SCRX 6 & 7- Studying Efficacy & Biodistribution on NOD/SCID mice

Background

Topic of interest: Lung tumors in mice [PDX- (or LU124) & PDX+ (or LU95)]

Treatment available now: PBD (Pyrrolobenzodiazepine)

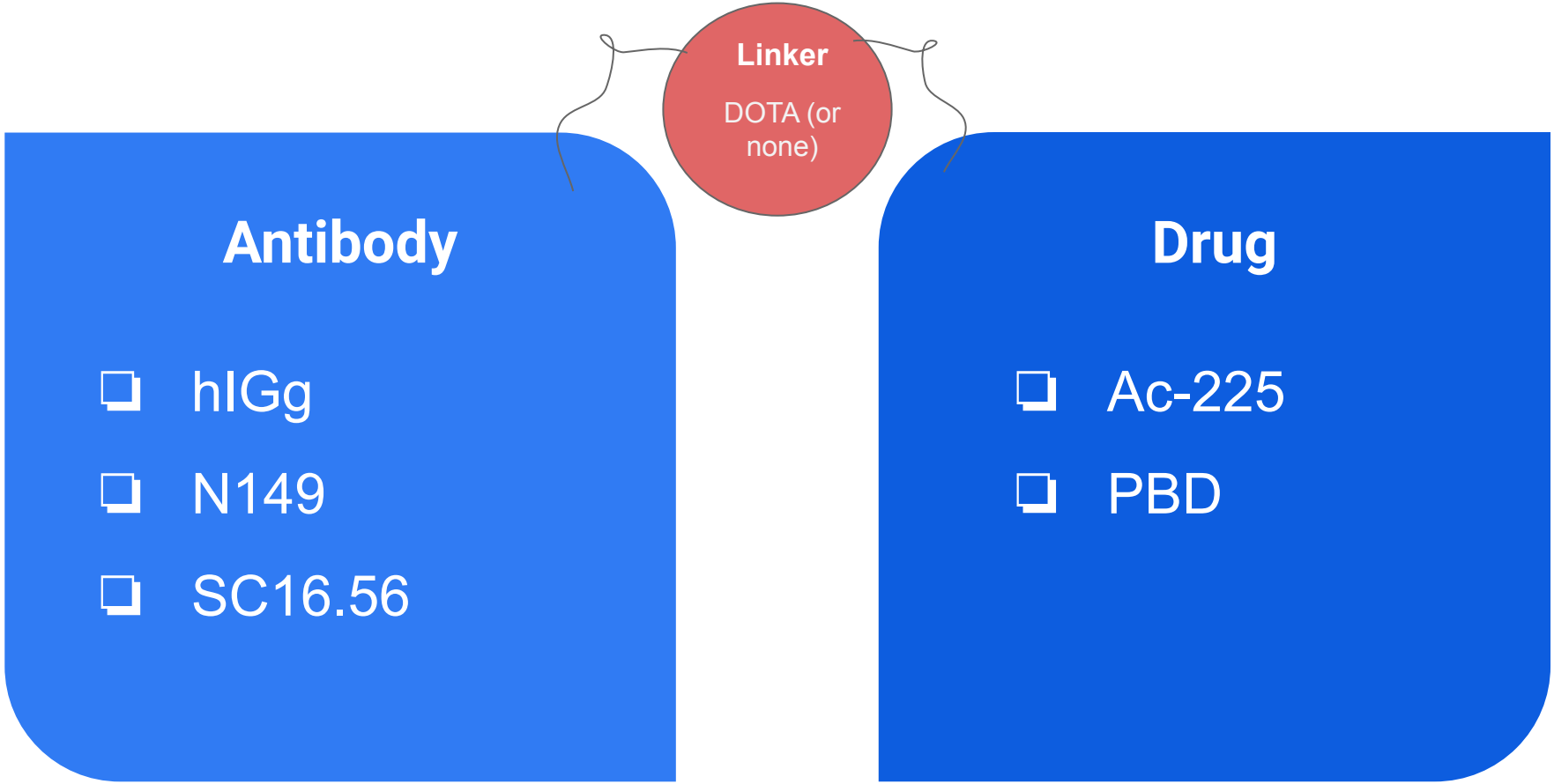
- May be toxic to kidneys
- Effective against cells expressing the DLL3 proteins
    - PDX+ has a higher expression of DLL3 compared to PDX-*

*Saunders LR, Bankovich AJ, Anderson WC, Aujay MA, Bheddah S, Black K, et al. A DLL3-targeted antibody-drug conjugate eradicates high-grade pulmonary neuroendocrine tumor-initiating cells in vivo. Science translational medicine. 2015 Aug 26;7(302):302ra136-302ra136.

Potential Solution, Experimental Setup

Actinium-225

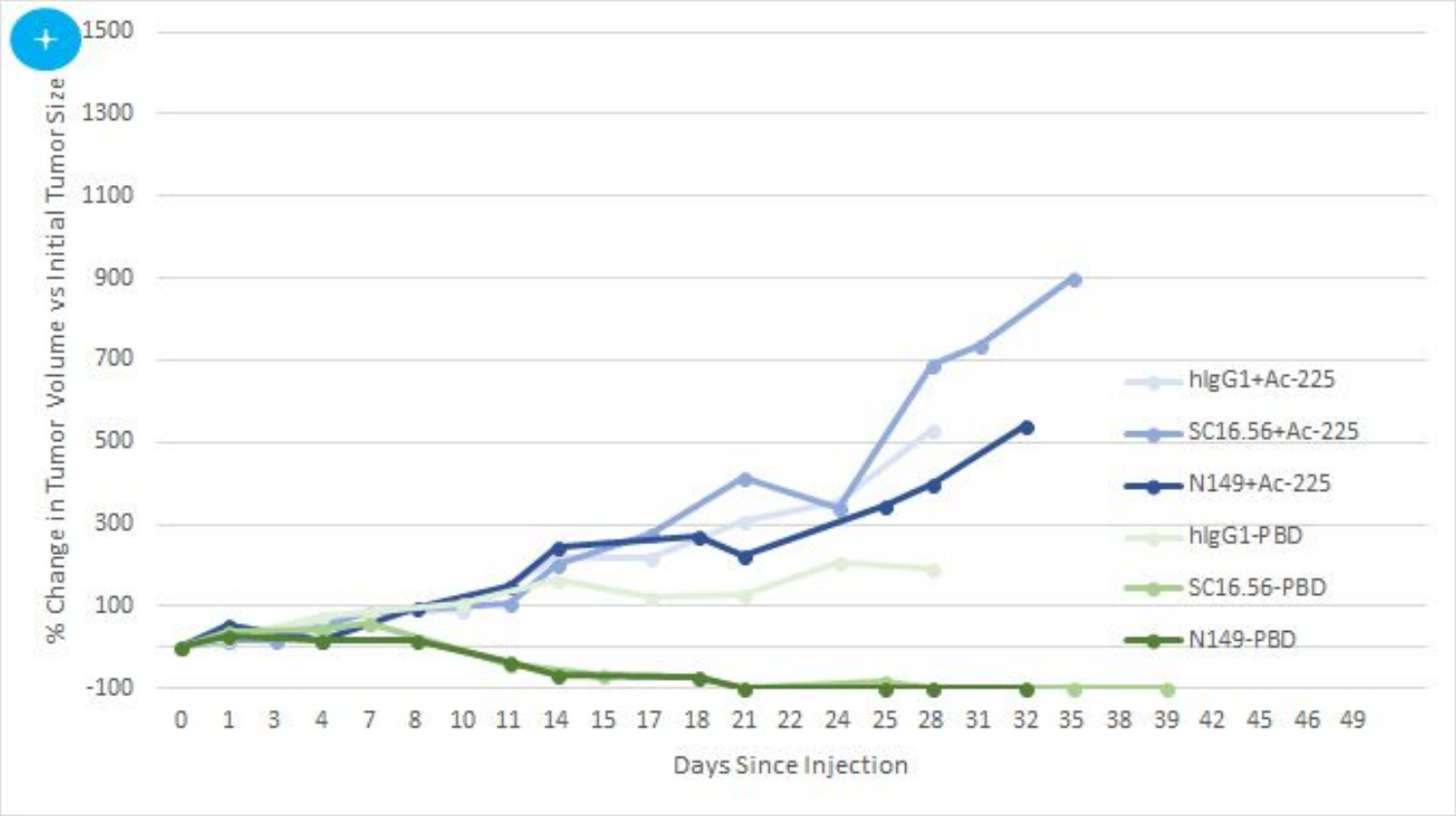
- Radioactive alpha emitter
- High LET
- Short half life
- Experimental groups injected with Actinium, control groups injected with PBD


Linker
DOTA (or none)
Antibody
hIGg
N149
SC16.56
Drug
Ac-225
PBD

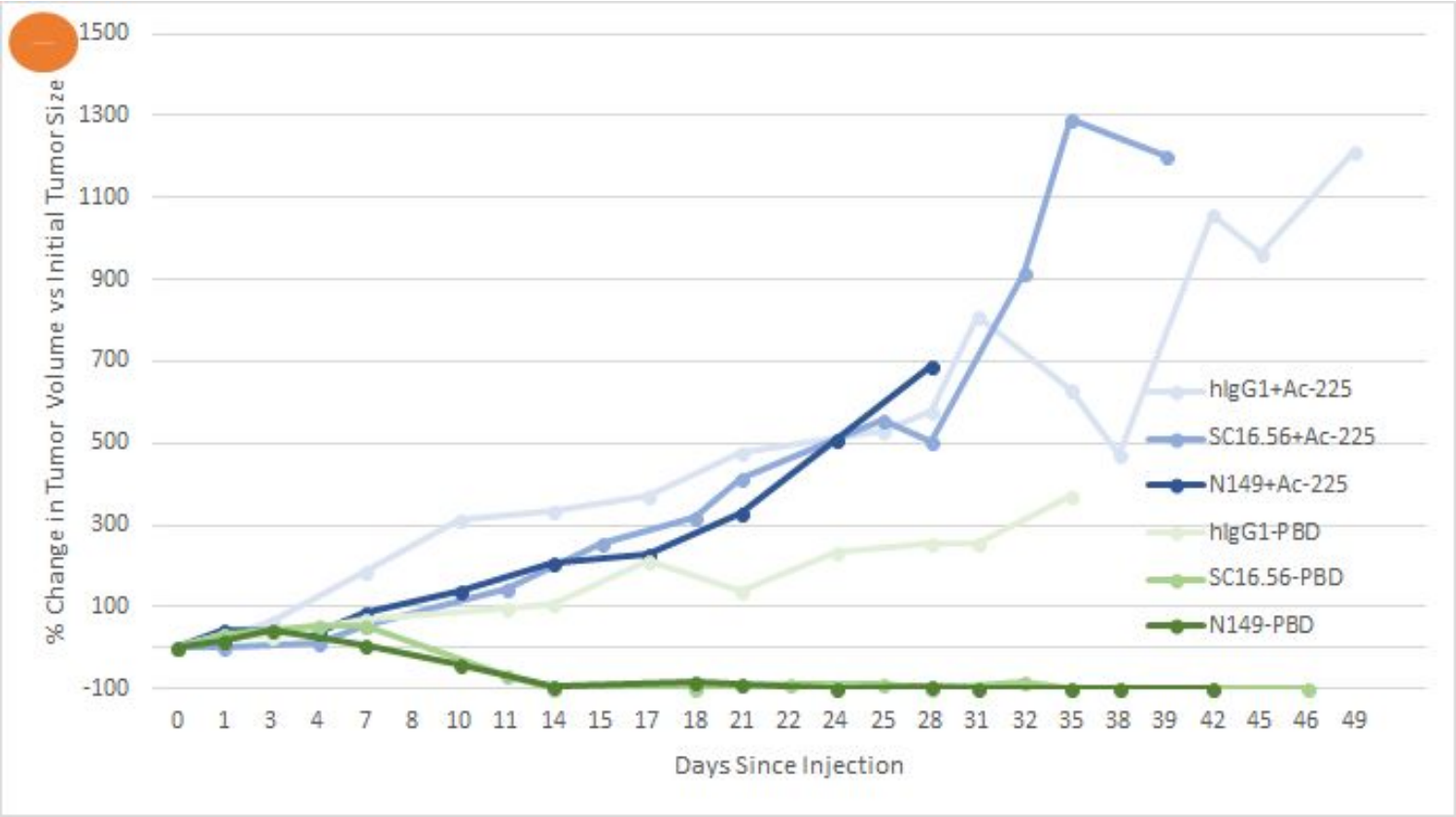
SCRX 6: Efficacy

Will ADCs work on lung tumors in mice?

How were PDX+ tumors affected by treatments?



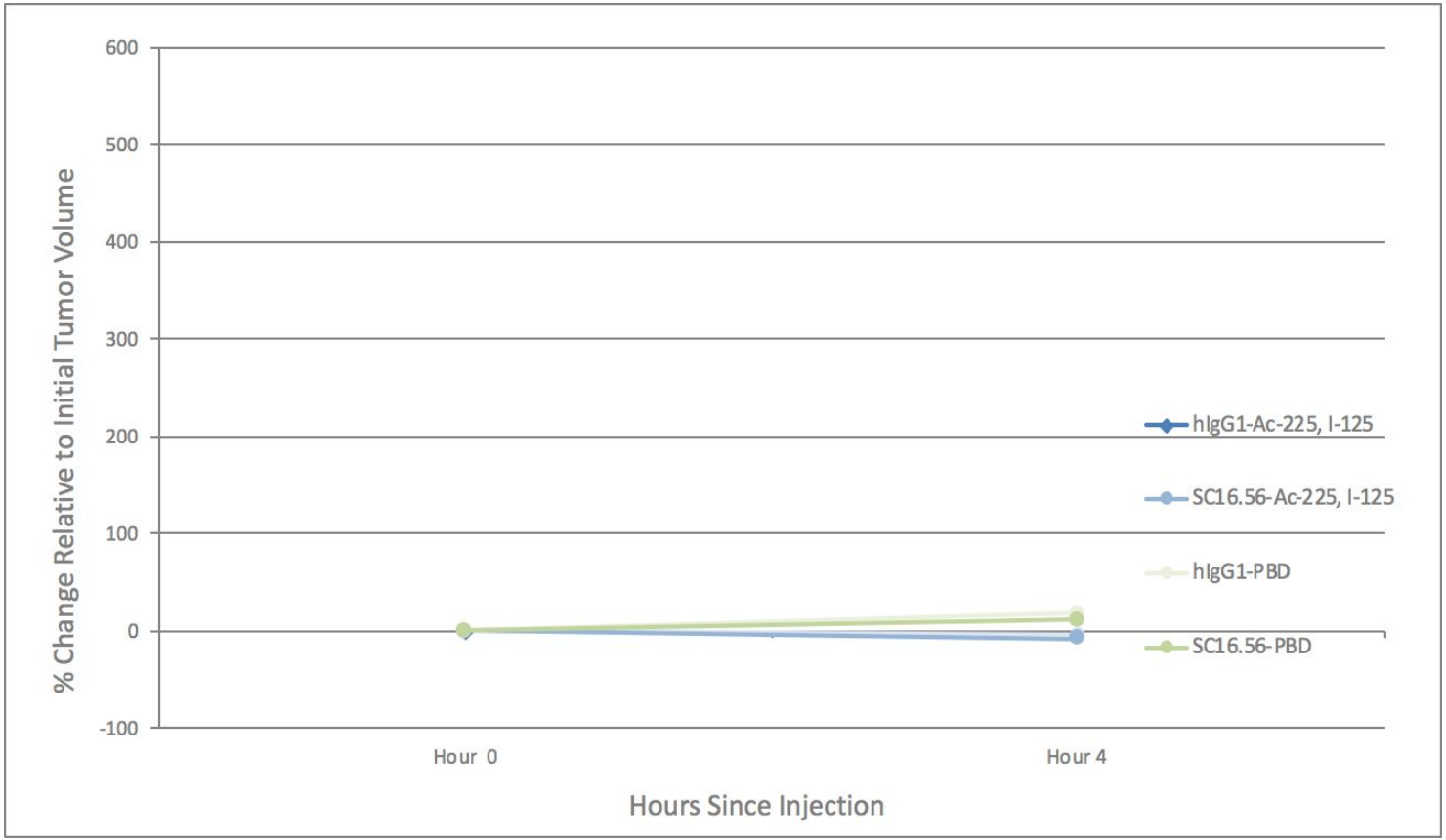
How did PDX- tumors respond differently?



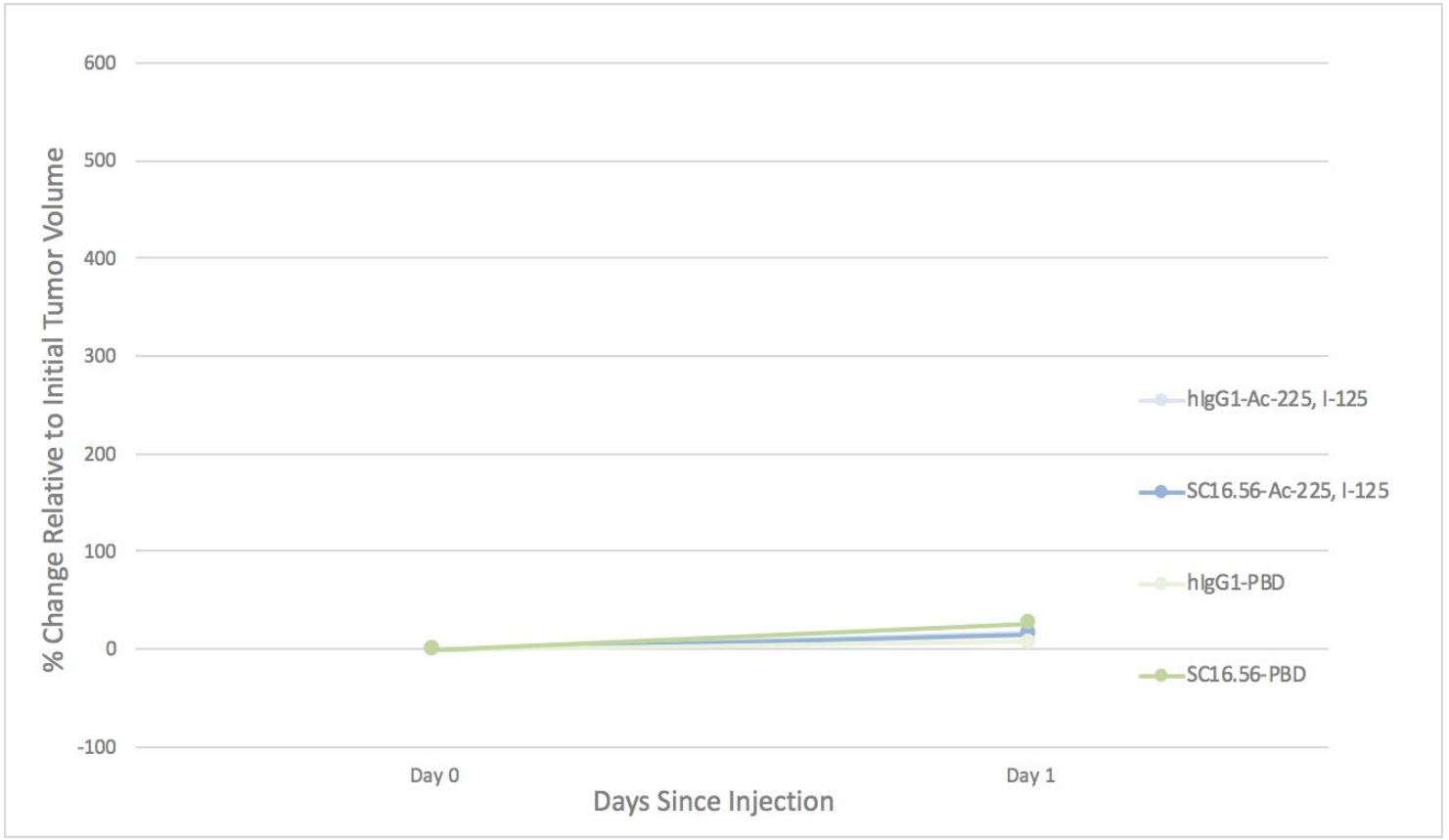
SCRX 7: Biodistribution

Where do ADCs go in PDX+ mice?

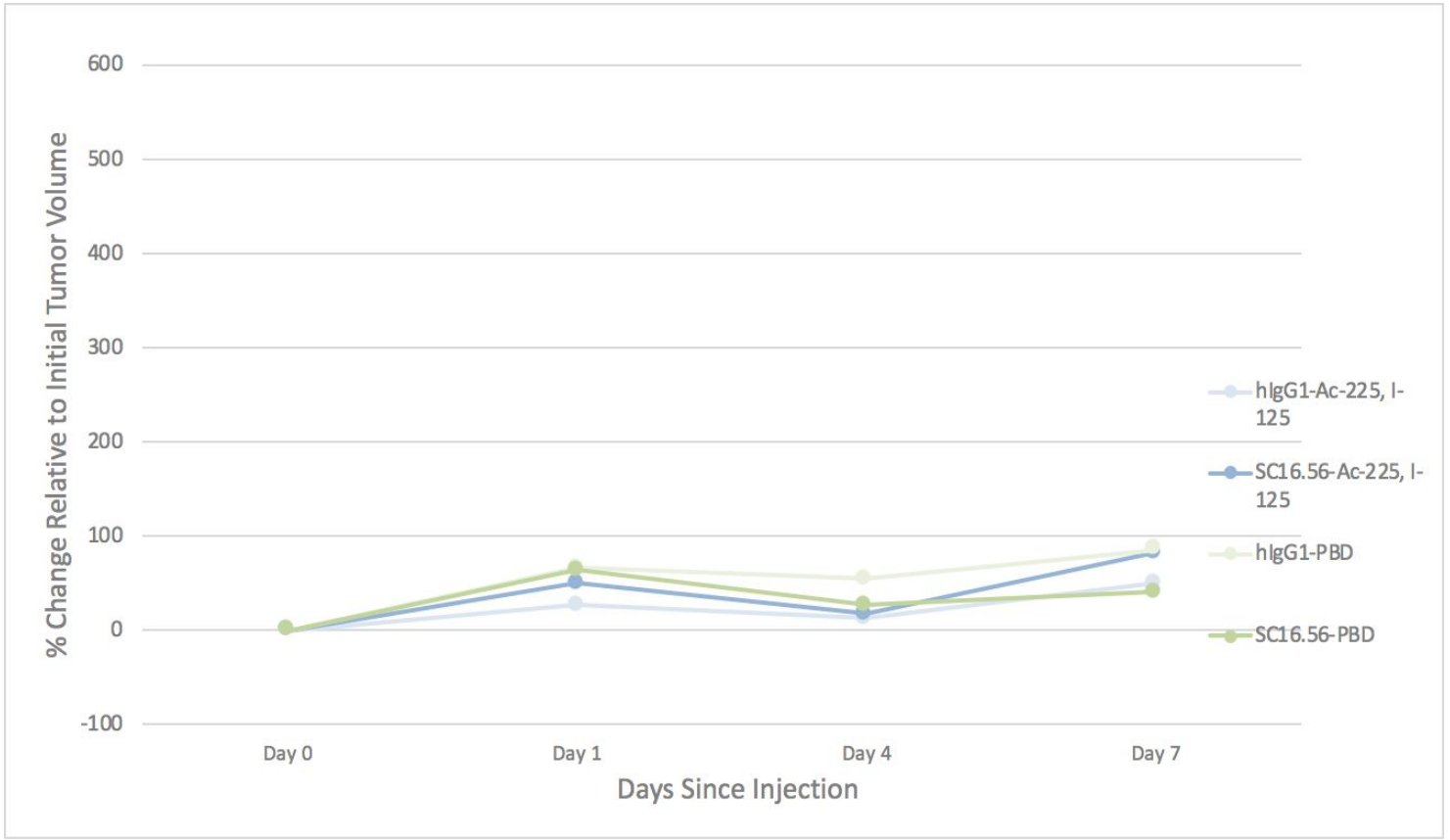
4 Hour Group


600
500
400
300
200
100
0
-100
% Change Relative to Initial Tumor Volume
Hour 0
Hour 4
Hours Since Injection
hIgG1-Ac-225, I-125
SC16.56-Ac-225, I-125
hIgG1-PBD
SC16.56-PBD

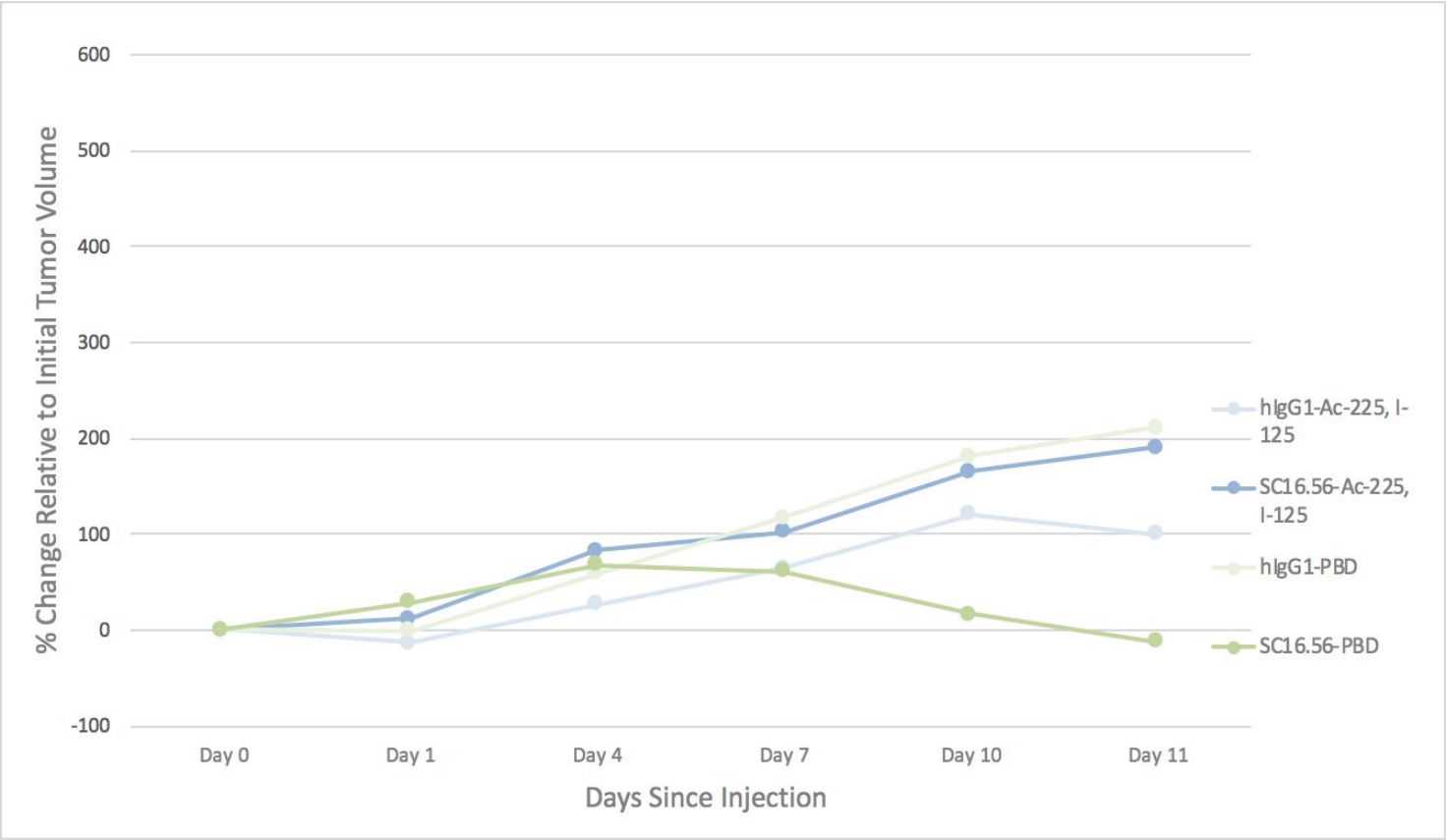
1 Day Group


600
500
400
300
200
100
0
-100
% Change Relative to Initial Tumor Volume
Day 0
Day 1
Days Since Injection
hIgG1-Ac-225, I-125
SC16.56-Ac-225, I-125
hIgG1-PBD
SC16.56-PBD

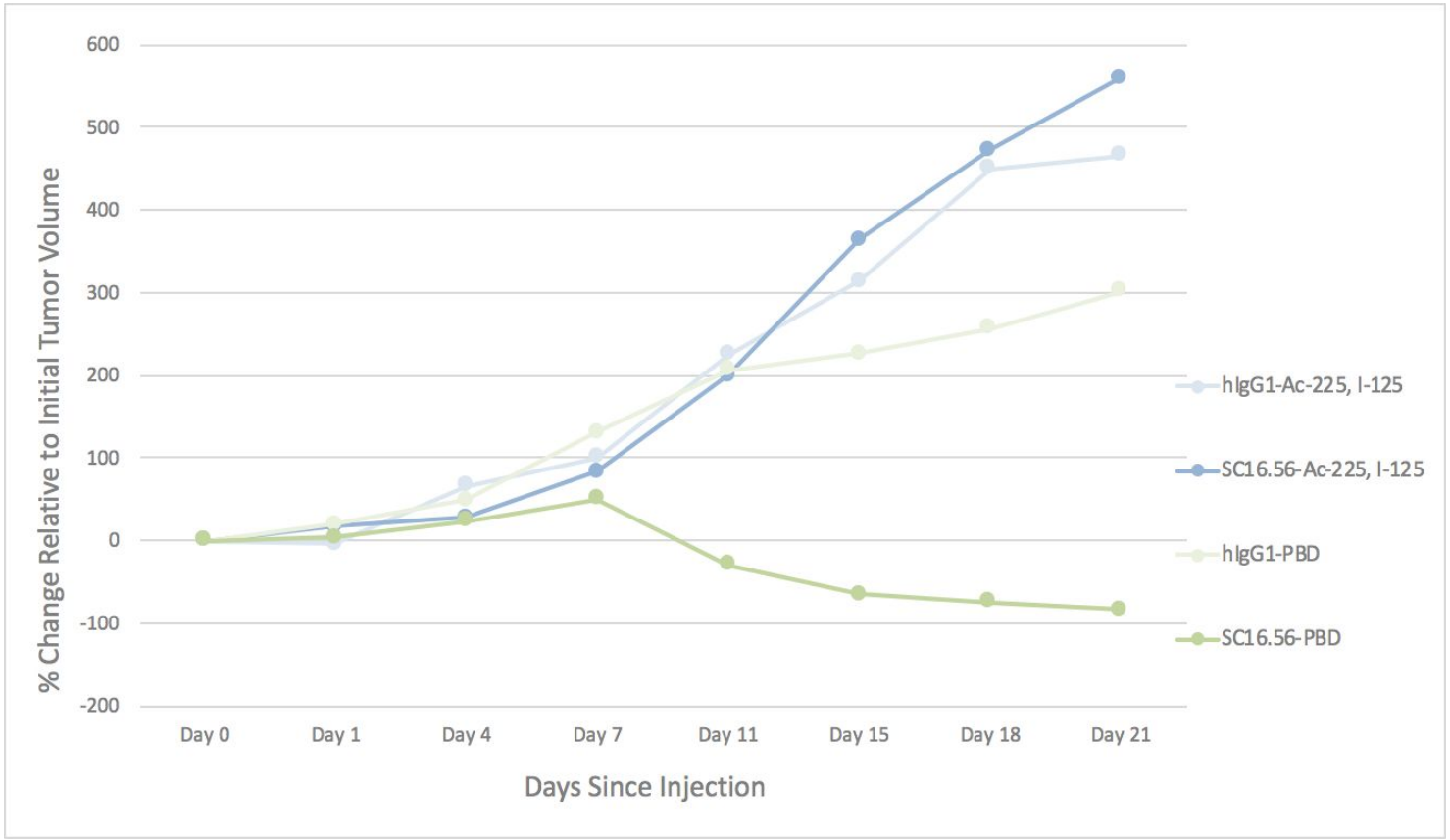
6 Day Group


600
500
400
300
200
100
0
-100
% Change Relative to Initial Tumor Volume
Day 0
Day 1
Day 4
Day 7
Days Since Injection
hIgG1-Ac-225, I-125
SC16.56-Ac-225, I-125
hIgG1-PBD
SC16.56-PBD

10 Day Group


600
500
400
300
200
100
0
-100
% Change Relative to Initial Tumor Volume
Day 0
Day 1
Day 4
Day 7
Day 10
Day 11
Days Since Injection
hIgG1-Ac-225, I-125
SC16.56-Ac-225, I-125
hIgG1-PBD
SC16.56-PBD

20 Day Group


600
500
400
300
200
100
0
-100
-200
% Change Relative to Initial Tumor Volume
Day 0
Day 1
Day 4
Day 7
Day 11
Day 15
Day 18
Day 21
Days Since Injection
hIgG1-Ac-225, I-125
SC16.56-Ac-225, I-125
hIgG1-PBD
SC16.56-PBD

SUMMARY

- Efficacy:
  - Controls are working
  - Actinium-225 doesn't seem to be working
  - Tumor sizes similar initially
  - Similar results across PDX+ and PDX- tumors

- Biodistribution:
  - SC 16.56-PBD works best in the long-term
  - Results of dissected organs in progress

FIN