1. GENERIC NAME
Itolizumab for Injection (r-DNA Origin)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Active ingredient: Itolizumab
Excipients: Histidine, Histidine Hydrochloride Monohydrate, Sucrose, Polysorbate 80
and Water for Injection as diluent
For full list of excipients, See Description (Section 7) for details.

3. DOSAGE FORM AND STRENGTH
Each vial contains:
Itolizumab (r-DNA origin) 100 mg
For i.v. infusion only. Single use vial. Lyophilised Powder
Itolizumab is a humanized recombinant anti-CD6 monoclonal antibody.
Alzumab-L® (Itolizumab for injection 100 mg/vial Lyophilised powder)
See Description (Section 7) for details.

Note: Alzumab® referred in this package insert is for Itolizumab injection 25 mg/5 mL solution and Alzumab-L® referred in this package insert is for Itolizumab for injection 100 mg/vial Lyophilised powder

4. CLINICAL PARTICULARS
4.1 Therapeutic indication
Alzumab-L® (Itolizumab for Injection) is indicated for the:
- Treatment of patients with active moderate to severe chronic plaque psoriasis who are candidates for systemic therapy.
- Treatment of Cytokine release syndrome (CRS) in moderate to severe Acute Respiratory distress syndrome (ARDS) patients due to (COVID-19).

Limitations of Use
The safety and efficacy of Itolizumab for Injection Alzumab-L® has not been studied in, (a) pediatric patients <18 years old; (b) patients with hepatic and renal impairment; (c) pregnancy and, (d) nursing mothers.

4.2 Posology and method of administration
Pre-Medication
Hydrocortisone 100 mg IV (or equivalent short acting glucocorticoid) and pheniramine 30 mg IV are given about 30 ± 10 minutes prior to each infusion. Alzumab-L® is intended for use under the guidance and supervision of a physician. The diluted infusion solution should be prepared by a trained medical professional using an aseptic technique, as follows:
- Calculate the dose and the number of Alzumab-L® vials needed. Alzumab-L® is provided as a sterile, preservative-free single-use vial for IV-Infusion, Lyophilized powder. Each vial contains 100 mg of Itolizumab (100 mg/vial). The vial is to be reconstituted using 1.1 mL WFI prior to use. The reconstituted solution for injection is a colorless to pale yellow solution at a concentration of 100 mg/mL at pH of 6.0±0.5. (see Pharmaceutical particulars sections). The reconstituted Alzumab-L® solution is stable in the vial for ~48 hours at 2-8°C and ~8 hours at 25°C. [see Pharmaceutical Particulars sections].
- Alzumab-L® should be administered via IV infusion in 250 mL of 0.9% Sodium Chloride solution (normal saline). For this, dilute the appropriate dose of Itolizumab for injection Alzumab-L® to 250 mL with sterile normal saline. Gently mix.

Note: Itolizumab infusion is not to be prepared in dextrose solution.
- Fully diluted Alzumab-L® solution should be allowed to reach room temperature prior to infusion. Before use, the fully diluted Alzumab-L® solution may be stored at room temperature, protected from light. Alzumab-L® is stable in an infusion bag containing 250 mL of normal saline for up to 12 hours at room temperature. Do not administer as IV push or bolus.It is recommended to administer the drug using a infusion set with an in-line, sterile, non-pyrogenic, low protein-binding filter (pore size of 0.2 µm). The infusion period can be extended up to 8 hours for medical reasons.

Note: Prior to initiating Alzumab-L® and periodically during therapy patients should be evaluated for active tuberculosis and tested for latent infection and history of severe allergy. History of known hypersensitivity reaction to any component of Alzumab-L® or any CHO proteins should be evaluated [see Special Warnings and Precautions for Use and Contraindications sections].

1) Plaque Psoriasis
The recommended dose of Alzumab-L® for the treatment of plaque psoriasis is 1.6 mg/kg given as IV infusion once every 2 wks for 12 wks, followed by 1.6 mg/kg every 4 wks up to 24 wks.

Approximately 50 mL of diluted Itolizumab for Injection Alzumab-L® reconstituted solution should be administered during the first hour, followed by remaining solution in the next hour.

2) Treatment of Cytokine Release Syndrome (CRS) in moderate to severe Acute Respiratory Distress Syndrome (ARDS) patients due to COVID-19
The recommended dose of Alzumab-L® is 1.6 mg/kg given as IV infusion as a starting dose. Based on the clinical status and serum inflammatory markers, additional dose of 0.8mg/Kg can be administered after 7 days based on the physician's discretion. First infusion of Itolizumab at 1.6mg/ kg must be initiated at 25 ml/h for the first hour. If well tolerated it can be increased to 50 mL/h to infuse the remaining amount. The infusion is to be completed over a period of 5-6h.
In case the dose had to be interrupted due to an infusion reaction, the dosing must be restarted very slowly after constant monitoring and appropriate management of vital signs and symptoms. If reaction appears upon re-challenge, dosing must be terminated.
If required, a second infusion of Itolizumab at 0.8mg/Kg is to be given after one week. The infusion can be completed over 3- 4 h.
The clinical trial data supports safety of up to 4 doses.
- The vials do not contain antibacterial preservatives. Therefore, any unused portion of the infusion solution should not be stored for reuse [see Pharmaceutical Particulars sections].
- No physical or biochemical compatibility studies have been conducted to evaluate the co-administration of Alzumab-L® with other agents. Alzumab-L® should not be infused concomitantly in the same IV line with other agents.
- Prior to administration, the reconstituted solution in the vial should be carefully inspected visually for particulate matter and discoloration. If visible opaque particles, discoloration or other foreign particulates are observed, the product should not be used.

4.3 Contraindications
Alzumab-L® should not be administered to patients having a history of severe allergy or known hypersensitivity reaction to any component of Alzumab-L® or any CHO proteins *(see Qualitative and Quantitative Composition)*.

4.4 Special warnings and precautions for use

Warning: Itolizumab is not recommended to be administered to patients who are on an invasive mechanical ventilator. No trials have been done on such patients

Infusion-related reactions and hypersensitivity reactions
During administration of Alzumab-L® some patients may develop acute infusion reactions. Symptoms may include chills/ rigors (common), nausea, flushing, urticaria, cough, hypersensitivity, pruritus, rash, wheezing, dyspnoea, oxygen desaturation (in ARDS patients), dizziness, headache and hypertension. Infusion reactions are most likely to occur during the first cycle of dosing and tend to decrease in severity and frequency upon subsequent infusions.
In the clinical trial Infusion reaction were grade 1 to grade 4 in severity. All of them resolved with appropriate symptomatic management. Acute infusion reactions should be treated using the standard of care; and physicians may need to delay dosing till the patient is stabilized.
In the COVID-19 trial (study III) of Alzumab® the infusion reactions occurred when they were given over 2 hours. However, the reactions were abated when the infusion rate was slowed and was given over 5-6 hours. For Infusion related information see section on Posology and Method of Administration.

Infections
In the psoriasis trial, overall, Alzumab®(Itolizumab Injection) did not appear to increase the rate of infections in patients compared to placebo, during the study. However, physicians should exercise caution before and during Alzumab-L® treatment in patients with a history of recurrent infections or underlying conditions which may predispose them to serious infections. Patients should be closely monitored closely for the development of signs and symptoms of an infection during and after the treatment with Alzumab-L® including patients who were evaluated negative for latent tuberculosis infection prior to initiating the therapy. In case of new infections or reactivation of latent infections during the treatment, Alzumab-L® should be discontinued and immediate treatment in accordance with standard medical practice should be instituted. During the TREAT-PLAQ study with Alzumab®, one case of tubercular lymphadenitis was reported after 4 wks of Itolizumab treatment, in a patient who had prior history of tuberculosis. The patient was withdrawn for safety reasons. During the study, one case of septic arthritis was reported, bacterial culture and acid-fast bacilli (AFB) culture of synovial fluid were negative and causality was inconclusive [see Undesirable Effects]. Overall, Alzumab® did not appear to increase rate of infections in patients compared to placebo, during the study.
Alzumab®and Alzumab-L® has not been studied in patients with a history of serious infections such as HIV-AIDS or active tuberculosis. The effect of Alzumab-L® in these special populations is unknown. Caution should be exercised while administering Itolizumab to immunocompromised patients with Human Immunodeficiency Virus (HIV), Hepatitis B, Hepatitis C infection and patients receiving or received chronic steroid therapy.
Prior to initiating the Alzumab-L® administration, patients should be screened for active or latent tuberculosis infection using Mantoux test and or chest X-ray and or IGRA.

Transient Lymphopenia
In the COVID-19 trial conducted with Alzumab®, patients with ALC < 500mm3 were excluded. Lymphopenia was observed post infusion; however, the lymphopenia was transient in nature and in general reversed within 7 days. The lymphopenia occurring is to be followed up. If persisting it has to be managed as per standard of care.

Use with other biologics
Alzumab-L® has not been studied in combination with other biological agents.

Vaccination
No data are available on the response to vaccination with live/attenuated vaccines or on the secondary transmission of infection by live vaccines in patients receiving Alzumab® and Alzumab-L® therapy. Based on its mechanism of action, Alzumab® and Alzumab-L® may blunt the effectiveness of some immunizations. It is recommended that live/attenuated vaccines not be given concurrently with Alzumab-L®. The patient's vaccination record and the need for immunization prior to receiving Alzumab-L® should be carefully investigated. The interval between vaccination and initiation Alzumab-L® therapy should be in accordance with current vaccination guidelines. Caution is advised in the administration of live vaccines to infants born to female patients treated with Alzumab-L® during pregnancy, since Alzumab-L® may cross the placenta.

Malignancies
None of the patients on Itolizumab injection Alzumab® treatment developed malignancies during the clinical trials.

4.5 Drugs interactions
Drug interaction studies have not been performed with Alzumab-L®.

5.6 Use in special populations
Pregnancy
As with other IgG antibodies, Itolizumab may cross the placenta during pregnancy. It is not known whether Alzumab-L® can cause fetal harm when administered to a pregnant woman, or whether it can affect reproductive capacity or fertility. Animal reproduction studies have not been conducted with Alzumab-L® as it does not recognize peripheral blood mononuclear cells within species other than humans, baboons and chimpanzees (see Nonclinical Properties section).
The available clinical experience is too limited to exclude a risk, and administration of Alzumab-L® is therefore not recommended during pregnancy.

Lactation
It is not known whether Itolizumab is excreted in human milk or absorbed systemically after ingestion. Because many drugs and immunoglobulin are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from Alzumab-L®, a decision should be made whether to discontinue nursing or to discontinue the drug, considering the importance of the drug to the mother.

4.7 Effects on ability to drive and use machines
Treatment with Alzumab-L®, is not expected to effect patient's ability to drive or use machines.

4.8 Undesirable effects
Clinical trial experience in patients
Safety data of Alzumab-L® has been derived from studies of Alzumab® (Itolizumab Injection) 2 randomized, multicentre studies in patients with chronic plaque psoriasis and 1 randomized, multicentre study in COVID-19 complications. Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in clinical trials of

Study I (T1hAb-CT1-001-07) was a randomized, single-blind, parallel-group, phase 2 study in 40 patients. Overall, 123 adverse events (AEs) were reported during the study. The most common AE was chills (5.69%), followed by pyrexia (4.88%). There was a relatively higher incidence of AEs with higher frequency of dosing at each dose. Numerically, the largest number of AEs (n=24) was reported for the highest dose administered in the trial (1.6 mg/kg every 2 wks).
Twenty-nine out of 40 (72.50%) patients in the study reported at least one AE during the study. Seventy-three out of 123 (59.35%) AEs were graded as mild, 46 (37.39%) were graded as moderate and 4 (3.25%) were graded as severe. There were 4 SAEs reported during the study. Three out of 4 SAEs reported were related to musculoskeletal and connective tissue disorders (e.g. arthralgia, other musculoskeletal pain and osteonecrosis) and one was erythrodermic psoriasis. There were 16 acute and 4 possible delayed infusion reactions. All these reactions were mild to moderate and the patients recovered completely. The incidence of infusion reactions was higher during the initial doses and decreased with subsequent dosing. All infusion reactions were mild to moderate in severi

Study II (TREAT-PLAQ) was a double-blind, placebo-controlled, one-way crossover phase 3 study in 225 patients. Overall, there were 289 AEs reported in 111 (49.8%) of the 223 patients in the safety population (i.e. patients who received at least one infusion) during 52-week treatment period. Sixty-six patients (29.6%) patients had mild AEs, 34 (15.2%) had moderate AEs, and 11 (4.9%) had severe AEs. The overall incidence of AEs and related AEs was not meaningfully different between patients randomized to treatment arms A, B and C. Overall incidence of AEs was 50%, 47.8% and 53.5% in treatment arm A, B and C, respectively. Incidence of related AEs was 26.7%, 28.9% and 30.3%, respectively. The most frequently reported AEs (in ≥5% of patients) were infusion-related reactions, pyrexia, upper respiratory tract infection and pruritus (Table 1).

Table 1 Most Frequently Occurring Adverse Events (in >5% of Patients) in the TREAT-PLAQ Study (Wks 1-52)

Infection
Several immunomodulatory agents approved for psoriasis (such as anti-TNF monoclonal antibodies) are known to increase the risk of infections. In the TREAT-PLAQ study, patients were monitored for infections (summarized in Table 2). In general, Itolizumab did not appear to increase the rate of infections as compared to placebo. During the placebo-controlled period, (wks 1-12) the proportion of patients with at least one infection was higher in the placebo arm (18.6%) than in arms A (11.1%) or B (8.9%). Over the course of the study, a total of 40 (17.9%) patients had at least one infection; 26 (11.7%) patients in the first 12 wks and 19 (8.5%) patients in wks 13 to 52 (5 patients had an infection in both periods).

Table 2 Incidence of Infections in TREAT-PLAQ Study

During the TREAT-PLAQ study, one case of septic arthritis was reported 8 months after the start of treatment, which was deemed related to the study drug by the investigator. However, bacterial culture and AFB culture of synovial fluid were negative. Total and differential counts of the patient were stable and in normal range throughout the study.
There was 1 case of tubercular lymphadenitis was observed after 4 wks of treatment (5 doses of Itolizumab, total dose of 3.2 mg/kg) in a patient who had a history of tuberculosis (15 years prior). The patient had WBC and differential counts in the normal range throughout the study participation. The patient was withdrawn from the study for safety reasons. All other infections reported were either mild or moderate in severity.

Vital signs
Vital signs (systolic and diastolic blood pressure, respiratory rate, mean and median pulse rates and temperature) were stable throughout the study.

Immunogenicity
The human anti-humanized antibody (HAHA) response to Itolizumab was evaluated through analysis of immunogenicity of Itolizumab at wks 4, 12, 28, and 52 in the TREAT-PLAQ study. Positive HAHA responses were observed in 51 (23.2%) patients through the study (23 from arm A, 19 from arm B and 9 from arm C). In arm C, 7 patients were positive prior to dosing (during the placebo-controlled phase) and 2 patients were positive after the crossover phase. Fourteen patients had positive titre at visit 1 (prior to dosing with Itolizumab).
There were a few incidences of positive HAHA response during the study. It is not known whether the HAHA detected were neutralizing or not; although positive immunogenic response in patients did not correlate with either infusion reactions or decreased efficacy.

Clinical laboratory abnormalities
Overall, there were no clinically meaningful differences between treatment arms with respect to the proportion of patients with abnormalities in haematology and clinical chemistry. There were 31 abnormal laboratory values that were reported as AEs in 18 patients. Twenty-six (83.9%) out of the 31 AEs were mild and 5 (16.1%) were moderate. Twenty-two (71%) of the 31 abnormal laboratory values were reported in the first 12 weeks of the study and 20 (64.5%) were related to different lipoprotein findings.
Other AEs that do not appear in Special Warnings and Precautions for Use or Undesirable effects sections that occurred at a rate of at least 1% and at a higher rate in the Itolizumab treated patients than the placebo group during the placebo-controlled period of TREAT-PLAQ study (Study II) irrespective of relationship to the study products are listed below:

Gastrointestinal disorders: diarrhoea, toothache, vomiting, gastritis, gastrointestinal inflammation.

General disorders and administration site conditions: Infusion-related reactions (acute and chronic), oedema peripheral, pain, chest pain.

Immune system disorders: hypersensitivity, anaphylactic reaction

Infections and infestations: abscess, folliculitis, gastroenteritis, lymphadenitis bacterial, lymph node tuberculosis, oral herpes, pyrexia, urinary tract infection, rhinitis, tooth abscess.

Metabolism and nutrition disorders: dehydration, hepatic steatosis, hypertriglyceridemia.

Musculoskeletal and connective tissue disorders: musculoskeletal pain, pain in extremity, arthralgia, back pain.

Nervous system disorders: headache, neuropathy peripheral, cerebrovascular accident.

Psychiatric disorders: Adjustment disorder with anxiety.
Renal and urinary disorders: dysuria.
Respiratory, thoracic and mediastinal disorders: cough, oropharyngeal pain, rhinorrhoea

Skin and subcutaneous tissue disorders: psoriasis, keloid scar, dermatitis exfoliative, pruritus, erythrodermic psoriasis.

Study III (ITOLI-C19-02-I-00) (COVID-19 with moderate to severe ARDS): In the trial conducted in moderate to severe ARDS patients with COVID-19 infection, where up to a maximum of 4 doses of Itolizumab injection (Alzumab®) were received, the most frequently reported treatment related emergent adverse event were lymphocyte count decrease, that was transient, and infusion related reaction.
The infusion reaction occurred only during the first infusion. 32% patients reported with infusion related reaction during the first infusion. Most of the infusion reaction presented as chills and were grade 1 and grade 2 in severity except for two events that were of grade 4 severity (anaphylactic reaction and infusion related reaction). The events were managed conservatively and were resolved. These infusion reactions occurred when they were given over 2 hours. However, the reaction were abated when the infusion was given over 5-6 hours For Infusion related reaction see section on Posology and Method of Administration.
There were 11 events of grade III Lymphopenia occurring post infusion and were transient in nature. They reversed spontaneously. The lymphopenia if occurring needs to be followed up. If persisting has to be managed appropriately.

4.9 Overdose
Doses up to 1.6 mg/kg have been administered to patients in clinical trials without evidence of dose-limiting toxicities. During the TREAT-PLAQ study (study II), one patient was overdosed by 23.2 mg with the cumulative dose of 50 mg during the first week of Itolizumab treatment. However, no AE was observed, and the patient was normal. In case of an overdose, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions or effects and appropriate symptomatic treatment instituted immediately.

4.10 Clinical Studies
Psoriasis
The efficacy and safety of Alzumab® was assessed in 2 randomized, multicentric studies (Study I and II) in patients 18 years of age and older with chronic, stable plaque psoriasis involving ≥10% body surface area, a minimum Psoriasis Area and Severity Index (PASI) score of ≥10. All patients had either failed or were intolerant to or had a contraindication to at least one prior systemic anti-psoriatic therapy.
The claim of efficacy is supported primarily by data from pivotal phase 3 trial (TREAT-PLAQ; Study II) in moderate to severe plaque psoriasis. Supporting efficacy data from this patient population was also collected from the phase 2 trial (Study I).
Pivotal Safety and Efficacy Study in Moderate to Severe ARDS patients due to COVID-19
The safety and efficacy of Alzumab® was assessed in Moderate to Severe ARDS patients due to COVID-19 in a multi-centric, randomized trial in patients 18 years of age and older with confirmed virological diagnosis of SARS-CoV2 infection (RT-PCR) (Study III).
Study I (Study T1hAb-CT1-001-07) was a 32-week, randomized, single-blind, parallel, phase 2 study to evaluate the efficacy and safety of Itolizumab in 40 patients of plaque psoriasis. Patients were randomized into 8 groups (5 patients per group), who received 0.4 or 0.8 mg/kg [once every week, once in 2 weeks (wks), once in 4 wks]; or 1.6 mg/kg (once in 2 wks or once in 4 wks). Patients were treated for 8 wks and were followed up for 24 wks. Efficacy parameters of the study included PASI, Physician's Global Assessment (PGA), Psoriasis Severity Scale (PSS); the Short Form-36 (SF-36), Dermatology Life Quality Index (DLQI) questionnaires to assess changes in patient quality of life; and reductions in epidermal as well as rete thickness.
In the overall study cohort (n=40), the mean PASI score decreased consistently for all patients from baseline visit to week 12. The mean PASI score at baseline was 22.32±8.84 which was significantly reduced to 7.62±7.80 at week 8 and 6.23±7.14 at the end of week 12 (p<0.0001). Overall, 72.5% of patients achieved PASI 50 and, 45% achieved PASI 75 at week 12. The reduction in mean PASI scores observed at the end of treatment phase (week 8) continued to persist till the end of week 12 in all dosing cohorts, 62.16% of patients improved or maintained their PASI improvement achieved at week 8 till week 12 after stopping the study drug. The PGA and PSS scores reduced consistently from baseline to week 12 (p<0.0001) for all groups in the study. Moreover, 65% of the patients achieved a score of "minimal" or "clear" by PGA scoring criteria. The proportion of patients with improvement in PASI and PGA scores at wks 8 and 12 is shown in Table 3. In addition, DLQI and SF-36 assessment suggested improvement in the quality of life in the patients owing to improvement of their skin lesions. Lastly, there were significant reduction in mean epidermal (p=0.0005) and rete thickness (p<0.0001) at week 12 compared to baseline; with maximal reduction in both epidermal and rete thickness seen at week 8.

Table 3 Summary of Itolizumab Efficacy Data in Phase 2 Study: Proportion of Patients Achieving Improvement in PASI and PGA Scores, at Week 8 and 12

Study II ("TREAT-PLAQ"; Study T1hAb-CT3-002-09) was a 52-week, randomized, double-blind, placebo-controlled, one-way cross over, pivotal phase 3 study to assess the efficacy and safety of Itolizumab (Alzumab®).
The study was conducted in three double blind phases post screening (2 wks) and washout phases (if necessary, up to 8 wks depending on current treatment):
- Placebo controlled phase (12 wks),
- Crossover of Placebo and consolidation treatment phase (16 wks) and,
- Randomized withdrawal phase (24 wks).

In this study, 225 patients were treated as follows:
Wks 1-12 (double-blind, placebo-controlled): Patients were randomized in a 2:2:1 ratio to following treatment arms: (A) Itolizumab 0.4 mg/kg every week for 4 wks, followed by 1.6 mg/kg every 2 wks for 8 wks; (B) Itolizumab 1.6 mg/kg every 2 wks for 12 wks; or (C) placebo for 12 wks.
Wks 12-24 (double-blind): Patients from arms A and B continued to receive Itolizumab at the dose of 1.6 mg/kg every 4 wks till wks 24; and patients from arm C received Itolizumab at 1.6 mg/kg every 2 wks till wks 24.
Wks 24-52: Week 24-28 was a treatment-free period.
Patients from arm C received Itolizumab at the dose of 1.6 mg/kg every 12 wks, and patients from arm A and B were re-randomized based on their PASI response:
- Patients who achieved ≥PASI 75 were randomized (1:1) to receive either Itolizumab 1.6 mg/kg every 12 wks or placebo (double-blind) till week 52;
- Patients who achieved ≥PASI 50 but <PASI 75 response received Itolizumab 0.4 mg/kg every week for 4 wks followed by 1.6 mg/kg every 4 wks (open-label);
- Patients failing to achieve PASI 50 were withdrawn from the study.

The last dosing visit (at wks 48) was followed by a 4-wks treatment-free follow-up period.
In the TREAT-PLAQ study, the primary endpoint was the proportion of patients achieving ≥PASI 75 at wks 12 in each Itolizumab cohort as compared to placebo. Other evaluated outcomes measured at different intervals were, (a) proportion of patients achieving PASI 50, 75, 90 and 100 from baseline in each Itolizumab cohort; (b) proportion of patients with PGA score in Table 4 "clear" or "minimal" and, (c) change in health-related quality of life as assessed by SF-36 and DLQI.
Two hundred and twenty patients were included in the efficacy population (full analysis set - intent-to-treat [FAS-ITT] population). The proportions of patients who achieved PASI 50, 75, 90 and 100 scores at week 12, 28 and 52 are displayed in Table 4. In the primary analysis, at week 12 both Itolizumab treatment arms A and B demonstrated significant efficacy over arm C (placebo from wks 1-12): 27% of patients from arm A, 36.4% from arm B and 2.3% from arm C achieved PASI 75 at week 12. The proportion of PASI 50 responders followed the same trend as for PASI 75. Thus, Itolizumab produced improvements in PASI 50 and PASI 75, both clinically meaningful outcomes for psoriasis patients.

Table 4 Summary of Itolizumab Efficacy Data in the TREAT-PLAQ Study: Proportion of Psoriasis Patients Achieving PASI 50, 75, 90 and 100 at Week 12, 28 and 52

Figure 1 represents the proportion of patients at each visit up to wks 28 who achieved PASI 75 by treatment arm. The rate of improvement in PASI score was similar in 2 arms (arm A and arm B), though delayed by about 4 wks for arm A, where patients received a lower dose in the first 4 wks compared to patients from arm B. After patients in arm C were crossed over to receive Itolizumab at wks 12, they showed rapid improvement, and by wks 20 the proportion of patients achieving PASI 75 was similar in all arms.

Figure 1: Proportion of Patients Achieving PASI 75 by Study Arm and Visit in the TREAT-PLAQ Study. Bars represent exact 95% confidence intervals.

[Note: At week 12, patients in arm C were crossed over to receive Itolizumab 1.6 mg/kg every 2 wks till week 24. Week 24 to 28 was treatment-free period].
Similar to the improvement in PASI scores, the proportions of patients who achieved PGA score "clear" or "minimal" were higher at week 12 for arm A (20%) and B (16%) than for arm C (5%); but by week 28, the proportions were similar for all three arms (21%, 26% and 23%) (Table 5). Quality of life, as assessed by the SF-36 and DLQI score, improved throughout the study. Improvement in DLQI scores was consistent with PASI scores. The proportion of patients who reported that the disease had only a small or negligible effect on their lives increased in each arm up to week 28.

Table 5 Summary of Itolizumab Efficacy Data in the TREAT-PLAQ Study: Proportion of Patients with PGA Score of "clear" or "minimal" at Week 12, 28 and 52

Study III (Study ITOLI-C 19-02-I-00) was a multi-centric, open label, two arm randomized trial to study the efficacy and safety of Itolizumab (Alzumab®) in COVID-19 complications in 30 patients. Patients were randomized into 2 groups in 2:1 ratio to receive (Arm A) best supportive care + Itolizumab and (Arm B) best supportive care (eg: Antibiotics, Antiviral, Steroids, LMWH, Hydroxychloroquine, multivitamin, oxygen therapy- as per institutional practice). Itolizumab was initiated at 1.6 mg/kg dose iv infusion, and if well tolerated, a weekly dose of 0.8mg/Kg depending on investigator's discretion for upto 4 doses. Majority of the patients were administered two doses.
A statistically significant difference (p = 0.0098) in the 1-month mortality rate was observed between the 2 treatment arms All patients dosed with Itolizumab consistently demonstrated significant improvement in oxygenation parameters.
Overall patients dosed showed decrease in inflammatory markers like ferritin and CRP compared to baseline. There was also a post-dosing reduction in other important markers of organ dysfunction and coagulopathy, such as LDH and D-Dimer, in several patients.
Post administration of Itolizumab, key inflammatory markers like IL-6 and TNF alpha showed a sharp reduction, as evidenced by the mean levels of IL-6 and TNF-alpha in comparison to the control arm which showed an increase.

Study III (Study ITOLI-C 19-02-I-00) was a multi-centric, open label, two arm randomized trial to study the efficacy and safety of Itolizumab (Alzumab®) in COVID-19 complications in 30 patients. Patients were randomized into 2 groups in 2:1 ratio to receive (Arm A) best supportive care + Itolizumab and (Arm B) best supportive care (eg: Antibiotics, Antiviral, Steroids, LMWH, Hydroxychloroquine, multivitamin, oxygen therapy- as per

Itolizumab is a humanized recombinant anti-CD6 mAb of immunoglobulin (Ig) G1 isotype that binds to domain 1 of CD6. The CD6 leukocyte differentiation antigen is a membrane glycoprotein mainly expressed on the surface of mature thymocytes, in most peripheral blood CD3+ T-cells and in a subtype of B-lymphocytes called B1a cells. In the peripheral blood T-cells, CD6 participates in cell activation as a co-stimulatory molecule. The ligand of CD6, Activated Leukocyte-Cell Adhesion Molecule (ALCAM) is widely distributed in normal tissues, including the thymus, spleen, lymph nodes and skin. Itolizumab immunomodulates human lymphocytes without interfering with the binding of CD6 to ALCAM.

Preclinical studies with T-cells showed that the antibody blocks intracellular Mitogen Activated Protein Kinase (MAPK) and Signal Transducer and Activator of Transcription-3 (STAT-3) signalling pathways, the secretion of pro inflammatory cytokines (including tumor necrosis factor-a, interferon-g and interleukin-6) and T-cell prolife