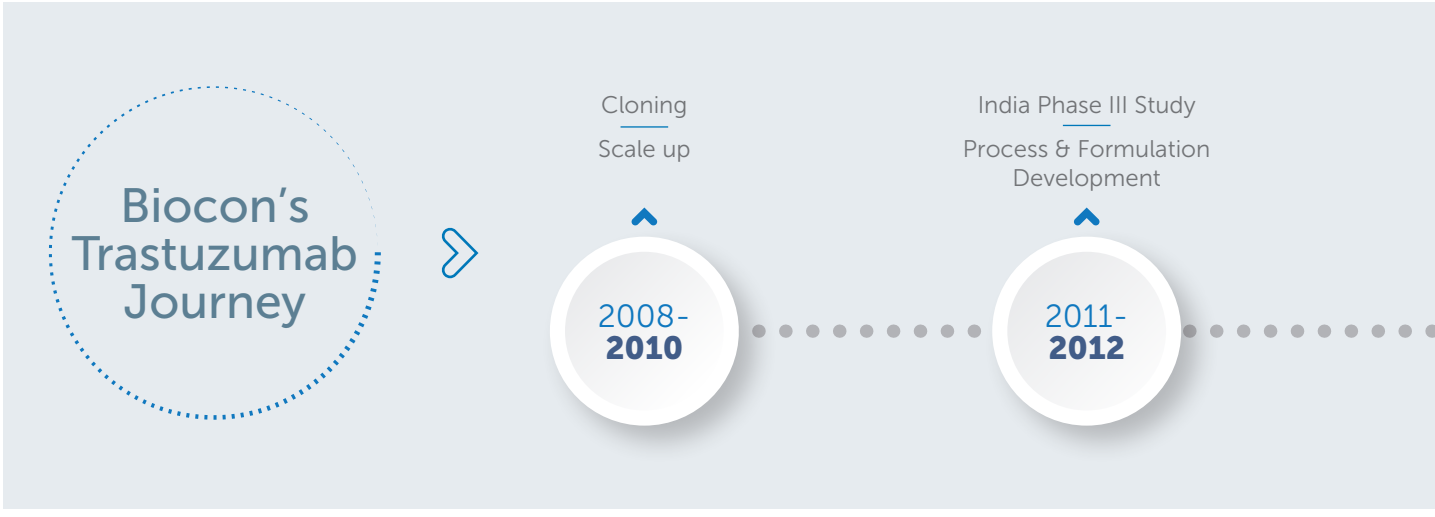
Regulatory Journey

Around 600 patients participated across our India Phase III and multi-centric global HERITAGE studies. The robust data package demonstrated that our product was highly similar to the reference product and no clinically meaningful differences existed between them in terms of safety, efficacy and immunogenicity.

In June 2016, we presented 24-week data from the HERITAGE study at the 2016 Annual Meeting of the American Society of Clinical Oncology (ASCO) in Chicago.

The package was submitted by our partner Mylan to the U.S. FDA as part of the Biologics License Application for biosimilar Trastuzumab in November 2016.

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



approved Ogivri™ (trastuzumab-dkst) for all indications included in the label of the reference product, including for the treatment of HER2-overexpressing breast cancer and metastatic gastric cancer.

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

In 2018, we presented the 48-week data from the HERITAGE study at ASCO's Annual Meeting in Chicago. The 48-week data further demonstrated that Ogivri™ is highly similar to the reference product and no clinically meaningful differences exist between them in terms of safety, purity and potency. We believe this positive data will enable wider adoption of our biosimilar Trastuzumab, thus expanding access to this therapy for cancer patients across the world.

Expanding Global Footprint

We demonstrated our commitment to enhance access to cutting-edge biologics therapy for cancer patients in emerging markets in 2018 when we became the first to get regulatory approvals for biosimilar Trastuzumab in Brazil and Turkey, two of the Top 4 emerging markets globally for this key breast cancer drug.

The U.S. FDA approval of our biosimilar Trastuzumab was not just a milestone for Biocon, but also for India's pharmaceutical industry. Representing a landmark achievement for the Biocon-Mylan collaboration, it is also an endorsement of our development, regulatory and manufacturing capabilities in the area of monoclonal antibodies. This journey has strengthened our resolve to continue to endure the challenges and stay on the chosen path of enabling access to affordable biotherapeutics.

CANMAb™ Approved & Launched in India

Global HERITAGE Study

2013-2014

Final Similarity Package

BLA Filing with U.S. FDA

2016

Ogivri™ Approved - Dec 2017

Post U.S. FDA ODAC's Unanimous (16-0) Vote for Approval in July 2017

2017