Clinical Trials in Myeloma and Related Disorders at PM Cancer Centre
(Version June 2026)

MULTIPLE MYELOMA TRIALS – NEWLY DIAGNOSED:

STUDY TITLE: DEVELOPMENT OF NK CELL- AND T CELL- ENGAGING BI- AND MULTI-SPECIFIC BIOLOGICS TO REDIRECT IMMUNE RESPONSES TOWASRDS PLASMA CELLS AND MYELOMA CELLS.
Study Number: NKT vs MM
Contact: Dr. Rodger Tiedemann/ Harjot Vohra- **Open Enrollment**

Inclusion Criteria

1. Age ≥ 18 years
2. Able to give informed consent
3. Diagnosed with or suspected of having multiple myeloma, or is a healthy volunteer
4. Able and willing to donate research specimens

Exclusion Criteria

1. Another active major non-plasma cell malignancy (but permitting non-metastatic skin tumors), previously treated with chemotherapy within the past 2 years
2. Known HIV or HTLV infection
3. Known symptomatic Covid-19 infection in the past 2 weeks
4. Any serious medical condition or psychiatric illness that would prevent the subject from signing the informed consent form.
5. Declined to participate.

AN INTEGRATED APPROACH TO CHARACTERIZE HIGH-RISK DISEASE IN MYELOMA AT PRINCESS MARGARET.
Protocol Number: HiPerMM
Contact: Dr. Suzanne Trudel /Harjot Vohra – **Open Enrollment**

Inclusion Criteria

1. Age ≥ 18 years
2. Ability to give informed consent
3. Newly diagnosed with active multiple myeloma
4. Eligible for autologous stem-cell transplantation (ASCT)
5. Classified as intermediate-high risk (stage III) or high risk (stage IV) risk as per the R2-ISS criteria
6. Able and willing to donate research specimens within the 1st month of induction treatment.

Exclusion Criteria

1. Patient deemed unfit or ineligible to proceed with ASCT.
2. Concurrent plasma cell disorder such as amyloid or POEMS, or other hematological malignancy
3. Any serious medical condition or psychiatric illness that would prevent the subject from signing the informed consent form.
4. Declined to participate.
5. Unable to speak or understand English necessary for completing the questionnaires and follow instructions.

Phase 3 Study of Teclistamab in Combination with Lenalidomide and Teclistamab Alone versus Lenalidomide Alone in Participants with Newly Diagnosed Multiple Myeloma as Maintenance Therapy Following Autologous Stem Cell Transplantation (MajesTEC-4)
Protocol Number: EMN30/64007957MMY3003 (MajesTEC4)
Contact: Dr. Donna Reece / Elena Talovikova–**Enrollment on hold at the site**

Inclusion Criteria

1. ≥18 years of age.
2. Must have **a new diagnosis of symptomatic multiple myeloma** according to **IMWG criteria** and have received 4 to 6 cycles of 3- or 4 drug induction therapy that includes a proteasome inhibitor and/or an IMiD with or without anti-CD38 monoclonal antibody and a single or tandem ASCT. Post ASCT consolidation is permitted for up to 2 cycles as long as the total number of induction plus consolidation cycles does not exceed 6.
    a. **NOTE**: Participants who receive up to the first 2 cycles of a 2-drug induction therapy may be eligible, provided the participants were deemed unable to tolerate a 3 or 4 drug therapy at start of treatment and the change to a 3 or 4 drug therapy was planned.
    b. **NOTE**: Must have measurable disease at the time of diagnosis defined as measurable M-protein in the serum (≥0.5 g/dL) or urine (≥200 mg/24h) or serum free light chain assay (defined as ≥10 mg/dL [≥100 mg/L] on involved light chain).
3. Must have received only one line of therapy and achieved at least a partial response (≥PR) as per IMWG 2016 response criteria based on the investigator's assessment. Participants with plasmacytomas at the time of diagnosis must meet IMWG 2016 response criteria for ≥PR based on repeat imaging utilizing the same modality
4. Must not be intolerant to the starting dose of lenalidomide (10mg)

5. Must have received high-dose chemotherapy and ASCT within 12 months of the start of induction therapy and be within 6 months of the last ASCT (7 months for participants who received consolidation) at the time of randomization.
6. Must not have received any maintenance therapy.
7. Have an Eastern Cooperative Oncology Group (ECOG) performance status score of 0-2 at screening and immediately prior to the start of administration of study treatment.
8. Have clinical laboratory values meeting the following criteria.

Hematology	
Hemoglobin	**≥8.0 g/dL (≥5 mmol/L; without prior RBC transfusion within 7 days before the laboratory test; recombinant human erythropoietin use is permitted)**
Platelets	≥75×109/L (without transfusion support or thrombopoietin receptor agonist within 7 days before the laboratory test)
Absolute neutrophil count	≥1.0×109/L (prior growth factor support is permitted but must be without support for 7 days for G-CSF or GM-CSF or 14 days for pegylated-G-CSF)
Chemistry	
AST and ALT	**≤2.5× upper limit of normal (ULN)**
Total bilirubin	**≤1.5×ULN; except in participants with congenital bilirubinemia, such as Gilbert syndrome (in which case direct bilirubin ≤1.5×ULN is required)**
CrCl	**≥30 mL/min based on Cockcroft-Gault formula calculation or a 24-hour urine collection**
Serum Calcium corrected for albumin	**≤14 mg/dL (≤3.5 mmol/L) or free ionized calcium ≤6.5 mg/dL (≤1.6 mmol/L)**

9. A woman of childbearing potential must have a negative serum pregnancy test within 10-14 days prior to the start of study treatment and again either a serum or urine pregnancy test within 24 hours of the start of study treatment and must agree to further serum or urine pregnancy tests during the study.
10. Must be willing and able to adhere to the lifestyle restrictions specified in this protocol. adherence to global/local Pregnancy Prevention Plan; not to donate blood, Tec-related hospitalizations, avoid driving during step-up dosing if Tec-Len patient

Exclusion Criteria

1. Any previous therapy with an immune cell redirecting agent or gene modified adoptive cell therapy (e.g., chimeric antigen receptor modified T cells, NK cells).
2. Discontinued treatment due to any AE related to lenalidomide as determined by the investigator.
3. History of allogeneic stem cell transplantation or prior organ transplant.
4. Progressive disease as per IMWG 2016 response criteria at any time prior to randomization.
5. Radiotherapy within 14 days or focal radiation within 7 days of C1D1.
6. Received a cumulative dose of corticosteroids equivalent to >40 mg of dexamethasone within the 14 days prior to C1D1.
7. Received a live, attenuated vaccine within 4 weeks before C1D1. Non-live vaccines or non-replicating authorized for emergency use (e.g., COVID-19) are allowed.
8. Excluded for any of the following:
    a. Any ongoing myelodysplastic syndrome or B cell malignancy (other than multiple myeloma)
    b. Any history of malignancy, other than multiple myeloma, which is considered at high risk of recurrence requiring systemic therapy
    c. Any active malignancy (i.e., progressing or requiring treatment change in the last 24 months) other than multiple myeloma. The only allowed exceptions are malignancies treated within the last 24 months that are considered cured:
        i. Non-muscle invasive bladder cancer (solitary Ta-PUN-LMP or low grade, <3 cm, no CIS)
        ii. Non-melanoma skin cancers treated with curative therapy or localized melanoma treated with curative surgical resection alone
        iii. Non-invasive cervical cancer
        iv. Breast cancer: adequately treated lobular carcinoma in situ or ductal carcinoma in situ or history of localized breast cancer (anti-antihormonal therapy is permitted)
        v. Localized prostate cancer (M0, N0) with a Gleason Score ≤7a, treated locally only (RP/RT/focal treatment)
        vi. Other malignancy that is considered cured with minimal risk of recurrence in consultation with the Sponsor's medical monitor.
9. Plasma cell leukemia, smoldering multiple myeloma, Waldenström's macroglobulinemia, POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, and skin changes), or primary light chain amyloidosis.
10. Central nervous system involvement or exhibits clinical signs of meningeal involvement of multiple myeloma. If either is suspected, brain magnetic resonance imaging (MRI) and lumbar cytology are required.
11. Stroke, transient ischemic attack, or seizure within 6 months of C1D1.
12. Contraindications or life-threatening allergies, hypersensitivity, or intolerance to any study treatment or its excipients.
13. Participant is pregnant or breast-feeding or planning to become pregnant while enrolled in this study or within 6 months after the last dose of

study drug.

14. Participant plans to father a child while enrolled in this study or within 3 months after the last dose of study drug.
15. Presence of the following cardiac conditions:
    a. New York Heart Association stage III or IV congestive heart failure
    b. Myocardial infarction or coronary artery bypass graft ≤6 months prior to C1D1
    c. History of clinically significant ventricular arrhythmia or unexplained syncope, not believed to be vasovagal in nature or due to dehydration
    d. Uncontrolled cardiac arrhythmia or clinically significant electrocardiogram (ECG) abnormalities.
16. Any of the following:
    a. Human immunodeficiency (HIV) virus-positive participants with 1 or more of the following:
        i. History of acquired immune deficiency syndrome (AIDS)-defining conditions
        ii. CD4 count <350 cells/mm3 at screening
        iii. Detectable viral load during screening or within 6 months prior to screening.
        iv. Not receiving highly active antiretroviral therapy (ART)
        v. Had a change in antiretroviral therapy within 6 months of the start of screening
        vi. Receiving antiretroviral therapy that may interfere with study treatment as assessed after discussion with the Medical Monitor.
17. Hepatitis B infection (i.e., HBsAg or HBV-DNA positive): In the event the infection status is unclear, quantitative viral levels are necessary to determine the infection status.
18. Active hepatitis C infection as measured by positive hepatitis C virus (HCV) - ribonucleic acid (RNA) testing. Participants with a history of HCV antibody positivity must undergo HCVRNA testing. If a participant with history of chronic HCV infection (defined as both HCV antibody and HCV-RNA positive) completed antiviral therapy and has undetectable HCVRNA 12 weeks following the completion of therapy, the participant is eligible for the study.
19. Concurrent medical or psychiatric condition or disease, that is likely to interfere with study procedures or results, or that in the opinion of the investigator would constitute a hazard for participating in this study, such as:
    a. Grade 3 or greater peripheral neuropathy
    b. Acute diffuse infiltrative pulmonary disease
    c. Evidence of active systemic viral, fungal, or bacterial infection, requiring systemic antimicrobial therapy
    d. History of autoimmune disease with the exception of:
        i. vitiligo not on systemic therapy
        ii. type I diabetes
        iii. prior autoimmune thyroid disease that is currently euthyroid based on clinical symptoms and laboratory testing
    e. Disabling psychiatric conditions (e.g., alcohol or drug abuse), severe dementia, or altered mental status
    f. Any other issue that would impair the ability of the participant to receive or tolerate the planned treatment at the investigational site, to understand informed consent or any condition for which, in the opinion of the investigator, participation would not be in the best interest of the participant (e.g., compromise the well-being) or that could prevent, limit, or confound the protocol-specified assessments.
    g. History of non-compliance with recommended medical treatments.
20. Participant had major surgery or had significant traumatic injury within 2 weeks prior to the start of administration of study treatment, or has not fully recovered from an earlier surgery, or has major surgery planned during the time the participant is expected to participate in the study or within 2 weeks after administration of the last dose of study treatment.
21. Have received an investigational drug (including investigational vaccines) or used an invasive investigational medical device within 4 weeks or 5 PK half-lives, whichever is longer, before C1D1 or is currently enrolled in an interventional investigational study except if only long-term survival data is collected and after Sponsor approval is obtained.

A SINGLE ARM, RESPONSE-ADAPTED, OPEN LABEL STUDY OF IBERDOMIDE, WEEKLY BORTEZOMIB AND DEXAMETHASONE (IBERBD) WITH ISATUXIMAB ADDED ON DEMAND FOR TRANSPLANT-INELIGIBLE, NEWLY DIAGNOSED MULTIPLE MYELOMA PATIENTS: THE BOREALIS TRIAL.
Protocol Number: CMRG010
Contact: Dr. Guido Lancman/Trisha Ramnanan – Open Enrollment

Inclusion Criteria

1. Age **≥ 65** years at the time of signing consent
2. Must be able to adhere to the study visit schedule and other protocol requirements.
3. Previously untreated, transplant ineligible, symptomatic multiple myeloma as defined by the criteria below.
   Both criteria A and B must be met:
   A). Clonal bone marrow plasma cells **≥10%** or biopsy proven bony or Extramedullary Plasmacytoma
   B). Any one or more of the following myeloma defining events
   I. Evidence of end organ damage that can be attributed to the underlying plasma cell proliferative disorder, specifically:
   - Hypercalcemia: serum calcium **>0.25** mmol/L (>1 mg/dL) higher than the upper limit of normal **or >2.75** mmol/L (>11 mg/dL)
   - Renal insufficiency: creatinine clearance **177** µmol/L (>2 mg/dL)
   - Anemia: hemoglobin value of >**2 g/dL** below the lower limit of normal, or a hemoglobin value **<10g/dL**
   - Bone lesions: one or more osteolytic lesions on skeletal radiography, CT, or PET-CT

II. Biomarker criteria or MDE:
- Clonal bone marrow plasma cell percentage **≥ 60%**
- Involved: uninvolved serum free light chain (FLC) ratio **≥100**
- **> 1** focal lesions on MRI studies (at least **5 mm in size**)

4. Must have Eastern Cooperative Oncology Group (ECOG) performance status score of 0, 1, or 2.
5. Life expectancy of **≥ 3 months.**
6. The following laboratory results must be met within **10 days** prior to first study drug administration:
   - Absolute neutrophil count (ANC) **≥ 1.0 x 109/L**. Growth factors cannot be given within 10 days of study drug administration.
   - Serum AST and ALT **≤ 1.5 x** upper limit of normal (ULN).
   - Creatinine clearance **≥ 30 mL**/min either directly measured via 24-hour urine collection or calculated using MDRD (Appendix 1).
   - Platelet count **≥ 50 x** 109/L. Platelet transfusions to help subjects meet eligibility criteria are not allowed within 10 days before study enrollment.
   - Hemoglobin **≥ 80 g/L.**

Exclusion Criteria

1. Previous treatment with anti-myeloma therapy (does not include radiotherapy, bisphosphonates, or a single short course of steroid i.e. less than or equal to dexamethasone 40 mg/day for 4 days not have been given within 14 days of treatment start).
2. Any serious medical condition that places the patient at an unacceptable risk if he or she participates in this study.
3. Pregnant or lactating females.
4. Renal failure requiring hemodialysis or peritoneal dialysis.
5. Prior history of malignancies, other than multiple myeloma, unless the patient has been free of the disease for ≥ 3 years. Except:
   - Basal cell carcinoma of the skin
   - Squamous cell carcinoma of the skin
   - Carcinoma in situ of the cervix
   - Carcinoma in situ of the breast
   - Incidental histological finding of prostate cancer
6. Patients who are unable or unwilling to undergo antithrombotic therapy
7. Peripheral neuropathy of ≥ grade 2 severity.
8. Known HIV positivity or active infectious hepatitis, type A, B, or C.
9. Primary AL (immunoglobulin light chain) amyloidosis and myeloma complicated by amyloidosis.
10. Plasma Cell Leukemia.
11. Evidence of cardiovascular risk including any of the following:
    - QTc interval **≥ 470** msecs. Note that the QT interval should be corrected for heart rate by Fridericia's formula (QTcF).
    - Evidence of current clinically significant uncontrolled arrhythmias; including clinically significant ECG abnormalities; including 2nd degree or 3rd degree atrioventricular (AV) block.
    - History of myocardial infarction, acute coronary syndromes, coronary angioplasty, or stenting or bypass grafting within six months of screening.
    - Class III or IV heart failure as defined by the New York Heart Association functional classification System.
    - Uncontrolled hypertension.
12. Patients requiring strong inhibitors or inducers of **CYP3A4/5.**
13. Patients that have undergone major surgery (as defined by the investigator) within 28 days of initiating study treatment
14. Patients with a gastrointestinal disease that may significantly alter the absorption of Iberdomide.
15. Patients that have received a live vaccine within **3 months** of initiating study treatment.

HEALTH-RELATED QUALITY OF LIFE AND CAREGIVER BURDEN ASSESSMENT IN MULTIPLE MYELOMA AND LYMPHOMA PATIENTS AND THEIR CAREGIVERS UNDERGOING OUTPATIENT AUTOLOGOUS STEM CELL TRANSPLANTATION AS COMPARED TO INPATIENT TRANSPLANTATIONS: A NEEDS ASSESSMENT

Non-Interventional

Contact: Dr. Anca Prica -**Open for Enrollment**

Inclusion criteria:

1. Males or females aged 18 years or older undergoing an autologous stem cell transplant for multiple myeloma, or Hodgkin or Non-Hodgkin Lymphoma
2. Able to provide consent
3. Able to read, write and speak English
4. Available primary caregiver for the caregiver QOL and burden component of study who is able to provide consent and read, write and speak English

Exclusion criteria:

1. Geographically inaccessible/will not be followed at Princess Margaret Cancer Centre for the 100d period post-transplant.
2. Unable to provide consent.

MULTIPLE MYELOMA TRIALS – RELAPSED OR REFRACTORY:

***MULTIPLE MYELOMA TRIALS* – SECOND LINE THERAPY**

Impact of Clonal Hematopoiesis (CHIP) on Toxicity and Outcomes in Lymphoma and Multiple Myeloma Patients Receiving CAR-T Cell Therapy or T-cell engaging Antibodies
Protocol: CHIP-IMPACTS
Contact: Dr. Christine Chen/Harjot Vohra– **Open for Enrollment**

Inclusion Criteria:

1. Age ≥18 years
2. Diagnosis of lymphoma or multiple myeloma
3. Planned to receive standard of care CAR T-cell therapy or TCE (myeloma patients only) as next line of therapy
4. Provides informed consent for serial blood sampling and clinical data collection

Exclusion Criteria:

1. History of myeloid malignancy (e.g., MDS, AML)
2. Individuals who have previously received CAR-T or T-cell engaging antibody (TCE) therapy.
3. Inadequate baseline blood sample for CHIP mutation will preclude further study participation

PHASE 1B/2A, MULTICENTER, OPEN-LABEL STUDY TO DETERMINE THE RECOMMENDED DOSE AND SCHEDULE, AND EVALUATE THE SAFETY AND PRELIMINARY EFFICACY OF MEZIGDOMIDE IN COMBINATION WITH ELRANATAMAB IN PARTICIPANTS WITH RELAPSED AND/OR REFRACTORY MULTIPLE MYELOMA
Protocol Number: CA0571040
Contact: Dr Guido Lancman / Olga Levina– Enrollment on hold- slot release expected in mid-August for expansion phase

Inclusion Criteria

Type of Participant and Target Disease Characteristics

1. Participant with a history of RRMM, and must:
   a) **Phase 1**: Have received 2 to 4 prior lines of anti-myeloma therapy. Participants must have previously received a regimen that included an immunomodulatory agent (eg, thalidomide, lenalidomide, pomalidomide) and a PI (eg, bortezomib, carfilzomib, ixazomib), either alone or in combination. Participants must have undergone at least 2 complete cycles of treatment unless progressive disease was the best response to the regimen. (Note: One line can contain several phases [eg, induction with or without hematopoietic stem cell transplant (HSCT) and with or without consolidation, and/or with or without maintenance therapy]).
   b) **Phase 2**: Have received 1 to 3 prior lines of anti-myeloma therapy.
      i) Achieved a response of minimal response or better to at least 1 prior anti-myeloma therapy.
      ii) A regimen that included lenalidomide and a PI (eg, bortezomib, carfilzomib, ixazomib), either alone or in combination.
   c) Have documented disease progression by the IMWG Uniform Response Criteria during or after their last anti-myeloma regimen.
   d) Participants must have measurable disease (as determined by local laboratory), including at least 1 of the following criteria:
      i) M-protein quantities ≥ 0.5 g/dL by sPEP
      ii) M-protein quantities ≥ 200 mg/24-hour urine collection by uPEP
      iii) Serum FLC levels > 100 mg/L (milligrams/liter) involved light chain and an abnormal kappa/lambda (κ/λ) ratio in participants without detectable serum or urine M protein
      iv) For participants with IgA myeloma whose disease can only be reliably measured by quantitative immunoglobulin measurement, a serum IgA level ≥ 0.50 g/dL
2. Participant consents to hospitalization requirements for elranatamab.
3. Participant consents to serial BMAs and/or BMBs during screening, study treatment, and at EOT.
4. Participant has an ECOG PS of 0 to 1.50

Age of Participant

5. Participant must be 18 years of age, inclusive, at the time of signing the ICF.

Reproductive Status

6. The investigator or designee shall counsel individuals of childbearing potential (IOCBP) participants (as defined in APPENDIX 3) and male (as assigned at birth) participants who are sexually active with IOCBP on the importance of pregnancy prevention, the implications of an unexpected pregnancy, and the potential of fetal toxicity occurring due to transmission of study intervention present in seminal fluid to a developing fetus, even if the participant has undergone a successful vasectomy or if the partner is pregnant.
   a) IOCBP must have 2 negative highly sensitive urine or serum, as required by local regulations, pregnancy test (minimum sensitivity 25 IU/L or equivalent units of human chorionic gonadotropin [HCG]). The first pregnancy test must be performed within 10 to 14 days prior to the

planned start of mezigdomide and the second pregnancy test must be within 24 hours prior to the start of study intervention. IOCBP must agree and adhere to all testing requirements in APPENDIX 3.

b) A female (as assigned at birth) is eligible to participate if they are not pregnant or breastfeeding and at least 1 of the following conditions applies:

i) Is not an IOCBP

OR

ii) Is an IOCBP and agree to use, and be able to comply with 2 forms of contraceptive methods including one that is highly effective (with a failure rate of < 1% per year) and one additional effective (barrier) method without interruption, as described in Protocol APPENDIX 3, during the intervention period and for at least 28 days after the last dose of mezigdomide or 115 days after the last dose of elranatamab, whichever is longer, and agrees not to donate eggs (ova, oocytes) for the purpose of reproduction while taking mezigdomide, during dose interruption, and for 28 days after the last dose of mezigdomide

OR

iii) Is an IOCBP and commits to complete abstinence (True abstinence is acceptable when this is in line with the preferred and usual lifestyle of the individual. Periodic abstinence [eg, calendar, symptothermal or post-ovulation methods], withdrawal [coitus interruptus] from heterosexual contact that could lead to pregnancy [based on sex assigned at birth], spermicide only, and lactation amenorrhea method [LAM] are not acceptable methods of contraception), and agrees not to donate eggs (ova, oocytes) for the purpose of reproduction while taking mezigdomide, during dose interruption, and for 28 days after the last dose of mezigdomide.

c) Male (as assigned at birth) participants will be required to:

i) Always use a condom (male and female condoms must not be used together) during any sexual activity (eg, vaginal, anal, oral) with a pregnant partner or an IOCBP, even if the participant has undergone a successful vasectomy (i.e., with documented azoospermia 90 days after the procedure) as described in Appendix 3. Male (as assigned at birth) participants should continue to use a condom during the intervention period, during dose interruption, and for at least 28 days after the last dose of mezigdomide or 115 days after the last dose of elranatamab, whichever is longer, and agrees not to donate sperm while taking mezigdomide, during dose interruption, and for 28 days after the last dose of mezigdomide. Note: azoospermic males are not exempt from contraceptive requirements.

OR

ii) Practice complete abstinence (True abstinence is acceptable when this is in line with the preferred and usual lifestyle of the individual. Periodic abstinence [eg, calendar, symptothermal or post-ovulation methods], withdrawal [coitus interruptus] from heterosexual contact that could lead to pregnancy [based on sex assigned at birth], spermicide only, and LAM are not acceptable methods of contraception), and agrees not to donate sperm while taking mezigdomide, during dose interruption, and for 28 days after the last dose of mezigdomide.

d) All participants regardless of reproductive status must agree to refrain from donating blood while taking mezigdomide, during dose interruptions, and for at least 28 days after the last dose of mezigdomide.

e) All participants must follow all other requirements defined in Protocol APPENDIX 3.

Exclusion Criteria

Medical Conditions

1. Participant with known current or history of CNS involvement of MM.
2. Participant has non-secretory MM, plasma cell leukemia, Waldenstrom's macroglobulinemia, POEMS syndrome, or amyloidosis.
3. Participant cannot tolerate oral medications and/or has gastrointestinal disease (within 3 months of screening) or any gastrointestinal surgery that may significantly alter the absorption of oral study treatment.
4. Ongoing Grade ≥ 2 peripheral sensory or motor neuropathy.
5. History of GBS or GBS variants, or history of any Grade ≥ 3 peripheral motor polyneuropathy.
6. Participant has impaired cardiac function or clinically significant cardiac disease, including any of the following:
   a) LVEF < 45% as determined by ECHO or MUGA scan at screening
   b) Myocardial infarction within 6 months before study treatment, or an unstable or uncontrolled disease/condition related to or affecting cardiac function (eg, unstable angina, congestive heart failure New York Heart Association Class III-IV)
   c) Uncontrolled clinically significant cardiac arrhythmia or clinically significant ECG abnormalities
7. Known HIV positive with an acquired immunodeficiency syndrome (AIDS)-defining opportunistic infection within the last year or a current CD4 count < 350 cells/µL. Participants with HIV are eligible if:
   a) Participants are established on ART for at least 4 weeks and have an HIV viral load of < 400 copies/mL prior to enrollment.
   b) Participants continue taking ART as clinically indicated and while enrolled on study.
   c) Participants' CD4 counts and viral load are monitored per SoC by a local health care provider.

Note: HIV-positive participants must be excluded where mandated locally.

8. Participant has known chronic, active HBV/HCV infection. Participants who had HCV but have received an antiviral treatment and show no detectable HCV viral RNA for 6 months are eligible. Participants with no active hepatitis B infection (eg, HBsAg negative, anti-HBc positive) who are under adequate prophylaxis per local SoC against HBV re-activation may be eligible; such participants must be screened using real-time PCR measurement of HBV levels; those who are PCR positive will be excluded. HBV prophylactic medication must not be strong CYP3A modulator. Participants who have received HBV vaccine and are HBsAb positive, HBcAb negative, and HBsAg negative are eligible for study entry.
9. Participant has a history of a VTE within 3 months prior to study entry (eg, deep-vein thrombosis or pulmonary embolism). Participants with VTE occurring > 6 months prior to study entry who require ongoing treatment with chronic therapeutic dosing of anti-coagulants (eg,

warfarin, low molecular weight heparin, Factor Xa inhibitors) are eligible for study entry.

10. Participant has a prior history of malignancies other than MM, except if the participant has been free of the disease for ≥ 3 years or if the participant had 1 of the following malignancies treated with curative intent without known recurrence:
    a) Basal cell carcinoma of the skin
    b) Squamous cell carcinoma of the skin in situ (stage 0)
    c) Carcinoma in situ of the cervix
    d) Carcinoma in situ of the breast
    e) Low-risk prostate cancer in active surveillance; low risk is defined as T1-T2a, Gleason ≤ 6 (Grade Group 1) and prostate-specific antigen ≤ 10 ng/mL (per the National Comprehensive Cancer Network [NCCN] and the European Society of Medical Oncology [ESMO] risk groups) or prostate cancer that has been treated with curative intent
11. Participant has a history or presence of clinically relevant CNS pathology such as epilepsy, seizure, paresis, aphasia, stroke, subarachnoid hemorrhage or CNS bleed, severe brain injuries, dementia, Parkinson's disease, cerebellar disease, organic brain syndrome, or psychosis.
12. Participant has inadequate pulmonary function as defined as SpO2 < 92% on room air.
13. Participant has active, uncontrolled, bacterial, viral, or fungal infection. Active infections must be resolved at least 21 days prior to enrollment. Treatment with systemic anti-infective agents must be completed at least 28 days prior to enrollment. Prophylactic use of systemic agents is permitted.
14. Lung imaging (eg, chest x-ray or lung CT) and SARS-CoV-2 PCR testing is mandated within 14 days prior to enrollment. Participants with a positive PCR test result within 14 days prior to enrollment or those suspected of having SARS-CoV-2 or evidence of active respiratory infection should be excluded from study enrollment.
15. Participant has any medical condition (eg, the presence of laboratory abnormalities), psychiatric, and/or social reason that places the participant at unacceptable risk or could confound interpretation of the data if he/she were to participate in the study per investigator or the sponsor discretion.

Prior/Concomitant Therapy

16. Inability to comply with restrictions and prohibited treatments as listed in Protocol Section 7.7.
17. Participant received prior therapy with mezigdomide.
18. Participant received prior treatment with TCE.
19. Participant received prior treatment with BCMA-targeting therapy, with the exception of participants who have received autologous BCMA-targeted CAR T-cell therapy > 6 months from the start of study therapy.
20. Participants have received prior allogeneic or autologous CAR T-cell therapy within 6 months, regardless of antigen target.
21. Participant has previously received allogeneic stem cell transplantation at any time or received autologous stem cell transplantation within 12 weeks of initiating study treatment.
22. Participant had prior systemic cancer-directed treatments or investigational modalities ≤ 5 half-lives or 4 weeks prior to starting study treatment, whichever is shorter. Participants must have recovered from any clinically significant non-hematologic toxicities (i.e., to Grade ≤ 1) of prior systemic anti-cancer directed treatments unless otherwise specified.
23. Participant received any of the following:
    a) Plasmapheresis within the last 28 days of initiating study treatment
    b) Radiation therapy, other than local palliative therapy for myeloma-associated bone lesions, within 14 days of initiating study treatment
    c) Participant had major surgery ≤ 2 weeks prior to starting study treatment. Participants must have recovered from any clinically significant effects of recent surgery.
24. Participant is on chronic systemic immunosuppressive therapy or corticosteroids (eg, prednisone or equivalent exceeding a total of 140 mg over the last 14 days). Intranasal, inhaled, topical, or local corticosteroid injections (eg, intra-articular injection), or steroids as premedication for ISRs (eg, CT scan premedication) are exceptions to this criterion.
25. Concurrent administration of strong CYP3A modulators (see Protocol Section 7.7.1) within 14 days of initiating study treatment.
26. Live vaccines are prohibited within 4 weeks prior to first dose of study drug.
27. Participant is unable or unwilling to undergo protocol-required thromboembolism prophylaxis (see Protocol Section 9.3.10.2).
28. Concurrent administration of proton-pump inhibitors (eg, omeprazole, esomeprazole, lansoprazole, pantoprazole) within 7 days or PCABs (eg, vonoprazan) within 2 days prior to initiating study treatment.

Physical and Laboratory Test Findings

29. Evidence of organ dysfunction or any clinically significant deviation from normal in PE, vital signs, ECG, or clinical laboratory determinations beyond what is consistent with the target population, and in addition to the other inclusion/exclusion criteria.
30. Participant has any of the following laboratory values (determined by local lab); qualifying laboratory value must occur at most recent measurement prior to cohort assignment and must be no more than 14 days prior to cohort assignment:
    a) ANC < 1.0 × 109/L (< 1000/ µL) and growth factor support is not allowed within 7 days prior to screening CBC (14 days if pegfilgrastim is used)
    b) Platelets < 75 × 109/L (< 75,000/µL) and platelet transfusions are not allowed within 7 days prior to screening CBC
    c) Hemoglobin < 8 g/dL (< 4.9 mmol/L)
    d) Potassium outside normal limits and cannot be corrected with supplements
    e) Corrected serum calcium > 13.5 mg/dL (> 3.4 mmol/L)
    f) Serum AST/SGOT and/or ALT/SGPT > 2.5 × ULN
    g) Serum bilirubin > 1.5 × ULN; > 3.0 mg/dL is allowed for participants with documented Gilbert's Syndrome
    h) eGFR < 30 mL/min or requiring dialysis. GFR will be calculated using the MDRD formula or measured in 24-hour urine collection (see

Protocol Section 9.2.4), or

i) INR ≥ 1.5× ULN and/or PTT ≥ 1.5× ULN (only for participants who are not on anticoagulants).

Allergies and Adverse Drug Reactions

31. History of severe allergic or anaphylactic reactions or hypersensitivity to monoclonal antibodies and related excipients, human proteins in the study interventions, or to other IMiDs (eg, lenalidomide, pomalidomide, thalidomide) or CELMoDs (eg, iberdomide).

Other Exclusion Criteria

32. Prisoners or participants who are involuntarily incarcerated. (Note: Under certain specific circumstances and only in countries where local regulations permit, a person who has been imprisoned may be included or permitted to continue as a participant. Strict conditions apply, and Sponsor approval is required.)
33. Inability to be venipunctured and/or tolerate venous access

A PHASE 1, MULTICENTER, OPEN-LABEL STUDY TO EVALUATE THE SAFETY AND PRELIMINARY EFFICACY OF BMS-986393 IN NOVEL COMBINATIONS IN PARTICIPANTS WITH RELAPSED AND/OR REFRACTORY MULTIPLE MYELOMA AND DETERMINE THE RECOMMENDED DOSE FOR EACH ADD-ON INVESTIGATIONAL COMPONENT

Protocol: CA0881005 (JUNO)

Contact: Dr. Christine Chen / Trisha Ramnanan **Enrollment on Hold by Sponsor until summer**

Inclusion Criteria

1) Signed Written Informed Consent
2) Type of Participant and Target Disease Characteristics
   a) Participant has a diagnosis of MM with relapsed and/or refractory disease. Participants must have confirmed progressive disease (as per IMWG criteria) on or within 12 months (measured from the last dose) of completing treatment with the last antimyeloma treatment regimen before study entry or have confirmed progressive disease within 6 months prior to Screening and who are subsequently determined to be refractory or non-responsive to their most recent anti-myeloma treatment regimen, except for participants with cellular therapy (eg, CAR T-cell therapy) as their last treatment, who may enroll beyond 12 months.
   b) **For Part 1** and first 10 participants in each Part 2 arm: Participants must have received at least 3 prior anti-myeloma treatment regimens (note: induction with or without hematopoietic stem cell transplantation [HSCT] and with or without maintenance therapy is considered 1 regimen).
      i) A regimen that included an immunomodulatory agent (eg, thalidomide, lenalidomide, pomalidomide) and a proteasome inhibitor (eg, bortezomib, carfilzomib, ixazomib), either alone or in combination. Participants must have undergone at least 1 complete cycle of treatment unless progressive disease was the best response to the regimen.
      ii) A regimen that included anti-CD38 (eg, daratumumab), alone or in combination.
      iii) Autologous HSCT, unless the participant was ineligible.
      iv) Prior therapy targeting BCMA and/or GPRC5D is permitted in all arms.
   c) **For Part 2**: Participants must have received at least 1 but not greater than 3 prior antimyeloma treatment regimens, including a proteasome and immunomodulatory agent.
      i) A regimen that included an immunomodulatory agent (eg, thalidomide, lenalidomide, pomalidomide) and a proteasome inhibitor (eg, bortezomib, carfilzomib, ixazomib), either alone or in combination. Participants must have undergone at least 1 complete cycle of treatment unless progressive disease was the best response to the regimen.
      ii) Prior therapy targeting BCMA is permitted in Arms B and C only.
3) Physical and Laboratory Test Findings
   a) Participant has adequate vascular access for leukapheresis.
   b) Participant has Eastern Cooperative Oncology Group (ECOG) performance status ≤ 1.
   c) Participant must have measurable disease, as determined by the central or local laboratory, defined as meeting at least 1 of the criteria below:
      i) M-protein ≥ 0.5 g/dL by serum protein electrophoresis (sPEP).
      ii) M-protein ≥ 200 mg/24-hour urine collection by urine protein electrophoresis (uPEP).
      iii) Serum free light chain (sFLC): levels of the involved light chain > 100 mg/L and an abnormal kappa/lambda (κ/λ) ratio in participants without measurable serum or urine M-protein.
      iv) Immunoglobulin A (IgA) myeloma whose disease can only be reliably measured by quantitative immunoglobulin measurement: a serum IgA level ≥ 0.5 g/dL.
   d) Participant has recovery to Grade ≤ 1 or baseline of any non-hematologic toxicities due to previous therapy, except alopecia (any Grade acceptable) and peripheral neuropathy (Grade ≤ 2 acceptable).
   e) Adequate organ function as determined by site's local laboratory defined as:
      i) Peripheral blood ANC ≥ 1.0 × 109/L without growth factor support within 7 days (14 days if pegfilgrastim), and platelet count ≥ 50 × 109/L without platelet transfusion support within 7 days of screening.
      ii) Creatinine clearance (CrCl) ≥ 45 mL/min, measured in 24-hour urine collection or calculated from serum creatinine using the Cockcroft-Gault equation, without the support of hydration within 3 days of renal assessment.
      iii) Aspartate aminotransferase/alanine aminotransferase ≤ 3.0× upper limit of normal (ULN) and total bilirubin < 1.5× ULN (or direct bilirubin < 1.5× ULN with documented Gilbert's syndrome).
      iv) Prothrombin time (PT) or international normalized ratio (INR), or partial thromboplastin time (PTT) ≤ 1.5×ULN.
      v) Adequate pulmonary function, defined as ≤ CTCAE Grade 1 dyspnea and saturated oxygen (SaO2 ≥ 92%) on room air.

vi) Adequate cardiac function, defined as left ventricular ejection fraction (LVEF) ≥ 45% as assessed by echocardiogram (ECHO) or multiple-gated acquisition (MUGA) scan performed within 8 weeks prior to or during the screening period.

4) Age of Participant

a) Participant must be 18 years of age at the time of signing the ICF.

5) Reproductive Status

a) Female of childbearing potential (FCBP) is a female who:

1) has achieved menarche at some point,

2) has not undergone a hysterectomy or bilateral oophorectomy, or

3) has not been naturally postmenopausal (amenorrhea following cancer therapy does not rule out childbearing potential) for at least 12 consecutive months (i.e., has had menses at any time in the preceding 12 consecutive months). FCBPs must:

i) Have 2 negative pregnancy tests as verified by the investigator prior to starting study therapy. They must agree to ongoing pregnancy testing during the course of the study, and after end of study therapy. This applies even if the participant practices complete abstinence* from heterosexual contact.

ii) The investigator is responsible for review of medical history, menstrual history, and recent sexual activity to potentially decrease the risk for inclusion of a person with an undetected pregnancy.

iii) Female participants must have documented proof that they are not of childbearing potential.

Exclusion Criteria

1) Medical Conditions

a) Uncontrolled medical, psychological, familial, sociological, or geographical conditions that do not permit compliance with the protocol, as judged by the investigator; or unwillingness or inability to follow the procedures required in the protocol.

b) Any condition that confounds the ability to interpret data from the study.

c) Known active or history of central nervous system (CNS) involvement of MM.

d) Active or history of plasma cell leukemia, Waldenstrom's macroglobulinemia, POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes) syndrome, or clinically significant amyloidosis.

e) Active autoimmune disease requiring immunosuppressive therapy.

f) Prior history of malignancies, other than MM, unless the participant has been free of the disease for ≥ 2 years except for the following non-invasive malignancies:

i) Basal or squamous cell carcinoma of the skin

ii) Carcinoma in situ of the cervix or breast

iii) Incidental histologic finding of prostate cancer (T1a or T1b using the TNM (tumor, nodes, metastasis) clinical staging system or prostate cancer that is curative

iv) Other completely resected Stage 1 solid tumor with low risk for recurrence

g) Active hepatitis B, hepatitis C, or any evidence of human immunodeficiency virus (HIV) infection at the time of Screening.

h) Participant has uncontrolled or active systemic fungal, bacterial, viral, or other infection despite appropriate anti-infective treatment at the time of leukapheresis.

i) Participant has impaired cardiac function or clinically significant cardiac disease, including any of the following:

i) A history of any 1 of the following cardiovascular conditions within 6 months prior to screening: Class III or IV heart failure as defined by the New York Heart Association, myocardial infarction, unstable angina, angioplasty or stenting, or other clinically significant cardiac disease.

ii) Uncontrolled clinically significant cardiac arrhythmia or clinically significant ECG abnormalities.

j) Participant cannot tolerate oral medications and/or has gastrointestinal disease that may significantly alter the absorption of oral study treatment.

k) Participant has a history or presence of clinically significant CNS pathology such as seizure disorder, aphasia, stroke, severe brain injuries, dementia, Parkinson's disease, or cerebellar disease, or presence of clinically active psychosis.

l) Participant has deep vein thrombosis or pulmonary embolism (non-infusion lineassociated) within 3 months prior to leukapheresis. Participants with venous thromboembolism (VTE) occurring > 3 months prior to leukapheresis who require ongoing treatment with chronic therapeutic dosing of anti-coagulants (eg, warfarin, low molecular weight heparin, Factor Xa inhibitors) are eligible for study entry.

m) Participant has a history of Grade ≥ 2 hemorrhage within 30 days of Screening

n) Participant has received any live vaccines against infectious disease within 8 weeks before BMS-986393 administration. Participant has received an approved or authorized SARS CoV-2 vaccine within 14 days prior to leukapheresis or initiation of LD chemotherapy. For vaccines requiring more than 1 dose, the full series (eg, both doses of a 2-dose series) should be completed at least 14 days prior to leukapheresis when feasible and when a delay in leukapheresis would not put the study participant at risk.

o) Participant in other interventional trial, including SARS-CoV-2 non-vaccine trials. If previously in another interventional trial, the participant may not have leukapheresis until the washout period of the investigational agent is achieved ≥ 28 days, or 5 half-lives, whichever is shorter (minimum 14 days).

2) Reproductive Status

a) FCBP who is pregnant, nursing (lactating), or breastfeeding, or who intends to become pregnant during participation in the study.

3) Prior/Concomitant Therapy

a) Inability to comply with restrictions and prohibited treatments as listed in Section 7.7: Concomitant Therapy.

b) Participant is unable or unwilling to undergo protocol-required thromboembolism prophylaxis.

c) Arm B: Concurrent administration of proton-pump inhibitors (eg, omeprazole, esomeprazole, lansoprazole, pantoprazole) including within 14 days prior to initiating mezigdomide.
d) Participant received prior therapy with alnuctamab (Arm A), mezigdomide (Arm B), or iberdomide (Arm C).
e) Arm B and Arm C: Concurrent administration of strong cytochrome P450 (CYP) 3A modulators within 14 days of initiating mezigdomide or iberdomide.
f) Participant has received prior treatment for MM with the following therapies, within the specified period:
i) Bendamustine within 6 months before leukapheresis
ii) Therapeutic doses of corticosteroids (defined as > 10 mg/day prednisone or equivalent) within 14 days before leukapheresis. Physiologic replacement, topical, intranasal, and inhaled steroids are permitted.
iii) Approved anti-MM antibody (eg, daratumumab) within 14 days before leukapheresis
iv) Any other systemic therapy approved for the treatment of MM within 14 days before leukapheresis, except T cell engaging agents, which are within 28 days
v) Any experimental biologics or any other therapy within 28 days or 5 half-lives before leukapheresis, whichever is shorter (minimum 14 days)
vi) Autologous HSCT (i.e., day of hematopoietic stem cell infusion) within 9 months before leukapheresis
vii) Allogeneic HSCT (i.e., day of hematopoietic stem cell infusion) within 12 months before leukapheresis, or has ongoing symptoms or treatment for chronic graft-versus-host disease (GVHD)
viii) Prior CAR T cell therapy administered within 3 months before leukapheresis
ix) Immunosuppressive therapies within 4 weeks before leukapheresis (eg, calcineurin inhibitors, methotrexate or other chemotherapeutics, mycophenolate, rapamycin, immunosuppressive antibodies such as anti-TNF, anti-IL6, or anti-IL6R)
x) Donor lymphocyte infusions within 6 weeks before leukapheresis
xi) Plasmapheresis within 14 days before leukapheresis
xii) Radiation that includes a large bone marrow field such as the pelvis or sternum within 14 days before leukapheresis

4) Allergies and Adverse Drug Reactions
a) History of allergy to fludarabine or cyclophosphamide (for participants receiving fludarabine/cyclophosphamide LDC) and bendamustine (for participants receiving bendamustine LDC).
b) History of allergy to monoclonal antibodies and related excipients (eg, tocilizumab) or known components of BMS-986393.
c) Arm B and Arm C: history of severe or clinically significant allergy to other IMiDs (eg, lenalidomide, pomalidomide, thalidomide) or CELMoDs (eg, iberdomide).

MULTIPLE MYELOMA TRIALS **– THIRD LINE THERAPY**

A PHASE ½ STUDY OF ETENTAMIG IN COMBINATION WITH A CELMoD AGENT FOR THE TREATMENT OF PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA.
Protocol Number: M24-555
Contact: Dr. Guido Lancman/Elena Talovikova– Open Enrollment Phase I (slots already allocated-Please check with the site)

Inclusion Criteria

1. ≥18 years of age.
2. Documented initial diagnosis of multiple myeloma according to IMWG diagnostic criteria
3. Must have the following:
   - Phase 1 Dose Escalation: subjects with 3-5 prior lines of therapies.
   - Phase 2 Dose Expansion and Selection: subjects with 1-3 prior lines of therapies, subjects with BCMA-targeted CAR-T-cell (completed at least 6 months prior to the first dose of study treatment) or BCMA-targeted ADCs (completed at least 30 days prior to the first dose of study treatment) are allowed.
4. Measurable disease at screening defined as per central laboratory with at least 1 of the following assessed within 28days prior to enrollment:
   - Serum monoclonal para protein (M-protein) level ≥ 0.5 g/dL (≥5 g/dL);
   - or Urine M-protein level ≥200 mg/24 hours;
   - or Serum Ig free light chain (FLC) ≥10 mg/dL (involved light chain) and an abnormal serum kappa lambda ratio only for subjects without measurable serum or urine M-protein.
5. Eastern Cooperative Oncology Group (ECOG) performance status grade of 0 or 1.
6. Clinical laboratory values:
   - **Hemoglobin** ≥8.0 g/dL; subject may receive red blood cell (RBC) transfusions in accordance with institutional guidelines to meet this criterion. Subjects may not have received a red blood cell (RBC) transfusion within 7 days prior to the hemoglobin result used for eligibility.
   - **Platelets** ≥ 75,000/mm3 . For subjects with >50% myeloma involvement in the marrow, a platelet count of ≥ 50,000 mm3 is allowed. Subjects may not have received a platelet transfusion within 7 days prior to the platelet count used for eligibility.
   - Absolute Neutrophil Count (ANC) ≥ 1,000/µL; subject may use growth factor support to achieve ANC eligibility criteria. Subjects may not have received a GCSF within 7 days prior to the ANC result used for eligibility.
   - Aspartate aminotransferase (AST) and alanine aminotransferase (ALT)≤3 ×ULN
   - Creatinine clearance ≥ 30 mL/min, measured by 24 hour urine collection or calculated using the MDRD formula

- Total bilirubin ≤ 2.0 × ULN (except for subjects with documented Gilbert's syndrome, in which case direct bilirubin ≤ 1.5 × ULN is required)
- Serum calcium corrected for albumin ≤14 mg/dL (≤3.5 mmol/L)

Exclusion Criteria

1. Prior antitumor therapy as follows, before the first dose of study drug:
   - Subject who has received prior etentamig treatment
     - Other prior BCMA-targeted or T cell engager therapies:
       - Phase 1, subjects with prior anti-BCMA therapy are excluded. Additionally, any subjects who received CD3-directed T cell-engager therapy as the last line are excluded.
       - Phase 2, subjects with prior BCMA directed T-cell engager therapy are excluded.
   - Subject who has received prior CELMoD (iberdomide or mezigdomide)
   - Subject who has received a peripheral ASCT within 12 weeks, or an allogeneic SCT within ≤6 months of the first dose of study drug treatment. Subjects with allogenic stem cell transplant should not have any symptoms of acute or chronic graft versus host disease.
2. Subjects who has unresolved AEs ≥Grade 1 (NCI CTCAE version 5.0) from prior anticancer therapy, except for alopecia or fatigue. Subjects with irreversible toxicity that is not reasonably expected to be exacerbated by any of the investigational products may be included (e.g., hearing loss) after consultation with the Sponsor or designee.
3. Subjects who has known active central nervous system involvement MM.
4. Subject who has history of clinically significant renal, neurologic, psychiatric, endocrine, metabolic, immunologic, cardiovascular, pulmonary, or hepatic disease within the last 6 months that in Investigator's opinion, would adversely affect the subject's participation in the study.
5. Subject who has known history of significant cardiovascular or pericardial disease, including uncontrolled angina, arrhythmia, recent myocardial infarction within 6 months of first dose, congestive heart failure cardiovascular disability status of New York Heart Association Class ≥3, severe cardiac insufficiency, or persistent QT interval corrected for heart rate (QTc) prolongation (>480 msec, QTc Fridericia)
6. Subject who has known history of other active malignancies, including myelodysplastic syndrome within the past 3 years with the following exceptions:
   - Adequately treated in situ carcinoma of the cervix uteri or the breast;
   - Basal cell carcinoma of the skin or localized squamous cell carcinoma of the skin;
   - Prostate cancer Gleason grade 6 or lower AND with stable Prostate Specific Antigen levels off treatment;
   - Previous malignancy with no evidence of disease confined and surgically resected (or treated with other modalitities) with curative intent and unlikely to impact survival during the duration of the study.
7. Subject who has evidence of active hepatitis B (HBsAg positive) infection based on screening blood testing. Hepatitis B testing must include HBsAg, antiHBc, and antiHBs.
8. Subject who has evidence of active hepatitis C infection based on screening blood testing;
   Subject may not be seropositive for hepatitis C (except in the setting of a sustained virologic response, defined as aviremia at least 12 weeks after completion of antiviral therapy)
9. Subject who has known active SARS-CoV-2 infection.
10. Subject who has known active infection with HIV.
11. Subject who has the following conditions:
    - Non-secretory MM;
    - Active Plasma cell leukemia, i.e., either 5% of peripheral white blood cells or >5.0 X 108/L circulating plasma cells by standard differential;
    - Waldenstrom's macroglobulinemai;
    - Light chain amyloidosis;
    - POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, and skin changes);
    - Major surgery within 4 weeks prior to first dose or planned study participation;
    - Acute infections within 14 days prior to the first dose of study drug requiring therapy (antibiotic, antifungal or antiviral)
12. Subject who has known or suspected hypersensitivity to the excipients contained in the formulation of etentamig, iberdomide (only for subjects receiving etentamig and Iber), or dexamethasone. Subject who had know allergies, significant sensitivity, or intolerance to constituents of the required premedications and the study drug (and its excipients) or derivatives.
13. Subject who has known history of clinically significant (per investigator's judgement) alcohol abuse within the last 6 months.

An Exploratory Phase 1b/2a Multicenter, Open-Label, Novel-Novel Combination Study to Assess the Safety, Pharmacokinetics, Pharmacodynamics, and Preliminary Efficacy of CC-92480 (BMS-986348) in Novel Therapeutic Combinations in Participants with Relapsed or Refractory Multiple Myeloma
Protocol Number: CA057-003
Contact: Dr. Donna Reece / Olga Levina – Open Enrollment (Next slot to open potentially in July-Arm E NOT available)

Inclusion Criteria

1. MM with relapsed or refractory disease and must:
   a. Have documented disease progression by the International Myeloma Working Group (IMWG) Uniform Response Criteria during or after their last myeloma therapy

   b. For Part 2 Dose Expansion: Be refractory to or have relapsed after at least 2 prior lines of therapy that include an IMiD, a proteasome inhibitor, an anti-CD38 mAb, and a T-cell redirecting therapy (TRT, eg, a CAR-T or T-cell engaging bispecific treatment) unless the participant is not a candidate for TRT.
2. Have measurable disease including at least 1 of the following criteria:
   a. M-protein quantities ≥ 1.0 g/dL by serum protein electrophoresis (sPEP)
   b. M-protein quantities ≥ 200 mg/24 hour urine collection by urine protein electrophoresis (uPEP)
   c. Serum free light chain (sFLC) levels > 100 mg/L of the involved light chain and an abnormal kappa/lambda (κ/λ) ratio in participants without measurable serum or urine M-protein
   d. Immunoglobulin class A (IgA) myeloma whose disease can only be reliably measured by quantitative immunoglobulin measurement, a serum IgA level ≥ 1 g/dL
3. Participant consents to serial bone marrow aspirations (BMAs) and/or biopsies (BMBs) during screening and study treatment, and may consent to BMA and/or BMB at the end of treatment
4. ECOG Performance Status of 0 or 1
5. ≥18 years of age
6. Females of childbearing potential (FCBP) must agree and adhere to all testing and contraception requirements in the mezigdomide (CC-92480) Global Pregnancy Prevention Plan (PPP).
7. Female of Child Bearing Potential participants and all male participants must follow study pregnancy prevention contraception requirements and Pregnancy Prevention Program. Varies depending on study treatment.
8. Male participant must agree to refrain from donating sperm or semen while on study treatment, during dose interruptions, and for up to 4 months after last dose of study treatment (duration dependent on study drug).
9. Female of Child Bearing Potential participants must agree to refrain from donating eggs or breastfeeding while on study treatment and up to 7 months after last dose of study treatment (duration dependent on study drug)
10. Must agree to refrain from donating blood while on study treatment, during dose interruptions, and for ≥ 28 days following last dose of study treatment.

Exclusion Criteria

1. Current or history of central nervous system involvement of MM
2. Plasma cell leukemia; Waldenstrom's macroglobulinemia; polyneuropathy, organomegaly, endocrinopathy, M-protein, and skin changes (POEMS) syndrome; or clinically significant light-chain amyloidosis.
3. Cannot tolerate oral medications and/or has gastrointestinal disease that may significantly alter the absorption of oral study treatments
4. Impaired cardiac function or clinically significant cardiac disease, including any of the following:
   a. Left ventricular ejection fraction (LVEF) < 45% as determined by echocardiography (ECHO) or multi-gated acquisition (MUGA) scan at screening
   b. Complete left bundle branch, bifascicular block, or other clinically significant abnormal electrocardiographic finding at screening
   c. A prolongation of QT interval on screening electrocardiogram (ECG) as defined by corrected QT interval (QTc) > 480 ms using Fridericia's QT correction formula; a history of or current risk factors for Torsades de Pointe (eg, heart failure, hypokalemia, or a family history of Long QT Syndrome); and concurrent administration of medications that prolong the QT/QTc interval
   d. Congestive heart failure (New York Heart Association Class III or IV)
   e. Myocardial infarction or stroke ≤ 6 months prior to starting study treatments
   f. Unstable angina or poorly controlled angina pectoris, including the Prinzmetal variant of angina pectoris
   g. Uncontrolled hypertension
5. HIV positive with an acquired immunodeficiency syndrome (AIDS)-defining opportunistic infection within the last year or a current CD4 count < 350 cells/µL. Participants with HIV are eligible if:
   a. They have received antiretroviral therapy (ART) for at least 4 weeks prior to starting study treatment as clinically indicated while enrolled on study.
   b. They continue taking ART as clinically indicated and while enrolled on study.
   c. CD4 counts and viral load are monitored per standard of care by a local health care provider.
6. History of hepatitis B or C virus or has virologic or serological evidence of hepatitis A, B, or C virus infection. Participants who had hepatitis C virus (HCV) but have received an antiviral treatment and show no detectable HCV viral ribonucleic acid (RNA) for 6 months are eligible.
7. History of concurrent second cancer requiring ongoing systemic treatment.
8. Prior malignancy other than MM, except if the participant has been free of disease for ≥ 3 years or the participant had 1 of the following non-invasive malignancies treated with curative intent without known recurrence:
   a. Basal or squamous cell carcinoma of the skin
   b. Carcinoma in situ of the cervix or breast
   c. Stage 1 bladder cancer
   d. Incidental histological findings of localized prostate cancer such as tumor Stage 1a or 1b (T1a or T1b) using the tumor, nodes, and metastasis (TNM) classification of malignant tumors OR prostate cancer that has been treated with curative intent
   e. Melanoma in situ
9. Participant has active, uncontrolled, or suspected infection.
10. Medical condition including the presence of laboratory abnormalities, which places the participant at unacceptable risk if he/she were to participate in the study.
11. History of retinal vein occlusion (RVO)

12. For trametinib-containing arms, participant with known risk factors for gastrointestinal perforation including history of diverticulitis and metastases to gastrointestinal tract. Note: Concomitant use of medicinal products with a recognized risk of gastrointestinal perforation is not exclusionary but should be avoided, if possible per protocol.
13. History of interstitial lung disease (ILD) or pneumonitis, or the participant has active dyspnea or other condition that may put the participant at increased risk of development of ILD or pneumonitis.
14. Pregnant, nursing, or breastfeeding, or who intend to become pregnant during participation in the study
15. Inability to comply with restrictions and prohibited treatments as listed in protocol.
16. For Part 1: Participant received prior therapy with CC-92480. For Part 2: Participant received prior therapy with CC-92480, tazemetostat, BMS-986158, or trametinib.
17. Previously received allogeneic stem-cell transplant at any time or received autologous stem-cell transplant within 12 weeks of initiating study treatment.
18. Received any of the following within 14 days prior to initiating study treatment:
    a. Plasmapheresis
    b. Major surgery (as defined by the investigator)
    c. Radiation therapy other than local therapy for myeloma associated bone lesions
    d. Use of any systemic anti-myeloma drug therapy
19. Used any investigational agents within 28 days or 5 half-lives (whichever is shorter) prior to study treatment.
20. Received immunosuppressive medication within 14 days prior to initiating study treatment. The following are exceptions to this criterion:
    a. Intranasal, inhaled, topical or local corticosteroid injections (eg, intra-articular injection)
    b. Systemic corticosteroids at doses that do not exceed 10 mg/day of prednisone or the equivalent
    c. Steroids as premedication for hypersensitivity reactions (eg, computed tomography [CT] scan premedication)
21. COVID-19 vaccine within 14 days prior to C1D1. For vaccines requiring more than 1 dose, the full series (eg, both doses of a 2-dose series) should be completed prior to C1D1.
22. Live/attenuated vaccine, including live vaccines for COVID-19, within 30 days prior to study treatment
23. Concurrent administration of strong CYP3A modulators including within 14 days prior to initiating study treatment
24. Concurrent administration of proton-pump inhibitors (eg, omeprazole, esomeprazole, lansoprazole, pantoprazole; etc.) including within 14 days prior to study treatment.
25. Unable or unwilling to undergo protocol-required thromboembolism prophylaxis
26. Evidence of organ dysfunction or any clinically significant deviation from normal by physical examination or in vital signs, by ECG, or by clinical laboratory determinations beyond what is consistent with the target population and in addition to the specific criteria above and below
27. Participant has any of the following laboratory values (determined by local lab); qualifying laboratory value must occur at most recent measurement prior to cohort assignment and must be no more than 14 days prior to cohort assignment:
    a. **Absolute neutrophil count (ANC)** < 1.0 x 10^9/L (< 1000/µL) without growth factor support within 7 days prior to screening complete blood count (CBC) (14 days if pegfilgrastim is used)
    b. **Platelets** < 75 x 10^9/L (< 75,000/µL) and no platelet transfusions within the 7-day period leading up to the screening CBC
    c. **Hemoglobin** < 8 g/dL (< 4.9 mmol/L) and no RBC transfusions are allowed within the 72-hour period leading up to the screening CBC
    d. **Potassium** outside normal limits and cannot be corrected with supplements
    e. **Corrected serum calcium** > 13.5 mg/dL (> 3.4 mmol/L)
    f. **Serum AST/serum glutamic oxaloacetic transaminase (SGOT**) and **ALT/serum glutamic pyruvic transaminase (SGPT)** > 3x ULN
    g. **Serum bilirubin** > 1.5x ULN; > 3.0 mg/dL is allowed for participants with documented Gilbert's Syndrome
    h. **Estimated glomerular filtration rate (eGFR)** < 45 mL/min/1.73 m^2 calculated using the Modified Diet in Renal Disease (MDRD) formula (see Appendix 7)
    i. **International normalized ratio (INR)** ≥ 1.5x ULN and **partial thromboplastin time (PTT)** ≥ 1.5x ULN (only for participants who are not on anticoagulants). Note: Participants receiving therapy for a thromboembolic event that occurred > 3 months prior to enrollment are eligible as long as they are on a stable regimen of anticoagulation with warfarin, low-molecular weight heparin, or another approved therapeutic anticoagulation regimen
28. History of severe allergic or anaphylactic reactions or hypersensitivity to a CRBN-modulating agent, BETi, EZH2i, MEKi, or any of their excipients
29. Current or recent (within 3 months of study intervention administration) gastrointestinal disease that could impact upon the absorption of study intervention
30. Any gastrointestinal surgery that could impact upon the absorption of study intervention

MULTIPLE MYELOMA TRIALS - FOURTH LINE OF THERAPY

PHASE I DOSE ESCALATION STUDY OF LIPOSOMAL CURCUMIN IN RELAPSED REFRACTORY MULTIPLE MYELOMA
Protocol Number: LipoCurc
Contact: Dr. Guido Lancman /Olga Levina – **Open Enrollment**

Inclusion Criteria

1. Is the patient able to understand and voluntarily sign an informed consent form (ICF)?
2. Is the patient ≥ 18 years of age at the time of signing the ICF?
3. Is the patient able to adhere to the study visit schedule and other protocol requirements?
4. Does the patient have documented diagnosis of relapsed and/or refractory MM with: (check one)

a. Documented evidence of progressive disease (PD) after achieving at least stable disease (SD) for ≥ 1 cycle during a previous MM treatment (i.e., relapsed MM) OR Disease progression during or within 60 days from the end of the most recent MM treatment (i.e., refractory MM).
b. Previously undergone treatment with an immunomodulatory drug (lenalidomide or pomalidomide), a proteasome inhibitor (bortezomib, ixazomib, carfilzomib) and an anti-CD38 drug (daratumumab or isatuximab), and exhausted available standard of care options.

5. Does the patient have a history of autologous stem cell transplant provided the transplant was > 12 weeks prior to study enrolment with no active infection?
6. Does the patient have a measurable disease defined as at least one of the following (these baseline laboratory studies for determining eligibility must be obtained within 28 days prior to start of study drug)?
   a. Serum M-protein ≥ 0.5 g/dl (≥ 5 g/l) Value……Date……..
   b. Urine M-protein ≥ 200 mg/24 h Value……Date……..
   c. Serum free light chains (FLC) assay: Involved FLC level ≥ 10 mg/dl (≥ 100 mg/l) and an abnormal serum free light chain ratio (< 0.26 or > 1.65) Value……Ratio……Date……..
   d. If the serum protein electrophoresis is unreliable for routine M-protein measurement, quantitative immunoglobulin levels on nephelometry or turbidometry will be followed. N/A
7. Does the patient have Eastern Cooperative Oncology Group (ECOG) performance status score of ≤ 2? ECOG = ____
8. If patient is of childbearing potential, does serum pregnancy test have a negative result?
   Patient commits to continued abstinence from heterosexual intercourse Or
   Patient abides by birth control requirements as described in protocol
   Birth control method: _____ Not applicable If N/A, please indicate reason: _____
9. If the patient is a man with a female partner of childbearing potential, does patient agree to use effective contraception from the time of first dose of study until 90 days after the last dose of study treatment to allow for clearance of any altered sperm.
   Not applicable If N/A, please indicate reason: ___
10. Is the patient able to take oral medications?
11. Does all prior treatment-related toxicities [defined by National Cancer Institute- Common Toxicity Criteria for Adverse Events (NCI-CTCAE), version 5] ≤ Grade 1 at the time of enrollment except for alopecia or be deemed to be irreversible (for example, steroid induced cataracts or peripheral neuropathy).
12. Are the following laboratory results met within 7 days of first study drug administration?
    a. Absolute neutrophil count (ANC) >1000 cells/dL (1.0 x 10^9/L). Growth factors cannot be given within 7 days of study drug administration.
    b. Serum AST and ALT ≤ 3 x upper limit of normal (ULN).
    c. Creatinine clearance ≥ 20 mL/min either directly measured via 24-hour urine collection or calculated using Cockroft-Gault
    d. Platelet count ≥ 50 x 109 /L. For subjects with > 50% myeloma involvement in the marrow, a platelet count of ≥30 x 109 /L is allowed. Subjects may not have received a platelet transfusion within 72 hours prior to the platelet count used for eligibility
    e. Hemoglobin ≥ 80 g/L. subject may receive red blood cell (RBC) transfusions in accordance with institutional guidelines to meet this criterion. Subjects may not have received a red blood cell (RBC) transfusion within 72 hours prior to the hemoglobin result used for eligibility; use of growth factors is allowed.
    f. Total bilirubin ≤ 1.5 x ULN, unless known to have Gilbert's disease.
    g. Albumin ≥ 2.0 g/dL (20 g/L).
    h. Calcium <1.2xULN.

Exclusion Criteria

Subjects meeting any of the following criteria will be excluded from enrolment in the study:

1. Known history of clinically active amyloidosis, POEMS syndrome, or patients with plasma cell leukemia defined as circulating plasma cell count exceeding 500/uL or 5% of the peripheral blood white cells at the time of screening
2 Any serious and/or unstable pre-existing medical, psychiatric disorder, or other conditions (including lab abnormalities) that could interfere with subject's safety, obtaining informed consent or compliance to the study procedures.
3 Pregnant or lactating females.
4 Subjects with previous or concurrent malignancies are allowed only if the second tumor is not contributing to the subject's illness. The subject must not be receiving active therapy, other than hormonal therapy for this disease and the disease must be considered medically stable for at least 2 years. The following are allowed:
   a. Adequately treated in situ carcinoma of the cervix uteri or the breast;
   b. Basal cell carcinoma of the skin or localized squamous cell carcinoma of the skin;
   c. In situ malignancy;
   d. Prostate cancer Gleason grade 6 or lower AND with stable Prostate Specific Antigen levels off treatment;
   e. Previous malignancy with no evidence of disease confirmed and surgically resected (or treated with other modalities) with curative intent and unlikely to impact survival during the duration of the study.
5 Evidence of cardiovascular risk including any of the following:
   a. QTc interval ≥ 470 m secs.
   b. Evidence of current clinically significant uncontrolled arrhythmias; including clinically significant ECG abnormalities; including 2nd degree (Type II) or 3rd degree atrioventricular (AV) block.
   c. History of myocardial infarction, acute coronary syndromes (including unstable angina), coronary angioplasty, or stenting or bypass grafting within six months of Screening.

d. Class III or IV heart failure as defined by the New York Heart Association functional classification system
e. Uncontrolled hypertension
f. Ejection fraction <40% as determined by echocardiogram

6 Active human immunodeficiency virus (HIV), hepatitis B virus (HBV) or hepatitis C virus (HCV) infection. Presence of hepatitis B surface antigen (HBsAg) or positive HBV PCR test at screening or within 3 months prior to first dose of study treatment. Participants with positive hepatitis B core antibody (HBcAb) can be enrolled, only if confirmatory negative Hepatitis B DNA is obtained AND patient is on hepatitis B prophylaxis (e.g. tenofovir or entecavir) before first dose of study drugs. Presence of isolated Hep B surface antibody (HBsAb) indicating previous vaccination will not exclude a participant. Positive hepatitis C antibody test result or positive hepatitis C RNA test result at screening or within 3 months prior to first dose of study treatment. Note: Participants with positive Hepatitis C antibody due to prior resolved disease can be enrolled, only if a confirmatory negative Hepatitis C RNA test is obtained. Hepatitis RNA testing is optional and participants with negative Hepatitis C antibody test are not required to also undergo Hepatitis C RNA testing. Patients with HIV with detectable viral load or with AIDS-defining features or illnesses will be excluded.

7 Current active liver or biliary disease (with the exception of Gilbert's syndrome or asymptomatic gallstones, liver metastases or otherwise stable chronic liver disease per investigator's assessment).

8 Evidence of severe or uncontrolled systemic diseases (e.g., unstable or uncompensated respiratory, hepatic, renal or cardiac disease).

9 Current or past history of clinically significant CNS disease, such as stroke, epilepsy, CNS vasculitis, neurodegenerative disease, or CNS involvement by MM

- Note that patients with a history of stroke who have not experienced a stroke or transient ischemic attack in the past 2 years and have no residual neurologic deficits as judged by the investigator are allowed.
- Note that patients with a history of epilepsy who have had no seizures in the past 2 years while not receiving any anti-epileptic medications are allowed.

10 Known active infection requiring treatment.

11 Receiving systemic immunosuppressive medications (including, but not limited to, azathioprine, methotrexate, and anti-tumor necrosis factor agents), with the exception of corticosteroid treatment <10mg/day prednisone or equivalent within 2 weeks. Inhaled corticosteroids for respiratory diseases are allowed.

12 Evidence of active mucosal or internal bleeding.

13 Significant urinary outflow obstruction

14 Radiotherapy or systemic therapy (standard or biologic anticancer agent) within 14 days of initiation of study drug treatment.

15 Use of an investigational drug within 21 days or five half-lives, whichever is shorter, preceding the first dose of study drug.

16 Major surgery within 28 days

17 Known immediate or delayed hypersensitivity reaction or idiosyncrasy to drugs chemically related to liposomal curcumin.

A PHASE 1B/2 DOSE-ESCALATION AND COHORT-EXPANSION STUDY TO DETERMINE THE SAFETY AND EFFICACY OF BGB-11417 AS MONOTHERAPY, IN COMBINATION WITH DEXAMETHASONE, DEXAMETHASONE/CARFILZOMIB, DEXAMETHASONE/DARATUMUMAB, AND DEXAMETHASONE/POMALIDOMIDE IN PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA AND t(11;14)

Protocol Number: BGB-11417-105

Contact: Dr. Christine Chen / Olga Levina – **Open for Enrollment (ONLY cohorts 6 & 7)**

Inclusion Criteria

1. ≥ 18 years old
2. Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 2
3. A confirmed diagnosis of multiple myeloma (must have an M-component in serum and/or urine)
4. Measurable disease defined as:
   a. M-spike ≥ 500 mg/dL, or
   b. Urine protein M-spike of ≥ 200 mg/day, or
   c. Serum free light chains ≥ 10 mg/dL, and an abnormal κ:λ ratio
5. Participant has documented relapsed or progressive MM on or after any regimen or who are refractory to the most recent line of therapy.
   Note:
   - Relapsed MM is defined as previously treated MM that progresses and requires initiation of salvage therapy but does not meet the criteria for refractory MM.
   - Refractory MM is defined as disease that is nonresponsive (failure to achieve minimal response or development of progressive disease) while on primary or salvage therapy or progresses within 60 days of last therapy.

   a. Patients in Part 1 should have relapsed or progressive disease and have had≥ 3 prior lines of therapy including a proteasome inhibitor, IMiD agent, and an anti-CD38 monoclonal antibody.
   b. Patients in Part 2 (Cohorts 1 and 2):
      i. Patients should have relapsed or progressive disease and have had ≥ 3 prior lines of therapy including a proteasome inhibitor, an IMiD, and an anti-CD38 monoclonal antibody.
   c. Part 2 (Cohorts 3, 4, and 5):
      i. Patients should have relapsed or progressive disease and have had ≥ 1 prior line of therapy.
      ii. Patients must have been exposed to a combination therapy containing an anti-CD38 monoclonal antibody.
      iii. Prior treatment with carfilzomib is allowed, but the patient must not be considered carfilzomib refractory by the investigator and not have received carfilzomib within the past 6 months.

6. Positivity for t(11;14) by a validated fluorescence in situ hybridization (FISH) assay in a predefined central laboratory:
   a. A fresh bone marrow aspirate sample must be collected at screening and sent to central laboratory for t(11;14) FISH testing.
   b. Enrollment requires centrally confirmed t(11;14) results.
7. Either > 100 days after autologous stem cell transplant or ≥ 6 months after allogeneic transplant and without active graft-versus-host disease (ie, requiring treatment)
8. At least 2 months should have elapsed after previous chimeric antigen receptor T-cell therapy
9. Adequate organ function defined as:
   a. Hemoglobin ≥ 8.0 g/dL within 7 days before first dose of study treatment, independent of growth factor support and transfusions
   b. Platelet count ≥ 75,000/µL within 7 days before first dose of study treatment, independent of growth factor support and transfusions
   c. Absolute neutrophil count (ANC) ≥ 1000/mm^3 [ANC = (% of segmented neutrophils + % of segmented bands) x total WBC count] within 7 days before first dose of study treatment
      NOTE: The screening hematology values confirming patient meets the ANC requirement must be dated at least 14 days following the most recent administration of peg-filgrastim (or other pegylated myeloid growth factors) and at least 7 days following the most recent administration of filgrastim or other myeloid growth factors
   d. ALT and AST ≤ 3 x upper limit of normal (ULN) and total bilirubin ≤ 2.0 x ULN
   e. Serum creatinine ≤ 1.5 x ULN or creatinine clearance ≥ 45 mL/min/1.73 m^2 calculated by the MDRD-6 formula.
      Web-based calculator available at:
      https://qxmd.com/calculate/calculator_141/mdrd-egfr-6-variable
10. Women of childbearing potential must have a negative serum pregnancy test ≤ 7 days before the first dose of study drug(s). In addition, they must use a highly effective method of birth control initiated before the first dose of study drug(s), for the duration of the study treatment period, and for 90 days after the last dose of sonrotoclax, dexamethasone, daratumumab, or pomalidomide, or 180 days after the last dose of carfilzomib, whichever is longer. See Appendix 10 for highly effective methods of birth control and the definition of childbearing
11. Nonsterile men must use a highly effective method of birth control along with barrier contraception for the duration of the study treatment period and for ≥ 90 days after the last dose of study drug. During this same period, they must not donate sperm. Sterile men must use barrier contraception. In addition, partners of these men who could become pregnant should also utilize a highly effective method of birth control. See Appendix 10 for highly effective methods of birth control and the definition of sterile.
12. Life expectancy ≥ 6 months
13. Able to comply with the requirements of the study
14. Ongoing toxicities from prior anticancer therapies should have resolved or decreased to ≤ Grade 1 in severity (except for alopecia)

Exclusion Criteria

1. Participant has any of the following conditions:
   a. Non secretory MM (Serum free light chains < 10 mg/dL)
   b. Solitary plasmacytoma
   c. Active plasma cell leukemia (5% of peripheral white blood cells)
   d. Waldenström macroglobulinemia
   e. Amyloidosis
   f. Polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes (POEMS) syndrome
2. Chronic respiratory disease that requires continuous oxygen and/or respiratory failure requiring assisted ventilation
3. Significant cardiovascular disease, including but not limited to:
   a. Myocardial infarction ≤ 6 months before screening
   b. Ejection fraction ≤ 50%
   c. Unstable angina ≤ 3 months before screening
   d. New York Heart Association Class III or IV congestive heart failure (see Appendix 5)
   e. History of clinically significant arrhythmias (eg, sustained ventricular tachycardia, ventricular fibrillation, or torsades de pointes)
   f. Heart rate-corrected QT interval > 480 milliseconds based on Fridericia's formula
   g. History of Mobitz II second-degree or third-degree heart block without a permanent pacemaker in place
   h. Uncontrolled hypertension at screening, defined as systolic blood pressure > 170 mmHg and diastolic blood pressure > 105 mmHg by ≥ 2 consecutive measurements
4. Prior therapy with BGB-11417 or other agents inhibiting Bcl-2 activity (eg, venetoclax)
5. Known infection with human immunodeficiency virus (HIV).
6. Serologic status reflecting active viral hepatitis B (HBV) or viral hepatitis C (HCV) infection as follows:
   a. Presence of hepatitis B surface antigen (HBsAg) or hepatitis B core antibody (HBcAb). Patients with presence of HBcAb, but absence of HBsAg, are eligible if HBV DNA is undetectable (limitation of sensitivity < 20 IU/mL), and if they are willing to undergo monthly monitoring for HBV reactivation.
   b. Presence of HCV antibody. Patients with presence of HCV antibody are eligible if HCV RNA is undetectable (limitation of sensitivity < 15 IU/mL).
7. Major surgery within 4 weeks prior to enrollment.
   Note: Major surgery is any invasive operative procedure in which an extensive resection is performed, eg, a body cavity is entered, organs are removed, or normal anatomy is altered. In general, if a mesenchymal barrier is opened (pleural cavity, peritoneum, or meninges), the surgery is considered major.
8. Acute infections requiring antimicrobial therapy (antibiotic, antifungal, or antiviral) that have not been resolved for > 14 days prior to Cycle 1 Day

1.
9. Need for chronic corticosteroid therapy (> 10 mg prednisone or equivalent daily).
10. Any other medical condition that, in the opinion of the investigator, would adversely affect the participant's participation in the study or will render the administration of study drug(s) hazardous or obscure the interpretation of safety or efficacy results.
11. Psychiatric or cognitive dysfunction precluding active participation with the study protocol.
12. Radiation therapy that could affect bone marrow (eg, encompassing ≥ 5% of total bone marrow).
13. Use of the following substances prior to the first dose of study drug(s):
    a. ≤ 30 days prior to the first dose of study drug(s)
       − Any biologic and/or anti-CD38-based therapy
    b. ≤ 14 days prior to the first dose of study drug(s)
       − Systemic chemotherapy or therapeutic radiation therapy (palliative radiation therapy for bone lesions is acceptable)
    c. ≤ 7 days prior to the first dose of study drug(s)
       − Corticosteroid given with antineoplastic intent
       − Dexamethasone for any indication
       − BTK inhibitor, tyrosine kinase inhibitor, or other targeted small molecule (with 5 half-lives ≥ 7 days) given with antineoplastic intent
14. A history of other active malignancies, including myelodysplastic syndrome, within the past 2 years prior to study entry, with the following exceptions
    a. Adequately treated in situ carcinoma
    b. Basal cell carcinoma of the skin or localized squamous cell carcinoma of the skin
    c. Prostate cancer ≤ Gleason Grade 6 and with stable prostate-specific antigen levels off treatment
    d. Previous malignancy, > 2 years with no evidence of disease, confined and surgically resected (or treated with other modalities) with curative intent, and unlikely to impact survival during the duration of the study
15. If patient had prior allogeneic stem cell transplant, there is evidence of ongoing graft-versus host disease.
16. Pregnant or lactating women.
17. Unable to swallow capsules or disease significantly affecting gastrointestinal function such as malabsorption syndrome, resection of the stomach or small bowel, bariatric surgery procedure, symptomatic inflammatory bowel disease, or partial or complete bowel obstruction.
18. Receiving any treatment with a moderate or strong CYP3A4 inhibitor (≤ 7 days or 5 half-lives) or moderate or strong CYP3A4 inducer (≤ 14 days or 5 half-lives) before first dose of sonrotoclax. See Appendix 6 for guidance on CYP3A inhibitors and inducers.

Note: For patients in the pomalidomide cohort, a mandatory washout period of 7 days must be completed for patients on strong CYP1A2 inhibitors prior to Cycle 1 Day 1.

19. History of hypersensitivity to excipient(s) of sonrotoclax, dexamethasone, carfilzomib, daratumumab, or pomalidomide.
20. Vaccination with a live vaccine ≤ 35 days before first dose of study drug(s).

Note: Seasonal vaccines for influenza are generally inactivated vaccines and are allowed. Intranasal vaccines are live vaccines and are not allowed. A non-live COVID-19 vaccine may be administered if recommended per local practice.

A PHASE 1 STUDY OF KTX-1001, AN ORAL, FIRST-IN-CLASS, SELECTIVE, AND POTENT MMSET CATALYTIC INHIBITOR THAT SUPPRESSES H3K36ME2 IN PATIENTS WITH RELAPSED AND REFRACTORY MULTIPLE MYELOMA

Protocol Number: K36MMSET-001

Contact: Dr. Suzanne Trudel /Trina Wang – Enrollment on hold by Sponsor

Inclusion Criteria

1. Voluntarily provide informed consent prior to initiation of study specific activities
2. ≥18 years of age.
3. Eastern Cooperative Oncology Group (ECOG) score ≤ 1
4. Patients must have a confirmed diagnosis of RRMM (as per IMWG).
   - Patients must have received at least 3 prior lines of therapy as defined by IMWG, including a PI, an IMiD, and an anti-CD38 antibody
   - Patients must have exhausted available therapeutic options that are expected to provide a meaningful clinical benefit, either through disease relapse, treatment refractory disease, intolerance, or refusal of the therapy
   - *For expansion cohorts in Part B only:* Have t(4;14) confirmed by standard of care fluorescence in situ hybridization (FISH) testing or GOF mutation in MMSET confirmed by local sequencing test.
5. Measurable disease, including at least 1 of the following criteria:
   - Serum M protein (detected by serum protein electrophoresis [SPEP]) ≥ 0.50 g/dL
   - For patients with immunoglobulin class A (IgA) myeloma whose disease can only be reliably measured by quantitative immunoglobulin measurement, a serum IgA ≥ 0.50 g/dL (IgA will similarly be used for response)
   - Urine M protein (detected by urine protein electrophoresis [UPEP]) ≥ 200 mg/24 h
   - Serum free light chain (sFLC) involved light chain ≥ 10 mg/dL (100 mg/L) provided sFLC ratio is abnormal
   - ≥ 1 extramedullary lesion on imaging, including ≥ 1 lesion that is ≥ 1 cm in size and able to be followed by imaging assessments (Dose Escalation Only)
   - Bone marrow plasma cells ≥ 10% (Dose Escalation Only)
6. Recovery to Grade ≤ 1 for any nonhematologic toxicities due to prior therapy, excluding alopecia or Grade 2 neuropathy
7. Ability and willingness to adhere to study visit schedule and protocol requirements

Exclusion Criteria

1. Treatment with the following therapies in the specified time period:
   - Radiation, chemotherapy, immunotherapy, or any other anticancer therapy ≤ 2 weeks prior to Cycle 1 Day 1 (C1D1)
   - Cellular therapies (eg, chimeric antigen receptor T cell) ≤ 8 weeks prior to C1D1
   - < 100 days post autologous transplant (prior to first dose)
   - ≤ 6 months post allogenic transplant prior to C1D1 or if > than 6 months from allogenic transplant, no active graft-versus-host disease requiring treatment
   - Major surgery ≤ 4 weeks from C1D1
2. History of or current plasma cell leukemia, POEMS (polyneuropathy, organomegaly, endocrinopathy, and skin changes) syndrome, solitary bone lesion or bone lesions as the only evidence for plasma cell dyscrasia, myelodysplastic syndrome, or a myeloproliferative neoplasm or light chain amyloidosis.
3. Active central nervous system (CNS) disease: patients with previously treated stable CNS disease are eligible
4. Inadequate bone marrow function defined by:
   - Absolute neutrophil count (ANC) < 1000 cells/mm3
   - Platelets (PLT) < 75,000 cells/mm3
   - Hemoglobin < 8 g/dL (may be transfused provided no evidence of active bleeding)
5. Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) > 2.5 × upper limit of normal (ULN)
6. Total bilirubin > 1.5 × ULN, > 2 × ULN for patients with documented Gilbert's syndrome
7. Prothrombin time (PT) or partial thromboplastin time (PTT) international normalized ratio (INR) > 1.5 × ULN, OR INR > 1.5 × ULN or within target range if on prophylactic anticoagulation
8. Creatinine clearance < 50 mL/min by Cockcroft-Gault formula
9. Active, ongoing, or uncontrolled systemic viral, bacterial, or fungal infection. Prophylactic medications, antimicrobials or antiretroviral therapies are permitted provided the agents are not prohibited
   - HIV-positive patients with CD4+ T-cell counts < 350 cells/µL or not on a stable antiretroviral regimen for > 4 weeks with a viral load > 400 copies/mL prior to enrollment may not be enrolled
   - Hepatitis C virus (HCV)-positive patients who have not completed curative antiviral treatment and have a quantifiable viral load may not be enrolled
   - Hepatitis B surface antigen (HBs-AG)-positive and hepatitis B core antigen (anti-HBc)-positive patients may be enrolled following a discussion with the Medical Monitor to discuss anti-hepatitis B virus (HBV) prophylaxis. Patients with chronic HBV infection should complete an anti-HBV therapy regimen with follow-up assessment for response and tolerability prior to initiating study medication
10. Use of prohibited medications, including acid reducing agents and strong inhibitors or inducers of CYP3A4, within 14 days or 5 half-lives prior to starting KTX-1001
11. Uncontrolled thromboembolic events or recent severe hemorrhage that, in the opinion of the Investigator or Medical Monitor would pose a risk to patient safety or interfere with the study evaluation, procedures, or completion
12. Any history of pulmonary embolism or deep vein thrombosis (DVT) within 1 month of enrollment. Therapeutic dosing of anticoagulants (eg, warfarin, low molecular weight heparin, Factor Xa inhibitors) is allowed for history of DVT if > 3 months from time of enrollment.
13. Active, unstable cardiovascular function; presence of any of the following:
   - Symptomatic ischemia
   - Uncontrolled clinically significant conduction abnormalities (eg, patients with ventricular tachycardia on antiarrhythmics are excluded; patients with first degree atrioventricular or asymptomatic left anterior fascicular block/right bundle branch block will not be excluded)
   - Congestive heart failure or New York Heart Association Class ≥ 3
   - Myocardial infarction within 3 months prior to C1D1
   - Uncontrolled hypertension
   - QTc > 470 ms
14. Active malignancy not related to myeloma that has required therapy in the last 2 years prior to enrollment or is not in complete remission. Exceptions to these criteria include successfully treated nonmetastatic basal cell or squamous cell skin carcinoma, or prostate cancer that does not require therapy. Other similar malignant conditions may be discussed with and permitted by the Medical Monitor
15. Malabsorption syndrome or other condition affecting oral absorption
16. Men and women of reproductive potential who are unwilling to practice acceptable methods of effective birth control while on study through 6 months (women) or 3 months (men) after receiving the last dose of study drug. Acceptable methods of effective birth control include sexual abstinence (refraining from heterosexual intercourse; men, women); vasectomy; tubal ligation; or a condom with spermicide (men) in combination with barrier methods, hormonal birth control or intrauterine device (women)
   - Pregnancy, or females planning on becoming pregnant while on study or through 6 months after last study drug administration; or females who are lactating/breast feeding or who plan to breastfeed while on study through 6 months after last study drug administration
   - Male patients must refrain from sperm donation, or attempt to conceive from study drug administration until 3 months after last dose of study drug
17. History or evidence of any other clinically significant disorder, condition, or disease (except for those outlined above) that, in the opinion of the Investigator or Medical Monitor would pose a risk to patient safety or interfere with the study evaluation, procedures or completion, including inability to find alternative concomitant medications that may be potential risk for drug-drug interaction (DDI)

A PHASE 3 RANDOMIZED STUDY COMPARING JNJ-79635322 AND AN ANTI-BCMAXCD3 BISPECIFIC ANTIBODY IN PARTICIPANTS WITH RELAPSED OR REFRACTORY MULTIPLE MYELOMA WHO HAVE RECEIVED AT LEAST 3 PRIOR LINES OF THERAPY INCLUDING A PI, AN IMID, AND AN ANTI-CD38 ANTIBODY

Protocol Number: 79635322MMY3001

Contact: Dr. Guido Lancman /Elim Chen – **Open Enrollment**

Inclusion Criteria

1. ≥18 years of age.
2. Documented initial diagnosis of multiple myeloma according to IMWG diagnostic criteria
3. Received at least 3 prior lines of antimyeloma therapy including a PI, an IMiD, and an anti-CD38 antibody.
4. Documented evidence of PD or failure to achieve a response (i.e., PR or better) to the last line of therapy based on investigator's determination of response by the IMWG criteria.
5. Have discontinued concurrent use of any other anticancer treatment (including nonpalliative radiotherapy) or investigational agent. Toxicity related to previous anticancer therapy must have resolved to resolved to Grade 1 or better (except alopecia, skin fibrosis or discoloration, dry mouth, endocrinopathy managed with replacement therapy, peripheral neuropathy, and dysgeusia, which must be Grade 2 or better).
6. Eastern Cooperative Oncology Group (ECOG) performance status grade of 0 to 2 at screening and Treatment
7. Renal function: Have an eGFR, calculated with the CKD-epi creatinine formula (Section 10.12), of >30 mL/min during the screening period.
8. Hepatic function: Participants are eligible if they have the following laboratory values during the screening period and within 1 day of the start of administration of study treatment:
    - AST and ALT<2.5×ULN
    - Total bilirubin <1.5×ULN
    - Bilirubin in case of known congenital nonhemolytic hyperbilirubinemias such as Gilbert's Syndrome, isolated total bilirubin ≥1.5×ULN with direct bilirubin <1.5×ULN
9. Clinical laboratory values:
    - **Hemoglobin** ≥7.5 g/dL, without use of transfusion or growth factors within 7 days **Platelets** ≥50×109/L (without transfusion support in the prior 7 days)
    - **Absolute Neutrophil Count (ANC)** 1≥0.75×103/µL (prior growth factor support is permitted but must be without support for 7 days for G-CSF or GM-CSF and for 14 days for pegylated G-CSF prior to the laboratory test
    - **Platelets** ≥50×103/µL, without use of transfusion or growth factors within 7 day

Exclusion Criteria

1. Serious underlying medical conditions, such as:
    a. Evidence of active systemic viral, fungal, or bacterial infection requiring systemic antiviral, antifungal, or antimicrobial therapy
    b. Active autoimmune disease requiring systemic immunosuppressive therapy within 6 months before start of study treatment
    c. Overt clinical evidence of dementia or altered mental status
    d. Any of the following within 6 months prior to first dose of study treatment: severe or unstable angina, myocardial infarction, seizure, major thromboembolic events (eg, pulmonary embolism, cerebrovascular accident [including TIA and stroke]), clinically significant ventricular arrhythmias or heart failure New York Heart Association functional classification Class III to IV
2. Active hepatitis of infectious origin.
    - Seropositive for hepatitis B:
    - Known hepatitis C infection or positive serologic testing for hepatitis C virus (anti-HCV) antibody.
    - Other clinically active liver disease of infectious origin.
3. Participants who are HIV-positive and meet any of the following
    - Detectable viral load (i.e., ≥50 copies/mL) at screening
    - CD4+ count ≤300 cells/mm3 at screening
    - Acquired immunodeficiency syndrome (AIDS)-defining opportunistic infection within 6 months of screening
    - Receive treatment other than continued HAART.
4. Plasma cell leukemia at the time of screening (≥5% circulating PCs in peripheral blood smear), Waldenstrom's macroglobulinemia, POEMS syndrome
5. Presence of any of the following:
    - Any ongoing myelodysplastic syndrome or B-cell malignancy
    - Any history of malignancy, other than MM, that is considered at high risk of recurrence requiring systemic therapy.
6. Suspected or known allergies, hypersensitivity, or intolerance to the excipients of JNJ- 79635322
7. Major surgery, (e.g., requiring general anesthesia) within 2 weeks before first dose, or will not have fully recovered from surgery, or has surgery planned during the time the participant is expected to participate in the study
8. Suspected or known allergies, hypersensitivity, or intolerance to teclistamab or its excipients (TECVAYLI USPI 2024).
9. Prior or concurrent exposure to any of the following, in the specified time frame prior to randomization:

- T-cell redirection therapy (eg, CAR-T, bispecific antibody) within 6 months.
- History of receiving both BCMA and GPRC5D-directed therapy
- History of receiving a BCMA-directed bispecific antibody
- An allogenic stem cell transplant within 6 months before first dose of study drug.
- Received a cumulative dose of corticosteroids equivalent to ≥140 mg of prednisone within the 14 days prior to first dose of study drug.

10. Received or plans to receive any live, attenuated vaccine within 4 weeks before the first dose of study treatment, during, or within 90 days after the last dose of study treatment.

AMYLOIDOSIS TRIALS:

A PHASE 1B/2 STUDY OF AZD0120 (ALSO KNOWN AS GC012F), A CHIMERIC ANTIGEN RECEPTOR T CELL THERAPY TARGETING CD19 AND B CELL MATURATION ANTIGEN IN PARTICIPANTS WITH RELAPSED OR REFRACTORY AL AMYLOIDOSIS.
Protocol Number: AZD0120-AL-201 - D831AC00001
Contact: Dr. Vishal Kukreti/Trina Wang – **Enrollment on hold by sponsor-release of new slots until Q3)**

Inclusion Criteria

Age

1. Must be ≥18 years of age, at the time of signing the informed consent.

Type of Participant and Disease Characteristics

2. Confirmed histopathological diagnosis of AL amyloidosis based on polarizing light microscopy of green bi-refringent material in Congo red stained tissue specimens and confirmation of AL derived amyloid deposits by at least one of the following: immunohistochemistry, immunofluorescence, mass spectrometry, characteristic electron microscopy appearance/immunoelectron microscopy. Confirmed diagnosis on historic biopsy is acceptable, with no requirement for repetition.
3. One or more organs currently or historically impacted by AL amyloidosis according to consensus guidelines
4. Measurable hematologic disease: dFLC > 20 mg/L or serum M-protein > 5g/L
5. Relapsed disease or refractory disease defined as a need for additional therapy after at least 1 line of anti-plasma cell-directed therapy. Prior therapies must include at least one CD38 monoclonal antibody and at least one proteasome inhibitor. Participants should not be in a CR at the time of inclusion. Participants who did not reach VGPR after at least 2 cycles of initial therapy can be included, as well as participants who initially attained a CR or VGPR with initial therapy with evidence of rising dFLC or rising M-protein, that the Investigator deems as requiring further anti-plasma cell directed treatment.
6. ECOG performance status of 0 to 1

Sex and Contraceptive/Barrier Requirements

7. Male or female
   Contraceptive use should be consistent with local regulations regarding the methods of contraception for those participating in clinical studies

   a. Male Participants:
      - Use of a condom plus an additional contraceptive method from the time of signing the ICF and throughout the study, until 12 months after receiving AZD0120 infusion or until CAR T cell DNA is no longer detectable by PCR (whichever is later) or 6 months after receiving the last dose of fludarabine or cyclophosphamide, whichever occurs last. In addition, male participants must refrain from sperm donation while on-study and for 12 months after receiving AZD0120 infusion or until CAR T cell DNA is no longer detectable by PCR, whichever is later.
      - NOTE: Non-pregnant female partners of male participants enrolled in this study should use acceptable contraception (Section 10.5) during their partner's participation in the study and until at least the same timeframe for their male partners.

   b. Female Participants:
      - FONCBP
      - Females receiving HRT and whose menopausal status is in doubt will be required to use one of the contraception methods outlined for FOCBP if they wish to continue using HRT during the study. Otherwise, HRT must be discontinued to allow confirmation of post-menopausal status prior to enrollment.
      - FOCBP must use one highly effective form of birth control from the time of signing the ICF, throughout the study and until 12 months after receiving AZD0120 infusion or until CAR T cell DNA is no longer detectable by PCR (whichever is later) or 12 months after receiving the last dose of fludarabine or cyclophosphamide, whichever occurs last. Cessation of contraception after this point should be discussed with the treating physician.
      - All FOCBP must have a negative serum and/or urine pregnancy test result at screening and thereafter as defined in SoA.
      - NOTE: Non-sterilized partners of FOCBP participants enrolled in this study should use acceptable contraception during their partner's participation in the study and until at least the same timeframe specified for their female partners.

Informed Consent

8. Capable of giving signed informed consent as described in Section 10.1.3 which includes compliance with the requirements and restrictions listed in the ICF and in this protocol.
9. Must be able and willing to adhere to the study visit schedule and other protocol requirements.

Exclusion Criteria

Any potential participant who meets any of the following criteria up until apheresis will be excluded from participating in the study:

Medical Conditions

1. Have any other form of amyloidosis other than AL amyloidosis
2. Have any other form of amyloidosis other than AL amyloidosis
   a. Mayo Stage IIIb AL amyloidosis (Wechalekar, 2013)
   b. NT-proBNP levels as follows:
      - NT-proBNP ≥ 2000 ng/L (Phase 1b dose escalation portion and Phase 2 lower NT-proBNP group)
      - NT-proBNP < 2000 and > 5000 ng/L (Phase 1b dose extension portion and Phase 2 higher NT-proBNP group).
   c. High-sensitivity cardiac troponin T > 75 ng/L
   d. NYHA Class III – IV
   e. LVEF < 45% by echocardiogram
   f. Medically refractory atrial or ventricular arrhythmias as determined by Investigator
   g. Symptomatic or medically refractory pleural effusions as determined by Investigator
   h. Decompensated heart failure
   i. Unexplained syncope, not believed to be vasovagal
   j. Standing systolic BP < 100 mm Hg or symptomatic orthostatic hypotension, defined as a decrease in systolic BP upon standing of > 30 mmHg despite medical management (eg, midodrine, fludrocortisones) in the absence of volume depletion
   k. Myocardial infarction, coronary revascularization or CABG ≤ 6 months prior to screening
   l. Pacemaker/ICD/CRT-D implantation within ≤ 6 months prior to screening
3. Severe Factor X deficiency (Factor X < 10%) or Factor X deficiency with significant risk of bleeding as determined by Investigator
4. Extensive GI involvement with evidence of active GI bleeding/risk of bleeding as determined by Investigator.
5. Oxygen saturation < 95% on room air
6. Prior therapies:
   a. CAR T cell therapy directed at any target
   b. Prior BCMA-targeting therapy
   c. Prior treatment with any FDA approved or investigational T cell engaging therapies (including T cell-directed bispecific or trispecific therapies) at any target within the last 6 months.
   d. An allogenic stem cell transplant within 6 months before apheresis. Participants who received an allogeneic transplant must be off all immunosuppressive medications for 6 weeks before apheresis without signs of GVHD.
   e. An autologous stem cell transplant ≤ 12 weeks before apheresis
   f. Prior therapy as follows, prior to apheresis:
      - Investigational product within 5 half-lives or ≤ 21 days (whichever is the shorter).
      - Monoclonal antibody treatment for AL within 21 days.
      - Cytotoxic/alkylating therapy within 21 days
      - Proteasome inhibitor therapy within 14 days.
      - Immunomodulatory agent therapy within 14 days.
      - Received a cumulative dose of systemic corticosteroids, equivalent to ≥ 70 mg of prednisone, within 7 days prior to apheresis.
7. Toxicity from previous anti-cancer or anti-PC-directed therapy did not resolve to baseline levels or to Grade 1 or less except for alopecia or peripheral neuropathy. For eligibility criteria related to hemoglobin, lymphocyte, platelet and neutrophil thresholds, refer to Exclusion Criteria 16 to 19.
8. Active plasma cell leukemia at the time of screening, Waldenstrom's macroglobulinemia or POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, and skin changes). IgM associated AL amyloidosis is permitted, as long as participant meets other eligibility criteria including requisite prior therapies.
9. Multiple myeloma defined as clonal bone marrow plasma cells ≥10% and any one or more of the following myeloma defining events (deemed as attributable to multiple myeloma by Investigator)
   a. Hypercalcemia: serum calcium > 0.25 mmol/L (> 1 mg/dL) higher than the ULN or > 2.75 mmol/L (> 11 mg/dL) OR
   b. Renal insufficiency: creatinine clearance < 40 mL per minute or serum creatinine > 177 µmol/L (> 2 mg/dL) OR
   c. Anemia: hemoglobin value of > 20 g/L below the lowest limit of normal, or a hemoglobin value < 100 g/L OR
   d. Bone lesions: one or more lesions on imaging tests (performed ≤ 3 months prior to signing the ICF or during Screening): skeletal radiography, CT, or PET/CT, or MRI.
   e. 60% or greater clonal plasma cells on bone marrow biopsy in screening

Note: a multiple myeloma diagnosis with a serum FLC ratio >100, as the only myeloma-defining event, does not constitute an exclusion.

10. Have history of any HLH and/or history of Grade 3 or higher CRS and/or neurotoxicities during prior T cell engaging therapy.
11. Have history of a prior malignancy, unless the participant has been disease-free with no evidence of recurrence for ≥ 2 years. The following are exceptions:
    - Basal cell carcinoma of the skin

- Squamous cell carcinoma of the skin in situ (Stage 0)
- Carcinoma in situ of the cervix
- Carcinoma in situ of the breast
- Incidental histologic finding of prostate cancer (T1a or T1b using the TNM [tumor, nodes, metastasis] clinical staging system) or prostate cancer that is curative

12. Exclusion criteria relating to neurological conditions:
    a. History of neurodegenerative disorders or significant neurological condition including but not limited to stroke, intracranial hemorrhage, severe brain injury, dementia, cerebellar disease, Parkinson's disease, organic brain syndrome or seizure within 6 months prior to apheresis.
    b. History of Guillain-Barre syndrome or its variants, or history of any Grade 3 or higher peripheral motor polyneuropathy.
13. Seropositive for HIV.
14. Vaccinated with live, attenuated vaccine within 4 weeks prior to apheresis.
15. Serologic status reflecting active hepatitis B or C:
    a. Patients who are anti-HBc antibody positive and who are surface antigen negative will need to have a negative PCR result before enrollment. Those who are hepatitis B surface antigen positive or hepatitis B PCR positive will be excluded.
    b. Patients who are hepatitis C antibody positive will need to have a negative PCR result before enrollment.
    c. Those who are hepatitis C PCR positive will be excluded. For participants with known history of HCV infection, confirmation of sustained virologic response is required for study eligibility, defined as ≥ 12 weeks after completion of antiviral therapy.
16. Hemoglobin < 8 g/dL (without prior red blood cell transfusion within 7 days before the laboratory test. For participants who meet the exclusion criteria at Screening, transfusion of red blood cells is permitted after Screening as needed to maintain a hemoglobin level ≥ 8.0 g/dL).
17. Platelets < 50,000/µL (participants above this threshold must not have received platelet transfusion support within 7 days before the laboratory test).
18. Absolute lymphocyte count < 300/µL
19. ANC < 1000/uL (prior growth factor support is permitted but must be without support in the 7 days prior to the laboratory test
20. AST or ALT >2.5×ULN
21. Total bilirubin >1.5×ULN; except in participants with congenital bilirubinemia, such as Gilbert syndrome (in which case direct bilirubin <1.5×ULN is required)
22. Calculated creatinine clearance < 30mL/min (per Cockcroft-Gault formula)
23. Known life threatening allergies, hypersensitivity, or intolerance to AZD0120 or its excipients, including DMSO, or to fludarabine and cyclophosphamide.
24. Serious underlying medical condition, such as:
    a. Evidence of serious active viral, bacterial, or uncontrolled systemic fungal infection
    b. Active autoimmune disease or a history of autoimmune disease requiring treatment within 3 years
    c. Overt clinical evidence of dementia or altered mental status.
    d. IBD requiring treatment within the past 5 years
25. Any issue that would impair the ability of the participant to receive or tolerate the planned treatment at the investigational site, to understand informed consent or any condition for which, in the opinion of the Investigator, participation would not be in the best interest of the participant (eg, compromise the well-being) or that could prevent, limit, or confound the protocol-specified assessments.
26. Pregnant or breast-feeding, or planning to become pregnant while enrolled in this study and within 12 months post-AZD0120 infusion or until CAR T cell DNA is no longer detectable by ddPCR, whichever occurs last.
27. Plans to father a child while enrolled in this study and within at least one-year post- AZD0120 infusion or until CAR T cell DNA is no longer detectable by ddPCR, whichever occurs last.
28. Major surgery within 4 weeks prior to apheresis, or has major surgery planned between apheresis and infusion of AZD0120, or within 4 weeks after study drug infusion with AZD0120.

(Note: participants with planned surgical procedures to be conducted under local anesthesia may participate).

CHRONIC LYMPHOCYTIC LEUKEMIA & WALDESTROM'S TRIALS

THE USE OF PERIPHERAL BLOOD CELL-FREE DNA (CFDNA) FOR GENETIC PROFILING IN PATIENTS WITH LYMPHOPLASMACYTIC LYMPHOMA (LPL) AND WALDENSTROM'S MACROGLOBULINEMIA (WM)
Protocol Number: PM-WM001
Non-Interventional
Contact: Dr. Christine Chen/Harjot Vohra -**Open Enrollment**

Inclusion criteria:

1. Males or females aged 18 years or older at the time of signing consent
2. A confirmed diagnosis of lymphoplasmacytic lymphoma or Waldenstrom's Macroglobulinemia
3. Treatment-naïve or previously treated
4. Known to Princess Margaret Cancer Centre with routine standard of care laboratory testing available

Exclusion criteria:

1. Any serious medical condition, laboratory abnormality, or psychiatric illness that would prevent the subject from signing the informed consent form
2. Currently undergoing treatment for active malignancy, NOT indolent lymphoma

A PHASE 2 STUDY TO EVALUATE THE EFFICACY AND SAFETY OF MK-1026 IN PARTICIPANTS WITH HEMATOLOGIC MALIGNANCIES.
Protocol Number: MK-1026-003-09
Contact: Dr. Christine Chen/ Olga Levina – Open Enrollment only for Part 2, Cohort J (WM patients)

Inclusion Criteria

The criteria listed below pertain to Cohort J in Part 2, which is currently open for enrollment. The relevant information has been extracted in accordance with protocol Amendment 9.0 (PA9.0) dated 21 August 2025, and incorporated into the key eligibility criteria below.

Participants eligible for inclusion in this study must be relapsed or refractory to existing treatment. The definition of relapsed/refractory disease is as follows:

The following disease-specific criteria must be met according to the WHO classification of hematological malignancies

1. Part 2 (Cohort J) has a confirmed diagnosis of CLL/SLL with:

- Part 2 Cohort J: CLL/SLL participants whose disease relapsed or was refractory to prior therapy with a covalent/irreversible BTKi and BCL2i (both classes of therapies are required). Additional use of noncovalent/reversible BTKi is permitted provided participant's disease relapsed/was refractory to such therapy. CLL participants must have received and failed, been intolerant to, or determined by their treating physician to be a poor PI3Ki candidate or ineligible for a PI3Ki per local (institution) guidelines. The participant is not eligible if response cannot be assessed after stopping BTKi and BCL2i. The participant will be eligible once disease progression or refractory status is determined.

NOTE: As of Protocol Amendment 09, at least 10 CLL/SLL participants whose disease relapsed or was refractory to prior therapy with a covalent/irreversible BTKi, BCL2i and noncovalent/reversible BTKi (all three classes of therapies are required) will be enrolled into Cohort J.

- Active disease for CLL/SLL clearly documented to initiate therapy. At least 1 of the following criteria should be met:
- Evidence of progressive marrow failure as manifested by the development of, or worsening of, anemia and/or thrombocytopenia. Cut-off levels of Hb <10 g/dL or platelet counts <100 × 109/L are generally regarded as indication for treatment. However, in some patients, platelet counts <100 × 109/L may remain stable over a long period; this situation does not automatically require therapeutic intervention.
- Massive (i.e., >+6 cm below the left costal margin) or progressive or symptomatic splenomegaly.
- Massive nodes (i.e., ≥10 cm in longest diameter) or progressive or symptomatic lymphadenopathy.
- Progressive lymphocytosis with an increase of ≥50% over a 2-month period, or LDT <6 months. LDT can be obtained by linear regression extrapolation of absolute lymphocyte counts obtained at intervals of 2 weeks over an observation period of 2 to 3 months; participants with initial blood lymphocyte counts ≥30 × 109/L may require a longer observation period to determine the LDT. Factors contributing to lymphocytosis other than CLL (e.g., infections, steroid administration) should be excluded.
- Autoimmune complications including anemia or thrombocytopenia poorly responsive to corticosteroids.
- Symptomatic or functional extra nodal involvement (e.g., skin, kidney, lung, spine).
- Disease-related symptoms as defined by any of the following:
    - Unintentional weight loss ≥10% within the previous 6 months
    - Significant fatigue (i.e., ECOG performance score 2 or worse; cannot work or unable to perform usual activities).
    - Fever of 100.5°F or 38.0°C for 2 or more weeks without evidence of infection.
    - Night sweats for ≥1 month without evidence of infection.

NOTE: CLL participants must have at least one parameter that can be objectively measured for response per iwCLL.
SLL participants must have measurable disease defined as at least 1 lesion that can be accurately measured in at least 2 dimensions with spiral CT scan. A minimum measurement must be >15 mm in the longest diameter.

- For SLL participants in Part 2: Participants with lymphoma must provide a lymph node biopsy for biomarker analysis from an archival (within 1 year relative to the date of sample submission to the central laboratory provided there was no intervening therapy) or newly obtained lymph node biopsy or bone marrow aspirate at Screening. If a lymph node biopsy is considered medically unsafe to perform, Sponsor consultation/approval is required for enrollment. CLL participants in Part 2 will only provide Cycle 1 Day 1 blood sample.

2. Have an ECOG performance status of 0 to 2 within 7 days before allocation.
3. Have a life expectancy of at least 3 months, based on the investigator assessment.
4. Have the ability to swallow and retain oral medication.
5. Participants who are HBsAg positive are eligible if they have received HBV antiviral therapy for at least 4 weeks and have undetectable HBV viral load prior to randomization.

NOTE: Participant should remain on antiviral therapy throughout study intervention and follow local guidelines for HBV antiviral therapy post completion of study intervention.

Hepatitis B screening tests are not required unless:

- Known history of HCV infection
- As mandated by local health authority

6. Participant with history of HCV infection are eligible if HCV viral load is undetectable at screening

NOTE: Participant must have completed curative antiviral therapy at least 4 weeks before randomization.

Hepatitis C Screening tests are not required unless:

- Known history of HCV infection
- As mandated by the local health authority

7. Have adequate organ function as defined in Table 7. Specimens must be collected within 7 days before the start of study intervention.

Table 7 Adequate Organ Function Laboratory Values

System	Laboratory Value
Hematological	
ANC	≥750/µL
Platelets	≥50 000/µL [a]
Hemoglobin	≥8.0 g/dL [a, b]
Renal	
Measured or calculated c CrCl (GFR can also be used in place of creatinine or CrCl)	≥30 mL/min
Hepatic	
Total bilirubin	≤1.5 ×ULN OR direct bilirubin ≤ULN for participants with total bilirubin levels >1.5 × ULN In participants with documented liver metastases and/or Gilbert's syndrome, total bilirubin of ≤3 × ULN
AST (SGOT) and ALT (SGPT)	≤2.5 × ULN (≤5 × ULN for participants with liver metastases)
Coagulation	
INR or PT aPTT	≤1.5 × ULN unless participant is receiving anticoagulant therapy as long as PT or aPTT is within therapeutic range of intended use of anticoagulants
ALT (SGPT) =alanine aminotransferase (serum glutamic pyruvic transaminase). ANC=absolute neutrophil count; aPTT=activated partial thromboplastin time; AST (SGOT)=aspartate aminotransferase (serum glutamic oxaloacetic transaminase); CLL=chronic lymphocytic leukemia; CrCl=Creatinine clearance; GFR=glomerular filtration rate; INR=International normalized ratio; pRBC=packed red blood cell; PT=prothrombin time; SLL=small lymphocytic leukemia; ULN=upper limit of normal. [a] No requirement in participants with significant bone marrow involvement. [b] Criteria must be stable for ≥1 week [c] CrCl should be calculated per institutional standard.	

Demographics

8. Is individual of any sex/gender, 18 years of age or older at the time of providing documented informed consent.

Male Participants

9. If capable of producing sperm, the participant agrees to the following during the intervention period and for at least the time needed to eliminate the study intervention after the last dose of study intervention. The length of time required to continue contraception for the study intervention is:
    - MK-1026: 12 days

- Uses a penile/external condom when having penile-vaginal intercourse with nonparticipant of childbearing potential who is not currently pregnant.
- Contraceptive use should be consistent with local regulations regarding the methods of contraception for those participating in clinical studies. If the contraception requirements in the local label for any of the study interventions are more stringent than the requirements above, the local label requirements are to be followed.

NOTE: If the participant is azoospermic (vasectomized or secondary to medical cause, documented from the site personnel's review of the participant's medical records, medical examination, or medical history interview), no contraception is required.

Female Participants

10. A participant assigned female sex at birth is eligible to participate if not breastfeeding during the study intervention period and at least 30 days after the last dose of study intervention (MK-1026). The number of days should be after 5 half-lives.

- A POCBP is eligible to participate if not pregnant and if a negative highly sensitive pregnancy test (urine or serum), as required by

local regulations, has been obtained within 24 hours (for a urine test) or 72 hours (for a serum test) before the first dose of study intervention. If a urine test cannot be confirmed as negative (e.g., an ambiguous result), a serum pregnancy test is required. Additional requirements for pregnancy testing during and after study intervention are in Section 8.3.5.

- A POCBP is eligible to participate if they use a contraceptive method that is highly effective (with a failure rate of <1% per year), with low user dependency, or if they adhere to penile-vaginal intercourse abstinence as their preferred and usual lifestyle (abstinent on a long-term and persistent basis), as described in Appendix 5, during the intervention period and for at least the time needed to eliminate the study intervention after the last dose of study intervention. The length of time required to continue contraception for the study intervention is:
  - MK-1026: 30 days

NOTE: The investigator should evaluate the potential for contraceptive method failure (i.e., noncompliance, recent initiation) in relationship to the first dose of study intervention. Contraceptive use by POCBPs should be consistent with local regulations regarding the methods of contraception for those participating in clinical studies. If the local contraception requirements for any of the study interventions are more stringent than the requirements above, the local label requirements are to be followed.

- Medical history, menstrual history, and recent sexual activity has been reviewed by the investigator to decrease the risk for inclusion of POCP with an early undetected pregnancy.

Informed Consent

11. The participant (or legally acceptable representative) has provided documented informed consent for the study.

Refer to Appendix 7 for country-specific requirements.

Other Inclusions

12. Participants with HIV are eligible if they meet ALL of the following criteria:

- The CD4 count is >350 cells/µL at Screening
- The HIV viral load is below the detectable level as per locally available testing
- Are on a stable ART regimen for at least 4 weeks before study entry.

NOTE: ART includes drugs which are NOT strong CYP3A4 inducers (participants receiving ART that are strong CYP3A4 inducers are not eligible to be included in the study).

- Are compliant with their ART

NOTE: If the participant has had an AIDS defining opportunistic infection in the past 12 months before Screening, they are not eligible to be included in the study.

- No HIV testing is required unless per local health guidelines.

Refer to Appendix 7 for additional country-specific requirements.

<u>Exclusion Criteria</u>

The participant must be excluded from the study if the participant meets any of the following criteria:

Medical Conditions

1. Part 2 participants: active HBV/HCV infection. See Inclusion Criteria 7 (HBV) and 8 (HCV) for requirements.
2. Has a history of malignancy ≤3 years before providing documented informed consent.

NOTE: participants with basal cell carcinoma of skin, squamous cell carcinoma o skin, or carcinoma in situ (e.g., Breast carcinoma, cervical cancer in situ) that have undergone potential curative therapy are not excluded. Participants with low-risk, early-stage prostate cancer (T1-T2a, Gleason score <6, and prostaticspecific antigen<10 ng/mL) either treated with definitive intent or untreated in active surveillance with SD are not excluded.

3. Has active CNS disease.
4. Has an active infection requiring systemic therapy.
5. Exclusion criterion removed.
6. Has a history or current evidence of any condition, therapy, laboratory abnormality or other circumstance that might confound the results of the study, or interfere with the participant's ability to cooperate with the requirements of the study, such that it is not in the best interest of the participant to participate, in the opinion of the treating investigator.
7. Has QTc prolongation (defined as a QTcF >470 msec) or other significant ECG abnormalities including second degree AV block type II, third degree AV block, or bradycardia (ventricular rate less than 50 beats/min).

NOTE: If triplicate ECG were performed, QTc prolongation is defined as a QTcF >470 msec on 2 out of 3 consecutive ECGs, and mean QTcF> 470 msec on all 3 ECG.

a) QTcF is calculated using Fridericia's Formula (QTcF = QT/ (RR^0.33).
b) Correction of suspected drug-induced QTcF prolongation or prolongation due to electrolyte abnormalities can be attempted at the Investigator's discretion, and only if clinically safe to do so with either discontinuation of the offending drug or switch to another drug not known to be associated with QTcF prolongation or electrolyte supplementation.

Prior/Concomitant Therapy

8. Has received prior systemic anticancer therapy within 5 half-lives or 4 weeks (if prior therapy was a monoclonal antibody) before C1D1.

NOTE: Participants must have recovered from all AEs due to previous therapies to ≤Grade 1 or baseline. Participants with ≤Grade 2 neuropathy may be eligible.

NOTE: If participant received major surgery, they must have recovered adequately from the toxicity and/or complications from the intervention before starting study intervention.

9. Currently being treated with the following drugs:
- P-gp substrates with a narrow therapeutic index
- CYP3A strong inducers
- CYP3A strong inhibitors

NOTE: A washout period of at least 5 times the half-life after the last dose of any of the above treatments is required for a participant to be eligible for study enrollment.

Prior/Concurrent Clinical Study Experience

10. Is currently participating in or has participated in a study of an investigational agent or has used an investigational device within 4 weeks before the first dose of study intervention.

NOTE: Participants who have entered the follow-up phase of an investigational study may participate as long as it has been 4 weeks after the last dose of the previous investigational agent.

11. Prior exposure to noncovalent, reversible BTK inhibitors.

NOTE: For Part 2 Cohort J, prior exposure to nemtabrutinib is not permitted. Additional prior use of noncovalent, reversible BTK inhibitor(s) other than nemtabrutinib is (are) permitted.

Diagnostic Assessments

12. Exclusion criterion removed

Other Exclusions

13. Has any clinically significant gastrointestinal abnormalities that might alter absorption.
14. Has a known severe hypersensitivity (≥Grade 3) to nemtabrutinib, its active substance and/or any of its excipients. Refer to the IB for a list of excipients.
15. History of severe bleeding disorders.

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