A PHASE 1 OPEN-LABEL, SAFETY, PHARMACOKINETIC, AND PRELIMINARY EFFICACY STUDY OF STRO-001, AN ANTI-CD74 ANTIBODY DRUG CONJUGATE, IN PATIENTS WITH ADVANCED B-CELL MALIGNANCIES, NCT03424603


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BACKGROUND

• CD74 is a transmembrane glycoprotein involved in MHC protein formation & transport
  - CD74 is expressed in ~90% of B-cell cancers including multiple myeloma (MM) and Non-Hodgkin Lymphoma (NHL)
  - Normal tissues have minimal CD74 expression
  - CD74 is rapidly internalized, making it an attractive target for antibody drug conjugates (ADCs)

• Sutro’s cell-free synthesis platform enables rapid production and high-throughput selection for optimization of ADC candidates.

• STRO-001 is a novel, specific and homogeneous anti-CD74 ADC (Figure 1) and contains two non-cleavable maytansinoid linker warheads per molecule.

• STRO-001 demonstrated potent in vitro cytotoxicity in MM and NHL cell lines.

• STRO-001 exhibited significant anti-tumor activity in MM (ARP-1 and MM-1S) and NHL (MM1C, MCL1) xenograft models in vivo.

• Toxology studies in cynomolgus monkeys did not produce any unexpected findings, treatment resulted in the intended pharmacodynamic effect, B-cell depletion.

• There is a persistent unmet need for novel, effective, well tolerated therapies for patients with relapsed or relapsed/refractory MM and NHL.

OBJECTIVES AND ENDPOINTS

PRIMARY OBJECTIVES

Part 1: Safety and tolerability of STRO-001, define the recommended phase 2 dose (RP2D)

Part 2: Anti-tumor activity of STRO-001

SECONDARY OBJECTIVES

Part 1: Characterize pharmacokinetics (PK) and immunogenicity of STRO-001

Part 2: Further examine toxicity and tolerability of STRO-001; further examine anti-tumor activity (duration of response (DoR) and progression free survival (PFS)), further assess PK of STRO-001

EXPLORATORY OBJECTIVES

Part 1: Preliminary assessment of anti-tumor activity; correlation of PK with clinical activity; assessment of biomarkers

Part 2: Correlation of PK with clinical activity; assessment of biomarkers

STRO-001-BCM1 STUDY DESIGN

• First-in-human, Phase 1 study in advanced B cell malignancies (BCM)

• Open-label, multicenter, dose escalation study with dose expansion to identify the maximum tolerated dose (MTD) and the recommended phase 2 doses (RP2D)

• Evaluate the safety, tolerability, and preliminary antitumor activity of STRO-001

• Open-label, multicenter, dose escalation study with dose expansion to identify the maximum tolerated dose (MTD) and the recommended phase 2 doses (RP2D)

• Evaluate the safety, tolerability, and preliminary antitumor activity of STRO-001

• Part 1: Dose Escalation- Separate cohorts for MM and NHL

• Part 2: Dose Expansion- Separate cohorts for MM, DLBCL, MCL, FL

• STRO-001 is given by intravenous (IV) infusion on Day 1 and Day 15 of 28 Day Cycles

• Accelerated dose titration followed by 3+3 design in Part 1

DOSE ESCALATION SCHEMA

DOSE ESCALATION SCHEMA

KEY ELIGIBILITY

KEY INCLUSION CRITERIA

- Confirmation of initial diagnosis

- Relapsed or relapsed/refractory disease

- Age ≥ 18 years

- Life expectancy > 3 months

- Adequate bone marrow and renal functions

- QTcF <500 msec

- Ability to comply with treatment, PK and test schedules

- NHL only- at least one measurable lesion

KEY EXCLUSION CRITERIA

- Active plasma cell leukemia and/or leukemic manifestations of lymphoma

- Chronic lymphocytic leukemia and Richter’s transformation, and prolymphocytic leukemia

- Known myeloidosis

- Ongoing immunosuppressive therapy, including systemic corticosteroids

- Sensory or motor neuropathy ≥ grade 2

- Clinically significant cardiac disease

- Positive serology for hepatitis B defined by a positive test for HBsAg

- History or clinical signs of meningeal or active CNS involvement

SIGNIFICANT EXCLUSION CRITERIA

- Significant concurrent, uncontrolled medical condition

- Patients requiring anti-coagulant therapy

ASSESSMENTS

- Chemistry and hematology labs are drawn on a weekly basis for Cycles 1-3, and every two weeks starting with Cycle 4

- Weekly clinical evaluations are conducted during Cycle 1; thereafter, clinical evaluations are conducted on infusion days (Day 1 and Day 15 of each cycle)

- Samples for PK analysis occur at specific times on Days 1, 2, 8, 15, 16, 22, and 29 of treatment and at the end of treatment (EOT) visit

- Tumor assessments are performed at screening, C3, C5, C7 and then every 3 cycles thereafter (C10, C13, etc.) and at EOT

- MM patients: Skeletal survey, bone marrow aspiration/biopsy, (only repeated if needed to confirm a response), FLC and kappa/lambda ratio, M protein

- NHL patients: CT/PET CT scans

STUDY PROGRESS

- The STRO-001-BCM1 study is registered with Clinicaltrials.gov, number NCT03424603

- The study is currently recruiting patients with MM and NHL at the following clinical sites: City of Hope, Duarte CA (Drs. Krishnan and Popplewell); Medical College of Wisconsin, Milwaukee WI (Drs. Shah and Chhabra); Virginia Cancer Specialists Fairfax VA (Dr. Spira); Rocky Mountain Cancer Center Aurora CO (Dr. Burke); Texas Oncology Austin TX (Dr. Melear)

- For more information, please contact STRO-001ClinDev@sutrobio.com or call Shannon Matheny at 650-676-4610

REFERENCES

5. Richter's transformation, and prolymphocytic leukemia
6. Chronic lymphocytic leukemia and Richter’s transformation, and prolymphocytic leukemia
7. Known myeloidosis
8. Ongoing immunosuppressive therapy, including systemic corticosteroids
9. Sensory or motor neuropathy ≥ grade 2
10. Clinically significant cardiac disease
11. Positive serology for hepatitis B defined by a positive test for HBsAg
12. History or clinical signs of meningeal or active CNS involvement
13. Significant concurrent, uncontrolled medical condition
14. Patients requiring anti-coagulant therapy