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. Humanigen recently filed for EUA for lenzilumab in COVID-19 patients.

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) which will evaluate lenzilumab in combination with remdesivir in hospitalized patients with COVID-19
- Positive results from a multi-center case-cohort study published by Mayo Clinic in patients hospitalized with COVID-19 pneumonia

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.

In May 2021, Humanigen submitted an application for *Emergency Use Authorization* for lenzilumab in COVID-19

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

June
- Positive data announced from patients treated at Mayo Clinic under compassionate use
- Additional positive analysis announced of lenzilumab versus remdesivir

July
- HGEN expands partnership with Catalent Biologics to ramp up manufacturing of lenzilumab
- **NIH selects lenzilumab for ACTIV-5/Big Effect Trial**

August
- Lenzilumab Phase 3 trial expanded to Brazil
- Lenzilumab demonstrates positive results in a case-control study published by Mayo Clinic

September
- DSMB recommends Phase 3 trial to continue without modification
- HGEN partners with Lonza and Thermo Fisher for lenzilumab manufacturing

October
- First patient dosed in NIH ACTIV-5/Big Effect Trial

November
- HGEN announces CRADA with US government to develop lenzilumab
- Encouraging interim analysis supports the potential for lenzilumab over and above current standard of care

2021

January
- HGEN partners with EVERSANA to support launch and commercialization of lenzilumab
- HGEN announces addition of BARDA and Expansion of CRADA with US government
- HGEN announces CDMO with Emergent BioSolutions, expands agreement with Ajinomoto
- **HGEN completes enrollment in lenzilumab Phase 3 study**

February
- HGEN announces cGMP Manufacturing Agreement with Avid Bioservices

March
- Humanigen expands anti-GM-CSF Patent Portfolio
- **Humanigen reports positive Phase 3 topline results**

May
- **Humanigen submits application to FDA for EUA for lenzilumab in COVID-19**

June
- **Humanigen initiates submission for Marketing Authorization to MHRA**

For more information, contact Grace Catlett: **gcatlett@rxmedyn.com**

ADDITIONAL INDICATIONS

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

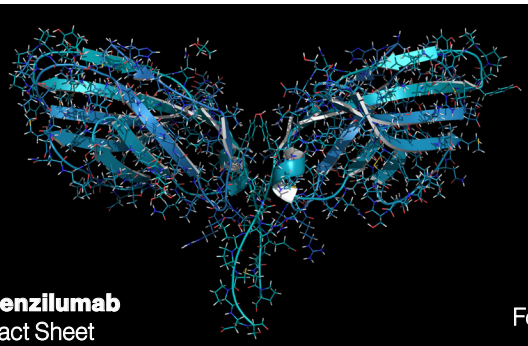
- Potential to improve efficacy of CAR-T therapies while simultaneously preventing cytokine storm (also referred to as cytokine release syndrome, or CRS) and reducing associated neurologic toxicities and other serious, potentially life-threatening effects
  - Positive data announced in ZUMA-19, a Phase 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 all commercially available CD19 CAR-T therapies in DLBCL.
- 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	Submitted
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 200 patients				
ZUMA-19 Break CAR-T Efficacy/ Toxicity Linkage	Prophylaxis as sequenced therapy with Yescarta in r/r DLBCL	Completed No Safety Issues No Severe CRS				
Prevention/Treatment of Acute GvHD	Allogeneic HSCT	Advanced planning				
Chronic myelomonocytic leukemia (CMML)	Lenzilumab + azacitidine in NRAS, KRAS or CBL mutant-positive newly-diagnosed patients	Advanced planning				

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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