Humanigen

NEWS RELEASE

The Lancet Respiratory Medicine Publishes Peer-Reviewed Paper and Independent Expert Commentary on Positive Phase 3 Lenzilumab Results

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- Lenzilumab is a variant-agnostic therapeutic that targets the dysregulated host immune response, an approach which may be of greater value than targeting the virus in hospitalized patients1
- Per the paper, the implication from all the available evidence is that “Lenzilumab significantly improved survival without invasive mechanical ventilation in hospitalised patients with COVID-19 who were treated concurrently with other available therapies”2
- Results of the LIVE-AIR Phase 3 trial demonstrate treatment of hospitalized COVID-19 patients with lenzilumab results in a statistically significant 54% relative improvement in the likelihood of survival without the need for invasive mechanical ventilation (“SWOV”)

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 today **The Lancet Respiratory Medicine (“Lancet”)**, an internationally trusted, peer-reviewed source of clinical, public health, and global health knowledge, published positive results from Humanigen’s LIVE-AIR Phase 3 randomized, controlled trial of lenzilumab in hospitalized COVID-19 patients, as well as an independent expert commentary. The Lancet paper concludes “LIVE-AIR showed that lenzilumab treatment of hospitalised patients with COVID-19 can improve the likelihood of survival without the need for mechanical ventilation, with a safety profile similar to that of placebo.”2

“Publication of LIVE-AIR results in this peer-reviewed medical journal is a major achievement. Our goal was to demonstrate that lenzilumab, a variant-agnostic therapy, could address the unmet need in treatment of COVID-19 patients by reducing death or mechanical ventilation. The results describe the positive impact lenzilumab has on improving survival without the need for invasive mechanical ventilation in COVID-19 patients upon hospitalization,” said Cameron Durrant, Chairman and CEO, Humanigen. “As the paper describes ‘60% of LIVE-AIR patients were on room air or low-flow oxygen support. … (Raising) the possibility that lenzilumab might be positioned for use before

ICU admission and progression of respiratory failure requiring high-flow oxygen and non-invasive or invasive ventilation.'"2

"This study of the treatment to prevent hyperinflammatory immune response that occurs in some patients infected with SARS-CoV-2 is important," said Zelalem Temesgen, M.D., Mayo Clinic infectious disease researcher and principal investigator. "The need is great for more therapies for newly hospitalized patients prior to respiratory failure to reduce mortality or mechanical ventilation."

Lenzilumab is not authorized, or approved, in any country.

"One of the key components of the detrimental hyperinflammatory response in COVID-19 is granulocyte-macrophage colony-stimulating factor (GM-CSF). ... excessive GM-CSF production can contribute to the dysregulated immune response in severe COVID-19, in which, upstream of IL-1 and IL-6, activated T cells target neutrophils and macrophages. Agents that interfere with its actions have high plausibility for benefit, not just in COVID-19, but in other acute inflammatory conditions,"1 noted the commentary.

The Lancet paper notes differences in CRP levels for LIVE-AIR patients compared to those of clinical trials for another immunomodulator to suggest these "findings might indicate the therapeutic potential of targeting a single upstream cytokine earlier in the disease process, guided by baseline CRP. ... The study contributes to the emerging body of evidence about how CRP concentrations relate to the pathogenesis of COVID-19 and to patient and treatment selection."2 Related to the value of a CRP-guided approach to treatment of COVID-19 patients, the commentary noted "further study of a CRP-guided approach, possibly targeting patients with lower CRP concentrations, earlier in their disease course, ... could therefore be warranted."1

For hospitalized patients, "we now know that targeting the dysregulated host response is of greater value than targeting the virus."1 The high level of uncertainty and concern surrounding the emergence of the Omicron variant highlights the ongoing need for variant-agnostic therapies.

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 over a 24-hour period. 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=0.040).

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 its 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 2 study to evaluate its efficacy and safety when combined with other commercially available CD19 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 will build 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.

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 has submitted lenzilumab to Medicines and Health Regulatory Agency in the United Kingdom for a rolling review towards potential Marketing Authorization. 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 aGvHD 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: Humanigen’s beliefs as to the potential benefits of lenzilumab as a treatment for hospitalized COVID-19 patients; its beliefs as to the potential of lenzilumab to improve patient survival when used before ICU admission and progression of respiratory failure; statements regarding the therapeutic potential of targeting a single upstream cytokine earlier in the COVID-19 disease process; its efforts to request and receive Conditional Marketing Authorization for lenzilumab in COVID-19 in the UK and other territories; and its other plans to initiate or participate in planned clinical trials and otherwise explore the effectiveness of lenzilumab and other candidates in its development portfolio as therapies for other inflammation and immune-oncology indications.

Forward-looking statements are subject to a number of risks and uncertainties including, but not limited to, the risks inherent in the company’s lack of profitability and need for additional capital to conduct its business; its dependence on partners to further the development of its product candidates; the uncertainties inherent in the development, attainment of the requisite regulatory authorizations and approvals and launch of any new pharmaceutical product; challenges associated with manufacturing and commercializing a biologic such as lenzilumab; the outcome of pending or future litigation; and the various risks and uncertainties described in the "Risk Factors" sections and elsewhere in Humanigen's periodic and other filings with the Securities and Exchange Commission.

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. The Company undertakes no obligation to revise or update any forward-looking statements made in this press release to reflect events or circumstances after the date hereof or to reflect new information or the occurrence of unanticipated events, except as required by law.

References

1. Leavis, H. et al. (2021). Comment: Stimulating severe COVID-19: the potential role of GM-CSF antagonism. The Lancet Respiratory Medicine. **https://doi.org/10.1016/S2213-2600(21)00539-7**
2. Temesgen, Z. et al. (2021). Lenzilumab in hospitalised patients with COVID-19 pneumonia (LIVE-AIR): a phase 3, randomised, placebo-controlled trial. The Lancet Respiratory Medicine. **https://doi.org/10.1016/S2213-2600(21)00494-X**

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