Press Release

Biocon Presented Insights into Clinical Study That Enabled DCGI Approval of Itolizumab for COVID-19

Bengaluru, Karnataka, India – July 13, 2020

Biocon Ltd. (BSE code: 532523, NSE: BIOCON), an innovation-led global biopharmaceuticals company, today presented key insights into the results of the pivotal study, which demonstrated the primary endpoint of one-month mortality and other efficacy endpoints were statistically . This led to the Drug Controller General of India (DCGI) approving this novel biologic therapy for restricted emergency use in India.
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Kiran Mazumdar-Shaw, Executive Chairperson, Biocon, said: *"Itolizumab is a 'Made in India,' 'Innovated in India,' first-in-class anti-CD6 monoclonal antibody, which has a seven-year proven track record of safety as doctors in India have been prescribing this biologic therapy to treat acute psoriasis. As Itolizumab has been approved in India and given that we are in the middle of a medical emergency, the regulator has approved Biocon's product for emergency use based on compelling data from a pivotal clinical trial involving a cohort of 30 patients. The two-arm, randomized study met both the primary and secondary endpoints, with the Itolizumab arm demonstrating statistically significant advantage over the control arm, culminating in the drug's approval for restricted emergency use by the DCGI. The study results show that Itolizumab's unique mechanism of action can bring down mortality in moderate to severe ARDS patients due to COVID-19."*

A multi-centric, open label, two-arm randomized Phase 2 clinical trial was conducted in 30 eligible patients at four hospitals across Mumbai and New Delhi. Twenty patients were randomized to receive Itolizumab plus best supportive care, while 10 patients received best supportive care alone in the control arm. The primary endpoint was mortality at the end of one month.

At the end of the treatment period, Itolizumab demonstrated statistically significant advantage over the control arm in one-month mortality rate. All 20 patients on drug arm who were administered Itolizumab improved or were stable after Day 14 onwards. Whereas three out of ten patients in the control arm with best standard of care died. Key efficacy parameters of lung function such as PaO2 and SpO2 (oxygen saturation) improvement without increasing FiO2 (oxygen flow) also showed

statistically significant advantage for the Itolizumab arm over the control arm. All patients on the Itolizumab arm were weaned off oxygen by Day 30, and none needed ventilator support unlike the control arm.

Key secondary endpoints of clinical markers of inflammation such as IL-6, TNF-α, serum ferritin, d-dimer, LDH and CRP showed clinically significant suppression post Itolizumab dosing and correlated well with clinical improvement in symptoms and chest X-ray images.

Itolizumab was overall well tolerated and found to be safe with infusion reactions manageable with slowing infusion rate.

Itolizumab when administered to patients with moderate to severe ARDS due to COVID-19 effectively controlled hyper-activation of the immune system in response to the SARS-CoV-2 virus and reduced morbidity and mortality related to the 'cytokine storm'. Older patients and those with co-morbidities like diabetes and hypertension, who were treated with Itolizumab, recovered well.

The results of Biocon's clinical trial support the hypothesis that Itolizumab's novel immune-modulating mechanism of action is effective in addressing the severe 'cytokine storm' experienced by COVID-19 patients.

These results are in line with findings from a similar clinical trial in Cuba, where 76 COVID-19 patients were treated with Itolizumab. At the end of the trial, 79% of severely ill patients were discharged from the ICU after 14 days of treatment, while moderately ill patients showed a reduction in the rate of disease progression.

The DCGI's approval for restricted emergency use of Itolizumab to treat COVID-19 patients with moderate to severe complications is timely as it will urgently provide physicians and patients with a new treatment option at a time when novel coronavirus infections are surging in India.

Dr Rahul Pandit, Director of Critical Care Services, Fortis Hospital, Mumbai, said: *"There are not many drugs currently available to block the COVID-19-induced cytokine release syndrome (CRS), which patients typically experience at the start of the second week of the viral infection. I used only a single dose of Itolizumab on my patients at the onset of CRS and the drug's mechanism of action of immunomodulation suppressed the pro-inflammatory cytokines, and the patients showed clinical improvement."*

Dr Vishal Gore, Physician and Intensivist, Markandeya Hospital and CNS Hospital, Solapur, said: *"COVID-19 patients who present co-morbidities such as diabetes and hypertension have a higher chance of experiencing the 'cytokine storm' as a result of the novel coronavirus infection. I administered Itolizumab to a few of my patients who were showing serious COVID-19 complications, and this drug has by far given the best experience. None of the patients treated with Itolizumab suffered from sepsis or other bacterial infections after using the drug. The drug is also affordable considering that it can reduce three to four days in ICU on a ventilator, which can be far more expensive."*

Dr. Sandeep Athalye, Chief Medical Officer, Biocon Biologics, said: "*As a patient-centric organization, I am very pleased that our team responded to the need of the hour and repurposed Itolizumab for this new indication that is now saving lives. In addition to the encouraging clinical trial results, we have seen similar promising efficacy in over 150 patients treated under compassionate use by many doctors. We will be publishing the trial data as well as real world data to further strengthen the body of evidence for Itolizumab. We hope to reach all the patients who need this product in time and are now working towards ramping up to meet those needs."*

Other Findings

The clinical trial showed that if Itolizumab is best administered in the pulmonary phase of the COVID-19 infection when the cytokine build-up is starting, and the patient is experiencing shortness of breath and exhibiting abnormal chest images. It prevents progression to the hyperinflammation phase (cytokine storm) and other complications such as coagulation and organ failure.

Also, the current approaches targeting IL-6 receptor blocking inhibits signalling of IL-6 alone and benefit some patients. However, the administration of Itolizumab leads to reduction in several inflammatory cytokines such as IL-6, IL-2, TNF-α and IL-17, offering a wider suppression of cytokines.

Partner Equillium Plans Global Clinical Trial of Itolizumab in COVID-19

Equillium, Biocon's commercial partner for Itolizumab in the U.S., Canada, Australia and New Zealand, is moving quickly to initiate a global study of Itolizumab that would support approval of the therapeutic in the U.S. and elsewhere so that the therapy may become available in the shortest time possible to the greatest number of patients worldwide.

Equillium is currently studying Itolizumab under two open U.S. INDs for the treatment of acute graft-versus-host disease (aGVHD) and lupus nephritis, as well as conducting an additional clinical study in uncontrolled asthma in Australia and New Zealand.

Availability of Itolizumab in India

Each ALZUMAb® (Itolizumab) injection is presented as a 25mg/5mL solution, which costs Rs 7,950 per vial. Based on an average body weight of 60 kg, the therapy cost of a single dose comprising four vials is estimated to be ~Rs 32,000 (MRP).

Biocon has been successful in making adequate supplies available to patients in the multi-centric clinical trial that just concluded in India. The Company has the manufacturing capacity and the supply and distribution network in place, which we are now looking to ramp up further to reach a larger number of patients across the country. Currently, there is a huge demand and Biocon wants to ensure Itolizumab first reaches those patients who need them the most. Concurrently, we are ramping up production capacity to meet surging demand.

About Itolizumab

Itolizumab is a 'first-in-class,' humanized IgG1 monoclonal antibody (mAb) that selectively targets CD6 cells. This anti-CD6 mAb inhibits activity and trafficking of Teff cells by selectively targeting the CD6/ALCAM pathways. CD6 is a pan T-cell marker involved in co-stimulation, adhesion and maturation of T-cells. Itolizumab, by binding to CD6, down regulates T-cell activation, causes reduction in synthesis of pro-inflammatory cytokines and possibly plays an important role by reducing T-cell infiltration at sites of inflammation.

Biocon developed and received approval for Itolizumab in the treatment of chronic plaque psoriasis in India in 2013, demonstrating the product was safe and well tolerated. Itolizumab is produced at commercial scale at Biocon's cGMP bio-manufacturing facility that is regulated by the U.S. Food & Drug Administration.

In May 2017, Itolizumab was outlicensed for the U.S. and Canada markets to U.S.-based biotechnology company Equillium. During FY20, the scope of the licensing agreement with Equillium for Itolizumab was expanded to include Australia and New Zealand. Itolizumab holds broad potential as a 'pipeline in a product' with multiple high-value indications applicable with three clinical studies underway across the globe in acute graft-versus-host disease (aGVHD), severe asthma and lupus nephritis.

About Itolizumab's Mechanism of Action in COVID-19

Upon COVID-19 viral invasion, the antigen presenting cells (APCs) in the airways/lungs, such as dendritic cells and macrophages, initiate the innate and adaptive T cell responses. This is done through an interaction between CD6 (a surface glycoprotein on the T-cells) and ALCAM (activated leukocyte cell adhesion molecule) which

modulates T-cell activation. Itolizumab, our novel biologic, is an anti-CD6 humanized IgG1 anti-inflammatory monoclonal antibody that binds to domain 1 of CD6 and inhibits T-cell priming, activation and differentiation. This reduces the release and overproduction of pro-inflammatory cytokines through Th1 and Th17 and contains and controls the cytokine storm associated with COVID-19 complications.

About Biocon Limited

Biocon Limited, publicly listed in 2004, (BSE code: 532523, NSE Id: BIOCON, ISIN Id: INE376G01013) is an innovation-led global biopharmaceuticals company committed to enhance affordable access to complex therapies for chronic conditions like diabetes, cancer and autoimmune. It has developed and commercialized novel biologics, biosimilars, and complex small molecule APIs in India and several key global markets as well as generic formulations in the US and Europe. It also has a pipeline of promising novel assets in immunotherapy under development. www.biocon.com Follow-us on Twitter: @bioconlimited

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Forward-Looking Statement: Biocon

This press release may include statements of future expectations and other forward-looking statements based on management's current expectations and beliefs concerning future developments and their potential effects upon Biocon and its subsidiaries/ associates. These forward-looking statements involve known or unknown risks and uncertainties that could cause actual results, performance or events to differ materially from those expressed or implied in such statements. Important factors that could cause actual results to differ materially from our expectations include, amongst other: general economic and business conditions in India and overseas, our ability to successfully implement our strategy, our research and development efforts, our growth and expansion plans and technological changes, changes in the value of the Rupee and other currency changes, changes in the Indian and international interest rates, change in laws and regulations that apply to the Indian and global biotechnology and pharmaceuticals industries, increasing competition in and the conditions of the Indian and global biotechnology and pharmaceuticals industries, changes in political conditions in India and changes in the foreign exchange control regulations in India. Neither Biocon, nor our Directors, or any of our subsidiaries/associates assume any obligation to update any particular forward-looking statement contained in this release.

The content of this Press Release was updated to reflect the final Clinical Study Report on Itolizumab