Humanigen

NEWS RELEASE

Lenzilumab Treatment Response in Hospitalized COVID-19 Patients Correlates with C-Reactive Protein Levels

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- Multi-variate analysis of LIVE-AIR Phase 3 data demonstrates that elevated baseline C-Reactive Protein (“CRP”) is the most predictive feature for progression to invasive mechanical ventilation (“IMV”) or death and may be a useful biomarker to guide therapeutic intervention
- Patients with baseline CRP<150 mg/L who received lenzilumab had a more than 2.5-fold higher likelihood to survive without IMV than patients who received placebo (p<0.001)
- Findings suggest hospitalized COVID-19 patients who are early in the hyper-immune response, with lower baseline CRP levels (CRP<150 mg/l), achieve even greater clinical benefit from lenzilumab treatment

BURLINGAME, Calif.--(BUSINESS WIRE)-- Humanigen, Inc. (Nasdaq:HGEN) (“Humanigen”), a clinical-stage biopharmaceutical company focused on preventing and treating an immune hyper-response called ‘cytokine storm’ with its lead drug candidate, lenzilumab, announced that a manuscript detailing the results of an analysis of CRP levels from the LIVE-AIR Phase 3 study is available on medRxiv (**https://www.medrxiv.org/content/10.1101/2021.12.30.21267140v1**) . The results indicate the greatest clinical benefit of lenzilumab treatment may be achieved in hospitalized COVID-19 patients with lower baseline CRP levels, which typically occur earlier in the progression of the disease.

Granulocyte-macrophage colony-stimulating factor (GM-CSF) is an early upstream mediator and orchestrator of the hyperinflammatory immune response following SARS-CoV-2 infection and serves to activate and expand inflammatory myeloid cells. Increases in CRP are driven by elevations of myeloid cell derived downstream cytokines. Highly elevated levels of CRP (>150 mg/L) may indicate a stage of the hyperinflammatory immune response by which sufficient myeloid activation has already occurred, rendering GM-CSF neutralization less adequate to prevent further disease progression.

This analysis and publication provide evidence that a biomarker-driven approach utilizing baseline CRP levels to

guide therapeutic intervention and patient selection may improve outcomes in patients hospitalized with COVID-19.

“We are encouraged by these results” said Dr. Dale Chappell, Chief Scientific Officer, Humanigen. “In the context of other GM-CSF targeting therapies having failed to progress in development for COVID-19, these results confirm the importance of patient selection and understanding disease processes when designing clinical trials. Importantly, ACTIV-5/BET-B, a potentially confirmatory Phase 2/3 study, utilizes CRP<150 mg/L to define the primary analysis population.”

Dr. Cameron Durrant, Chief Executive Officer, Humanigen, added, “The PREACH-M study in chronic myelomonocytic leukemia being conducted at 5 centers in Australia has begun dosing patients. Both the SHIELD study in CAR-T and the RATinG study in acute Graft versus Host Disease (aGvHD) are planned to begin enrolling in the first half of 2022, in the US and the UK respectively. Additional COVID studies which will be completed or initiated in 2022 include the NIH-sponsored ACTIV-5/BET-B study in the US and Korea and the C-SMART study being conducted in Australia. All are late-stage, clinical studies. Further strengthening the Humanigen pipeline is our Phase 1 program focused on ifabotuzumab in solid tumors.”

About the LIVE-AIR, Phase 3 Study of Lenzilumab

This study was a randomized, double-blind, placebo-controlled, multi-center Phase 3 trial for the treatment and prevention of serious and potentially fatal outcomes in patients hospitalized with COVID-19 pneumonia. The primary objective was to assess whether lenzilumab, in addition to other treatments, which included dexamethasone (or other steroids) and/or remdesivir, could prevent or alleviate the immune-mediated ‘cytokine storm’ and improve survival without ventilation, or ‘SWOV’ (sometimes referred to as ‘ventilator-free survival’). SWOV is a composite endpoint of time to death and time to invasive mechanical ventilation (IMV) and SWOV is an important clinical endpoint that measures not only mortality, but the morbidity associated with mechanical ventilation. Approximately 94% of patients received dexamethasone (or other steroids), 72% received remdesivir, and 69% received both.

The LIVE-AIR study enrolled 520 patients in 29 sites in the US and Brazil who were at least 18 years of age; experienced blood oxygen saturation (SpO2) of less than or equal to 94%; or required low-flow supplemental oxygen, or high-flow oxygen support, or non-invasive positive pressure ventilation; and were hospitalized but did not require IMV. Following enrollment, subjects were randomized to receive three infusions of either lenzilumab or placebo, with each infusion separated by eight hours. The LIVE-AIR study achieved its primary endpoint of survival without ventilation measured through day 28 following treatment (HR: 1.54; 95%CI: 1.02-2.32, p=0.04) and the results have been published in Lancet Respiratory Medicine.

About Lenzilumab

Lenzilumab is a proprietary Humaneered® first-in-class monoclonal antibody that has been proven to neutralize

GM-CSF, a cytokine of critical importance in the hyperinflammatory cascade, sometimes referred to as cytokine release syndrome, or cytokine storm, associated with COVID-19 and other indications. Lenzilumab binds to and neutralizes GM-CSF, consequently improving outcomes for patients hospitalized with COVID-19. Humanigen believes that GM-CSF neutralization has the potential to reduce the hyper-inflammatory cascade known as cytokine release syndrome common to chimeric antigen receptor T-cell (CAR-T) therapy and acute Graft versus Host Disease (aGvHD).

In CAR-T, lenzilumab successfully achieved the pre-specified primary endpoint at the recommended dose in a Phase 1b study with Yescarta® in which the overall response rate was 100% and no patient experienced severe cytokine release syndrome or severe neurotoxicity. Based on these results, Humanigen plans to test lenzilumab in a randomized, multicenter, potentially registrational, Phase 3 study to evaluate its efficacy and safety when combined with Yescarta and Tescarta CAR-T therapies in non-Hodgkin lymphoma. Lenzilumab will also be tested to assess its ability to prevent and/or treat aGvHD in patients undergoing allogeneic hematopoietic stem cell transplantation.

A study of lenzilumab is also underway for patients with chronic myelomonocytic leukemia (CMML) exhibiting RAS pathway mutations. This study builds on evidence from a Phase 1 study, conducted by Humanigen, that showed RAS mutations are associated with hyper-proliferative features, which may be sensitive to GM-CSF neutralization.

Lenzilumab is an investigational product and is not approved or authorized in any country.

About Humanigen

Humanigen, Inc. (Nasdaq: HGEN) (“Humanigen”), is a clinical-stage biopharmaceutical company focused on preventing and treating an immune hyper-response called ‘cytokine storm’. Lenzilumab is a first-in class antibody that binds to and neutralizes granulocyte-macrophage colony-stimulating factor (GM-CSF). Results from preclinical models indicate GM-CSF is an upstream regulator of many inflammatory cytokines and chemokines involved in the cytokine storm. Early in the COVID-19 pandemic, investigation showed high levels of GM-CSF secreting T cells were associated with disease severity and intensive care unit admission. Humanigen’s Phase 3 LIVE-AIR study suggests early intervention with lenzilumab may prevent consequences of a full-blown cytokine storm in hospitalized patients with COVID-19. Humanigen is developing lenzilumab as a treatment for cytokine storm associated with COVID-19 and CD19-targeted CAR-T cell therapies and is also exploring the effectiveness of lenzilumab in other inflammatory conditions such as acute Graft versus Host Disease in patients undergoing allogeneic hematopoietic stem cell transplantation, eosinophilic asthma, and rheumatoid arthritis. For more information, visit **www.humanigen.com** and follow Humanigen on LinkedIn, Twitter, and Facebook.

Forward-Looking Statements

All statements other than statements of historical facts contained in this press release are forward-looking statements. Forward-looking statements reflect management's current knowledge, assumptions, judgment, and

expectations regarding future performance or events. Although management believes that the expectations reflected in such statements are reasonable, they give no assurance that such expectations will prove to be correct, and you should be aware that actual events or results may differ materially from those contained in the forward-looking statements. Words such as "will," "expect," "intend," "plan," "potential," "possible," "goals," "accelerate," "continue," and similar expressions identify forward-looking statements, including, without limitation, statements regarding the ACTIV-5/BET-B study and the PREACH-M, SHIELD, RATinG and C-SMART studies, and other statements regarding our plans relating to lenzilumab and ifabotuzumab.

Forward-looking statements are subject to a number of risks and uncertainties including, but not limited to, the risks inherent in our lack of profitability and need for additional capital to grow our business; our dependence on partners to further the development of our product candidates; the uncertainties inherent in the development, attainment of the requisite regulatory authorizations and approvals and launch of any new pharmaceutical product; the outcome of pending or future litigation; and the various risks and uncertainties described in the "Risk Factors" sections of our latest annual and quarterly reports and other filings with the SEC.

All forward-looking statements are expressly qualified in their entirety by this cautionary notice. You should not rely upon any forward-looking statements as predictions of future events. We undertake no obligation to revise or update any forward-looking statements made in this press release to reflect events or circumstances after the date hereof, to reflect new information or the occurrence of unanticipated events, or to update the reasons why actual results could differ materially from those anticipated in the forward-looking statements, in each case, except as required by law.

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