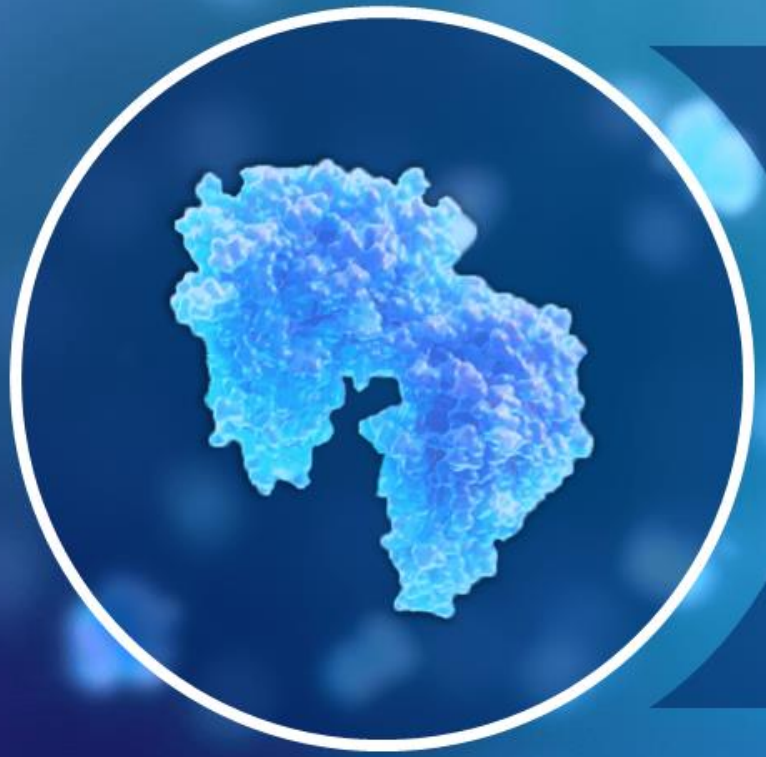
Humanigen



Humanigen, Inc.

Executive Overview
September 2022

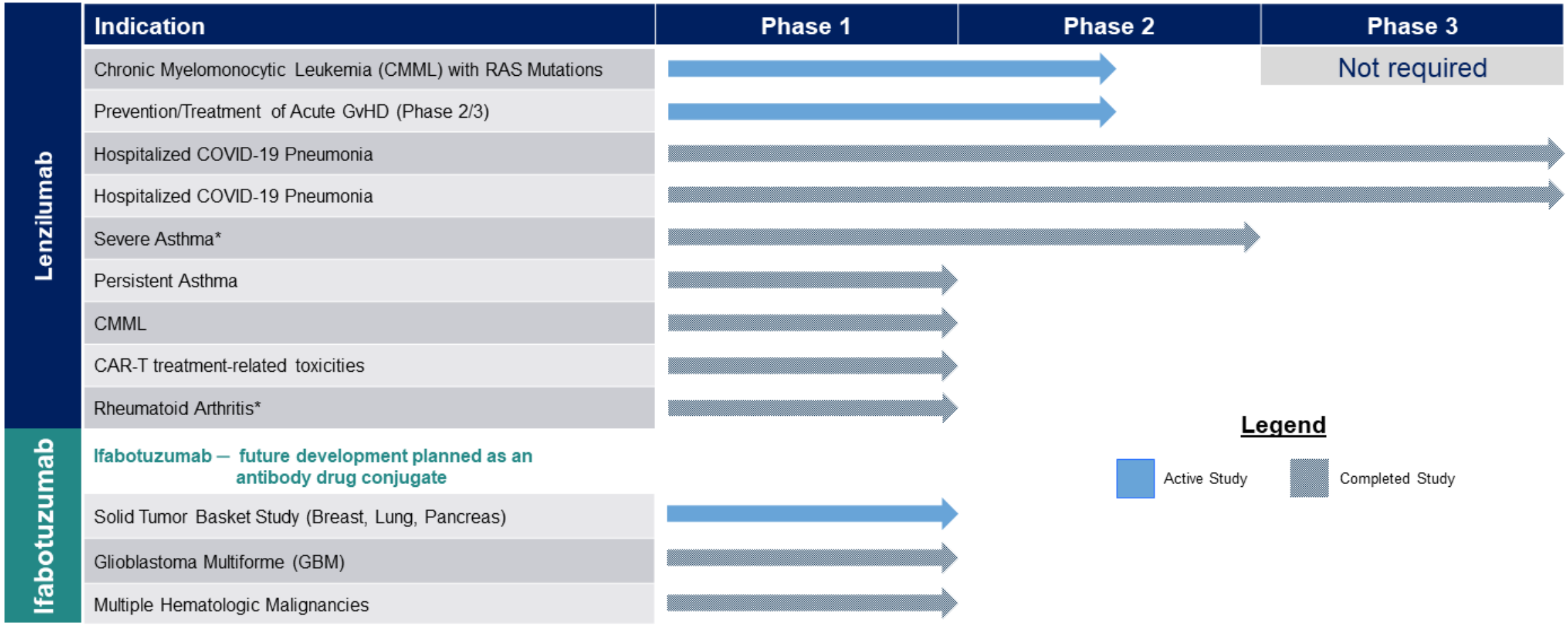
Cautionary Note Regarding Forward-Looking Statements

All statements other than statements of historical facts contained in this presentation 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.

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; 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 or arbitration; 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 press release to reflect events or circumstances after the date hereof, to reflect new information or the occurrence of unanticipated events, or 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.

Pipeline Includes Antibodies Targeting GM-CSF and EphA-3



*historical clinical results provide basis for global partnering discussions

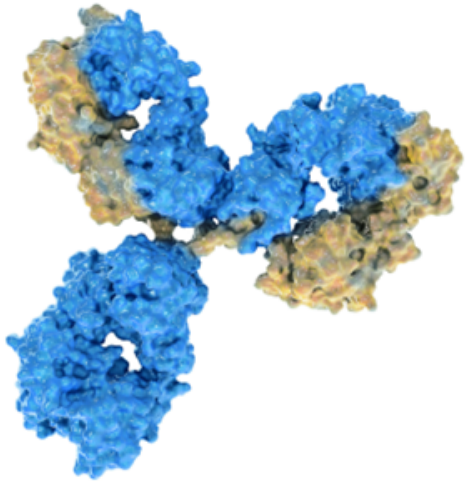
Lenzilumab Humaneered® to Tackle Serious and Potentially Life-Threatening Conditions

Humaneered Best-in-Class Antibody

- ✓ Neutralizes GM-CSF to prevent and treat Cytokine Storm
- ✓ Highest binding affinity
- ✓ Slowest off-rate

Multiple Current Indications

- ✓ Target hyper-proliferative features of Chronic Myelomonocytic Leukemia (CMML) with RAS mutations
- ✓ Prevention/early treatment of Acute Graft vs. Host Disease (aGvHD)
- ✓ Companion treatment with CAR-T to prevent neurotoxicity and cytokine release syndrome, and potentially improve efficacy (IIT requests under review)
- ✓ Examining potential inclusion of lenzilumab in platform studies for COVID-19
- ✓ Historical results from Eosinophilic Asthma and Rheumatoid Arthritis to be used for global partnering discussions



Chronic Myelomonocytic Leukemia (CMML)

- CMML is an orphan cancer with US prevalence of 6,000 patients
  - Incidence US: 1,700 Patients annually
  - Incidence US, UK, and Australia: 2,125 patients[1]
- As an orphan indication, CMML may qualify lenzilumab for certain regulatory and commercial advantages that accelerate development and approval
  - Regulatory submission and potential approval by the Therapeutic Goods Administration in Australia; may be expanded through Project Orbis to United States and United Kingdom[2]
  - FDA approvals for CMML have been achieved with limited numbers of patients[3,4]
- CMML is an aggressive and poorly understood cancer with 3-year overall survival of approx. 20%[5]
- There are gene mutations in more than 90% of CMML cases, TET2 mutations occur in approx. 60% of cases; associated w/improved prognosis[6]
- RAS pathway mutations (up to 50% of cases[7]) associated w/poorer outcomes; may respond to GM-CSF neutralization[5,8,9]
- Currently there is a high unmet need for additional therapeutic options
- Humanigen has conducted a Phase 1 study of lenzilumab in CMML demonstrating GM-CSF inhibition is a viable therapeutic strategy[9]
- Bridge to other myeloid leukemias with RAS mutations such as JMML, MDS/MPN, and AML

1. Incidence extrapolated by applying NIH SEER incidence rate of five per one million people found at https://seer.cancer.gov/statistics-network/explorer/ to the population of U.S., UK, and Australia, Prevalence data also from NIH SEER. 2. FDA Project Orbis https://www.fda.gov/about-fda/oncology-center-excellence/project-orbis. 3. Costa, R., et. al. (2010, Dec. 10) Activity of azacitidine in chronic myelomonocytic leukemia, *Cancer,* https://acsjournals.onlinelibrary.wiley.com/doi/10.1002/cncr.25759. *4.* Inqovi prescribing information (2020, July), https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/212576s000lbl.pdf. 5. Padron, E, et. al. (2013, June 20) GM-CSF–dependent pSTAT5 sensitivity is a feature with therapeutic potential in chronic myelomonocytic leukemia. *Blood.* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4347259/. 6. Zhao, W., et. al. (2022) The prognostic value of the interaction between ASXL1 and TET2 gene mutations in patients with chronic myelomonocytic leukemia: a meta-analysis. *Hematology.* https://doi.org/10.1080/16078454.2021.1958486. *7.* https://doi.org/10.1158/1078-0432.CCR-09-2112. *8.* Carr, R. et. al. (2021, May 18) RAS mutations drive proliferative chronic myelomonocytic leukemia via a KMT2A-PLK1 axis. *Nature Communications.* https://www.nature.com/articles/s41467-021-23186-w. 9. Patnaik, M. et. al. (2019, Nov. 13) A Phase 1 Study of Lenzilumab, a humaneered recombinant Anti-Human Granulocyte-Macrophage Colony- Stimulating Factor (anti-hGM-CSF) Antibody, for Chronic Myelomonocytic Leukemia (CMML). *Blood.* https://doi.org/10.1182/blood-2019-131181.

Strategic Rationale for Lenzilumab Development in Hematologic Malignancies

JMML

- Stem cell transplant mainstay, 50% remain uncured
- Ultra orphan pediatric indication
- Priority review voucher potential

CMML

- Completed Phase 1*
- Relatively inexpensive & speedy development
- Potential for expedited review and breakthrough status
- Phase 2 open label actively enrolling n=36 with planned interim analysis

MDS

- Overlap with CMML and a larger patient population
- Existing treatment options limited and suboptimal response rates
- 1/3 progress to AML

AML

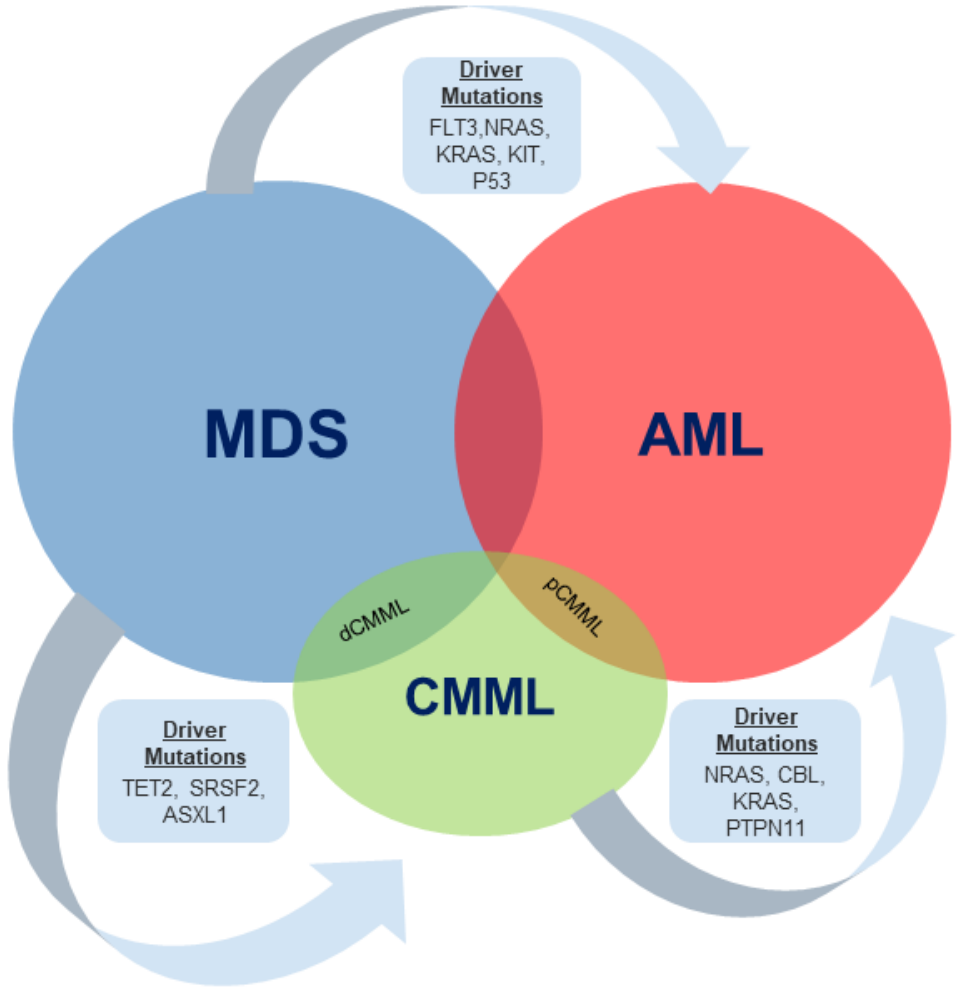
- Remains difficult to treat
- Chemotherapy remains backbone of existing therapies
- Secondary AML resulting from transformation of MDS and CMML patients

*Patnaik, M. et. al. (2019, Nov. 13) A Phase 1 Study of Lenzilumab, a humaneered recombinant Anti-Human Granulocyte-Macrophage Colony- Stimulating Factor (anti-hGM-CSF) Antibody, for Chronic Myelomonocytic Leukemia (CMML). *Blood*. https://doi.org/10.1182/blood-2019-131181.

RAS Pathway Mutations are a Key Driver for Proliferative Disease and Transformation to AML

RAS-pathway activation is a crucial pathophysiologic process for GM-CSF hypersensitivity, myeloproliferation, progressive disease and transformation of both MDS and CMML into AML

In CMML there are proliferative CMML (pCMML) subtypes in which oncogenic RAS pathway mutations (NRAS, CBL, KRAS and PTPN11) are initiating driver mutations, associated with poor outcomes and leukemic transformation



RAS, an abbreviation of "rat sarcoma" used to identify members of a family of 36 human genes tied to development of more than 30% of all human tumors, but just three (KRAS, NRAS, and HRAS) play the most prominent role.

Source: Keeton, A. et. al. (2017, January 15) The RAS-effector interaction as a drug target. *Cancer Research*. doi:10.1158/0008-5472.CAN-16-0938

dCMML, dysplastic subtype of Chronic Myelomonocytic Leukemia,
pCMML, proliferative subtype of Chronic Myelomonocytic Leukemia

RAS Pathway Key Driver in Development of Proliferative CMML

CMML is a clinically, molecularly, and biologically heterogenous disease historically classified as either dysplastic or proliferative based on white blood cell count[1]

Patients with proliferative CMML (pCMML) have significantly lower median overall survival (19 months vs. 30 months) than dysplastic (dCMML),[1] and while more than 90% of CMML patients have gene mutations,[2] RAS pathway mutations are initiating driver mutations associated with pCMML subtypes with poor outcomes[1]

RAS-pathway activation is a crucial pathophysiologic process for GM-CSF hypersensitivity, myeloproliferation, progressive disease and transformation into acute myeloid leukemia (AML)

Progression of CMML Gene Mutations

TET2 and SRSF2 mutations are early initiating events

↓

Subsequent acquisitions of ASXL1 and other mutations usually give rise to dysplastic CMML

↓

Acquisition of ASXL1, JAK2V617F, and RAS pathway mutations give rise to proliferative CMML

↓

15%-30% of CMML transforms into AML[3]

1. Carr, R. et. al. (2019, Nov. 13) Clinical Categorization of Chronic Myelomonocytic Leukemia into Proliferative and Dysplastic Subtypes Correlates with Distinct Genomic, Transcriptomic and Epigenomic Signatures. *Blood*. https://doi.org/10.1182/blood-2019-123877. 2. Jian, J. et. al. (2021, April 16) Mutations in chronic myelomonocytic leukemia and their prognostic relevance. *Clinical and Translational Oncology*. https://doi.org/10.1007/s12094-021-02585-x.
3. Renneville, A. et.al. (2021, June 26) Increasing recognition and emerging therapies argue for dedicated clinical trials in chronic myelomonocytic leukemia. *Leukemia*. https://doi.org/10.1038/s41375-021-01330-1.

GM-CSF Sensitivity Demonstrated in Chronic Myelomonocytic Leukemia[1]

An in-vitro study demonstrated the vast majority of CMML patient samples respond more vigorously to GM-CSF treatment

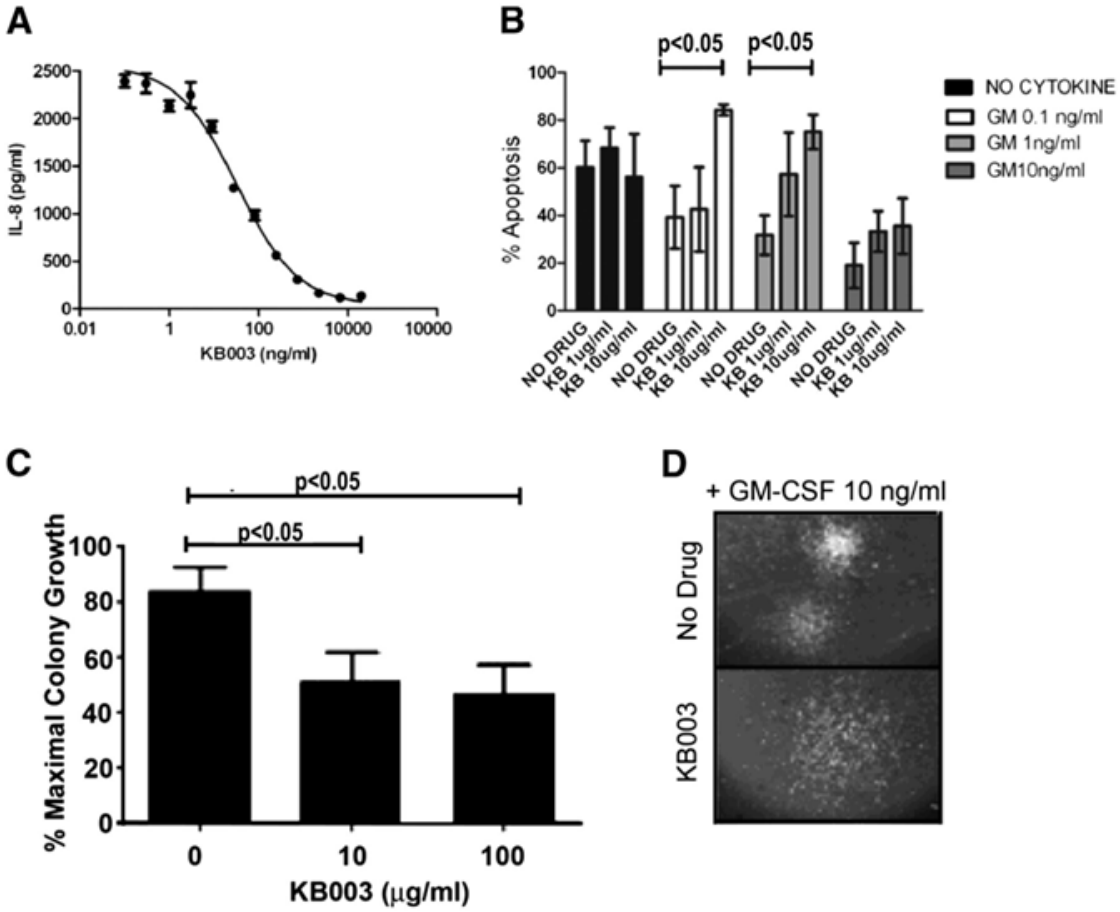
- GM-CSF neutralization significantly decreased the number of colonies and morphologic organization in CMML

Patients with signaling mutations (RAS mutations) have greater sensitivity to GM-CSF.

Molecular events contributing to monocyte differentiation or proliferation may be similar in JMML and CMML.

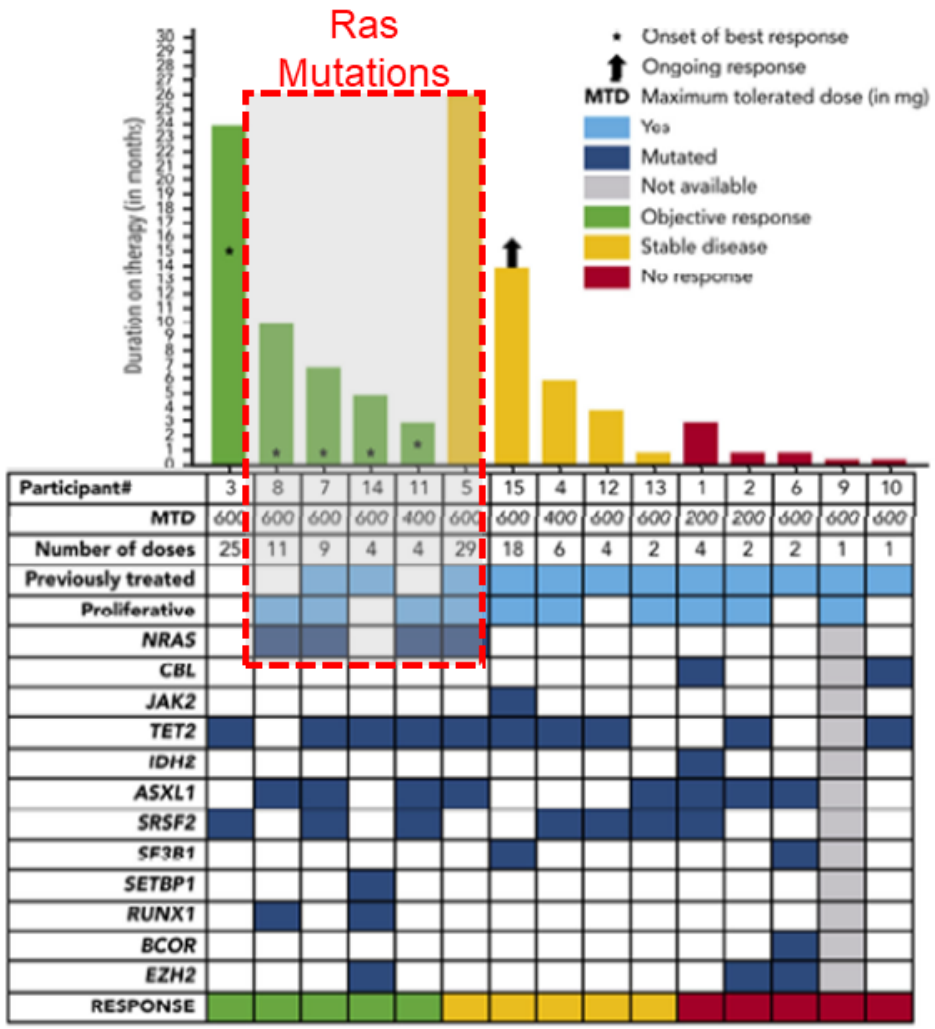
- The genetic events leading to GM-CSF hypersensitivity in JMML are also linked to mutations involving the Ras pathway

GM-CSF signaling cascade is an excellent CMML therapeutic target, and clinical studies are required to test lenzilumab in this indication



1. Padron, E, et. al. (2013, June 20) GM-CSF–dependent pSTAT5 sensitivity is a feature with therapeutic potential in chronic myelomonocytic leukemia. Blood. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4347259/

Completed Phase 1 Study in CMML
Highest Response in RAS Pathway[1]



GM-CSF inhibition identified as an excellent target for CMML

- Phase 1 data indicate 33% durable clinical benefit

RAS pathway mutations are more sensitive to GM-CSF

- Phase 1 data indicate 75% objective response in patients with RAS mutation

Lenzilumab well tolerated

- Safety database from more than 650 patients across multiple studies

1. Patnaik, M. et. al. (2019, Nov. 13) A Phase 1 Study of Lenzilumab, a humaneered recombinant Anti-Human Granulocyte-Macrophage Colony- Stimulating Factor (anti-hGM-CSF) Antibody, for Chronic Myelomonocytic Leukemia (CMML). Blood. https://doi.org/10.1182/blood-2019-131181

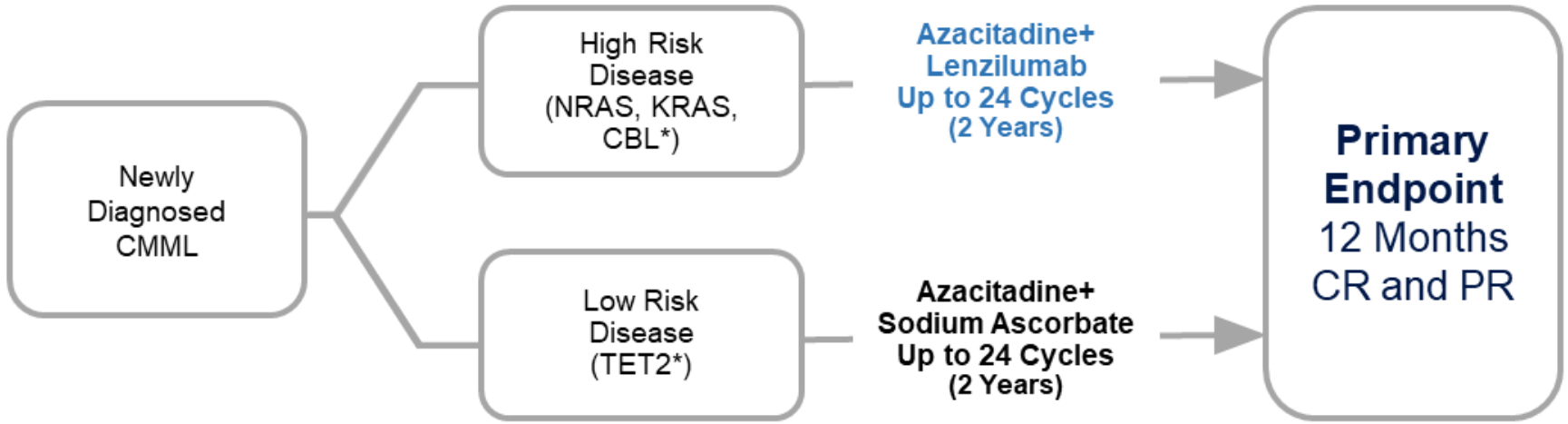
PREACH–M Trial Phase 2 for CMML

Partners

SAHMRI
South Australian Health & Medical Research Institute

THE UNIVERSITY of ADELAIDE

Trial Design



*TET2, NRAS, KRAS, and CBL are gene mutations

Potential Expansion Into Additional Cancers w/RAS Mutation (US Data)

Cancer Type	Est. Prevalance	RAS Mutation Rate	Est. Incidence with RAS	Est. Prevelance with RAS
Acute Myeloid Leukemia	70,000	15%	2,000	10,500
Myelodysplastic Syndromes	60,000	5%	600	3,000
Chronic Myelomonocytic Leukemia	6,000	50%	900	3,000
Juvenile Myelomonocytic Leukemia	200	90%	100	180
Total	136,200		3,600	16,680

Sources: AML - http://ashpublications.org/hematology/article-pdf/2016/1/348/1249582/hem088327.pdf; MDS - http://ashpublications.org/blood/article-pdf/133/10/1049/1556859/blood844621.pdf;
CMML - http://aacrjournals.org/clincancerres/article-pdf/16/8/2246/1995814/2246.pdf; JMML - http://ashpublications.org/blood/article-pdf/133/10/1060/1556886/blood844688.pdf Prevalence: https://seer.cancer.gov/

Acute Graft vs. Host Disease (aGvHD)
A Potentially Life-Threatening Complication of Stem Cell Transplants

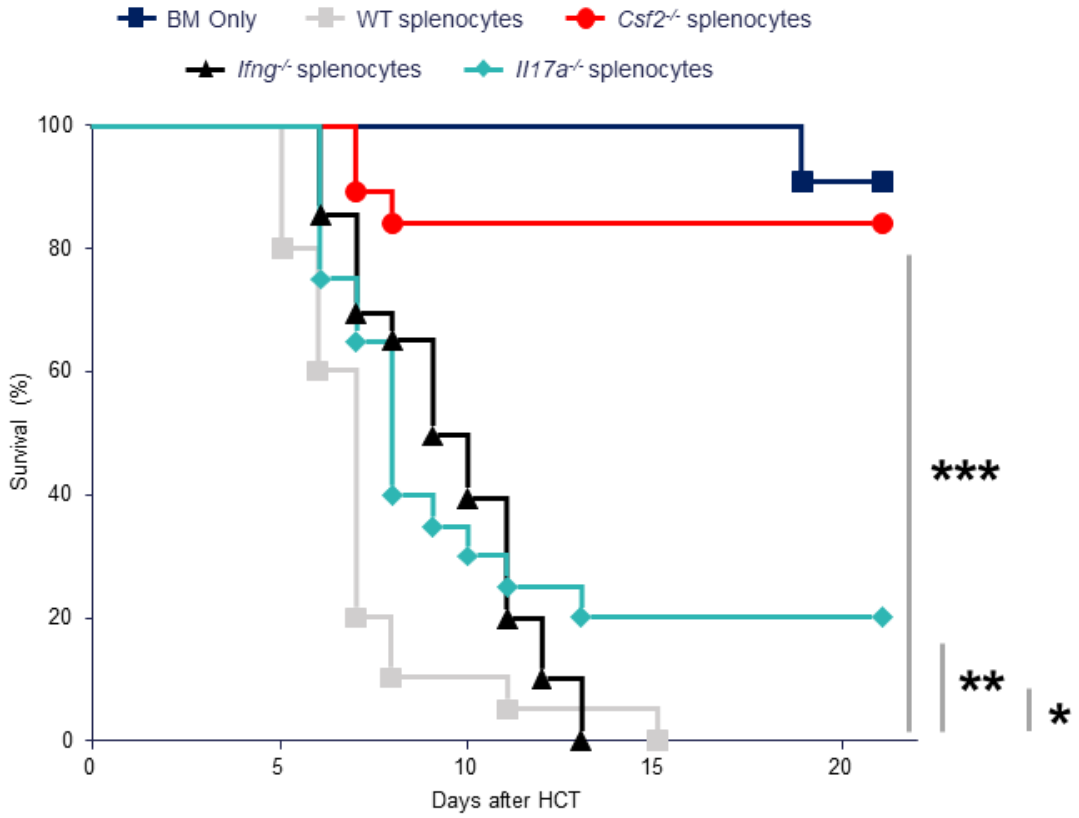
- Hematopoietic Cell Transplantation (HCT) is a potentially curative treatment for both malignant cancers and other non-cancer indications, being utilized in 2019 for more than 28,000 patients across Europe and the U.S.[1]
- 50%-70% of HCT patients develop aGvHD, a potentially life-threatening complication of allogeneic stem cell transplants[2]
- Only 25%-30% of patients with Grade III aGvHD and 1-2% of patients with Grade IV aGvHD survive >2 years[3]
- Treatments – Steroids and Chemotherapy
- Mount Sinai Acute GvHD International Consortium (MAGIC) identifies aGvHD patients who are at higher risk of non-relapse mortality and has the potential to guide therapy[4]
- GM-CSF inhibition has been identified as an attractive target for early treatment of aGvHD[5]
- RATinG study utilizes novel trial design incorporating MAGIC criteria to identify patients for early treatment with lenzilumab, a GM-CSF neutralizing antibody
- Potential Commercial Implications: Orphan Drug Designation (ODD); Fast Track; Breakthrough; Priority Review; Accelerated Review

1. Current use and outcome of hematopoietic stem cell transplantation: CIBMTR US summary slides, 2021 available at https://www.cibmtr.org/ReferenceCenter/SlidesReports/SummarySlides/pages/index.aspx and Hematopoietic cell transplantation and cellular therapy survey of the EBMT: monitoring of activities and trends over 30 years. *Bone Marrow Transplantation*. https://www.nature.com/articles/s41409-021-01227-8
2. Jiang, H. et. Al. (2021, Oct. 5) T Cell Subsets in Graft Versus Host Disease and Graft Versus Tumor. *Frontiers in Immunology*. https://doi.org/10.3389/fimmu.2021.761448.
3. Malard, F. et. al. (2020) Treatment and unmet needs in steroid-refractory acute graft-versus-host disease. *Leukemia*. https://www.nature.com/articles/s41375-020-0804-2.
4. Srinagesh, H. et. al. (2019, Dec. 10) The MAGIC algorithm probability is a validated response biomarker of treatment of acute graft-versus-host disease. *Blood Advances*. https://doi.org/10.1182/bloodadvances.2019000791.
5. Gartlan, K. et. al. *(2019)* Donor T-cell–derived GM-CSF drives alloantigen presentation by dendritic cells in the gastrointestinal tract. *Blood Advances*. https://doi.org/10.1182/bloodadvances.2019000053

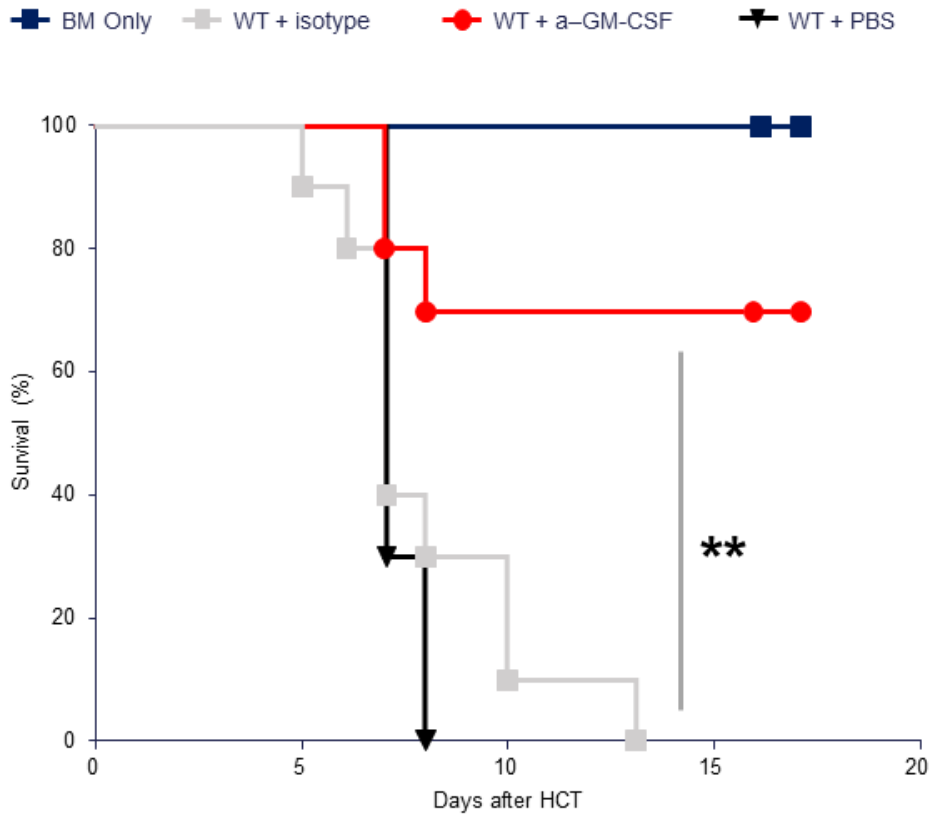
GM-CSF Blockade Reduces GvHD Mortality

Proof-of-concept study demonstrates role of GM-CSF in GvHD

GM-CSF k/o (CSF2-/-) improves GvHD survival

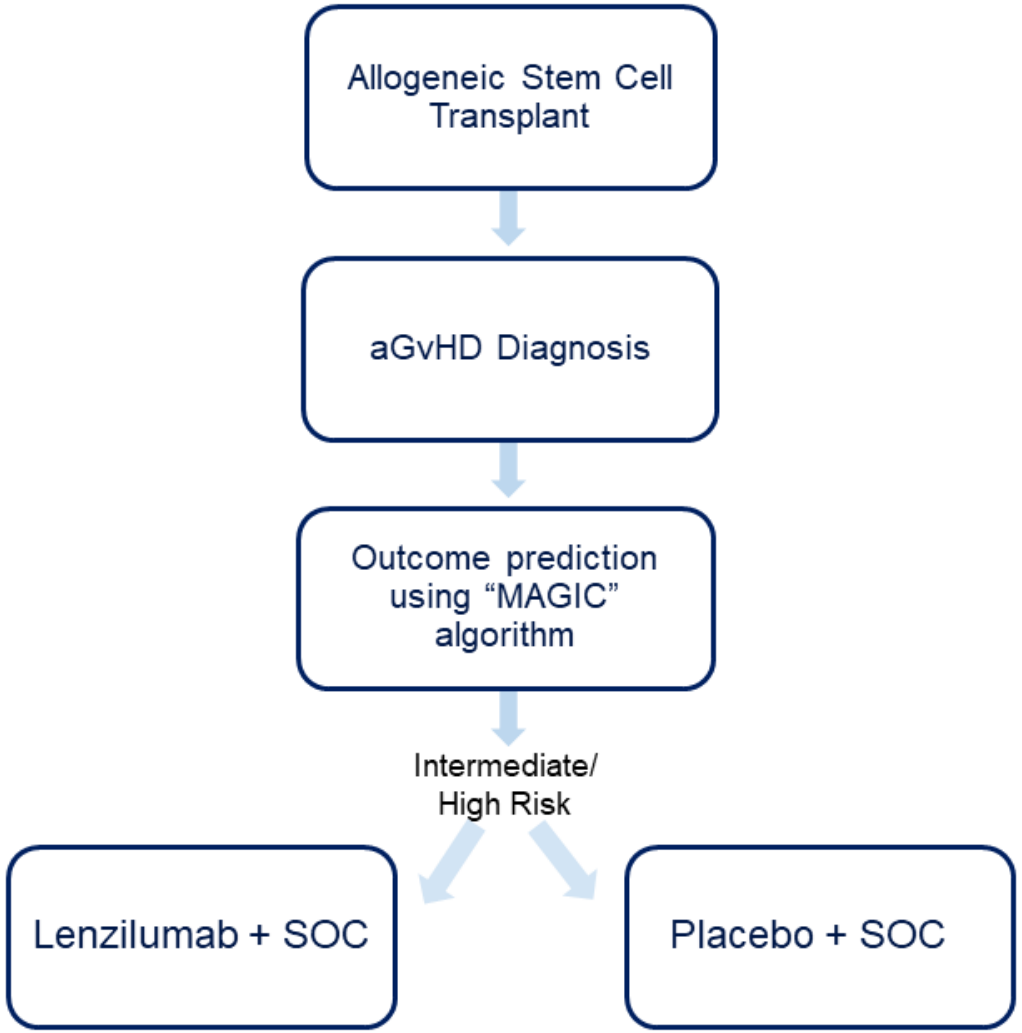


Anti-GM-CSF antibody improves GvHD survival



Tugues et al., Sci. Transl. Med. 10, eaat8410 (2018)

RATinG: Randomized, Double Blind, Placebo Controlled Study in aGvHD

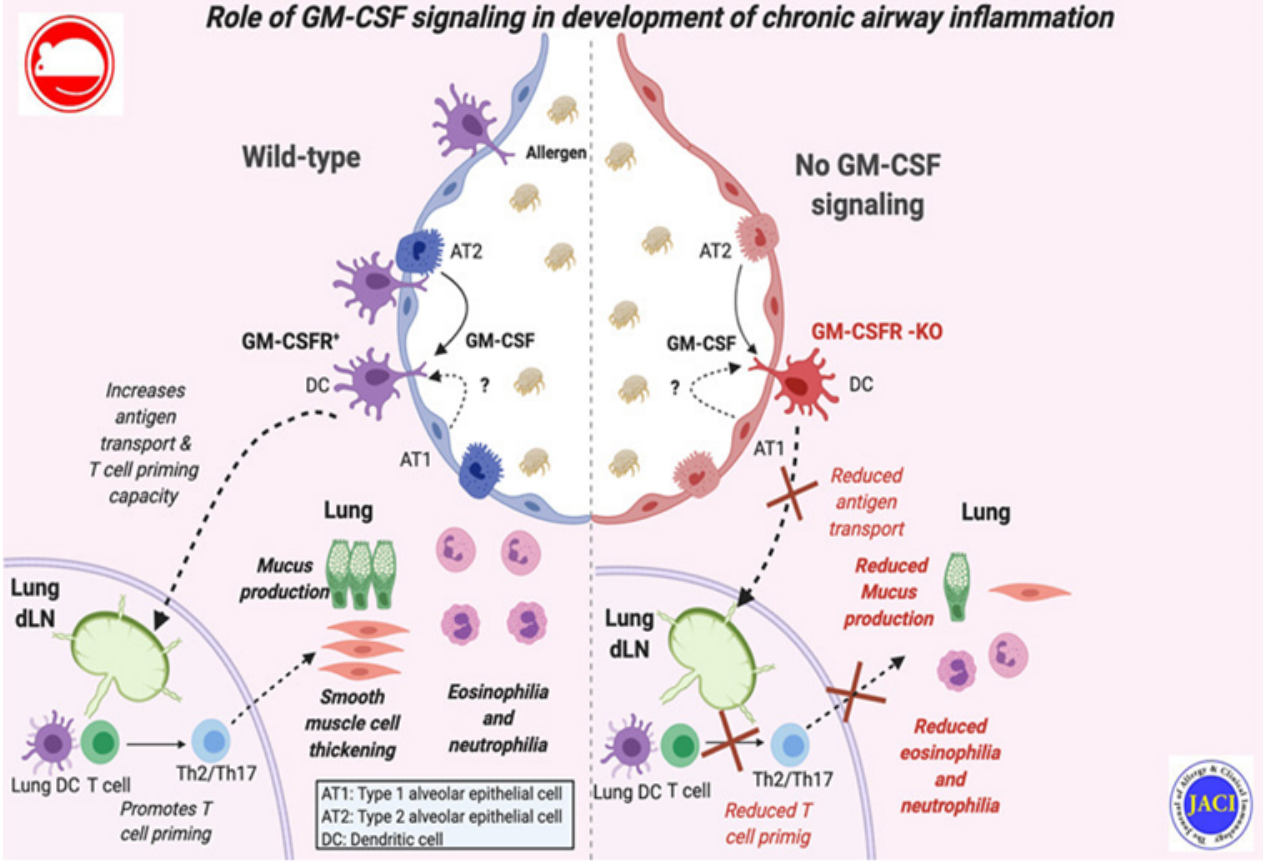


- ☑ Peer Review
- ☑ Protocol Development
- ☑ IRAS Completion
- ☑ Contracts
- ☑ Site Feasibility
- ☑ Biomarker assay development
- ☑ Updated IB
- ☑ Regulatory Submission
- ☑ Regulatory Approval
- ☑ Site initiation Visits
- ○ FPI

FPI 2022

D-B, double-blind; P-C, placebo-controlled; MAGIC, Mount Sinai Acute Graft Versus Host Disease International Consortium algorithm of two biomarkers used to separate patients into two groups with dramatically different non-relapse mortality and overall survival; SOC, standard of care; IRAS, integrated research application system; IB, investigator brochure; FPI, first patient in (enrolled into) a study

Rationale of Lenzilumab in Eosinophilic Asthma



GM-CSF signaling intrinsically promotes accumulation of eosinophils in the lung during allergic airway inflammation

GM-CSF induces chemokinesis and promotes eosinophil survival in vitro, which likely contribute to eosinophil accumulation in the airways in *vivo*

GM-CSF controls lung dendritic cell function

- promotes T-cell-dependent recruitment of neutrophils to the airways

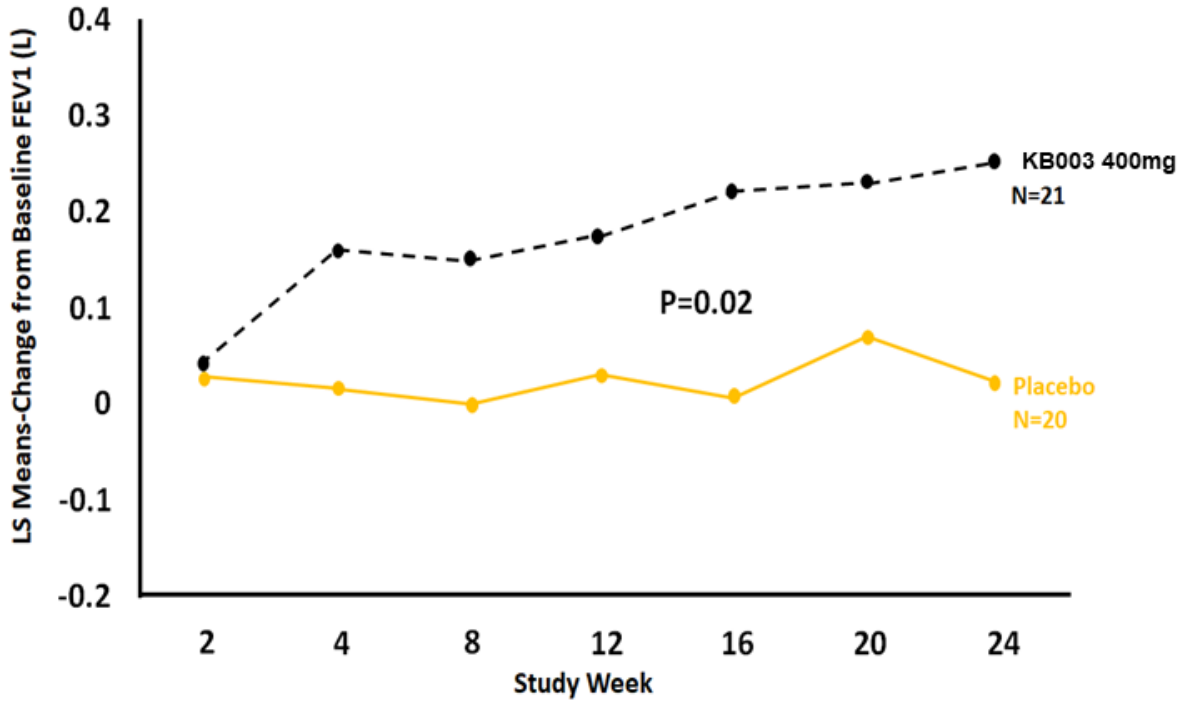
GM-CSF regulates lung dendritic cell antigen uptake, transport, and TH2/TH17 cell priming in an intrinsic fashion

- drives pulmonary granulocyte recruitment and contributes to development of airway hyperresponsiveness in chronic disease

https://doi.org/10.1016/j.jaci.2020.12.638

Phase 2, Double-blind, Placebo-controlled, Randomized Study to Evaluate the Safety, Tolerability, and Efficacy of Lenzilumab in Severe Asthma Inadequately Controlled by Corticosteroids

- 160 subjects randomized; 81% (63) of subjects randomized to drug received all of the 7 doses per protocol
- Subjects in the lenzilumab group had treatment-emergent AE similar to placebo; No treatment related SAE
- 4 subjects in the lenzilumab group vs. 2 in placebo reported an infusion-related reaction (mild-mod, no severe infusion-reactions)
- No deaths were reported or Pulmonary Alveolar Proteinosis (PAP) diagnosis reported
- Statistically significant improvement in FEV1 (227 mL) in pre-specified eosinophilic asthma group

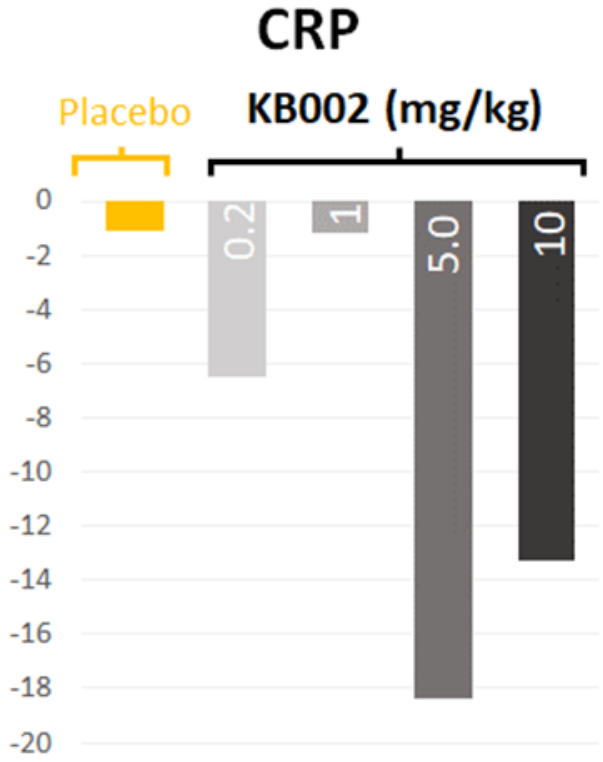


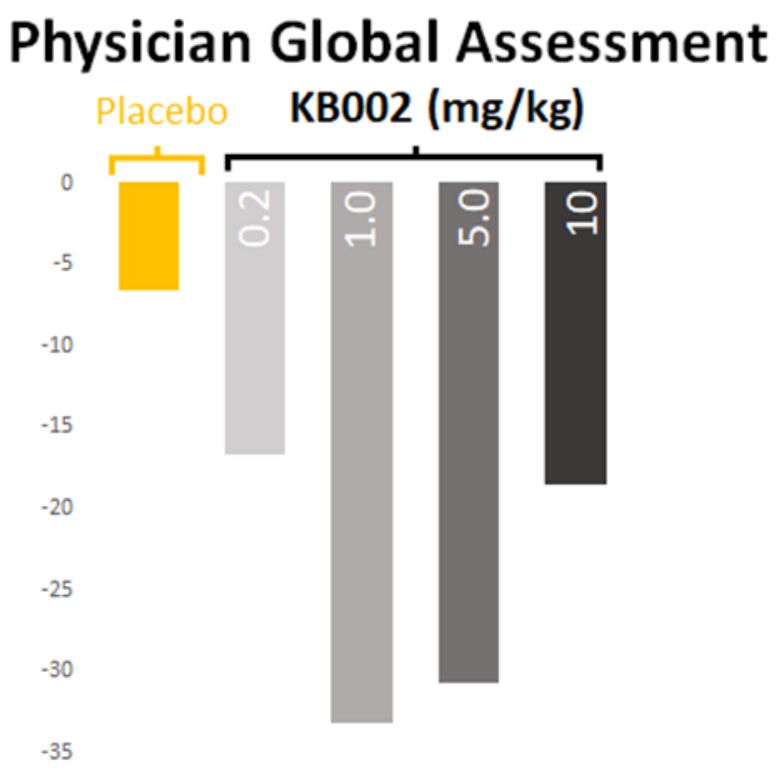
Difference from Placebo in Mean Change from Baseline FEV1 (mL)

Trial	Week 24	
Nucala (75mg IV)*	5	
Nucala (100mg SC)**	76	
Nucala (100mg SC)**	114	
Lenzilumab (400mg IV)***	227	p=0.02

Molfino NA, et al. *BMJ Open* 2016;6:e007709. doi:10.1136/bmjopen-2015-007709

Phase 1 Study:
KB002 in moderate to severe RA uncontrolled with methotrexate





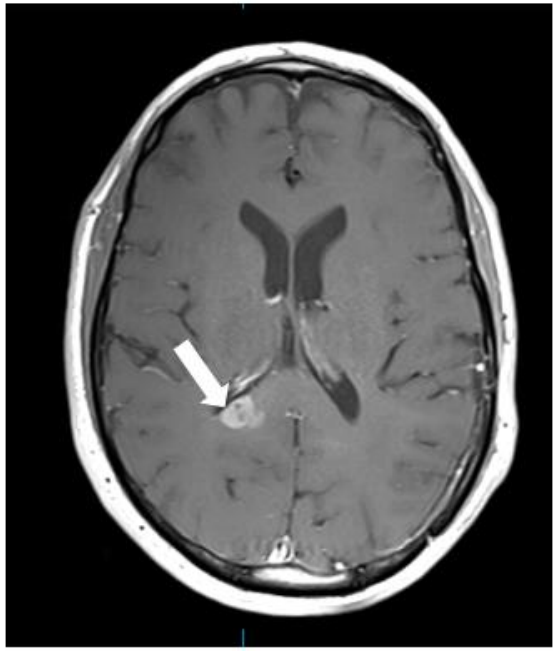
- Overall, a single dose of KB002 was well tolerated at all dose levels
- No clinically significant safety signals or clinically meaningful adverse safety trends
- No trends in developing neutropenia, infections, or respiratory dysfunction, especially in relationship to signs and symptoms of PAP through day 29.
- Analyzing additional concomitant medications collected through day 120 did not reveal worrisome trends or change the overall safety conclusions.

Humanigen, Inc. – Data on file

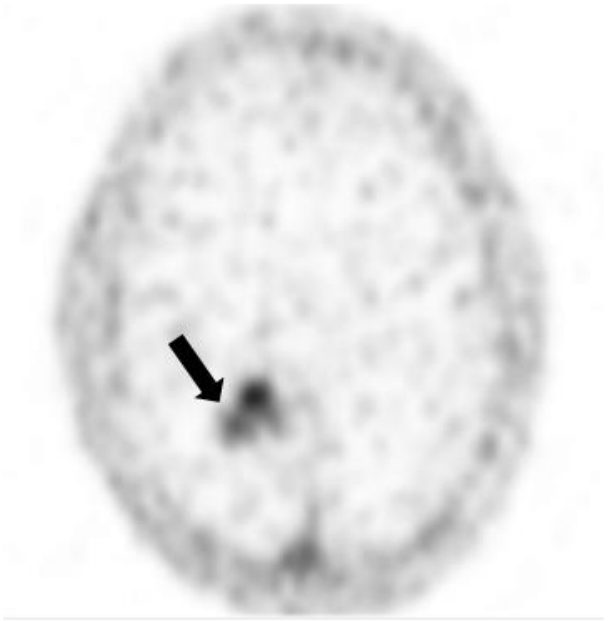
Phase 1 Ifabotuzumab Data in Glioblastoma Multiforme (GBM) Proof of Concept

Radio-labelled ifabotuzumab showed rapid, specific targeting of GBM tumor

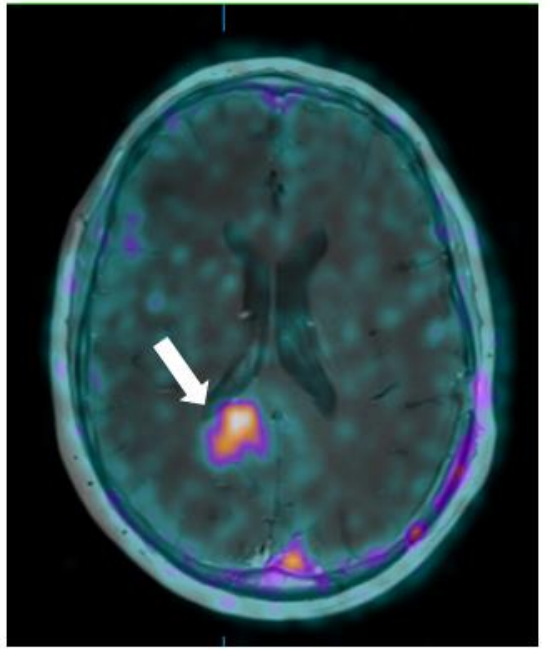
No normal tissue uptake of ^{89}Zr-ifabotuzumab



MRI (T1 + C)



^{89}Zr-ifabotuzumab PET



^{18}F-FDG PET

Source: Scott, A., et al. (2021). Phase I safety and bioimaging trial of ifabotuzumab in patients with glioblastoma (OP-0854). *European Journal of Nuclear Medicine and Molecular Imaging* September 24, 2021;48, s299 https://doi.org/10.1007/s00259-021-05547-1

Humanigen (Nasdaq: HGEN) Late-Stage Pipeline of Proprietary Humaneered® Antibodies

Late-stage pipeline supported by large safety database for a therapeutic with a mechanism of action that has broad applicability

- CMML
  - Initial assessment from open label data expected in 2023H1
- aGvHD
  - First patient to be enrolled 2022
  - Initial interim assessment on first 20 patients
- CAR-T
  - Assessing IIT requests

Advancing antibody drug conjugate (ADC) using proprietary antibody for solid tumor targeting

- ifabotuzumab
  - ADC optimization underway
  - Plan solid tumor basket study (GBM, Breast, Lung, Pancreas)

Historical data in RA and EA provide potential for Global Partnering

- GM-CSF RA readouts by year-end provide opportunity to discuss new MOA
- EA subset of patients statistically significant

VISIT OUR SITE

Humanigen

Thank You For Your Attention