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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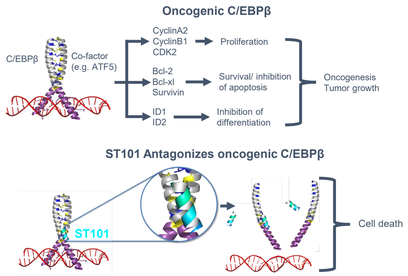
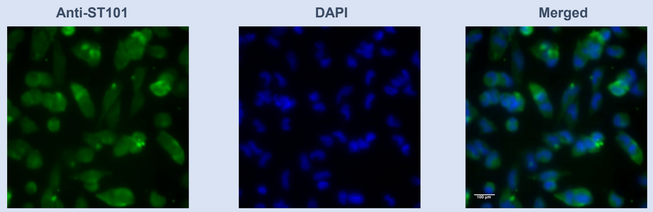
ST101 novel mechanism of action



- Target (C/EBPβ) is prognostic and widely expressed in many cancers
- Down-regulates genes involved in survival, proliferation, and de-differentiation
- Broad-spectrum, tumor-specific preclinical activity in solid and hematological cancers
- Crosses the blood brain barrier

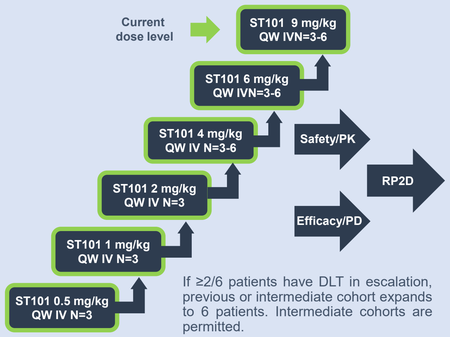
- ST101 disrupts the interaction of C/EBPβ with cofactors such as ATF5, depriving cells of oncogenic signals they are dependent upon and resulting in selective tumor cell death.



- 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.

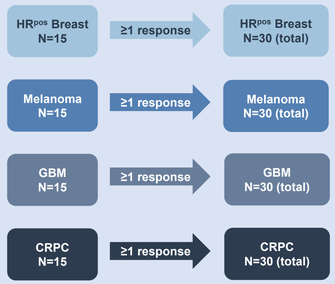
Study design

Phase 1: Dose Escalation

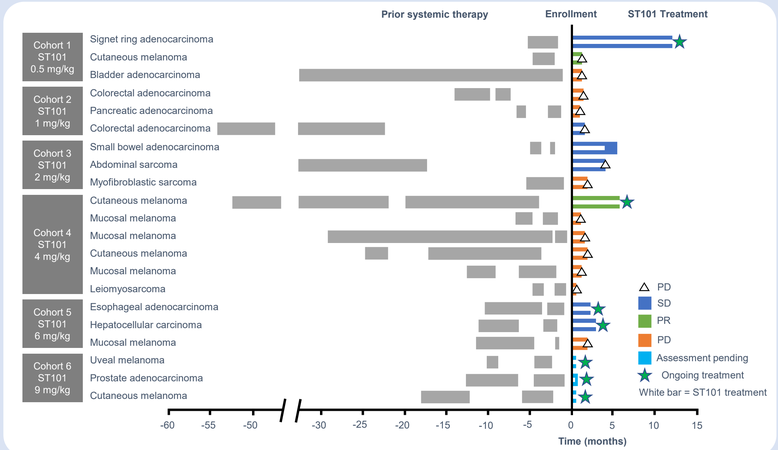


If ≥2/6 patients have DLT in escalation, previous or intermediate cohort expands to 6 patients. Intermediate cohorts are permitted.

Phase 2: Dose Expansion

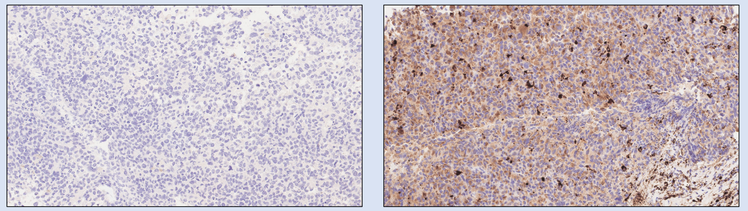


Study status



Enrollment Status. Seven of 21 enrolled patients are ongoing. One patient had a confirmed PR at week 23, two patients had SD at the week nine assessment, one patient had SD out to week 45, and three 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



A. Pretreatment B. Cycle 2 post-treatment

ST101 is detected in post-infusion biopsies: ST101 is detected in post-infusion biopsies: Immunohistochemistry was performed on tumor biopsy specimen obtained during screening or within 24 hours of ST101 exposure in Cycle 2. Panel A represents a pretreatment 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)

AEs = adverse events; C/EBPβ = CCAAT/enhancer-binding protein β; CRPC = castration resistant prostate cancer; DLT = dose-limiting toxicity; EOI = end of infusion; GBM = glioblastoma multiforme; HRpos = hormone receptor positive; IRR = infusion-related reaction; IV = intravenous; MoA = mode of action; PD = pharmacodynamic PK = pharmacokinetic; PR = partial response, QW = once weekly; RP2D = recommended Phase 2 dose; SAE = serious adverse event, SD = stable disease

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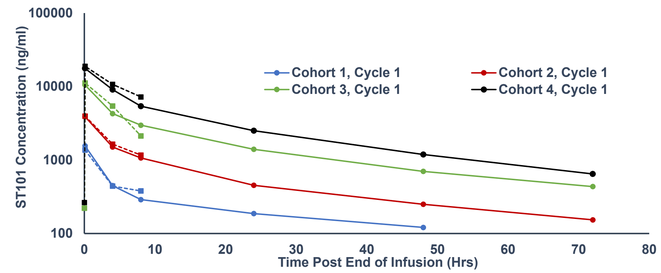
PK is dose-proportionate with no accumulation



ST101 Pharmacokinetics: Mean C_{max} and $AUC_{(0-t)}$ were comparable between Day 1 of Cycles 1 and 2 in the first four cohorts. Mean C_{max} and $AUC_{(0-inf)}$ increased slightly higher than dose proportional between cohorts. Mean T1/2 where calculable was 18 to 41.2 hours across cohorts. Data indicates no significant accumulation of ST101.

Majority of AEs are infusion related

Adverse event	DL1 (n=3)	DL2 (n=3)	DL3 (n=3)	DL4 (n=6)	DL5 (n=3)	DL6 (n=3)	All (%)
IRR symptoms	1	2	3	5	2	3	67
Anorexia	1	1	-	-	1	1	19
Nausea	-	1	-	3	-	-	19
Vomiting	1	-	-	2	1	-	19
Fatigue	1	1	-	-	-	-	10
Dehydration	1	-	1	-	-	-	10
Headache	1	-	-	-	1	-	10
Hypophosphatemia	-	-	-	1	-	1	10

Most AEs were IRRs (G1-2) IRRs are effectively managed by:

- Slowing infusion rate
- Infusion interruptions
- H1/H2 antagonists
- Leukotriene antagonist (montelukast)

Conclusions

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

Encouraging safety profile

- No DLTs or ST101-related SAEs
- Most common AEs are manageable G1-2 IRRs
- Pruritus and urticaria

PR observed in a cutaneous melanoma patient with evidence of long-lasting stable disease up to 1 year across various tumor types

Positive pharmacologic characteristics:

- Modeling supports the use of flat dosing
- 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

Study sponsored by Sapience Therapeutics Inc.
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Presenting author disclosure

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