Efficacy, safety, pharmacokinetic and pharmacodynamic data from phase 1 dose escalation of a novel therapeutic peptide, ST101, targeting the oncogenic transcription factor C/EBPβ, in patients with advanced and metastatic solid tumors

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ST101 novel mechanism of action

- ST101 disrupts the interaction of C/EBPβ with cofactors such as AT5, depleting cells of oncogenic signals they are dependent upon and resulting in selective tumor cell death.
- PK is dose-proportionate with no accumulation

Cohort 4, Cycle 1

Study status

Enrollment Status. Seven of 21 enrolled patients are ongoing. One patient had a confirmed PR at week 3, two patients had SD at the week one assessment, one patient had SD but went to week 40, and six patients have not been assessed to date. Thirteen patients progressed while on study and one patient discontinued treatment to pursue surgery.

ST101 detected in post-infusion tumor biopsies

- U251 cells were exposed to 300 nM ST101 for 5 minutes. Cell and nuclear penetration was assessed by IF staining using a rabbit polyclonal antibody against ST101.
- ST101 is detected in post-infusion biopsies: Immunohistochemistry was performed on tumor biopsy specimens obtained during screening or within 24 hours of ST101 exposure in Cycle 2. Panel A represents a pre-treatment biopsy. Panel B represents a post-treatment biopsy in cycle 2. All biopsies were obtained in cohort 4 (4 mg/kg). Brown indicates ST101 immunostaining; blue represents hematoxylin counterstain. Early indication of decreased tumor cell proliferation post-ST101 (data not shown).

PK is dose-proportionate with no accumulation

Majority of AEs are infusion related

- slowness of infusion rate
- Infusion interruptions
- Fatigue
- Rash
- Hypophosphatemia

Most AEs were IRRs (G1-2) IRRs are effectively managed by:
- Slowing infusion rate
- H1/H2 antagonists
- Leukotriene antagonist (montelukast)

Conclusions

- Positive pharmacologic characteristics:
  - Modeling supports the use of flat dosing
  - PK is dose-proportional with no significant accumulation
  - ST101 uptake detected in tumor biopsies
  - Modeling supports the use of flat dosing

Study is enrolling well in Cohort 6 at 9 mg/kg

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  - No DLTs or ST101-related SAEs

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