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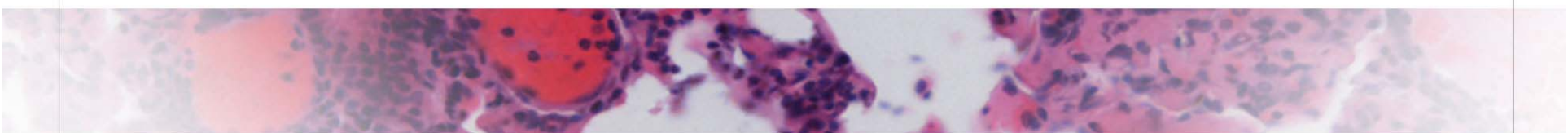

Preliminary Results of a Phase 1 Study of Flotetuzumab, a CD123 x CD3 Bispecific DART® Protein, in Patients with Relapsed/Refractory Acute Myeloid Leukemia and Myelodysplastic Syndrome

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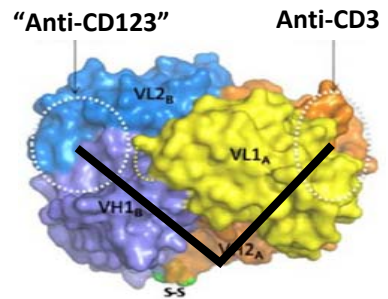
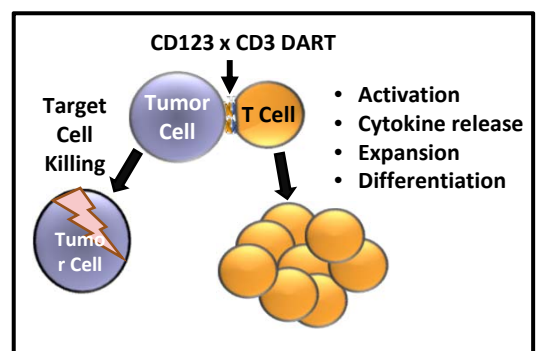
**Equal contribution*

Flotetuzumab: CD123 x CD3 Bispecific DART Protein

- DART bispecific platform
  - Multiple applications across different diseases
  - Predictable manufacturability
  - Long-term stability
  - Ability to tailor half-life and valency



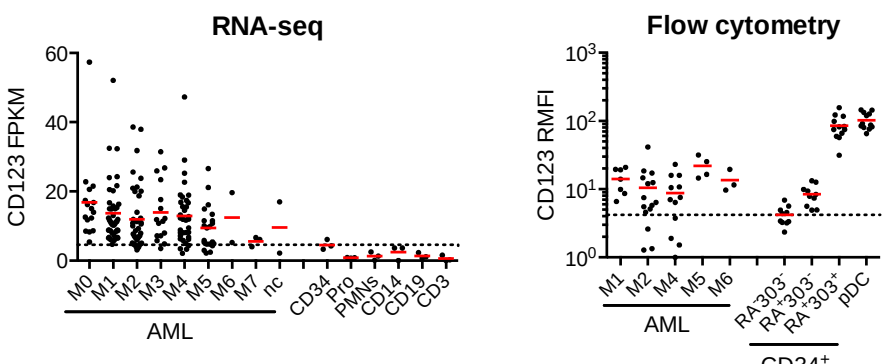
- Optimal variable light and heavy chain pairing allows for tighter conformation and closer proximity between effector (CD3+) cells and target (CD123+) cells
- Flotetuzumab (MGD006/S80880) mode of action: redirected T-cell killing of CD123+ Cells



Root, et al. Antibodies 2016, 5, 6
Chichili, et al. Sci Transl Med. 2015 May 27;7(289)

IL-3 Receptor α (IL-3Rα): CD123

- Low affinity ligand binding subunit of IL-3R
- Binds IL-3 and heterodimerizes with common β subunit of GM-IL-5-IL-3 receptor complex to induce proliferative and anti-apoptotic signaling
- Differentially overexpressed in 93% of AML patients
- Correlation between CD123+ cells frequency and prognosis

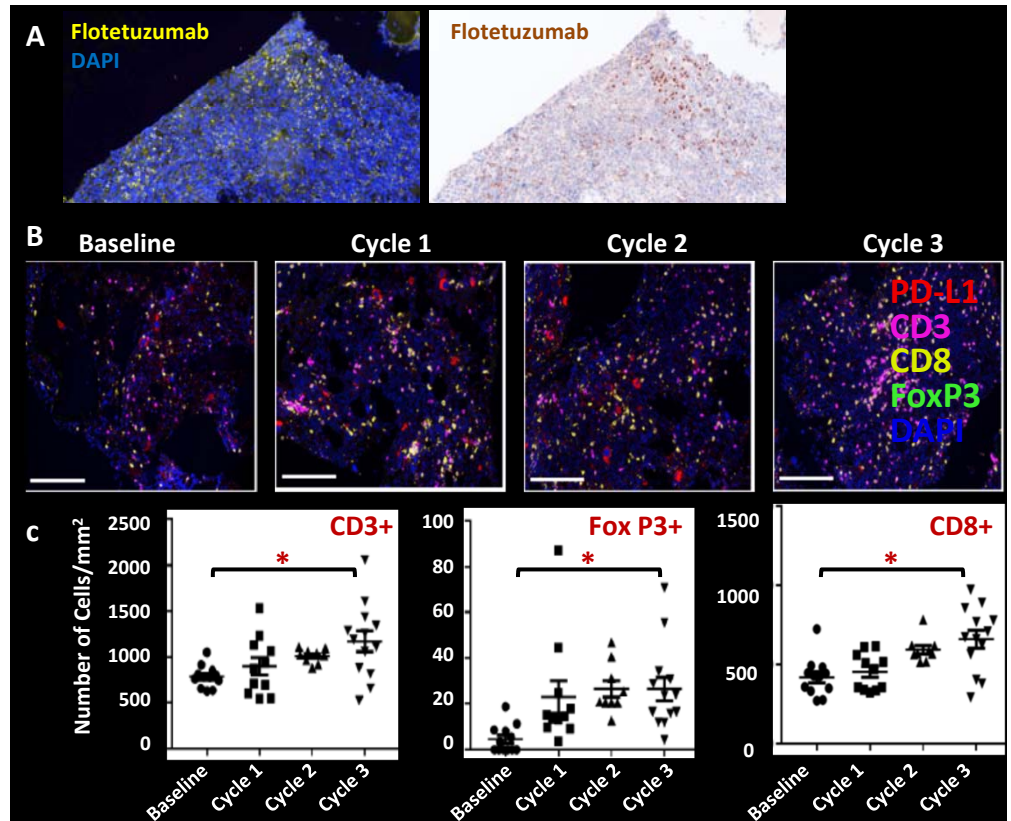


Disease	CD123 Positivity
AML	93%
MDS	>50%
CML	>50 - 77.5%
B-cell ALL	80 - 99%
Classical Hodgkin's Lymphoma	50 - 60 %
Hairy Cell Leukemia	100%
CLL	10%
Systemic Mastocytosis	>50 - 100%
pDC Leukemia	100%

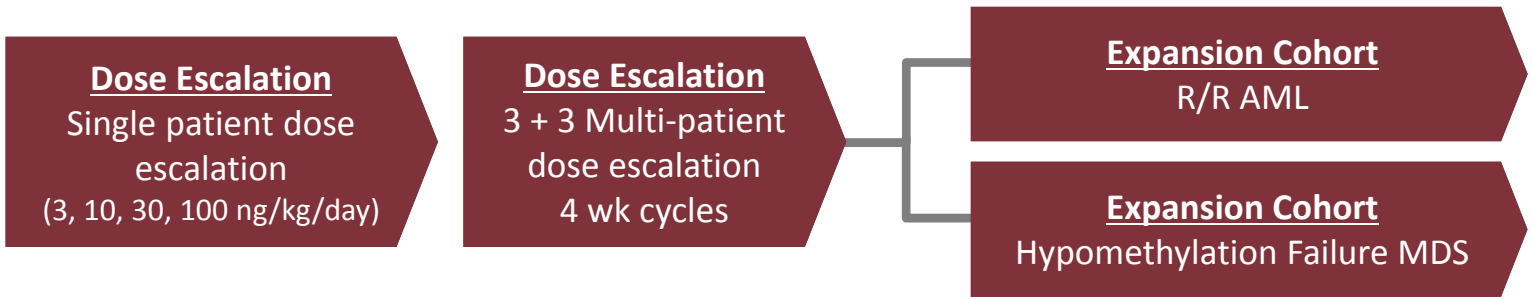
Jordan, et al. Leukemia. 2000 Oct; 14(10):1777-84; Jin, et al. Cell Stem Cell 2009 Jul 2;5(1):31-42; Munoz, et al. Haematologica 2001 Dec;86(12):1261-9; O'Brien and Rizzieri Cancer Invest 2013 May;31(4):215-20; Testa, et al. Blood. 2002 Oct 15; 100(8):2980-8; Tettamanti, et al. Br J Haematol 2013 May; 161(3):398-401; Vergez, et al. Haematologica 2011 Dec;96(12):1792-8

Flotetuzumab: CD123 x CD3 Bispecific DART Protein

- Multiplex immunohistochemistry images of an AML patient treated with flotetuzumab
- Bone marrow FFPE tissue was immunolabeled and quantified for MGD006 (fig A), PD-L1, CD3, CD8, FoxP3 and DAPI (fig B)
- Statistically significant increases in density of T-cells, including CD3+, FoxP3+ and CD8+, on treatment (* *p<0.05*)



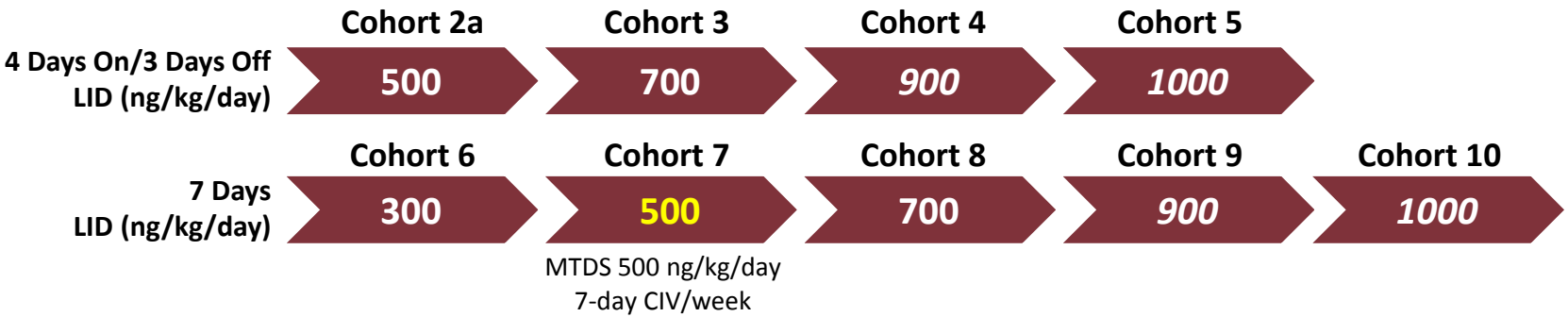
Flotetuzumab Phase 1 Study Design



(N=24 each cohort)

- Flotetuzumab Phase 1 key inclusion/exclusion criteria
  - Refractory AML unlikely to benefit from cytotoxic chemotherapy
  - Patients with MDS who have experienced treatment failure with induction therapy or hypomethylating therapy and have ≥10% marrow blasts
  - Prior history of allogeneic stem cell transplant is exclusionary
- Flotetuzumab Phase 1 study objectives
  - Safety and preliminary clinical activity
  - Optimize approach to delivery and supportive care (manage CRS while minimizing corticosteroid use)
  - Define PK, PD and PK/PD relationships

Dosing Scheme in Multi-Patient Dose Escalation



Lead-in Dose (LID)	• Week 1: 30 ng/kg/day x 3 days, 100 ng/kg/day x 4 days
Cycle 1 Weeks 2-4	• Arm A: (Cohorts 2-5): 4 days on, 3 days off schedule • Arm B: (Cohorts 6-10): 21 days continuous infusion
Cycle 2 and Beyond	• 4 days on, 3 days off schedule

Flotetuzumab Phase 1 Patient Demographics†

Characteristic		All Patients (n=57)
Age	Mean ± SD	63.6 ± 14.28
	Median (Range)	67.0 (29.0, 84.0)
Gender [n (%)]	Female	25 (43.9)
Diagnosis [n (%)]	AML	52 (91.2)
	MDS	5 (8.8)
AML Subclassification	Relapse	10 (19.2)
	Refractory	**28 (53.8)**
	HMA Treatment failure (≥ 2 cycles)	14 (26.9)
AML Risk Stratification (ELN 2017)	Favorable	3 (5.8)
	Intermediate	18 (34.6)
	Adverse	**26 (50)**
	Unknown	5 (9.6)
MDS IPSS Risk Category	High	2 (40.0)
	Intermediate-1	1 (20.0)
	Intermediate-2	2 (40.0)

† Data cut-off November 30, 2017

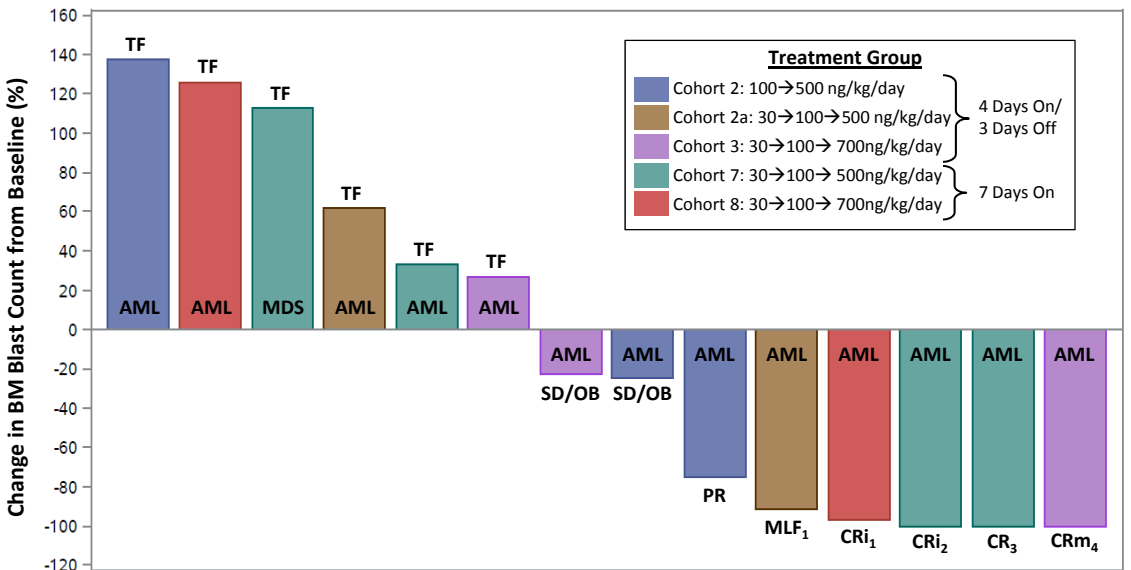
Flotetuzumab Phase 1 Study Safety: Overview*

Adverse Event	Related to Flotetuzumab	
	All (N=57)	≥ Gr 3
Infusion related reaction/CRS	46 (80.7)	9 (15.8)
Pyrexia	14 (24.6)	2 (3.5)
Nausea	13 (22.8)	
Chills	8 (14.0)	
Platelet count decreased	8 (14.0)	7 (12.3)
Lymphocyte count decreased	8 (14.0)	8 (14.0)
White blood cell count decreased	7 (12.3)	6 (10.5)
Anemia	6 (10.5)	6 (10.5)
Fatigue	8 (14.0)	
Vomiting	8 (14.0)	
Diarrhea	7 (12.3)	1 (1.8)
Edema peripheral	6 (10.5)	
Hypocalcaemia	7 (12.3)	2 (3.5)
C-reactive protein increased	6 (10.5)	2 (3.5)
Alanine aminotransferase increased	6 (10.5)	1 (1.8)
Blood bilirubin increased	6 (10.5)	
Hypomagnesaemia	6 (10.5)	

**Cut-off date: November 30, 2017; Includes events occurring in ≥10% of the population.*

Anti-Leukemic Activity at Threshold Dose ≥ 500 ng/kg†

Of 14 patients treated with flotetuzumab in dose escalation phase at threshold dose ≥ 500 ng/kg/day who received ≥ one cycle of treatment and had post-treatment bone marrow biopsy



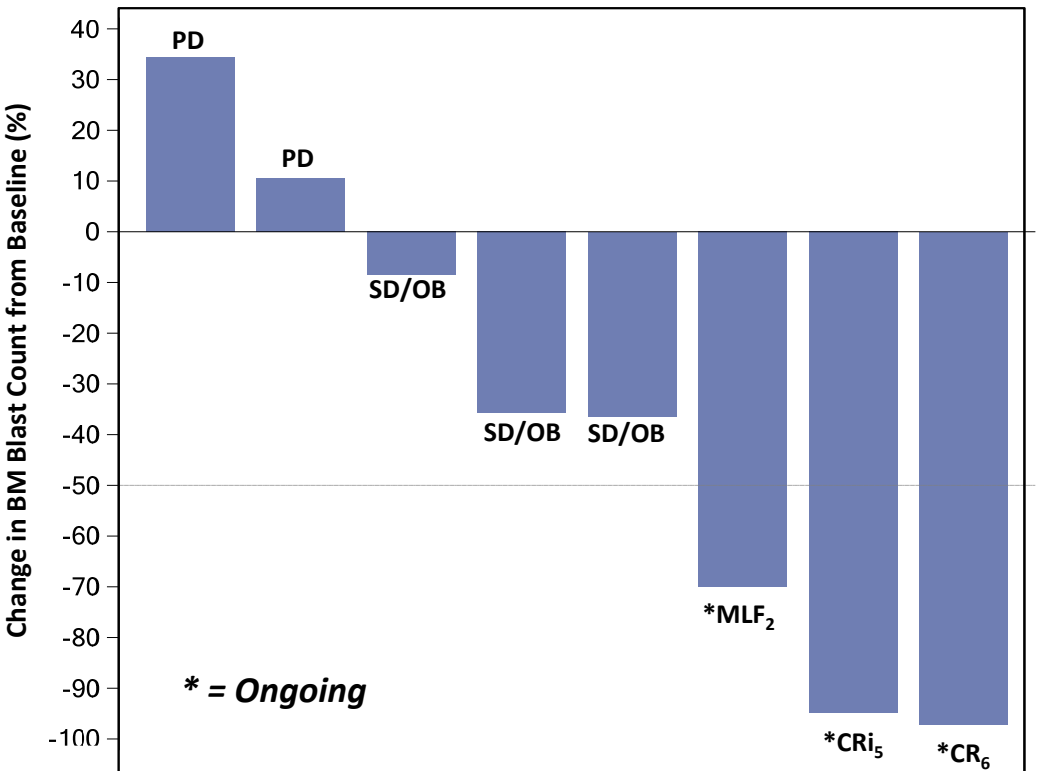
- Rapid responses after single cycle of therapy in majority of patients that respond (cycles ≤ 2)
- Anti-leukemic activity observed in 8/14 pts (57%)
- Objective resp. rate (CR/CRi/MLF/PR): 6/14 pts (43%)
- CR Rate: 4/14 (28%) (CR/CRi)

CR = Complete Response; CRm = molecular CR; CRi = Complete Response with incomplete hematological improvement; MLF = Morphologic Leukemia-free state; PR = Partial Response; SD/OB = Stable Disease/Other Anti-Leukemic Benefit; PD= Progressive Disease; (Modified ELN 2017 criteria)

† Data cut-off Aug. 1, 2017; presented at ESMO 2017

Expansion Cohort-Evaluable Population

- Cohort expansion at MTDS (500 ng/kg/day 7-day CIV) will enroll 24 AML and 24 MDS patients
- 11 AML patients dosed to date, with eight evaluable at data cut-off
- Six patients (75%) have evidence of anti-leukemic activity; three patients are still ongoing
- Expansion cohort open in 13 sites worldwide (7 US, 6 EU)



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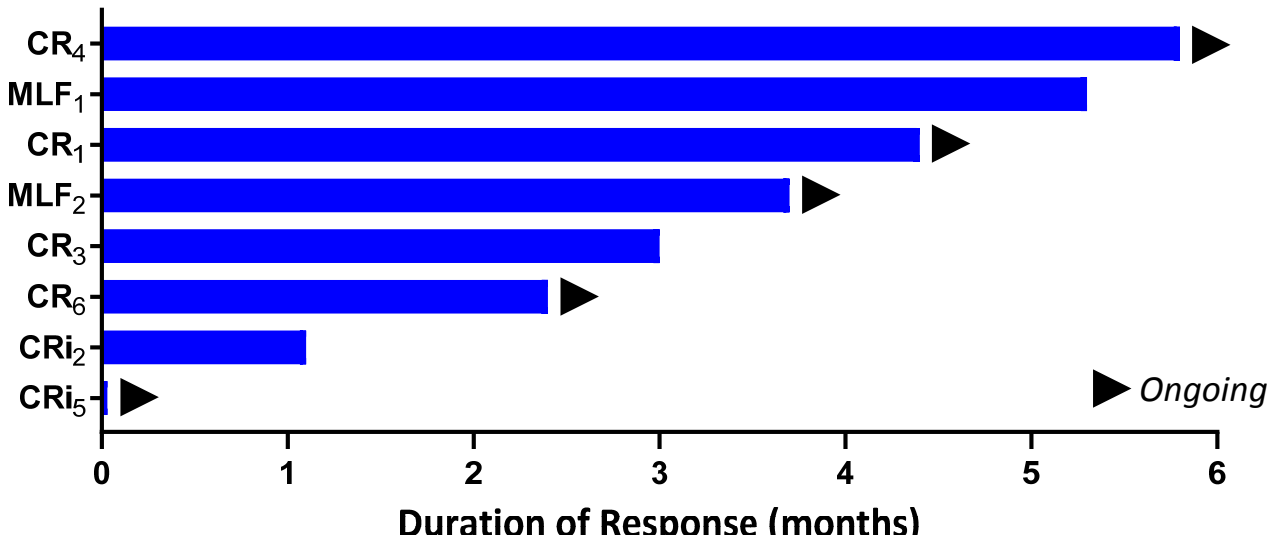
† Data cut-off December 4, 2017

Flotetuzumab Phase 1 Duration of Response†

- Durable responses in patients that achieve MLF, CRi, CR
- Duration of response ranges from 1.0 to 5.8 months, with 5 patients still ongoing



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† Data cut-off November 30, 2017

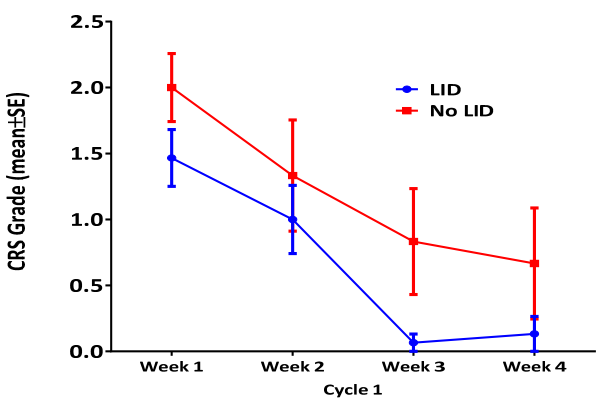
Conclusions

- Flotetuzumab is a potent CD123 x CD3 bispecific DART molecule that redirects T-cells to kill CD123-positive AML blasts, in vitro and/or in vivo
- In patients with AML, flotetuzumab has an acceptable safety profile to date
- Encouraging initial anti-leukemic activity at ≥ 500 ng/kg/day (threshold dose) in AML pts
- Anti-leukemic activity even in high risk patients (adverse cytogenetics)
- Cohort expansion now ongoing and enrolling at 13 sites in US and EU

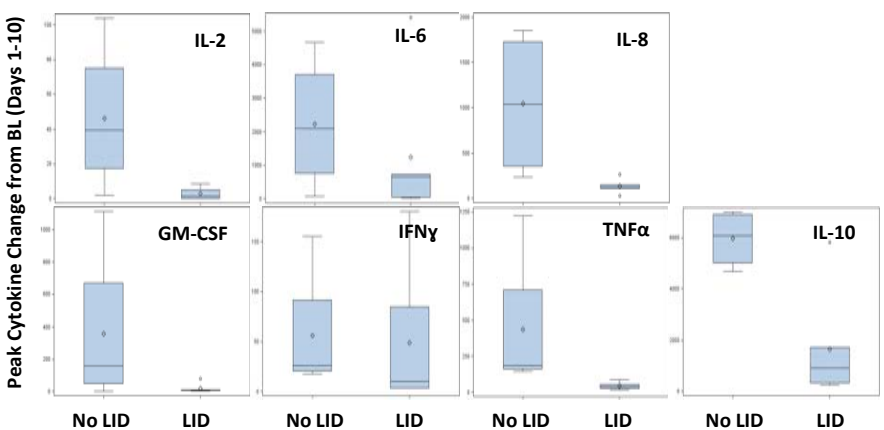
Next Steps: Dosing Refinement

- Step-wise (two-step, lead-in dose) administration allows for safe escalation of dose and improved efficacy
- See ***Poster # 3856:*** *"Lead-in Optimization to Mitigate Cytokine Release Syndrome in AML and MDS Patients Treated with Flotetuzumab, a CD123 x CD3 DART® Molecule for T-cell Redirected Therapy" (Mon., Dec. 11: 6:00 - 8:00pm)*

Mean Grade Decrease of 0.54 at Same Dose Level



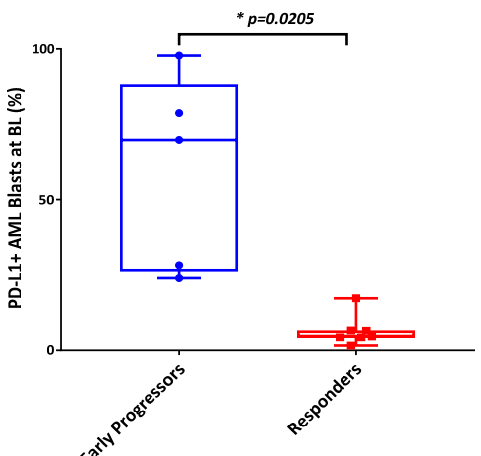
Decrease Overall Peak Cytokine Levels



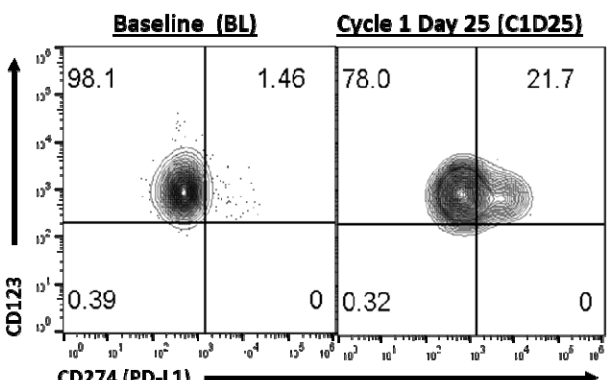
Next Steps: Combination with PD-1 Inhibitors

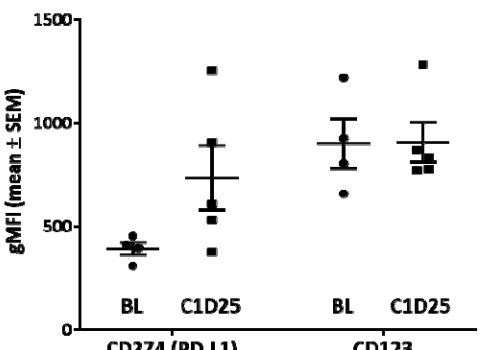
- Translational data outlines population and timing of optimal combination
- *See **Poster # 1365:** "Preliminary Translational Results from an Ongoing Phase 1 Study of Flotetuzumab, a CD123 x CD3 DART®, in AML/MDS: Rationale for Combining Flotetuzumab and Anti-PD-1/PD-L1 Immunotherapies" (Sat., Dec. 9: 5:30 - 7:30pm)*

PD-L1 Expression is Associated with Decreased Flotetuzumab Activity in Vivo



PD-L1 Upregulation in Residual Bone Marrow Blasts upon Flotetuzumab Treatment





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