

BRINGING BREAKTHROUGH THERAPIES TO PATIENTS

October 2024



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Mveloma



Company Overview





- Founded in 2013 and listed on LSE since 2017 (LSE: HEMO), with its operations located in New York City at its state-of-the-art research and manufacturing facility
- Our mission is to develop breakthrough therapies for the treatment of blood diseases, including Acute Myeloid Leukemia (AML), rare solid cancers and emerging viral infections
- We are progressing several distinct and complementary product candidates, as well as platform technologies as an engine for novel product development:
 - **HEMO-CAR-T**: Clinically ready next generation CAR-T cell therapy positioned to treat adult and pediatric patients with relapsed/refractory AML and a subset of ALL
 - **CDX**: Advanced design bispecific antibody for the treatment of relapsed/refractory AML, a subset of ALL and conditioning of bone marrow transplantation
 - **Chimeric Bait Receptors (CBR)**: Novel cell therapy for the treatment of cancer and viral infections

Leadership Team





Sir Marc Feldmann *Chairman*



- Medicine and PhD in Immunology from the Walter and Eliza Hall Institute of Medical Research
- Discovered the pivotal role of TNF in rheumatoid arthritis and led development of anti-TNF antibodies, the world's best selling drug class
- Received multiple prizes for his discovery including Crafoord prize in Sweden, Albert Lasker Clinical Medical Research Award (2003), and Canada-Gairdner award



Vladislav Sandler, PhD Chief Executive Officer, Co-Founder WHARVARD HARVARD EINSTEIN Weill Cornell

- Widely published stem cell scientist with decades of experience in scientific research at world leading institutes such as Children's Hospital at Harvard Medical School, the Salk Institute for Biological Sciences, Harvard University, Albert Einstein College of Medicine, and Weill Cornell Medical College as well as Advanced Cell Technologies, Inc
- Awarded the inaugural Daedalus Fund Award for Innovation at Cornell



Peter Redmond UK-based Director

UNIVERSITY OF

- Over 30 years' experience in corporate finance and venture capital
- Has reconstructed AIM companies which have subsequently been acquired and established operating businesses
- Director of Gem Resources plc



Alexis M. Sandler, JD Non-Executive Director, COO & Co-Founder

- Co-founder and COO in US
- Attorney specialising in IP
- 15 years of experience representing a range of companies and institutions

Scientific, Clinical, Business Advisors and Team Principals



- PhD in Cellular Molecular Developmental Biology
- Discovered importance of HER2 in tumor resistance and developed trastuzumab/ Herceptin to treat breast cancer
- In 2019 received Albert Lasker-De Bakey Clinical Research Award for discovery of trastuzumab/Herceptin
- Warren Alpert Prize for treatment of breast cancer



Koen van Besien, MD

University Hospitals Weill Cornell

- Professor of Medicine and Director of the Stem Cell Transplant Program at the NYP-Weill Cornell College of Medicine
- Developed novel methods of transplantation for patients who lack matching donors
- >200 publications in peer reviewed journals
- Editor in Chief of the journal Leukemia and Lymphoma

Alan Walts, PhD

- Venture Partner at Advent Life Sciences, Director at Eloxx, Executive Chairman of Artax
- 25 years Genzyme in BD, business strategy, R&D, management of Genzyme's corporate venture fund, Genzyme Ventures (now Sanofi Ventures)
- Founder and director of The Termeer Foundation



Genentech

Elina Shrestha, PhD Director of Preclinical Development

- NYU Grossman School of Medicine
- PhD in Cellular Molecular Biology
- Developed HEMO-CAR-T prototype
- Supervised IND-enabling studies and filing IND for HEMO-CAR-T



Ronen Ben Jehuda, PhD **Principal Scientist**

TECHNION Israel Institute

- PhD in Physiology
- Responsible for the development of CBR
- Responsible for the development manufacturing of HEMO-CAR-T

Pipeline Overview



• Our Lead asset, HEMO-CAR-T for relapsed/refractory (r/r) AML is expected to enter the clinic in H2 2024



Note: IND-enabling studies for CMR and/or AME for rare cancers 2024-2025

Established Capability for Program Execution



Science/Quality/Analytical/CMC/Pre-clinical/Regulatory/Clinical Capabilities

- R&D and manufacturing In-House
- Quality system In-House
- cGMP cell manufacturing In-House
- cGLP analytical release testing In-House
- CMC, Regulatory, Clinical Trials Management Outsourced

R&D and Manufacturing Capacity

- Custom built 10,000 sf. R&D/Manufacturing facility
- Two qualified ISO7 clean rooms for cGMP cell therapy manufacturing
- Fully equipped R&D laboratory
- Access to animal facilities (Columbia University)

Floorplan of Hemogenyx's New York facility





CAR-T manufacturing process

AML Market and Treatment Paradigm







A Bone Marrow or Hematopoietic Stem Cell Transplant (HSCT) is a potentially <u>life-saving option</u> in treating blood diseases such as Relapsed or Refractory Acute Myeloid Leukemia and BPDCN

BPDCN: Blastic plasmacytoid dendritic cell neoplasm; C/D: Complete/durable remission

* https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2021/cancer-facts-and-figures-2021.pdf

** https://www.globenewswire.com/news-release/2020/07/22/2066107/0/en/Acute-Myeloid-Leukemia-Therapeutics-Market-To-Reach-USD-3-56-Billion-By-2027-Reports-And-Data.html



r/r AML is Almost Universally Fatal

- Most patients lack sensitivity to currently available therapies
- The only curative treatment is allogeneic HSCT but:
 - Poor outcomes following allogeneic HSCT
 - O Less than 50% success rate in patients with chemorefractory disease

Conditioning regimens have safety concerns

- All current conditioning regimens for HSCT are very toxic and have severe side effects that can be life-threatening
- Toxicity of conditioning prevents wider use of HSCT for the treatment of both malignant and non-malignant diseases
- Toxicity of conditioning limits the age range of potential recipients

Hemogenyx Pharmaceuticals is currently developing therapies to address unmet needs in the treatment of AML



CAR-T program

for treatment of relapsed/refractory Acute Myeloid Leukemia



HEMO-CAR-T: a novel CAR-T therapy for AML

Autologous 3rd generation CAR-T therapies:

- Mechanism of Action: cytotoxic T lymphocyte (CTL)-mediated cytolysis
- Clinically Proven safety

HEMO-CAR-T:

- Targeting FMS-like tyrosine kinase 3 receptor (FLT3) which is highly expressed by AML blasts in a majority of patients
- Improved vector design for safety
- No off-target binding other than FLT3
- No FLT3 Ligand (FLT3L) competition, avoiding possible reduction of HEMO-CAR-T efficacy
- Proven *in vitro* and *in vivo* antitumor activity
- Potential as a **conditioning regimen** for AML patients
- **Phase 1 ready**: first patients in Q4 2024 <u>MD Anderson</u>

CAR-T mediated cytotoxicity





HEMO-CAR-T: Pathway to the clinic

Current Status

- Preclinical development is complete
 - Preparation cGMP material, release testing and stability
 - IND-enabling studies (e.g. UPENN, Hemogenyx Pharmaceuticals)
 - Safety studies
 - Potential for functional activity (elimination of AML and HSC/HP)
 - HEMO-CAR-T manufacturing by Hemogenyx Pharmaceuticals PQ runs
 - IND has been cleared by US FDA and Phase 1 trial is projected to be initiated in 2024
 - CRO to run clinical trials has been contracted Prevail Infoworks
 - Two clinical sites are being established: University of Pennsylvania and MD Anderson Cancer Center done
 - A clinical-grade test for FLT3 expression patient's inclusion into the trial is developed
 - Orphan drug designation to be applied for at the start of clinical trials



Clinical Plan

- Initial clinical study will be conducted in relapsed or refractory FLT3⁺ adult AML patients pre-qualified for HSC/HP transplantation to obtain preliminary data on safety (dose escalation), tolerability and partial efficacy – up to 18 patients
- The study will be expanded into pediatric R/R AML and KMT2A rearranged acute lymphoblastic leukemia (ALL) to obtain preliminary data on safety, tolerability and partial efficacy
- Potential upside for early signal of activity demonstrated as:
 - Elimination of malignant cells (FLT3⁺ AML)
 - Elimination of HSC/HP (myeloablative conditioning)



CDX program

for treatment of relapsed/refractory Acute Myeloid Leukemia



CDX: a Novel Humanized FLT3-CD3 Bispecific Antibody

- An "off the shelf" (non patient-specific) product
- Eliminates AML-derived cells transplanted into humanized mice and conditions humanized mouse bone marrow *in vivo*
- **High affinity** binding to FLT3
- No FLT3 Ligand (FLT3L) competition
- Unique bi-specific structure: bi-valent FLT3 and bi-valent CD3 binding
- Highly Potent and allows to target low-FLT3 expressing cells of different sizes
- **Designed to minimize** potentially dangerous non-specific T-cell activation
- **Cross-reacts with Rhesus monkeys** that will be used for further *in vivo* testing
- **Functional synergy** with epigenetic modifying drugs, BET inhibitors and checkpoint inhibitors or conditioning regimens for HSCT
- Market Expansion: effective and non-toxic conditioning would extend the use of HSCT to older and more frail patients and potentially target several additional indications including autoimmune and rare genetic disorders
- Exclusively licensed global rights and developed in **collaboration with Eli Lilly**

I Binds to FLT3 (HSC, AML, DC)
I Binds to CD3 (T cells)



CDX: Potential Path to IND and Clinical Plan



Activity	Year 1	Year2
 Preclinical ADME/toxicology studies Rhesus monkeys (cross-reactive species) to demonstrate: Safety Potential for functional activity (elimination of HSC/HP) 		
Establishment of master cell line, process development and formulation		
Preparation cGMP material, release testing and stability		
IND Enabling Studies		
Pre-IND Meetings		

Clinical Plan

- Initial clinical study to be conducted in relapsed or refractory FLT3⁺ AML and ALL patients pre-qualified for HSC/HP transplantation to obtain preliminary data on safety (dose escalation), tolerability and Ph II dose (expected initiation in 2025/2026)
- The study will be expanded into pediatric R/R AML and KMT2A rearranged acute lymphoblastic leukemia (ALL)
- Potential upside for early signal of activity demonstrated as:
 - Elimination of malignant cells (FLT3⁺ AML)
 - Elimination of HSC/HP (myeloablative conditioning)



Chimeric Bait Receptor Platform







A **novel paradigm** for targeting **Cancer, Neurodegenerative disease** treatments and creating **Antivirals**

<u>Mechanism of action</u>: Programming or redirection of myeloid immune cells such as macrophage using novel synthetic proteins

Expected significant advantages:

As CBR-programmed macrophages:

- a. Penetrate solid tumors
- b. Modulate solid tumor microenvironment for better efficacy
- c. Better safety profile than standard-of-care treatments
- d. Immunize host against targeted malignant cells

As Antivirals:

- a. Single therapeutic targeting multiple viral infections
- b. Long shelf life at ambient temperature
- c. Easy deployment/administration at ambient temperature

Synthetic Macrophage Receptors - Design Concepts







Intellectual Property



Intellectual Property Position



- Hemogenyx has a strong Intellectual Property position and know-how
- Patents cover compositions of matter and methods of use for the CAR-T and CDX programs, in major jurisdictions
- In addition, other granted US patents are:
 - "Method of eliminating hematopoietic stem cells/hematopoietic progenitors (HSC/HP) in a patient using bi-specific antibodies"
 - "Post-natal hematopoietic endothelial cells and their isolation and use"
- Seminal patent application (current PCT) covering CBR platform
- More are in prosecution or planned to be filed in 2025
- Patent protection is expected to around 2037-2042, excluding any potential extensions or further applications
- Freedom to operate has been conducted for all current product candidates





Advancing product candidates towards the clinic

- HEMO-CAR-T therapy for the treatment of relapsed/refractory AML and subset of ALL in adults and pediatric patients; IND cleared by US FDA and Phase
 I trial is projected to be initiated in H2 2024
- CDX bi-specific antibody for the treatment of relapsed/refractory AML, subset of ALL in adults and pediatric patients and conditioning of bone marrow transplantation; developed in collaboration with Eli Lilly & Co. with exclusive world-wide license
- CMR (Chimeric Macrophage Receptor) for rare cancers

Conclusion

- Experienced team
- Established in-house capability for program execution, including manufacturing
- Deep translational program pipeline
- Advancement to the clinic of HEMO-CAR-T in Q4 2024
- Large and fast-growing market (>\$1.5B p.a. for two leading product candidates)
- Strong IP portfolio
- Clear path to the clinic; first clinical trial expected to commence in Q4 of 2024
- Proprietary Chimeric Bait Receptor platform for treatment of rare cancers and emerging viral infections



Thank You!

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