2022 ASCO® ANNUAL MEETING

Abstract #8003
Phase I study of CART-ddBCMA: a CART-Therapy Utilizing a Novel Synthetic Binding Domain for the Treatment of Subjects with Relapsed or Refractory Multiple Myeloma

Matthew J. Frigault, MD[1,2]; Jacalyn Rosenblatt, MD[3]; Noopur S. Raje, MD[1,2]; Daniella Cook, BS[1,2]; Andrew J Yee, MD[1,2]; Emma K. Logan[3]; Christine Cornwell[4]; Kamalika Banerjee, MS[4]; Anand Rotte, PhD[4]; Christopher R. Heery, MD[4]; David Avigan, MD[3]; Andrzej Jakubowiak[5]; and Michael R. Bishop, MD[5]

[1]Massachusetts General Hospital Cancer Center, Boston, MA; [2]Harvard Medical School, Boston, MA; [3]Beth Israel Deaconess Medical Center, Boston, MA; [4]Arcellx, Inc., Gaithersburg, MD;[5]The David and Etta Jonas Center for Cellular Therapy, University of Chicago, Chicago, IL

PRESENTED BY:
Dr Matthew Frigault MD
Administrative Director, Cellular Therapy Service, MGH

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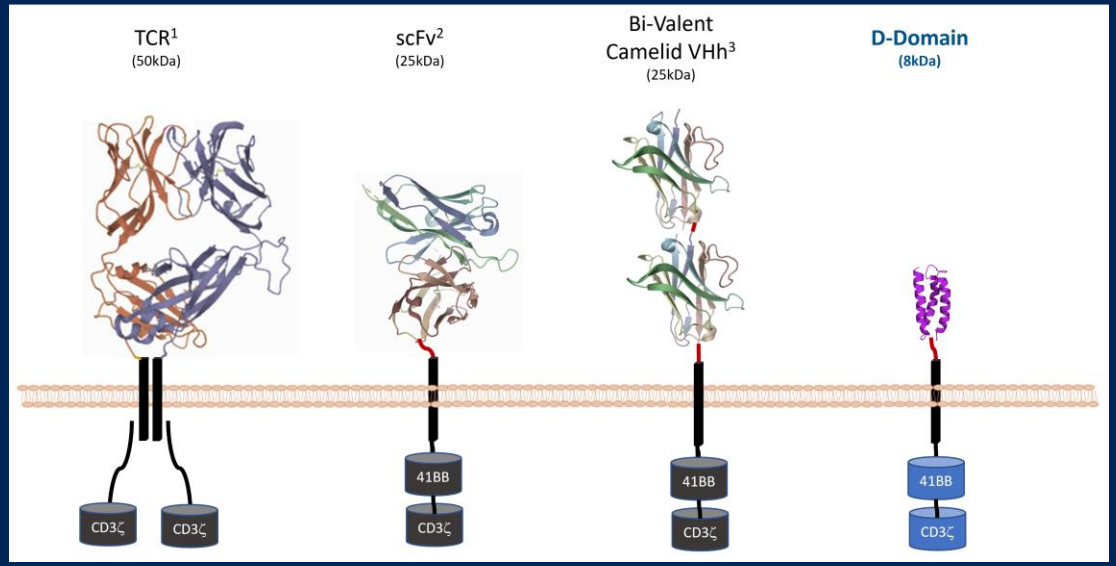
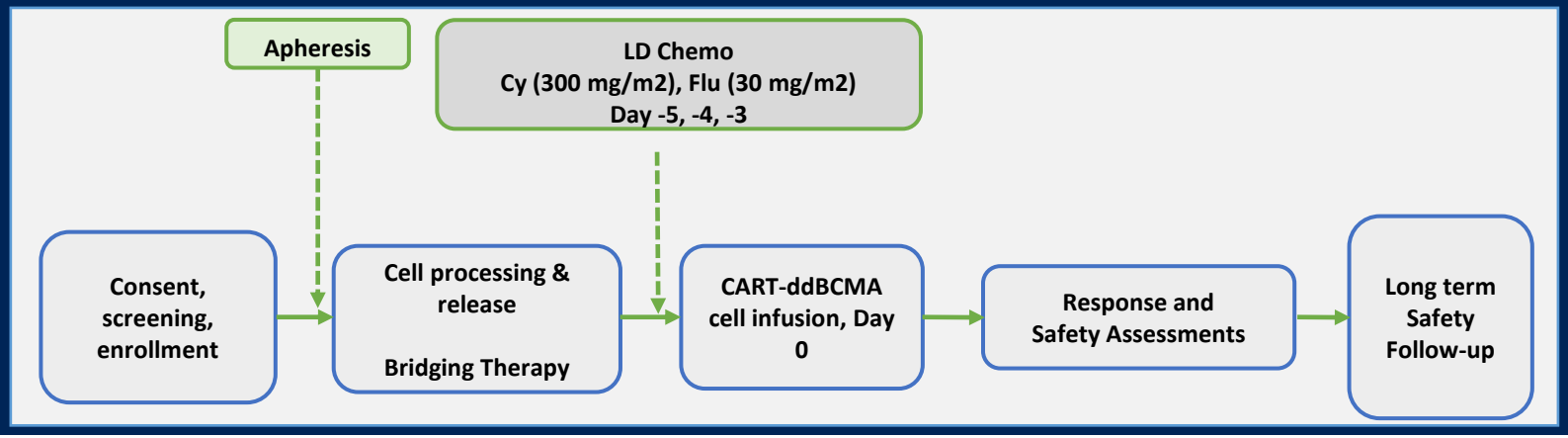
Background and Methods

- CART-ddBCMA is an autologous CAR-T containing a novel computationally designed synthetic protein[1,2] binding domain (non-scFv) engineered to reduce the risk of immunogenicity and is highly stable
- Phase 1 first-in-human trial is in progress, enrolling patients with relapsed or refractory myeloma
  - Prior IMiD, PI, and CD38-targeted therapy
  - Received ≥3 prior therapies or triple refractory
  - 2 Dose Levels evaluated, 6 subjects in each dose escalation cohort.
    - DL1 = 100 x 10^6 CAR+ cells; DL2 = 300 x 10^6 CAR+ cells
  - Expansion cohort is enrolled at DL1



[1] Chan, KF. et al. 2018.,Nat Commun 9:1026-1026
[2] Bjerragaard-Anderson, K., et al 2018. Sci. Rep., 8:10836-10836.
[3] https://commons.wikimedia.org/wiki/File:1l3V_(Lama_VHH_domain_unligated).png#file



[1]Rotte, et al. "BCMA targeting CAR T cells using a novel D-domain binder for multiple myeloma: clinical development update." *Immuno-Oncology Insights 2022; 3(1), 13–24*
[2]Frigault et al. "Phase 1 Study of CART-ddBCMA for the treatment of subjects with relapsed and refractory Multiple Myeloma." Blood Advances 2022; bloodadvances.2022007210. doi: https://doi.org/10.1182/bloodadvances.2022007210.

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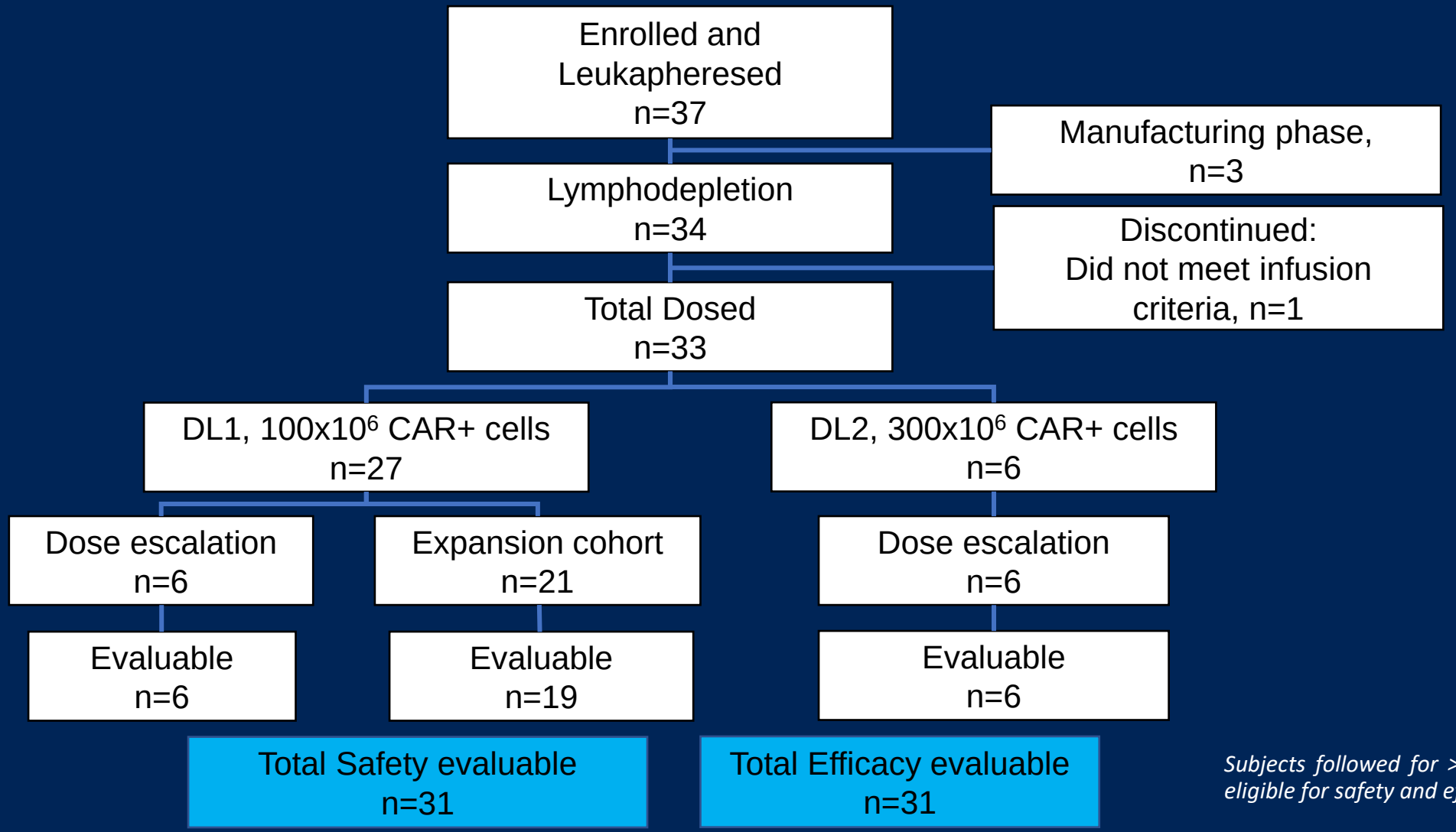
Patient Disposition



Subjects followed for >1 month f/u are eligible for safety and efficacy analysis.

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Patient Demographics (as of 03 MAY 2022)

Characteristics	Dose Level 1 100 million CAR-T (n=25)	Dose Level 2 300 million CAR-T (n=6)	Total (n=31)
Age, median (min-max)	68 (44-76)	60 (52-65)	66 (44-76)
Gender	13 Male (52%) 12 Female (48%)	5 Male (83%) 1 Female (17%)	18 Male (58%) 13 Female (42%)
BMPC ≥50%	7 (28%)	5 (83%)**	12 (39%)
Extra-medullary disease	9 (36%)	3 (50%)	12 (39%)
Prior Lines of Therapy, Median (min – max) *	5 (3 – 7)	4 (3 – 16)	5 (3 – 16)
Triple refractory	19 (76%)	5 (83%)	24 (77%)
Penta refractory	17 (68%)	4 (67%)	21 (68%)
IgG myeloma IgA myeloma Light chain only	14 4 5	5 0 1	19 4 6

*Two subjects with ongoing data entry excluded
**Data updated since ASH 2021 after full data entry was complete.

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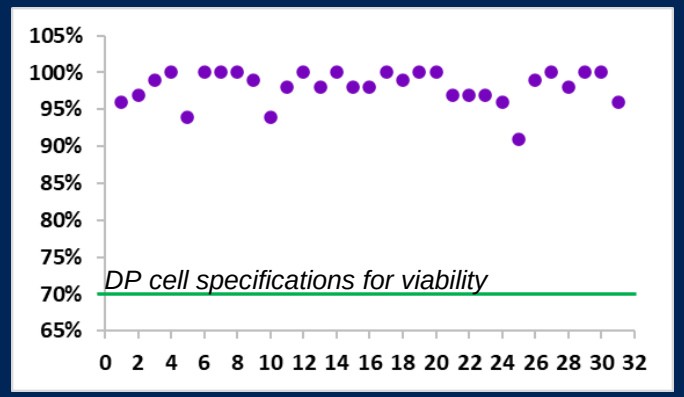
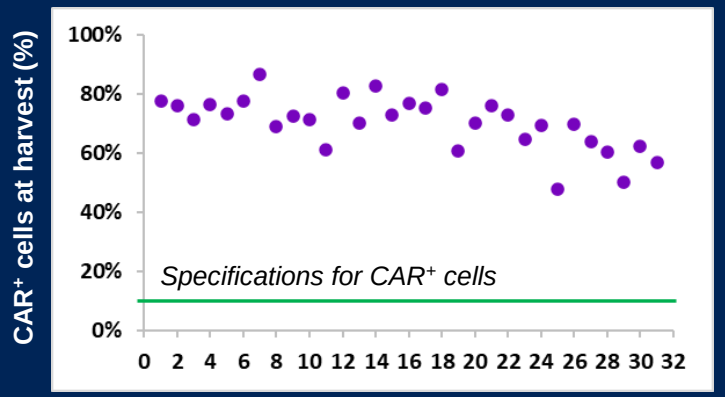
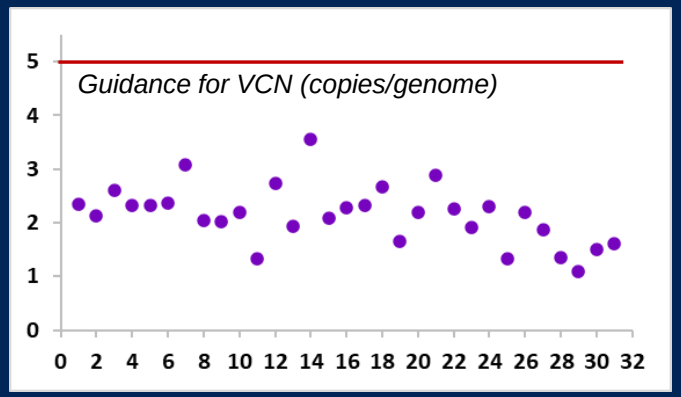
CART-ddBCMA Manufacturing Results in Consistent Product Profile



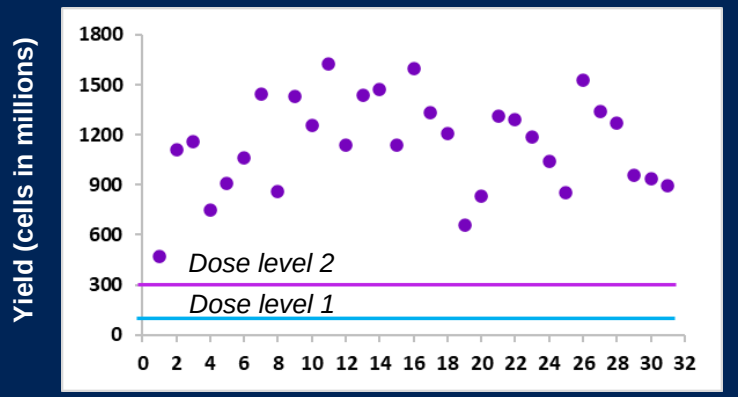
High cell viability: median 99% viable cells



Low inter-patient variability in CAR+ cells: median 72% CAR+ cells



Low inter-patient variability in CAR expression/cell: median 2.2 copies/cell



High yield: ≥3 doses of DL1 can be administered from a single manufacture run

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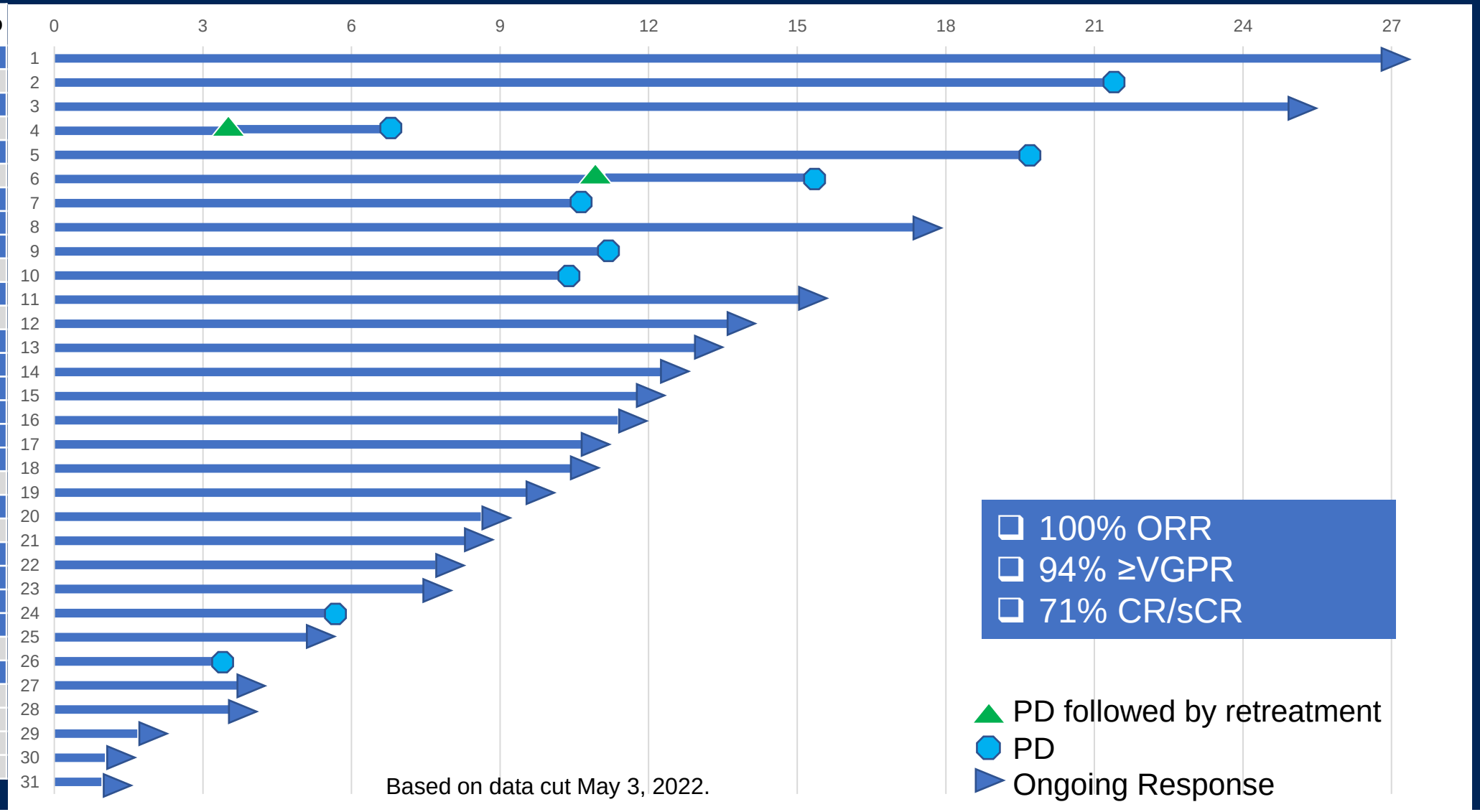
CART-ddBCMA: 100% ORR and Durable Responses

	Best ORR	Best MRD
100M CAR+ T cells	sCR	10^{-6}
	sCR	NE
	sCR	10^{-6}
	PR	POS
	sCR	10^{-6}
	PR	NE
300M CAR+ T cells	CR	10^{-5}
	sCR	10^{-6}
	VGPR	10^{-6}
	CR	NE
	sCR	10^{-6}
	sCR	10^{-4}
100M CAR+ T cells (expansion)	sCR	10^{-6}
	CR	10^{-5}
	CR	10^{-5}
	sCR	10^{-6}
	VGPR	10^{-6}
	VGPR	10^{-6}
	sCR	POS
	CR	10^{-5}
	sCR	NE
	VGPR	10^{-6}
	sCR	10^{-6}
	sCR	10^{-6}
	VGPR	10^{-6}
	CR	NE
	VGPR	10^{-5}
	sCR	TBD
	CR	TBD
	VGPR	TBD
	sCR	TBD



- 100% ORR
- 94% ≥VGPR
- 71% CR/sCR

- PD followed by retreatment
- PD
- Ongoing Response

Based on data cut May 3, 2022.

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CART-ddBCMA Responses Deepen Over Time

	CART-ddBCMA		
Minimum follow-up (mo)	**1**	**6**	**12**
Sample Size (n)	31	24	16
Median Follow-up (mo)	12.1	13.3	17.7
EMD # (%)	12 (39%)	12 (50%)	8 (50%)
ORR	100%	100%	100%
CR rate	22 (71%)	18 (75%)	13 (81%)
% of patients in ongoing response:			
@ 6 months	-	92% (22/24)	94% (15/16)
@ 12 months	-	-	69% (11/16)

Based on data cut May 3, 2022.

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Adverse Event Profile (as of 03 MAY 2022)

Grade 3/4 AEs (non-CRS/ICANS) ≥5% after cell infusion (N=31)	
Hematologic	
Neutrophil count decreased	24 (77.4%)
Anemia	15 (48.4%)
Thrombocytopenia	13 (41.9%)
Lymphocyte count decreased	12 (38.7%)
Febrile neutropenia	6 (19.4%)
White blood cell count decreased	6 (19.4%)
Non-hematologic	
Hypertension	3 (9.7%)
Cellulitis	2 (6.5%)
Hyponatraemia	2 (6.5%)
Hypotension	2 (6.5%)
Sepsis	2 (6.5%)

CAR-T-associated AEs Per ASTCT criteria	100 million (N=25)		300 million (N=6)	
Cytokine Release Syndrome (CRS)	**Grade 1/2**	**Grade 3**	**Grade 1/2**	**Grade 3**
	22 (88%)	**0**	**5 (83%)**	**1 (17%)**
Median onset (min-max)*	2 days (1-8 days)		2 day (1-2 days)	
Median duration (min-max)	8 days (3-13 days)		5 days (3-10 days)	
Neurotoxicity (ICANs)	**Grade 1/2**	**Grade 3**	**Grade 1/2**	**Grade 3**
	5 (20%)	**1 (4%)**	**0**	**1 (17%)**
Median onset (min-max)*	4.5 days (3-6 days)		7 days	
Median duration (min-max)	7.5 days (4 - 11 days)		23 days	
Toxicity Management				
Tocilizumab	19		5	
Dexamethasone	13		2	

Subjects followed for <1 month are not yet evaluable for safety analyses.

* *Infusion Day 0 is considered Study Day 1*

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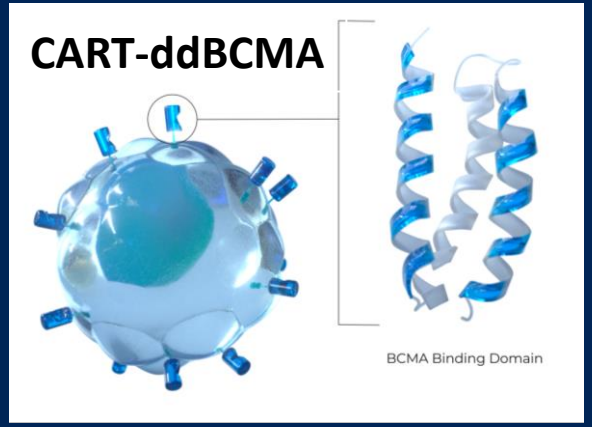
CART-ddBCMA Phase 1: Conclusions

- **CART-ddBCMA utilizes a novel, synthetic highly stable binding domain**
  - 2 dose levels studied (100 and 300 million CAR+ T-cells); MTD not reached
  - High CAR-T cell viability, low inter-patient variability in CAR+ cells and high CAR-T cell yield
  - Phase 1 expansion at 100 million CAR+ T cells resulted in selection of this dose as RP2D
- **Adverse Event Profile appears potentially differentiated from other CAR T products**
  - No tissue-targeted toxicities observed
  - No cases grade 3 (or greater) CRS, 1 case (4%) Grade 3 ICANS event at RP2D (n=25)
  - No delayed neurotoxicity or parkinsonian-like events observed in entire population (n=31)
- **100% ORR per IMWG across both dose levels**
- **Deep and durable responses observed in patients with poor prognostic factors**
  - **All Patients (39% EMD): 31/31 (100%) ORR; 22/31 (71%) CR/sCR**, 7/31 (23%) VGPR, 2/31 (6%) PR; ≥VGPR = 29/31 (94%)
  - **Pts w/ 6 mo f/u (50% EMD): 24/24 (100%) ORR; 18/24 (75%) CR/sCR**, 4/24 (17%) VGPR, 2/24 (8%) PR; ≥VGPR = 22/24 (92%)
  - **Pts w/ 12 mo f/u (50% EMD): 16/16 (100%) ORR; 13/16 (81%) CR/sCR**, 1/16 (6%) VGPR, 2/16 (13%) PR; ≥VGPR = 14/16 (88%)
- **Pivotal phase 2 trial initiation this year**



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