Preliminary results of a Phase 1 dose escalation study of the first-in-class anti-CD74 antibody drug conjugate (ADC), STRO-001, in patients with advanced B-cell malignancies


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INTRODUCTION

• 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)1-3
• Normal tissues have minimal CD74 expression
• CD74 is rapidly internalized, making it an attractive target for antibody drug conjugates (ADCs)
• STRO-001 is a novel, specific and homogeneous anti-CD74 ADC, containing 2 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 (AP1- and IMA15), NHL diffuse large B-cell (DLBC; SU-DHL-6) and NHL mantle cell lymphoma (Ioma 1, IMW-31) xenograft models in vivo.
• Toxicology studies in cynomolgus monkeys did not produce any unexpected findings; treatment resulted in the intended pharmacodynamic effect, without toxicity.

OBSERVATIONAL (ENDPOINTS)

• Primary Objectives (Endpoints)
  - Dose escalation: Safety & tolerability of STRO-001 (adverse events); Define RP2D (dose limiting toxicities)
  - Dose expansion: Anti-tumor activity of STRO-001 (overall response rate)
• Secondary Objectives (Endpoints)
  - Dose escalation: Characterize pharmacokinetics (PK) and immunogenicity (anti-drug antibodies (ADA))
  - Dose expansion: Toxicity, time to event endpoints, PK (AUC), duration of progression, progression free survival, additional PK
• Exploratory Objectives
  - Dose escalation: Preliminary efficacy, PK correlation with efficacy, biomarkers
  - Dose expansion: Further PK correlation with efficacy, biomarkers

METHODS

STRO-001 BCM1 STUDY DESIGN

• Part 1: Dose Escalation- Separate cohorts for MM and NHL
  - Part 2: Dose Expansion- Separate cohorts for MM, DLBC, NCL, MM.

SUTR-001 is given by IV infusion on Day 1 and Day 15 of 28 day Cycles

CONCLUSIONS

• STRO-001 is the first ADC generated with novel cell-free protein synthesis technology and site-specific conjugation to be tested in the clinic
• STRO-001 has been well tolerated, most AEs are grade 1 or 2.
• No unexpected toxicity signals have been observed
• Two thrombocytopenia DLTs have been observed in 2 patients with very bulky baseline disease (>15 cm).
• Enrollment is ongoing at 0.65 mg/kg in MM cohort and 0.91 mg/kg in NHL cohort.
• Preliminary PK profile in 3 patients reveals an estimated half-life for total antibody of 37-47 hours.
• Anti-drug antibodies (ADA) have not been detected.
• Preliminary anti-tumor activity (1 L and 1 PR) has been observed in two patients with DLBC.

REFERENCES

1. Stutro et al., Nature Medicine, 2017