Humanigen

LENZILUMAB™ OVERVIEW

Lenzilumab (LENZ), 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
- Is currently being evaluated to prevent/treat cytokine storm in patients with a range of conditions, including patients undergoing CAR-T therapy and patients hospitalized with severe and critical COVID-19 pneumonia

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.

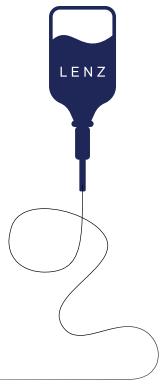
The ability of LENZ to neutralize the cytokine GM-CSF, which is key in the initiation of cytokine storm, holds potential to improve the time to recovery and reduce the progression to respiratory failure, requiring invasive mechanical ventilation, or death in hospitalized patients with severe or critical COVID-19.

Key studies include:

- Ongoing global Phase 3 registration study of LENZ in approximately 300 severe and critical hospitalized COVID-19 patients (NCT0435152)
- NIH-sponsored Big Effect Trial (BET) which will evaluate LENZ in combination with remdesivir in 200 hospitalized patients with COVID-19
- Positive results from a multi-center case-control study published by Mayo Clinic in patients with severe and critical COVID-19 pneumonia

Having previously published data demonstrating the ability of LENZ to prevent and/or treat cytokine storm, LENZ 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. Remdesivir is the only currently authorized treatment for COVID-19.

Humanigen aims to advance LENZ through the regulatory pathway for potential *Emergency Use Authorization* in late 2020.



LENZ IN COVID-19 DEVELOPMENT TIMELINE 2020

MARCH
- Cytokine storm identified in COVID-19 patients
- HGEN expands LENZ clinical focus to include COVID-19 based on mechanism of action

APRIL
- FDA approves Emergency IND of LENZ for **compassionate use**
- Treatment of patients begins at **Mayo Clinic** under compassionate use
- FDA approves initiation of **LENZ Phase 3 study**

MAY
- First patient dosed in LENZ Phase 3 study

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

JULY
- HGEN expands partnership with Catalent Biologics to ramp up manufacturing of LENZ
- **NIH selects LENZ for Big Effect Trial**

AUGUST
- LENZ Phase 3 trial expanded to Brazil
- LENZ demonstrated 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 LENZ manufacturing

ADDITIONAL INDICATIONS & CLINICAL PIPELINE

Additional trials are underway to evaluate the potential of LENZ 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
  - The ZUMA-19 pivotal study, conducted in collaboration with Kite Pharma, a Gilead Company, is designed to investigate the ability of LENZ to break the efficacy/toxicity link with Yescarta® (axicabtagene ciloleucel) in adults with relapsed/refractory diffuse large B-cell lymphoma (DLBCL)
- Early intervention in adults at high risk for acute graft versus host disease (GvHD) after alloegeneic HSCT in partnership with IMPACT Clinical Trials (UK)
- Treatment of refractory chronic myelomonocytic leukemia (CMML) patients with RAS pathway mutations
  - Evaluating lenzilumab plus azacytidine in NRAS, KRAS or CBL mutant-positive, newly-diagnosed patients (Australia)

LENZ CLINICAL-STAGE PIPELINE

Indication		Phase 1	Phase 2	Phase 3
COVID-19 NCT04351152	Prevention/treatment of cytokine storm in partnership with Mayo Clinic			
COVID-19	Prevention/treatment of cytokine storm NIAID/DMID sponsored			
ZUMA-19 Break CAR-T efficacy/toxicity linkage	Prophylaxis as sequenced therapy with Yescarta in r/r DLBCL			
Prevention/treatment of Acute GvHD	Allogenic HSCT			
Chronic Myelomonocytic Leukemia (CMML)	LENZ+Azacitidine in NRAS, KRAS, or CBL mutant-positive newly-diagnosed patients			
CMML	Monotherapy in salvage patients			
Eosinophilic Asthma	Inadequately controlled asthma			

SAFETY PROFILE

LENZ has been shown to be safe in clinical settings following administration to 125 patients in multiple indications, including severe respiratory conditions and leukemia, with no serious or adverse events.

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