ARCELLX

Abstract 3313
Phase 1 Study of CART-ddBCMA for the Treatment of Subjects with Relapsed and/or Refractory Multiple Myeloma

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Background and Methods

CART-ddBCMA is an autologous CAR-T containing a novel synthetic protein[1,2] binding domain (non-scFv) engineered to reduce the risk of immunogenicity and is highly stable

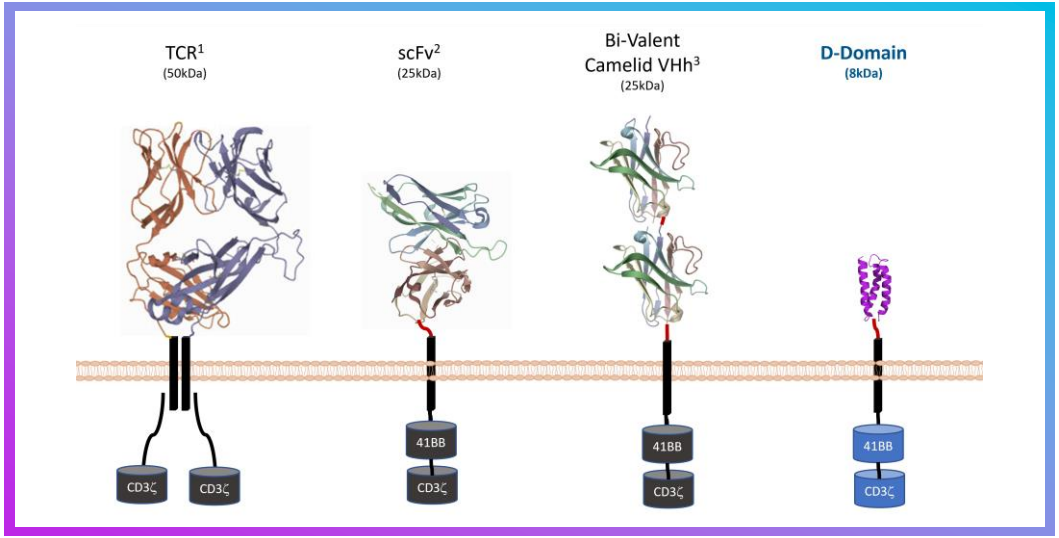
Phase 1 first-in-human trial has completed enrollment of relapsed and/or refractory myeloma

- Prior IMiD, PI, and CD38-targeted therapy required
- Received ≥3 prior therapies or triple refractory

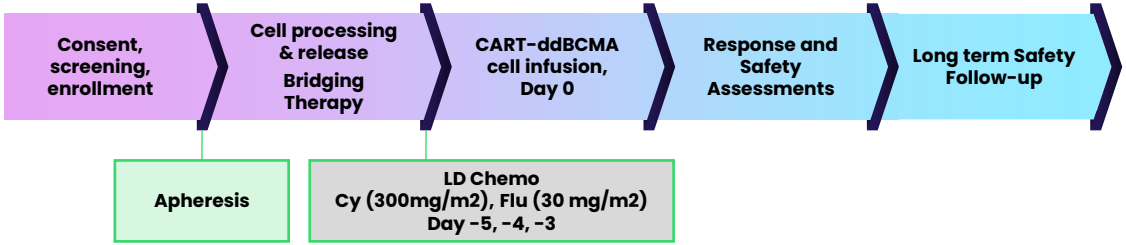
2 Dose Levels evaluated, 6 subjects in each dose escalation cohort

- DL1 = 100 x 10^6 CAR+ cells;
  DL2 = 300 x 10^6 CAR+ cells

Expansion cohort is enrolled at DL1

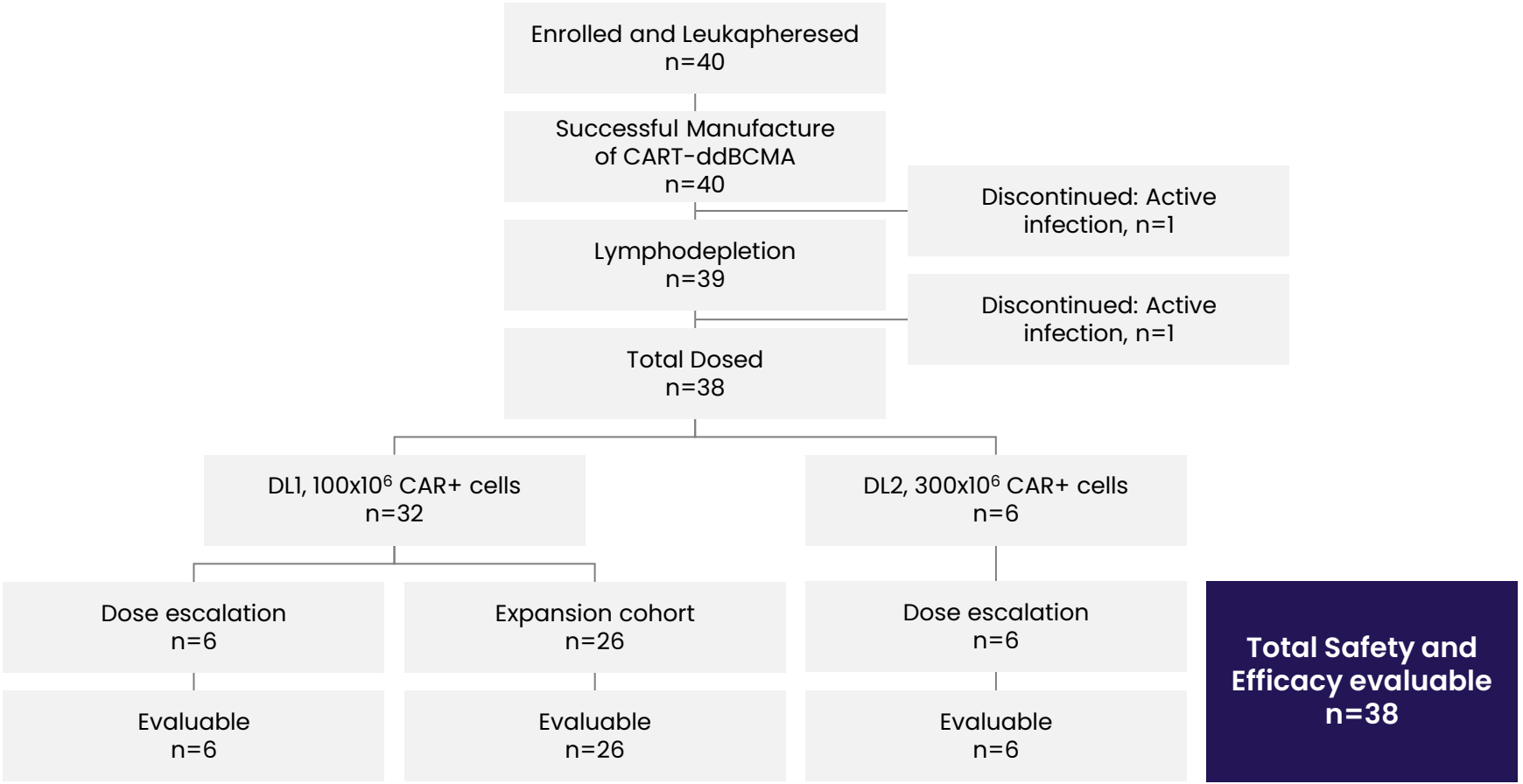


[1] Chan, KF. et al. 2018.,Nat Commun 9:1026-1026
[2] Bjerragaard-Anderson, K., et al 2018. Sci. Rep., 8:10836-10836.
[3] https://commons.wikimedia.org/wiki/File:113V_(Lama_VHH_domain_unligated).png#file



[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.

Patient Disposition



Patient Demographics (as of 31 Oct 2022)

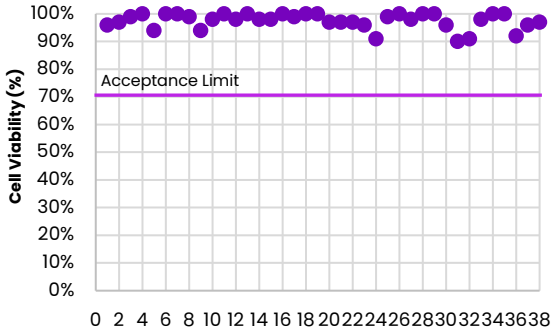
Characteristics	Dose Level 1 100 million CAR-T (n=32)	Dose Level 2 300 million CAR-T (n=6)	Total (n=38)
Age, median (min - max)	66 (44 - 76)	60 (52 - 65)	66(44 - 76)
Gender	18 Male (56%) 14 Female (44%)	5 Male (83%) 1 Female (17%)	23 Male (61%) 15 Female (39%)
ECOG PS*			
0	9/32 (28%)	3/6 (50%)	12/38(32%)
1	23/32 (72%)	3/6 (50%)	26/38 (68%)
High Risk Prognostic Feature	16/32 (50%)	6/6 (100%)	22/38 (58%)
BMPC ≥60%	6/32 (19%)	3/6 (50%)	9/38 (24%)
ISS Stage III (B2M ≥ 5.5)	3/32 (9%)	2/6 (33%)	5/38 (13%)
Extra-medullary disease	10/32 (31%)	3/6 (50%)	13/38 (34%)
High Risk Cytogenetics**	9/32 (28%)	2/6 (33%)	11/38 (29%)
Prior Lines of Therapy, Median (min - max)	5 (3 - 7)	4 (3 - 16)	4 (3 - 16)
Triple refractory***	32/32 (100%)	6/6 (100%)	38/38 (100%)
Penta refractory	21/32 (66%)	5/6 (83%)	26/38 (68%)
IgG myeloma	19	5	24
IgA myeloma	6	0	6
Light chain only	5	1	6

*Eastern Cooperative Oncology Group Performance Status Scale
**Defined as Del 17p, t(14;16), t(4;14).
***Note: modified from ASCO 2022 due to data cleaning efforts.

CART-ddBCMA Manufacturability: Reliable Process, Consistent Product

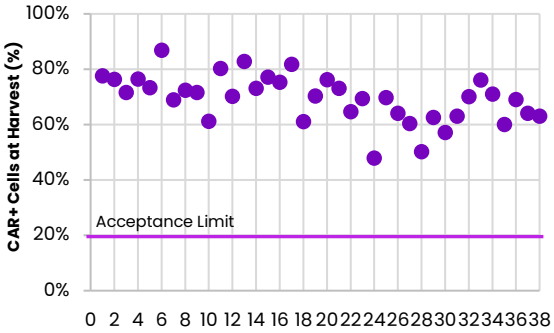
100% of initiated cell product runs released to date

Cell Viability

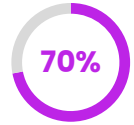


High cell viability: median 98% viable cells

CAR Positivity



Low inter-patient variability in CAR⁺ cells: median 70% CAR⁺ cells



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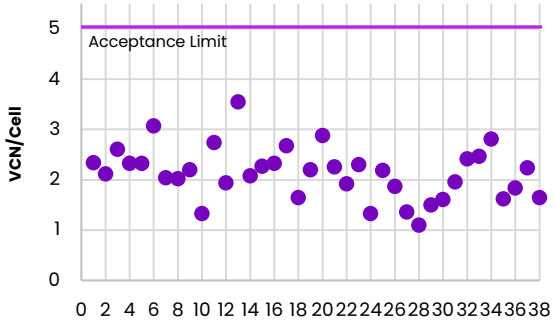
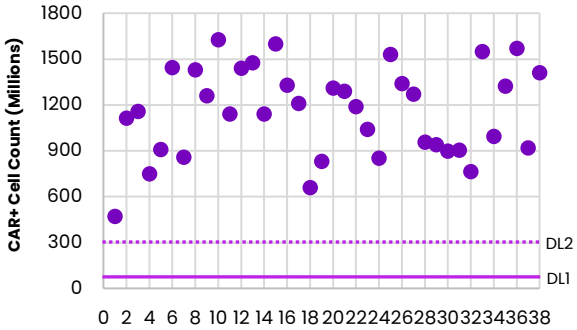


Low inter-patient variability in CAR expression/cell: median 2.2 copies/cell

Total Manufactured Cells

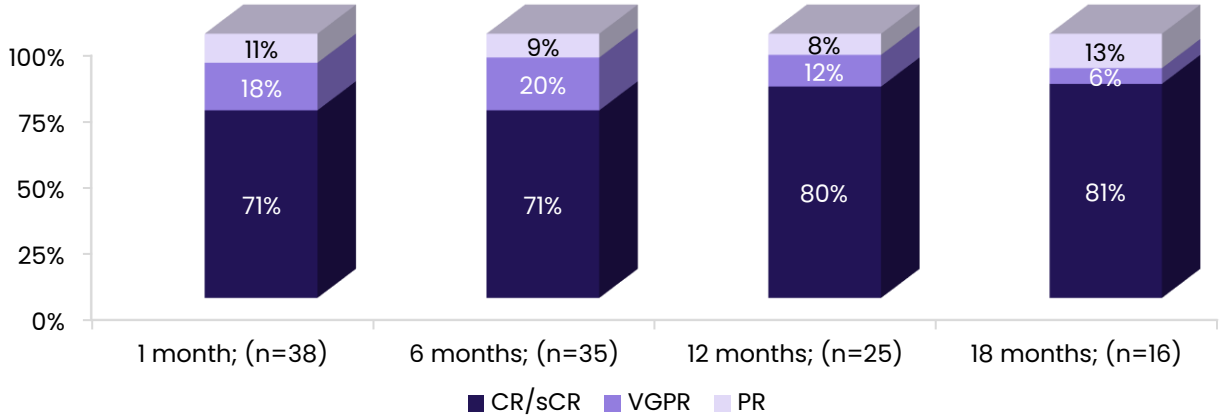


High yield: ≥3 doses of DL1 can be administered from a single manufacture run

Potential for Best-in-Class Treatment

*Patient initiated subsequent therapy prior to official PD.
**Subject 30 died of cardiac arrest secondary to drug overdose.
MRD abbreviations: NE = not evaluable, failed calibration; POS = positive; Pending = sample being analyzed

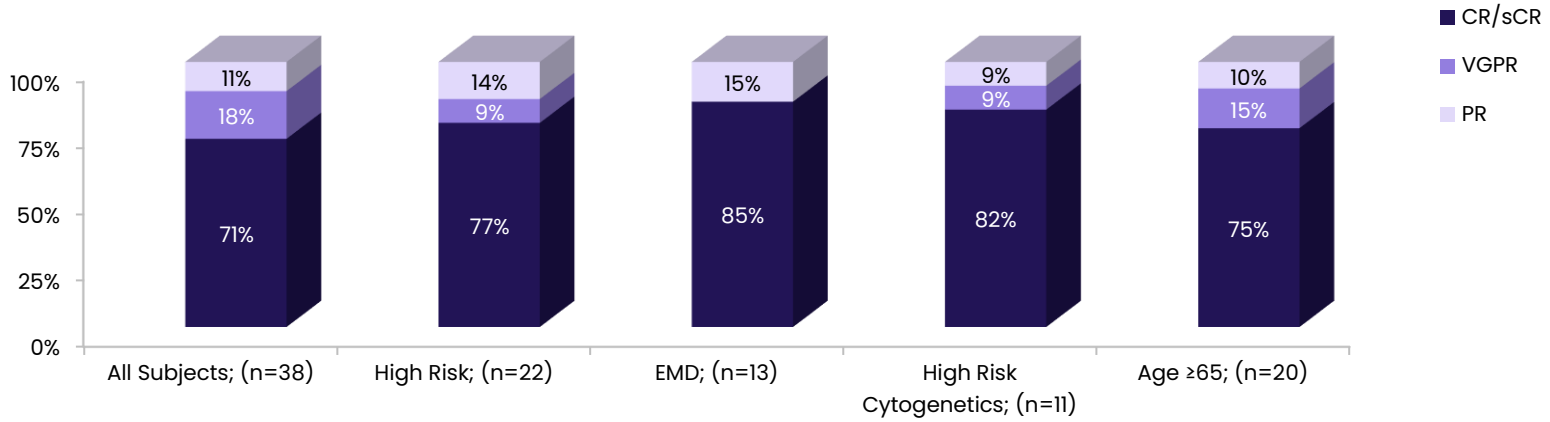
CART-ddBCMA Responses Deepen Over Time



Minimum months since infusion (M)	1	6	12	18
Sample Size (n)*	38	35	25	16
Median Follow-up (mo)	15.0	16.4	18.9	22.9
High Risk Features** # (%)	22 (58%)	21 (60%)	19 (76%)	13 (81%)
ORR	100%	100%	100%	100%
CR/sCR rate***	27 (71%)	25(71%)	20 (80%)	13 (81%)

*Includes patients who were dosed at least M months prior or have had follow visit at Mth-month as of 11/22/22.
**High risk features defined as presence of EMD, BMPC ≥ 60, or B2M ≥ 5.5
***Calculated using number of patients who reached CR/sCR divided by number treated at least 1, 6, 12, or 18 months prior

Responses in Subgroups



	Patients n (%)	6-month PFS % (95% CI)	12-month PFS % (95% CI)	18-month PFS % (95% CI)
Overall	38 (100%)	91.8% (76.7%, 97.2%)	72.7% (52.2%, 85.5%)	64.6% (43.7%, 79.4%)
≥ 65 years	20 (52.6%)	95.0% (69.4%, 99.3%)	82.3% (54.3%, 94.0%)	75.4% (46.7%, 90.1%)
Complete Responders	27 (71.1%)	96.2% (75.7%, 99.4%)	86.0% (62.3%, 95.3%)	80.7% (55.9%, 92.4%)
High Risk Features*	22 (57.9%)	90.5% (67.0%, 97.5%)	69.2% (43.7%, 84.9%)	63.4% (38.0%, 80.7%)
Extramedullary disease	13 (34.2%)	91.7% (53.9%, 98.8%)	64.2% (30.2%, 84.8%)	64.2% (30.2%, 84.8%)
High Risk Cytogenetics	11 (28.9%)	80.8% (42.3%, 94.8%)	69.2% (31.1%, 89.1%)	69.2% (31.1%, 89.1%)

*High risk features defined as presence of EMD, BMPC ≥ 60, or B2M ≥ 5.5

CART-ddBCMA: 100% ORR, High CR Rate, and Durable Responses Demonstrate Potential for Best-in-Class Treatment

	CART-ddBCMA		LEGEND-2	CARTITUDE-1	
Minimum follow-up (mo.)	**1**	**18**	**1**	**1.5**	**13.5 (est.)**
Sample Size (n)	38	16	57	97	
Median Follow-up (mo.)	15.0	22.9	8	12.4	24
EMD %	34%	50%	30%	13%	13%
ORR	**100%**	**100%**	**88%**	**97%**	**98%**
CR rate	**71%**	**81%**	**68%**	**67%**	**83%**
Kaplan Meier Estimate PFS Rate	All subjects		LEGEND-2 All subjects	CARTITUDE-1 All subjects	
@ 6 months	91.8% (76.7%, 97.2%)		~82%	87%	
@ 12 months	72.7% (52.2%, 85.5%)		~70%	~75%	
@18 months	64.6% (43.7%, 79.4%)		~41%	~67%	

Based on preliminary data cut October 31, 2022
LEGEND-2 estimates are based on KM curves from Zhao BMC 2018 (Figure 2a) and CARTITUDE-1 estimates are based on KM curves from Martin JCO 2022 (Fig 2a).

Adverse Event Profile (as of 31 Oct 2022)

Grade 3/4 AEs (non-CRS/ICANS) ≥5% after cell infusion (N=38)	
Hematologic	
Neutrophil count decreased	29 (76.3%)
Anemia	22 (57.9%)
Thrombocytopenia	15 (39.4%)
Lymphocyte count decreased	13 (36.8%)
White blood cell count decreased	7 (18.4%)
Febrile Neutropenia	6 (15.8%)
Non-hematologic	
Hypertension	3 (7.9%)
Hyponatremia	2 (5.3%)
Pain in extremity	2 (5.3%)
Cellulitis	2 (5.3%)
Sepsis	2 (5.3%)

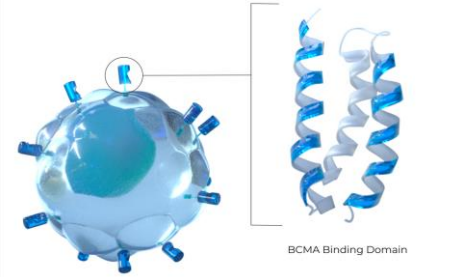
CAR-T-associated AEs Per ASTCT criteria	100 million (N=32)		300 million (N=6)	
Cytokine Release Syndrome (CRS)	**Grade 1/2**	**Grade 3**	**Grade 1/2**	**Grade 3**
	30 (94%)	**0**	**5 (83%)**	**1 (17%)**
Median onset (min-max)*	2 days (1-12 days)		2 day (1-2 days)	
Median duration (min-max)	8 days (2-14 days)		5 days (3-10 days)	
Neurotoxicity (ICANs)	**Grade 1/2**	**Grade 3**	**Grade 1/2**	**Grade 3**
	5 (16%)	**1 (3%)**	**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	27 (84%)		5 (83%)	
Dexamethasone	20 (63%)		2 (33%)	

*Infusion Day 0 is considered Study Day 1

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
- Consistency in manufacturing (100% success) highlighted by high CAR-T cell viability, low inter-patient variability in CAR+ cells and high CAR-T cell yield



100% ORR

per IMWG across both dose levels

Deep and durable responses

- **All Patients: 38/38 (100%) ORR; 27/38 (71%) CR/sCR**, 7/38 (18%) VGPR, 4/38 (11%) PR; ≥VGPR = 34/38 (89%)
- **Pts w/ 12 mo f/u: 25/25 (100%) ORR; 20/25 (80%) CR/sCR**, 3/25 (12%) VGPR, 2/25 (8%) PR; ≥VGPR = 23/25 (92%)
- **Pts w/ 18 mo f/u: 16/16 (100%) ORR; 13/16 (81%) CR/sCR**, 1/16 (6%) VGPR, 2/16 (13%) PR; ≥VGPR = 14/16 (88%)

Median Duration of Response Not Reached for Overall Population

- PFS Rate: @6 months 92%, @12 months 73%, @ 18 months 65%

Durable responses in patients with high-risk features

- PFS rate 63% @18 months in population defined by EMD, BMPC ≥ 60%, and/or B2M ≥ 5.5

24 of 27 (89%) of MRD evaluable subjects achieved Negativity at ≥10^{-5}

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 (3%) Grade 3 ICANS event at RP2D (n=32)
- No delayed neurotoxicity or parkinsonian-like events observed in entire population (n=38)

Pivotal Phase 2 Trial is now enrolling!
(RP2D, 115±10 million CAR+ T cells)