

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

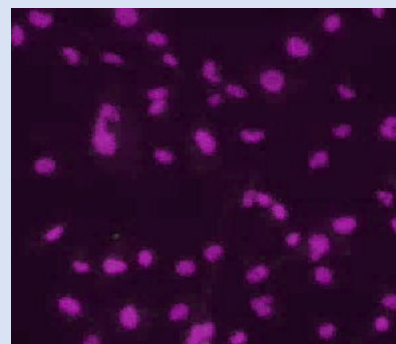
Falchook G, McKean M, Lakhani N, Arkenau T, Symeonides S, Evans J, Lim E, Rotolo J, Michel R, Bexon A.

Sarah Cannon Research Institute at HealthONE, Denver, CO, Sarah Cannon Research Institute, Tennessee Oncology, Nashville, TN, START Midwest, Grand Rapids 49546, MI, Sarah Cannon UK and UCL, London, United Kingdom, Edinburgh Cancer Research Centre, MRC Institute of Genetics and Molecular Medicine, University of Edinburgh, Edinburgh, United Kingdom, University of Glasgow, Beatson West of Scotland Cancer Centre, Glasgow, United Kingdom, Division of Hematology and Oncology, Herbert Irving Comprehensive Cancer Center, Columbia University Medical Center, New York, NY, Sapience, Harrison, NY, Bexon Clinical Consulting, Montclair, NJ

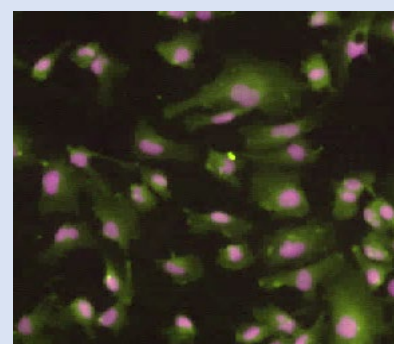
Abstract: LB114

ST101 novel mechanism of action

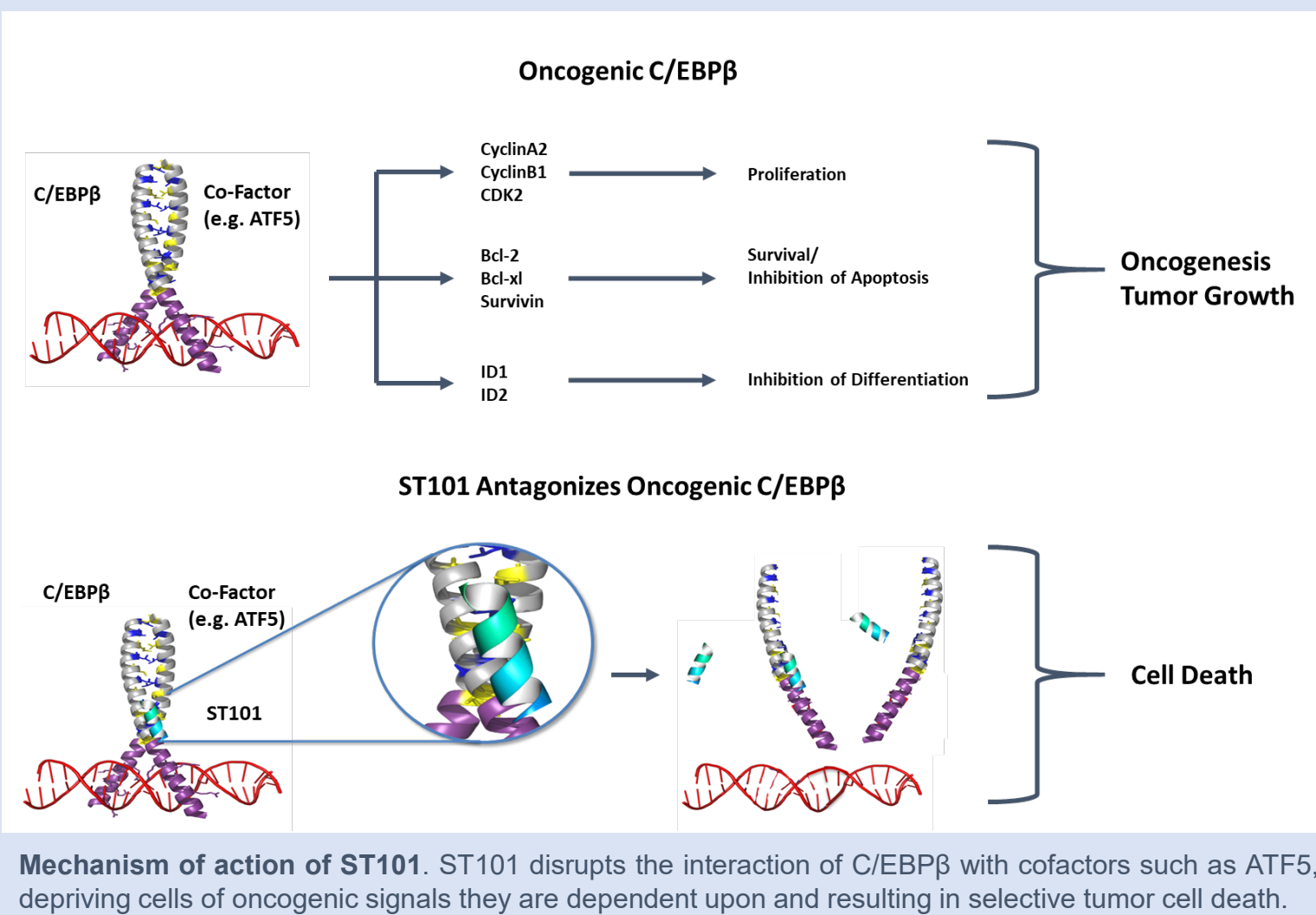
- Target (C/EBPβ) is prognostic and widely expressed in many cancers leading to tumor specific activity
- Crosses the blood brain barrier
- Down-regulates genes involved in survival, proliferation, and de-differentiation
- Broad-spectrum preclinical activity
- Potential treatment of solid and hematological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



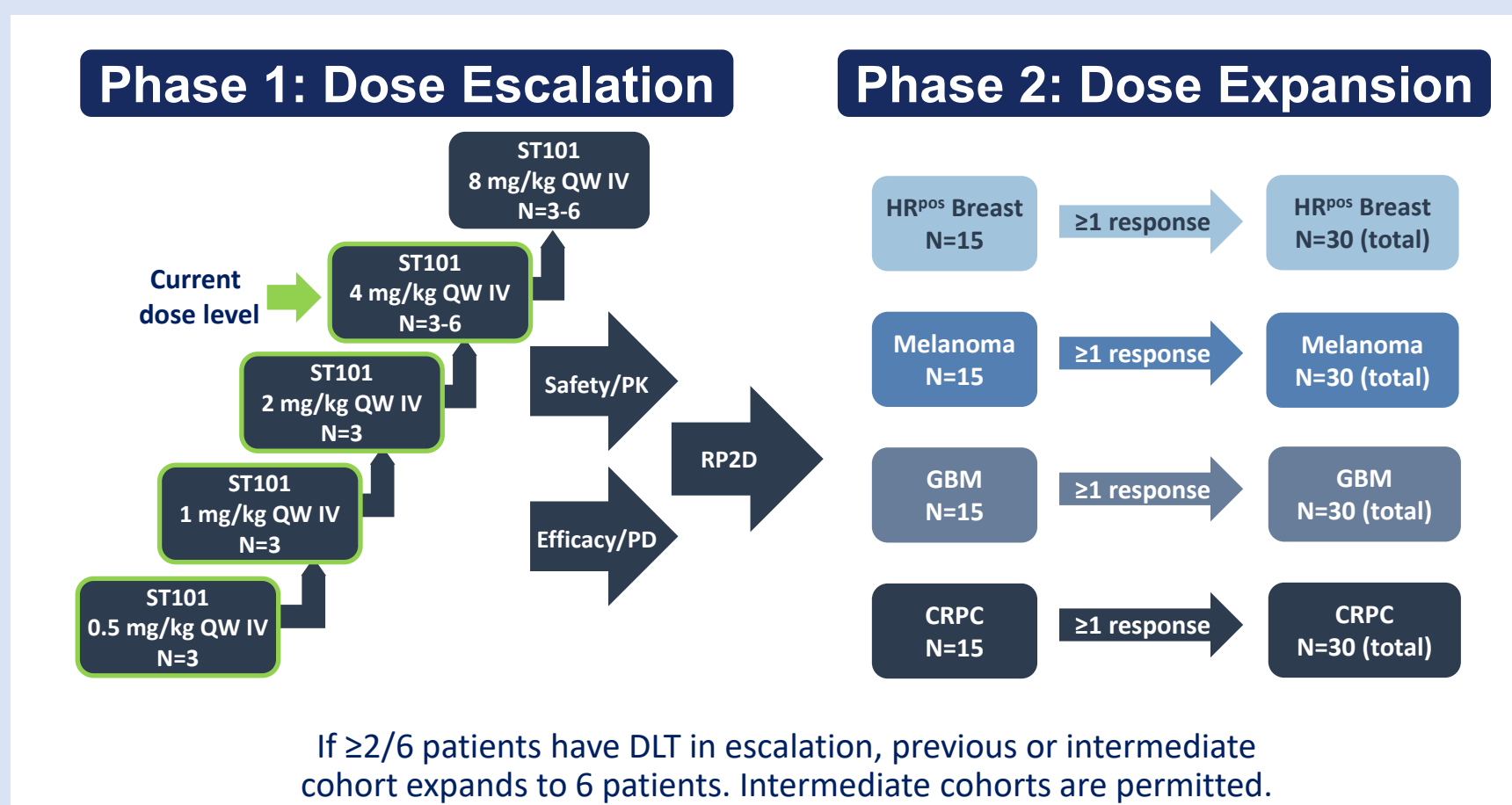
ST101 enters cells and antagonizes C/EBPβ activation: A) U251 cells were exposed to 300 nM ST101 for 5 minutes. Cell and nuclear penetration was assessed by IF staining using a rabbit polyclonal antibody against ST101. DAPI shown in purple and ST101 shown in green.



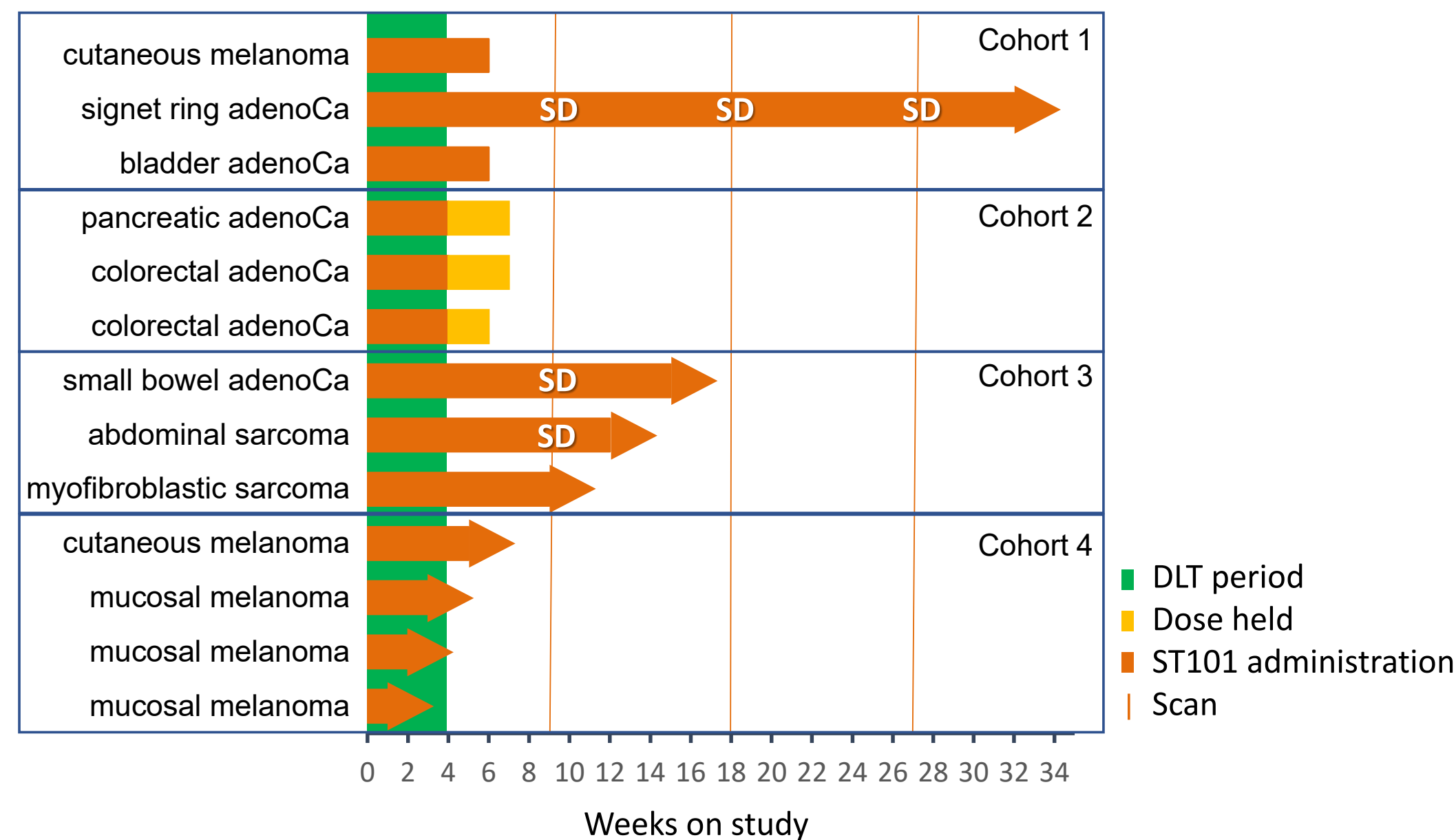
ST101 MoA



Study design

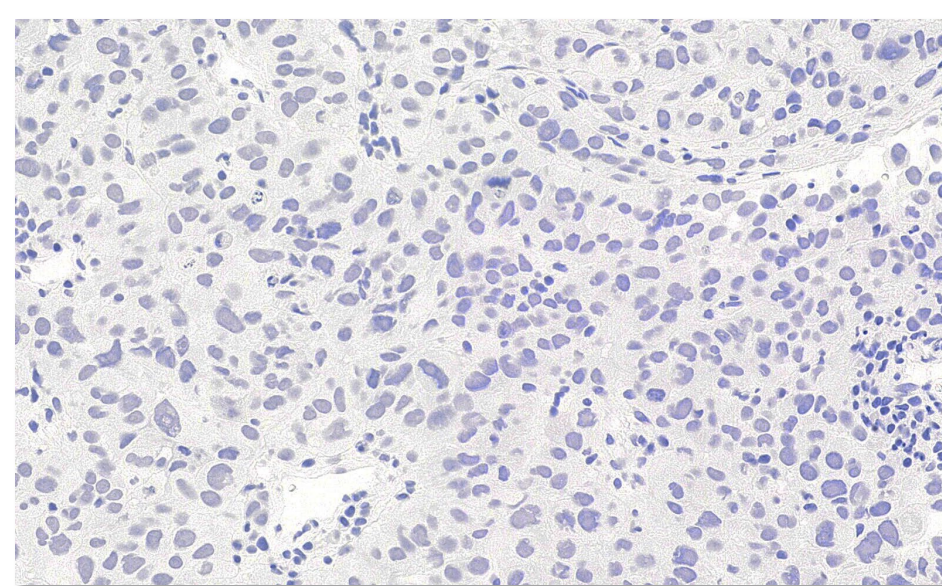


Study status

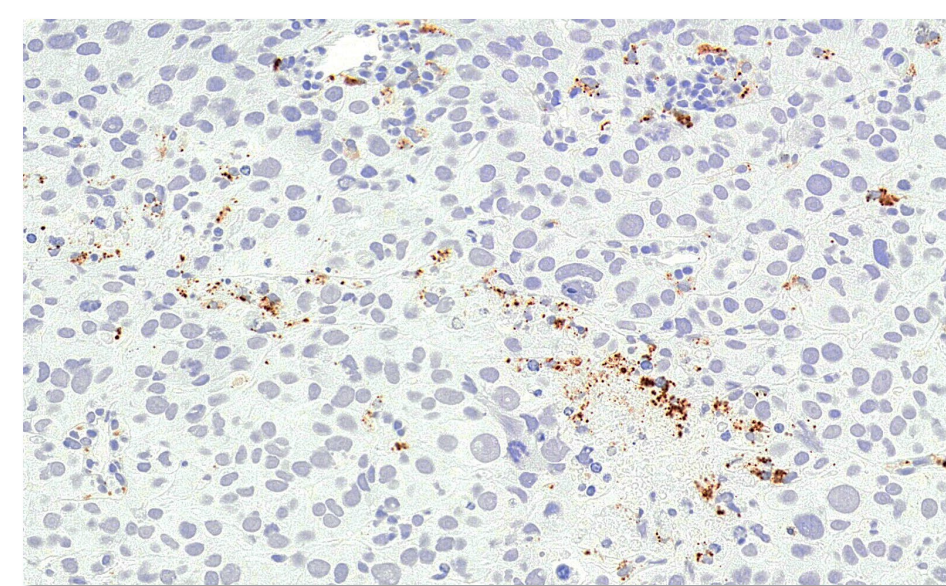


Enrollment Status. One patient has been enrolled for 29 weeks and continues to do well. Three patients had stable disease at the week nine assessment with one patient having stable disease out to week 27. Five patients progressed while on study and three patients have not been assessed to date.

ST101 detected in post-infusion tumor biopsies



A: Pretreatment



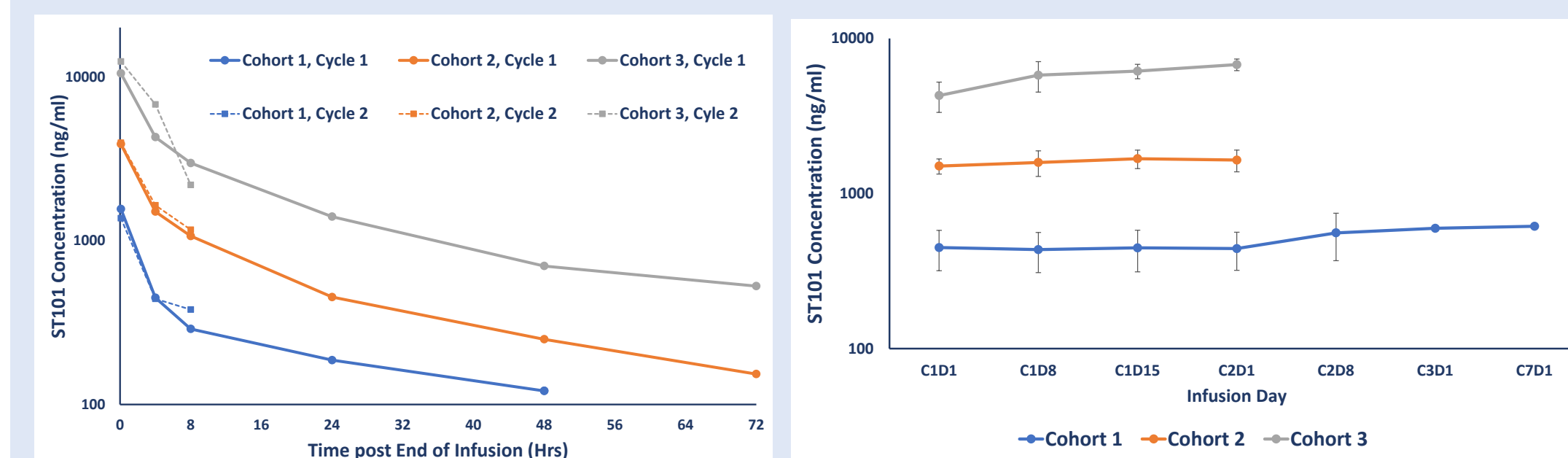
B: Cycle 2 post-treatment

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 hrs 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 1 (0.5 mg/kg). Brown indicates ST101 immunostaining; blue represents hematoxylin counterstain.

ADAs = anti-drug antibodies; AEs = adverse events; C/EBPβ = CCAAT/enhancer-binding protein β
CRPC = castrate-resistant prostate cancer; DLT = dose-limiting toxicity; EO1 = end of infusion; GBM = glioblastoma multiforme
HR^{pos} = hormone receptor positive; IRR = infusion-related reaction; MoA = mode of action; PD = pharmacodynamic
PK = pharmacokinetic; SD = stable disease

Contact information: abexon@sapiencetherapeutics.com

PK is dose-proportionate with no accumulation



ST101 Pharmacokinetics: Panel A represents ST101 mean plasma concentrations across all three cohorts for Cycle 1 (EO1 to 72 hrs. post EO1) and Cycle 2 (EO1 to 8 hrs. post EO1). Mean C_{max} and $AUC_{(0-1)}$ were comparable between Day 1 of Cycles 1 and 2 in all three Cohorts. Mean C_{max} and $AUC_{(0-1)}$ increased slightly higher than dose proportional between cohorts. Mean T_{1/2} where calculable was 18 to 31 hours across the three cohorts. Panel B represents ST101 mean plasma concentrations at 4 hrs. post EO1 across all three cohorts at each dosing interval. Data indicates no significant accumulation of ST101.

Minimal AEs are infusion related

AE	DL1 (n=3)	DL2 (n=3)	DL3 (n=3)	DL4 (n=4)	All (%)
IRR symptoms	1	2	2	4	69
Fatigue	1	1	-	-	15
Dehydration	1	-	1	-	15
Anorexia	-	1	-	-	8
Diarrhea	-	1	-	-	8
Nausea	-	1	-	-	8
Pain	-	1	-	-	8
Weakness	-	1	-	-	8
Lymphopenia	-	-	-	1	8
Hypoalbuminemia	-	-	-	1	8

Measure	DL1 (n=3)	DL2 (n=3)	DL3 (n=3)	DL4 (n=4)	All (%)
Antihistamines	1	1	2	4	62
Acetaminophen/paracetamol	-	1	2	4	54
Corticosteroids	-	-	2	4	46
Interrupted infusion	-	-	2	4	46
Slowed infusion	-	-	2	4	46
NSAIDs	-	2	-	-	15

Management of IRRs

AEs Observed by Cohort

Conclusions

- Study is enrolling well in Cohort 4 at 4 mg/kg
- Encouraging safety profile
 - No DLTs or ST101-related SAEs
 - 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