Humanigen

LENZILUMAB OVERVIEW

Lenzilumab, Humanigen's lead product candidate, is a late clinical-stage monoclonal antibody developed with Humaneered® technology designed to optimize antibody properties.

- Shown to neutralize immune signaling ability of granulocyte-macrophage colony-stimulating factor (GM-CSF), a key cytokine responsible for the initiation of the inflammatory cascade and immune hyper-response known as cytokine storm.
- Currently being developed to prevent/treat cytokine storm in patients with a range of conditions, including patients undergoing CAR-T therapy and patients hospitalized with COVID-19.

POTENTIAL IN TREATING COVID-19

Several studies suggest that cytokine storm and elevated levels of GM-CSF are correlated with the worst clinical outcomes in COVID-19 pneumonia, including acute respiratory distress syndrome, lung injury, multi-organ failure and death.

The ability of lenzilumab to neutralize the cytokine GM-CSF, which is key in the initiation of cytokine storm, has been shown to improve the relative likelihood of survival without need for invasive mechanical ventilation, and in some patients time to recovery and need for intensive care (ICU).

Key studies include:

- Positive results from LIVE-AIR, a global Phase 3 registration study of lenzilumab in 520 hospitalized COVID-19 patients (NCT0435152)
- NIH-sponsored ACTIV-5/Big Effect Trial (BET-B) which will evaluate lenzilumab in combination with remdesivir in hospitalized patients with COVID-19, enrollment completed
- Peer review publication in The Lancet Respiratory Medicine of LIVE-AIR results

Having previously published data demonstrating the ability of lenzilumab to prevent and/or treat cytokine storm, lenzilumab has the potential to be used as a monotherapy or in combination with a direct- acting antiviral, like remdesivir, in COVID-19, given the differing mechanisms of action.

LENZILUMAB IN COVID-19 DEVELOPMENT TIMELINE

2020

- **March** — Cytokine storm identified in COVID-19 patients
- HGEN expands lenzilumab clinical focus to include COVID-19 based on mechanism of action
- FDA approves Emergency IND of lenzilumab for **compassionate use**
- **April** — Treatment of patients begins at **Mayo Clinic** under compassionate use
- FDA approves initiation of **lenzilumab Phase 3 study**
- **May** — First patient dosed in lenzilumab Phase 3 study
- **July** — HGEN expands partnership with Catalent Biologics to ramp up manufacturing of lenzilumab
- **NIH selects lenzilumab for ACTIV-5/Big Effect Trial**
- **August** — Lenzilumab demonstrates positive results in a case-control study published by Mayo Clinic
- **September** — HGEN partners with Lonza and Thermo Fisher for lenzilumab manufacturing
- **October** — First patient dosed in NIH ACTIV-5/Big Effect Trial

2021

- **January** — **HGEN completes enrollment in lenzilumab Phase 3 study**
- **March** — **Humanigen reports positive Phase 3 topline results**
- **December** — **LIVE-AIR results published in The Lancet Respiratory Medicine**
- **Meetings with FDA, EMA, and MHRA confirms inclusion of results from ACTIVE-5/BET-B study in request for authorization**

2022

- **January** — ACTIV-5/BET-B full enrollment in 400+ patients with CRP levels <150 mg/L
- **Confirms development plan with FDA for SHIELD study, lenzilimab in CAR-T**

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ADDITIONAL INDICATIONS

Additional trials are underway to evaluate the potential of lenzilumab in other settings, including:

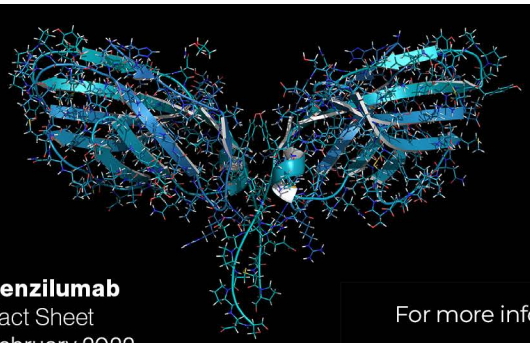
- Potential to improve efficacy of CAR-T therapies while simultaneously reducing associated neurologic toxicities (ICANS) and other serious, potentially life-threatening effects
  - Positive data announced in ZUMA-19, a Phase 1b study of lenzilumab in adults with relapsed/refractory diffuse large B-cell lymphoma (DLBCL). Humanigen plans to initiate a randomized, multicenter, potentially registrational, Phase 2 study to evaluate the efficacy and safety of lenzilumab combined with Yescarta/Tecartus CAR-T therapies in non-Hodgkin lymphomas (NHL).
- Early intervention in adults at high risk for acute graft versus host disease (GvHD) after allogeneic hematopoietic stem cell transplantation (HSCT) in partnership with IMPACT Clinical Trials (UK)
- Treatment of refractory chronic myelomonocytic leukemia (CMML) patients with RAS pathway mutations
  - Evaluating lenzilumab plus azacitidine in newly-diagnosed CMML patients who express NRAS/KRAS/CBL mutations (Australia)

LENZILUMAB CLINICAL-STAGE PIPELINE

Indication			Phase 1	Phase 2	Phase 3
COVID-19	Prevention/treatment of cytokine storm in partnership with Mayo Clinic	Achieved Primary Endpoint 520 patients			
COVID-19	Prevention/treatment of cytokine storm NIAID/DMID sponsored	Enrolling complete			
CAR-T ICANS	Prophylaxis as sequenced therapy with Yescarta and Tecartus	FPI 2022			
Prevention/Treatment of Acute GvHD	Allogeneic HSCT	FPI 2022			
Chronic myelomonocytic leukemia (CMML)	Lenzilumab + azacitidine in NRAS, KRAS or CBL mutant-positive newly-diagnosed patients	Enrolling			

SAFETY PROFILE

Lenzilumab has been evaluated across multiple indications, including severe respiratory disorders and hematologic malignancies. To date, there have been no safety issues and no serious adverse events attributed to lenzilumab.



Humanigen has developed a neutralizing, IgG1, monoclonal antibody against human GM-CSF, using proprietary Humaneered® technology.

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