Tumor uptake and dose-proportional PK of ST101 - a peptide antagonist of C/EBPβ – in patients with advanced unresectable and metastatic solid tumors


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ST101 novel mechanism of action
- Target (C/EBPβ) is prognostic and widely expressed in many cancers leading to tumor specificity
- Crosses the blood brain barrier
- Down-regulates genes involved in survival, proliferation, and de-differentiation
- Broad-spectrum preclinical activity
- Potential treatment of solid and hematological malignancies

ST101 MoA
- ST101 enters cells and antagonises C/EBPβ, abrogating cell survival
- ST101 disrupts the interaction of C/EBPβ and its target, degrading growth factor receptor signaling and blocking tumor cell death
- ST101 enters cells and antagonises C/EBPβ, abrogating cell survival

Study status
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- ST101 detected in post-infusion tumor biopsies
- A: Pretreatment
- B: Cycle 2 post-treatment

PK is dose-proportional with no accumulation
- ST101 Pharmacokinetics: Panel A shows ST101 plasma concentrations across all three cohorts for Cycle 1 (EOI to 72 hrs post EOI) and Cycle 2 (EOI to 8 hrs post EOI). Mean C_{max} and AUC_{0-4} were comparable between Day 1 of Cycles 1 and 2 in all three cohorts. Mean C_{max} and AUC_{0-4} increased slightly higher than dose proportions across cohorts. Mean T_{1/2} decreased slightly from 14.6 to 11.5 hours across the three cohorts. In addition, ST101 monotherapy was generally well tolerated across all cohorts with no significant accumulation of ST101.

Minimal AEs are infusion related
- AEs Observed by Cohort
- Management of IRRs

Conclusions
- Study is enrolling well in Cohort 4 at 4 mg/kg
- Encouraging safety profile
- No AEs or ST101-related AEs
- Most common AEs are manageable G1-2 IRRs
- Itch and urticaria
- Positive pharmacologic characteristics
- PK is dose-proportional with no significant accumulation
- ST101 uptake detected in tumor biopsies by IHC
- Early indications of decreased tumor cell proliferation post ST101
- Evidence of long-lasting stable disease