



NEWS RELEASE

NIH Advances ACTIV-5/BET-B Trial Evaluating Lenzilumab from a Phase 2 Exploratory Study to a Phase 2/3 Study for the Treatment of COVID-19

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- ACTIV-5/BET-B trial amended in the context of Humanigen's positive Phase 3 lenzilumab LIVE-AIR study
- Primary endpoint focuses on survival without ventilation by day 28 in patients with baseline C-reactive protein (CRP) levels less than 150 mg/L
- Study modification may enable Humanigen to use ACTIV-5/BET-B as a confirmatory study to support a future Biologics License Application (BLA)
- Approximately half of the 400 patients are already enrolled in ACTIV-5/BET-B

BURLINGAME, Calif.--(BUSINESS WIRE)-- Humanigen, Inc. (Nasdaq: HGEN) ("Humanigen"), a clinical-stage biopharmaceutical company developing a first-in-class GM-CSF neutralizing antibody to prevent and treat an immune hyper-response called 'cytokine storm' across multiple therapeutic indications, has announced that the NIH has advanced the ACTIV-5/BET-B study to a Phase 2/3 study and modified the primary endpoint to survival without ventilation ("SWOV"), the same endpoint used in the Phase 3 LIVE-AIR study.

The amended ACTIV-5/BET-B study now includes 400 patients overall. Up to sixty US sites will be participating in the study. Humanigen is providing lenzilumab and assisting the NIH to achieve the timely completion of the study. NIH is sponsoring and funding this study.

"We appreciate the close collaboration with NIH on this important study," said Adrian Kilcoyne, MD, Chief Medical Officer, Humanigen. "The ACTIV-5/BET-B study design has been adapted to align with the design of LIVE-AIR and may help support a future BLA for lenzilumab."

"Sharing the same endpoint as the LIVE-AIR study, the ACTIV-5/BET-B study reinforces the potential for lenzilumab to treat hospitalized COVID-19 patients," said Vincent Marconi, MD, Professor of Medicine at Emory University School of Medicine. "At Emory University, a key center in both the LIVE-AIR and ACTIV-5/BET-B studies, we believe these trials can identify the optimal patient population for lenzilumab. LIVE-AIR showed us that COVID-19 patients who at baseline had a CRP of less than 150 mg/L and are under 85 years of age had the greatest response to

lenzilumab. Using CRP as a biomarker to identify COVID-19 patients at risk for disease progression, in whom lenzilumab treatment can be initiated prior to full blown cytokine storm, would be lifesaving.”

“ACTIV-5/BET-B may provide prospective validation for lenzilumab in the treatment of COVID-19,” said Cameron Durrant, MD, Chief Executive Officer, Humanigen. “We believe ACTIV-5/BET-B, along with LIVE-AIR, will provide the sufficient size and statistical power typically required for a BLA to be submitted to FDA.”

About ACTIV-5/BET-B

The Accelerating Covid-19 Therapeutic Interventions and Vaccines (ACTIV) is a National Institutes of Health (NIH) directed public-private partnership to develop a coordinated research strategy for prioritizing and speeding development of the most promising treatments and vaccines.¹ ACTIV is led by a working group of senior scientists representing government, industry, non-profit, philanthropic, and academic organizations and is pursuing five fast-track focus areas most ripe for opportunity, one of which is accelerating clinical testing of the most promising vaccines and treatments. Within this focus area ACTIV-5 (Big Effect Trial, BET) is a series of randomized, double-blind, placebo-controlled trials using common assessments and endpoints to evaluate whether certain therapies, approved or investigational, show promise against COVID-19.

Within ACTIV-5, lenzilumab is the first and only anti-human GM-CSF treatment to be tested in ACTIV-5 as a concomitant therapy with remdesivir compared with remdesivir alone. Lenzilumab was selected from among 400 compounds that were considered for investigation in ACTIV.² The study began in October 2020 and was comprised of 200 adult hospitalized patients who need medical care for COVID-19 pneumonia and randomized (1:1) to the treatment groups.² Patients receive a loading dose of 200-mg intravenous (IV) remdesivir on day 1 followed by a 100-mg once-daily IV maintenance dose up to a 10-day total course while hospitalized. Lenzilumab (or placebo) is administered at 600-mg IV lenzilumab infusion every 8 hours starting on Day 1 for a total of 3 doses.² The original primary efficacy outcome was change in clinical status on an 8-point ordinal scale at Day 8 from the NIH-sponsored Adaptive COVID-19 Treatment Trial (ACTT, NCT 04280705).^{3,4}

Lenzilumab Clinical Evidence Supporting Modification of ACTIV-5/BET-B

Lenzilumab achieved the primary endpoint of the Phase 3 LIVE-AIR trial with a 1.54-fold relative improvement in the likelihood of SWOV compared to placebo. Lenzilumab also improved the relative likelihood of SWOV by 1.92-fold in the pre-specified subgroup of subjects who received both corticosteroids and remdesivir as well as a 3-fold improvement in the likelihood of SWOV in patients with a baseline CRP<150 mg/L and less than 85 years of age. In these patients, a 2.2-fold improvement in the likelihood of survival was observed with lenzilumab. No serious adverse events were attributed to lenzilumab, and the overall safety profile was comparable to placebo.

The LIVE-AIR, Phase 3 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 who were 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 alleviate the immune-mediated cytokine release syndrome (CRS) and improve SWOV. SWOV is a composite endpoint of time to death and time to IMV, which is a robust measure that is less prone to favor a treatment with discordant effects on survival or days free of ventilation.¹

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 (NIPPV); and were hospitalized but did not require IMV. Following enrollment, subjects were randomized to receive three infusions of either lenzilumab or placebo, each infusion separated by eight hours over a 24-hour period with other treatments. The primary endpoint was the difference between lenzilumab treatment and placebo treatment in SWOV through 28 days following treatment. Key secondary endpoints, also measured through 28 days, included ventilator-free days, duration of ICU stay, incidence of IMV, extracorporeal membrane oxygenation (ECMO), and/or death, time to death, all-cause mortality, and time to recovery. LIVE-AIR results have been submitted for potential publication in a peer-reviewed journal.

About Lenzilumab

Lenzilumab is a proprietary Humaneered® (“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 (“CRS”) or cytokine storm (CS), associated with COVID-19 and other indications. Lenzilumab binds to and neutralizes GM-CSF, consequently improving outcomes for hypoxic 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 pre-specified primary endpoint at the recommended dose in a Phase 2 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 all commercially available CD19 CAR-T therapies in DLBCL. Lenzilumab will also be tested to assess its ability prevent and/or treat aGvHD in patients undergoing allogeneic hematopoietic stem cell transplantation (HSCT).

About Humanigen

Humanigen, Inc. is developing its portfolio of clinical and pre-clinical therapies for the treatment of inflammation and immuno-oncology. Humanigen’s immediate focus is to prevent or minimize cytokine release syndrome that precedes severe lung dysfunction in hospitalized and hypoxic patients with COVID-19 pneumonia. Humanigen has

requested Emergency Use Authorization for this indication and is submitting lenzilumab to the Medicines and Health Regulatory Agency in the United Kingdom under an expedited rolling review seeking Marketing Authorization. Humanigen is also exploring the effectiveness of lenzilumab in other inflammatory conditions such as aGvHD and cytokine release syndrome associated with CAR-T. 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 our request for and receipt of an Emergency Use Authorization from FDA for lenzilumab in COVID-19; our request and receipt of Marketing Authorization or Conditional Marketing Authorization for lenzilumab in COVID-19 by the MHRA; and our other plans relating to lenzilumab to further development of 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, to reflect new information or the occurrence of unanticipated events, 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.

References

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