ASX ANNOUNCEMENT **15 May 2025**

ADVENT-AML Phase 1B clinical trial update

- **Two of three evaluable patients have achieved CRi – Complete Response with incomplete blood count recovery (remission) in Acute Myeloid Leukemia (AML)**
- **This clinical trial is designed to enroll 20 newly diagnosed AML patients who are not eligible for chemotherapy or allogeneic stem cell transplant.**
- **Known as ADVENT-AML, the trial combines standard of care AML treatment with CHM's CORE-NK technology to test a novel and potentially transformative new paradigm for AML patients**
- **ADVENT-AML is the first frontline AML trial to incorporate a cell therapy**

Melbourne, Australia, 15 May 2025: Chimeric Therapeutics (ASX:CHM, "Chimeric" or the "Company", is pleased to announce the ADVENT-AML Phase 1B clinical trial has **3 patients on frontline CHM CORE-NK protocol; 2 out of 3 patients have achieved CRi – Complete Response with incomplete blood count recovery.**

ADVENT-AML (www.clinicaltrials.gov/search?term=NCT05834244) is the first clinical trial to evaluate the synergy of Chimeric's CHM CORE-NK technology in combination with the current standard of care for AML patients. The Phase 1B ADVENT-AML clinical trial at MD Anderson Cancer Centre has completed enrollement of relapsed/refractory AML subjects in the dose finding portion of the trial where no safety concerns were observed. In this second cohort of the phase 1b trial, newly diagnosed AML subjects who are elderly or otherwise unsuitable for transplantation and have not been previously treated for AML, will be eligible for enrollment. The third of the three patients achieved Stable Disease, whereby the cancer is neither increasing nor decreasing in extent or severity.

This clinical trial is an investigator-initiated study currently open to enrollment at MD Anderson Cancer Center under Principal Investigator Abhishek Maiti MD, Assistant Professor in the Department of Leukemia. The study is evaluating the synergy of NK cell therapy in combination with the current standard of care, Azacitidine and Venetoclax. "This is great news for newly diagnosed AML patients who may benefit from our CORE-NK cells as their initial AML therapy," said Dr Rebecca McQualter, CEO of Chimeric Therapeutics. "We are excited to be pioneers in the cell therapy sector, with the first frontline cell therapy study in AML lead by MD Anderson Cancer Center".

The trial commenced in December 2024. Trial completion is subject to satisfactory enrollment of sufficient eligible patients, however, the Company currently anticipates the study is likely to complete in the December 2025 quarter.

The CORE-NK cells used in the ADVENT-AML clinical trial were manufactured and cryopreserved for "off-the-shelf" accessibility at the Cellular Therapy Integrated Services Laboratory at Case Western Reserve University where the CHM CORE-NK cells were developed.

ABOUT CHIMERIC THERAPEUTICS

Chimeric Therapeutics, a clinical stage cell therapy company focused on bringing the promise of cell therapy to life for more patients with cancer.

To bring that promise to life for more patients, Chimeric's world class team of cell therapy pioneers is focused on the discovery, development, and commercialization of the most innovative and promising cell therapies.

Chimeric currently has a diversified portfolio that includes first in class autologous CAR-T cell therapies and best in class allogeneic NK cell therapies. Chimeric assets are being developed across multiple different disease areas in oncology with 4 clinical stage programs.

CHM CDH17 is a first-in-class, 3rd generation CDH17 CAR-T invented at the world-renowned cell therapy centre, the University of Pennsylvania (Penn) in the laboratory of Dr. Xianxin Hua, professor in the Department of Cancer Biology in the Abramson Family Cancer Research Institute at Penn. Preclinical evidence for CDH17 CAR-T was published by Dr. Hua and his colleagues in March 2022 in Nature Cancer demonstrating complete eradication of tumours in 7 types of cancer in mice. CHM CDH17 is currently being studied in a phase 1/2 clinical trial in gastrointestinal and neuroendocrine tumours that was initiated in 2024.

CHM CORE-NK is a potentially best-in-class, clinically validated NK cell platform. Data from the complete phase 1A clinical trial was published in March 2022, demonstrating safety and efficacy in blood cancers and solid tumours. Based on the promising activity signal demonstrated in that trial, two additional Phase 1B clinical trials investigating CORE-NK in combination regimens have been initiated. From the CORE-NK platform, Chimeric has initiated development of new next generation NK and CAR NK assets.

CHM CLTX is a novel and promising CAR-T therapy developed for the treatment of patients with solid tumours. CLTX CAR T is currently being studied in a phase 1B clinical trial in recurrent / progressive glioblastoma. Positive preliminary data from the investigator-initiated phase 1A trial in glioblastoma was announced in October 2023.

Authorised on behalf of the Chimeric Therapeutics board of directors by Chairman Paul Hopper

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Study Overview

Brief Summary

To learn if adding a healthy person's natural killer (NK) cells to the combination of Azacitidine and Venetoclax can help to control AML. NK cells are cancer- and infection-fighting immune cells.

Detailed Description

Primary Objective:

- To evaluate Safety of the combination of azacitidine, venetoclax and allogeneic NK cells

Secondary Objective:

- To estimate overall response rate (ORR)
- To estimate rate of CR/CRi by 4 cycles of therapy
- To estimate rate of MRD negative by 6 cycles
- To estimate overall survival (OS)
- To estimate relapse-free survival (RFS)

Exploratory Objectives:

- To estimate rate of CRc MRD negative at any time
- To estimate event-free survival (EFS)
- To estimate duration of response (DOR)
- To estimate median time to blood count recovery
- To estimate median time to first response
- To estimate median time to negative MRD
- To evaluate persistence of NK cells in peripheral blood
- To explore biomarker of response and resistance
- Using propensity-score matching analysis (per post-hoc plan) to explore the difference in response, survival adverse events in contemporary historical control population treated with HMA-VEN

Official Title

A Phase Ib Trial of Azacitidine, Venetoclax and Allogeneic NK Cells for Acute Myeloid Leukemia (ADVENT-AML)

Conditions

Acute Myeloid Leukemia

Intervention / Treatment

- Drug: Azacitidine
- Drug: Venetoclax
- Drug: NK Cells

Other Study ID Numbers

- 2022-0941
- NCI-2023-03179 (Other Identifier) (OTHER: NCI-CTRP Clinical Trials Registry)

Eligibility Criteria
Description

Inclusion Criteria:

1. Patients need to have a confirmed diagnosis of AML, or MDS/AML with 10% to 19% blasts, per the International Consensus Classification 2022 or the WHO 2022 classification.43,44

   Dose escalation cohort:

2. Patients ≥18 years with R/R AML or R/R MDS/AML, other than acute promyelocytic leukemia (APL), or core binding factor (CBF) AML with no available standard treatment options.
3. Relapsed or refractory disease defined by standard criteria as follows
    1. Relapsed: Bone marrow blasts ≥5%, reappearance of blasts in the blood, or development of extramedullary disease following achievement of CR/CRi/MLFS
    2. Refractory: Failure to achieve CR/CRi/MLFS following initial treatment, with evidence of persistent leukemia by blood and/or bone marrow evaluation
    3. Appropriate prior therapy in order for patient to be deemed relapsed or refractory include the following

   i. 7+3 based induction: 2 cycles of for patients <60 years, and 1 cycle for patients who are either ≥60 years or unfit for intensive therapy ii. 1 cycle of induction regimen containing intermediate dose or higher of cytarabine iii. 2 cycles of venetoclax with HMA/LDAC +/- other agents iv. 4 cycles of HMA alone d. For patients in first relapse, the dose escalation cohort will only enroll patients in early first relapse, i.e., first remission duration of ≤12 months.

4. Patients relapsing after allo-SCT may be eligible if they have recovered from all transplant-related toxicities and are off all immunosuppression, with no more than grade 1 chronic GVHD. Physiologic dose of steroids (≤10 mg prednisone or equivalent) may be acceptable.
5. Patients with actionable mutations with available FDA-approved therapies, e.g., FLT3, IDH1/2 inhibitors may be enrolled after they have exhausted such available FDA approved treatment options.

   Dose expansion cohort:

   Dose expansion cohort will only enroll older/unfit patients with newly diagnosed adverse or intermediate risk AML or MDS/AML who are ineligible for intensive chemotherapy and/or are ineligible for or decline to receive allo-SCT (please refer to stratification in statistics section).

6. Adverse risk AML or MDS/AML defined per AML ELN 2022 recommendations.

7. Age ≥ 75 years, or
8. Age ≥ 18 years with at least one of the following comorbidities
    1. ECOG PS 2 or 3
    2. Left ventricular ejection fraction (LVEF) ≤ 50%
    3. Lung diffusing capacity for carbon monoxide (DLCO) ≤ 65% of expected
    4. Forced expiratory volume in 1 second (FEV1) ≤ 65% of expected
    5. Chronic stable angina or congestive heart failure controlled with medication
    6. Other comorbidity or conditions that the Investigator judges as incompatible with intensive chemotherapy, or allo-SCT which must be documented
9. Patients with antecedent aplastic anemia, myelodysplastic syndrome, or chronic myelomonocytic leukemia may be eligible if they had not received prior hypomethylating agent, BCL2 inhibitors, MCL1 inhibitors, chemotherapy (definitive or therapeutic intent), or allo-SCT for MDS. Acceptable prior therapies include erythropoietin stimulating agents, thrombopoietin receptor agonists, lenalidomide, luspatarcept, anti-thymocyte globulin, cyclosporine, and iron chelating agents.

    All patients:

10. Adequate hepatic function (direct bilirubin ≤ 2 x upper limit of normal (ULN) unless increase is due to Gilbert's disease or leukemic involvement, and AST and/or ALT ≤ 2.5 x ULN unless considered due to leukemic involvement, in which case direct bilirubin or AST and/or ALT ≤ 3 x ULN will be considered eligible.)
11. Adequate renal function with creatinine clearance ≥ 30 mL/min calculated by the Cockcroft-Gault formula or measured by 24-hour urine collection
12. The effects of these agents on the developing human fetus are unknown. For this reason, and because other therapeutic agents used in this trial may be teratogenic, women of childbearing potential and men must agree to use adequate contraception (hormonal or barrier method of birth control; abstinence) prior to study entry, for the duration of study participation, and for at least 90 days after last treatment. This includes all female patients between the onset of menses (as early as 8 years of age) and 55 years unless the patient presents with an applicable exclusionary factor which may be one of the following:
    - Postmenopausal (no menses in greater than or equal to 12 consecutive months).
    - History of hysterectomy or bilateral salpingo-oophorectomy.
    - Ovarian failure (follicle-stimulating hormone and estradiol in menopausal range, who have received whole pelvic radiation therapy).
    - History of bilateral tubal ligation or another surgical sterilization procedure.
13. Approved methods of birth control are as follows: Hormonal contraception (i.e., birth control pills, injection, implant, transdermal patch, vaginal ring), Intrauterine device (IUD), tubal ligation or hysterectomy, subject/partner post vasectomy, implantable or injectable contraceptives, and condoms plus spermicide. Not engaging in sexual activity for the total duration of the trial and the drug washout period is an acceptable practice; however, periodic abstinence, the rhythm method, and the withdrawal method are not acceptable methods of birth control. Should a woman become pregnant or suspect she is pregnant while she or her partner is participating in this study, she should inform her treating physician immediately.

14. Men treated or enrolled on this protocol must also agree to use adequate contraception prior to the study, for the duration of study participation, and 4 months after completion of treatment.
15. Ability to understand and the willingness to sign a written informed consent document.

Exclusion Criteria:

1. Patients with t(15;17), t(8;21), inv(16), or t(16;16) karyotypic abnormality
2. Patient has a white blood cell count > 15 x 10^9/L. Hydroxyurea, and/or cytarabine (up to 2 g/m2 total) used as supportive care is permitted to meet this criterion.
3. Patients who have received high-dose (e.g., > 10 mg prednisone or equivalent) systemic steroid therapy or any other form of immunosuppressive therapy within 1 week or 5 half-lives of first NK cell infusion date (cycle 1 Day 8), whichever is longer.
4. Patients with known symptomatic or uncontrolled CNS leukemia.
5. Patient has systemic fungal, bacterial, viral or other infection that is exhibiting ongoing signs/symptoms related to the infection without improvement despite appropriate treatment.
6. Any signs or symptoms of active CNS pathology within 6 months of screening including history of seizures requiring anti-epileptics, focal neurological deficit, stroke, dementia, brain injury, or organic brain pathology. Any subarachnoid hemorrhage or CNS bleed within 3 months of screening.
7. Patients with any severe gastrointestinal or metabolic condition which could interfere with the absorption of oral study medications as determined by the investigator.
8. Active and uncontrolled comorbidities including decompensated congestive heart failure NYHA class III/IV, clinically significant and uncontrolled arrhythmia as judged by the treating physician.
9. Known active hepatitis B (HBV) or Hepatitis C (HCV) infection with detectable viral DNA or RNA, respectively, or known HIV infection.
10. Corrected QT interval (QTc) > 480 msec or history of Torsades de pointes
11. Any other medical, psychological, or social condition that may interfere with study participation or compliance, or compromise patient safety in the opinion of the investigator.
12. Any previous or concomitant malignancy, except when the patient has completed definitive curative-intent treatment with chemotherapy and/or surgery and/or radiotherapy at least 3 months prior to enrollment. Patients having completed definitive treatment for the following conditions may be eligible immediately after completion of definitive curative-intent therapy, after healing of wounds, and no evidence of residual disease by examination, imaging, and/or cytology/pathology, e.g., non-melanoma skin cancers, or a carcinoma in-situ, e.g., ductal carcinoma in situ, urothelial cancer, cervical cancer, localized prostate cancer, pre-cancerous colon polyp, etc.
13. Weight <50 kg
14. Major surgery within 4 weeks prior to screening or a major wound that has not fully healed.
15. Patients under legal protection measure (guardianship, trusteeship or safeguard of justice) and/or uncontrolled psychiatric comorbidities, ongoing illicit substance abuse, inability, any impairment or unwillingness to comply with the treatments, follow-up, requirements and procedures of this clinical trial.
16. A known hypersensitivity or severe allergy to study drug components or diluents
17. Nursing women, women of childbearing potential (WOCBP) with positive urine or serum pregnancy test, or WOCBP who are not willing to maintain adequate contraception.

18. Pregnant women are excluded from this study because study agents may have the potential for teratogenic or abortifacient effects. Because there is an unknown but potential risk for adverse events (AEs) in nursing infants secondary to treatment of the mother with study agents, breastfeeding should be discontinued if the mother is treated on this study.

Design Details
Primary Purpose : Treatment
Allocation : Non-Randomized
Interventional Model : Single Group Assignment
Masking : None (Open Label)

Arms and Interventions

Participant Group/Arm	**Intervention/Treatment**
Experimental: Dose Escalation Dose Escalation to evaluate the combination of azacitidine, venetoclax and allogeneic NK cells in older/unfit participants with AML ineligible for intensive chemotherapy or allogeneic stem-cell transplantation (allo SCT).	Drug: Azacitidine • Given by IV (vein) • Other Names: ○ 5-azacytidine ○ 5-aza ○ Vidaza™ ○ 5-AZC ○ AZA-CR ○ Ladakamycin ○ NSC-102816 ○ Azacytidine Drug: Venetoclax • Given by PO • Other Names: ○ ABT-199 ○ GDC-0199

Participant Group/Arm	Intervention/Treatment
	Drug: NK Cells • Given by IV (vein)

Experimental: Dose Expansion
Dose Expansion to evaluate the combination of azacitidine, venetoclax and allogeneic NK cells in older/unfit participants with AML ineligible for intensive chemotherapy or allogeneic stem-cell transplantation (allo SCT).
	Drug: Azacitidine
	• Given by IV (vein)
	• Other Names:
	  ○ 5-azacytidine
	  ○ 5-aza
	  ○ Vidaza™
	  ○ 5-AZC
	  ○ AZA-CR
	  ○ Ladakamycin
	  ○ NSC-102816
	  ○ Azacytidine
	Drug: Venetoclax
	• Given by PO
	• Other Names:
	  ○ ABT-199
	  ○ GDC-0199
	Drug: NK Cells
	• Given by IV (vein)

What is the study measuring?

Primary Outcome Measures

Outcome Measure	Measure Description
Incidence of Adverse Events, Graded According to National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) Version (v) 5.0	