Humanigen

NEWS RELEASE

Humanigen Announces Clinical Trial Collaboration to Evaluate Lenzilumab in Acute Graft Versus Host Disease

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- Humanigen is supporting the University of Birmingham to conduct a Phase 2/3, potentially registrational, clinical trial at IMPACT stem cell transplant centers across the United Kingdom
- The “Risk Adapted Therapy in Acute GvHD”, or “RATinG”, study is expected to begin enrolling in 1H22

BURLINGAME, Calif.--(BUSINESS WIRE)-- Humanigen, Inc. (Nasdaq: HGEN), a clinical-stage biopharmaceutical company focused on preventing and treating an immune hyper-response called ‘cytokine storm’ with its lead drug candidate, lenzilumab, today announced it plans to support a Phase 2/3 study to evaluate lenzilumab for the early treatment of acute graft versus host disease (aGvHD) following allogeneic hematopoietic stem cell transplantation (HSCT) in collaboration with IMPACT, a world class accelerated trial network delivering innovative research for stem cell transplant patients in the UK. IMPACT delivers innovative research in partnership with the British Society of Blood and Marrow Transplantation and the University of Birmingham’s Cancer Research UK Clinical Trials Unit. The safety run-in component of the RATinG study is anticipated to be completed in 2022. The study is partially funded by IMPACT with Humanigen providing lenzilumab and the remaining funding for the study.

“The IMPACT partnership is committed to improving the outcomes of stem cell transplant patients. Management of aGvHD disease is an area of significant unmet need in stem cell transplantation and I am really excited to collaborate with Humanigen and IMPACT to deliver on the promise of this therapeutic approach for patients with high risk aGvHD,” said Professor Adrian Bloor MA, MB BChir, PhD, FRCP, FRCPath, Director of Stem Cell Transplantation, The Christie NHS Foundation Trust.

Lenzilumab neutralizes the immune signalling protein granulocyte-macrophage colony-stimulating factor (GM-CSF), which has been shown to initiate the inflammatory cascade that drives aGvHD, a serious condition with significant unmet needs that affects 30%-50% of all patients who undergo HSCT.1, 2

“We are pleased to be supporting the RATinG study in collaboration with IMPACT, the UK’s stem cell transplant clinical trials partnership, to evaluate lenzilumab, which represents a potential way to spare patients from the devastating effects of steroid refractory aGvHD after undergoing allogeneic HSCT,” said Cameron Durrant, Chairman and CEO, Humanigen.

About the Risk Adapted Therapy in Acute Graft versus Host Disease (RATinG) study

The RATinG study will evaluate lenzilumab in patients who have undergone allogeneic hematopoietic stem cell transplantation and been diagnosed with high-risk aGvHD. The trial will be conducted at up to 22 sites across the UK transplant network in two stages. The first stage of the study will treat 20 patients with lenzilumab before halting for an interim assessment of safety, efficacy, and futility. If an independent data monitoring committee deem the second stage to be feasible, then the trial will progress to its double-blind, randomized (1:1), second stage, which will enroll a minimum of 220 patients. A second interim analysis is planned to assess futility based upon the 28-day response rate to the first infusion in the first 150 evaluable patients.

Within seven days following clinical diagnosis of aGvHD, investigators will assess patients’ risk for steroid refractory aGvHD as measured by the Mount Sinai Acute GvHD International Consortium (MAGIC) biomarkers. Intermediate and high-risk groups will be treated with lenzilumab plus steroids in stage 1 and randomized to receive lenzilumab plus steroids or placebo plus steroids in stage 2. The stage 2 primary endpoint, non-relapse mortality, will be assessed once all patients have completed at least 6 months follow up.

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 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 Conditional 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 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.

About IMPACT

IMPACT is a partnership of organisations committed to improving the outcomes of stem cell transplant patients through the delivery of clinical trials across the UK. It is jointly funded by **Anthony Nolan**, **Leukaemia UK** and **NHS Blood and Transplant**. IMPACT aims to ensure patients benefit from scientific advances sooner by making it easier for transplant centres to work together to set up clinical trials, recruit patients and share data. The partnership allows transplant centres across the UK to work together to deliver clinical trials focused on stem cell transplantation. IMPACT provides funding for research nurses in eleven centres and works with a further eleven affiliated centres, which also participate in IMPACT trials. IMPACT trials are coordinated by the central hub, located at the University of Birmingham's Cancer Research UK Clinical Trials Unit (CRCTU).

About the University of Birmingham

The University of Birmingham is ranked amongst the world's top 100 institutions, and its work brings people from across the world to Birmingham, including researchers and teachers and more than 6,500 international students from nearly 150 countries.

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 potential of lenzilumab to be used as a treatment for aGvHD; statements regarding use of lenzilumab as a therapy for the treatment of patients hospitalized with COVID-19; statements about our efforts to seek Conditional Marketing Authorization of lenzilumab for COVID-19 in the UK; and statements regarding our plans to develop lenzilumab for CAR-T and other indications and our other plans relating to lenzilumab.

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 presentation 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. Gartlan, K. et al. (2019). Donor T-cell–derived GM-CSF drives alloantigen presentation by dendritic cells in the gastrointestinal tract. Blood Advances, 3(19), 2859–2865. **https://doi.org/10.1182/bloodadvances.2019000053**
2. Zeiser, R., and Blazar, B. (2017). Acute graft-versus-host disease — biologic process, prevention, and therapy. New England Journal of Medicine, 377(22), 2167–2179. **https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6034180/#!po=38.2353**

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