

**MGTA-145, in Combination with Plerixafor in a Phase 1 Clinical Study,
Mobilizes Large Numbers of Hematopoietic Stem Cells
and a Graft with Potent Immunosuppressive Properties
for Autologous and Allogeneic Transplant**

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Magenta Therapeutics

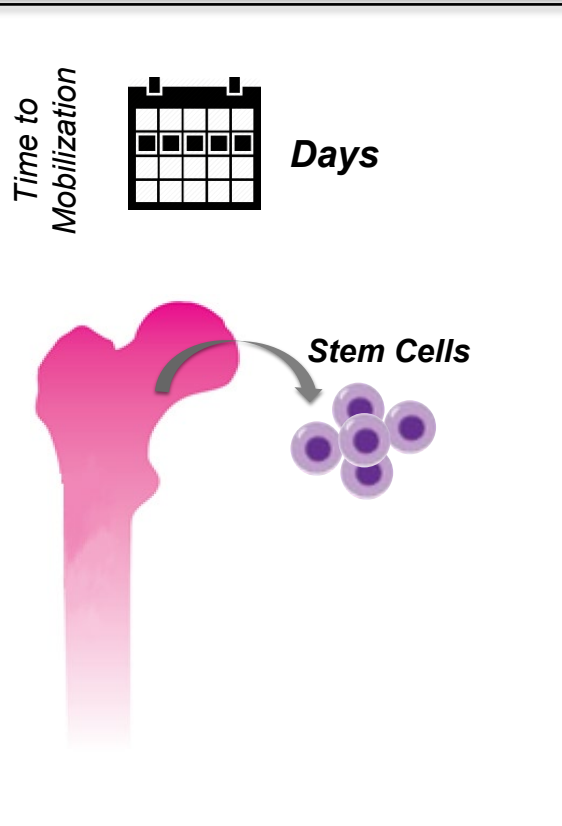
Disclosures

Magenta Therapeutics

- Employee, Salary, Ownership Interest, Intellectual Property

MGTA-145 + Plerixafor Enables Rapid and Robust Mobilization of Hematopoietic Stem Cells (HSCs)

G-CSF Induced Mobilization



65,000 transplants annually
70% use mobilized peripheral blood

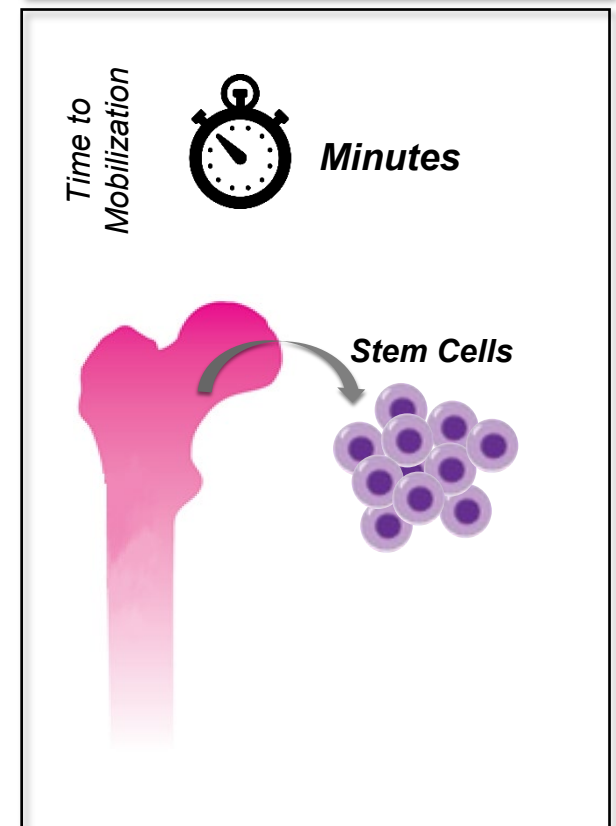
Limitations to Current Mobilization Standard of Care:

- Requires 5+ days
- Variable yields
- Adverse events, some for the duration of mobilization
- Contraindicated/precautions in certain diseases

Benefits of Novel Mobilization:

- Shortened mobilization phase
- Fewer/shorter duration of adverse events
- On demand mobilization enables more flexible scheduling

Magenta Mobilization



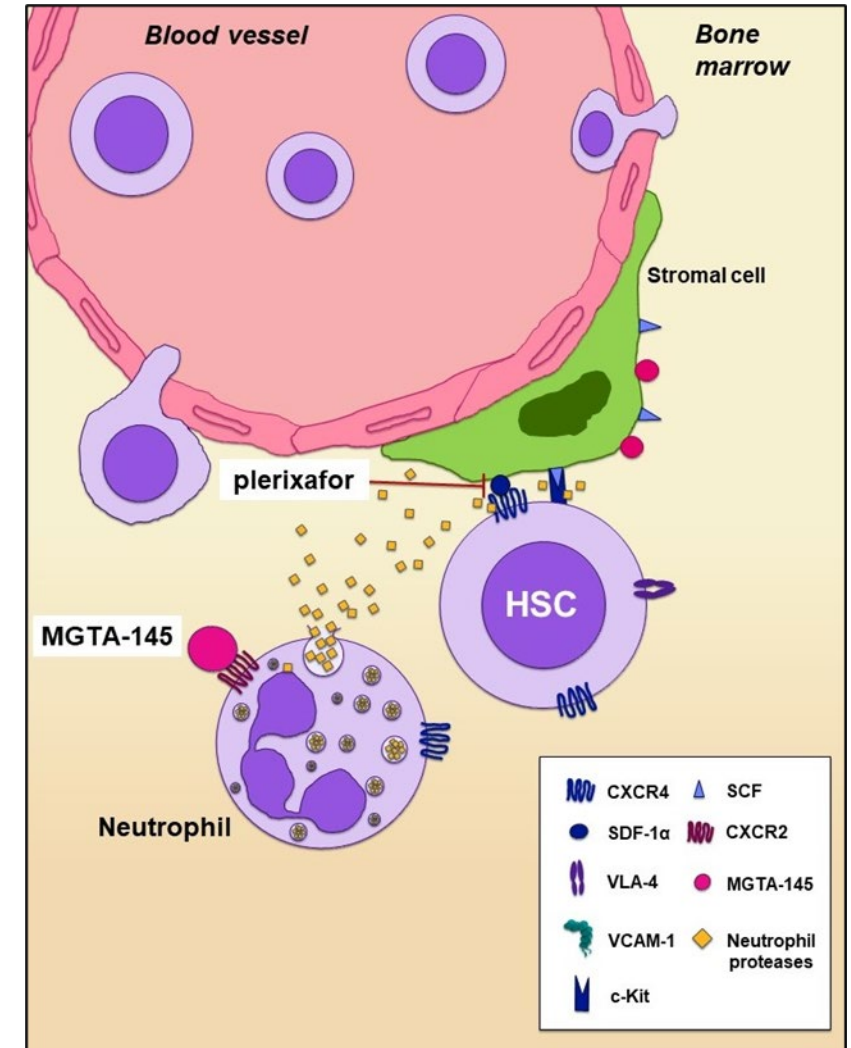
MGTA-145, In Combination with Plerixafor, Rapidly Mobilizes HSCs

NOVEL MOBILIZATION AGENT

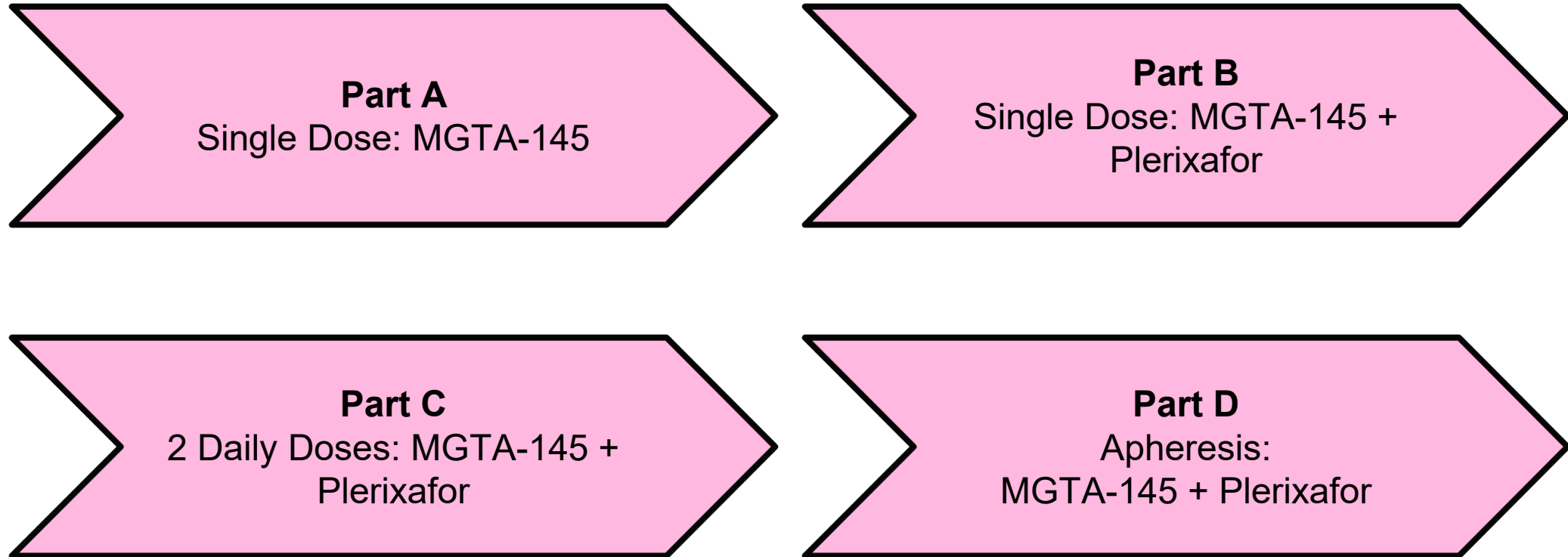
MGTA-145 (GroßT) *CXCR2 agonist* + **plerixafor** (AMD3100) *CXCR4 antagonist*

KEY FEATURES

- Rapid & robust mobilization of HSCs in mice and non-human primates
[Hoggatt et al, *Cell* 2018; Goncalves et al, *Blood* 2018; Karpova et al, *JCI* 2019]
- Single-day dosing and collection
- Well-tolerated
- Mimics physiological response



MGTA-145-101 Healthy Volunteer Study Schema



DiPersio et al. TCT 2020

Treatment Emergent Adverse Events

	Part A		Part B		Part C		Part D
	MGTA-145 (0.0075 - 0.3 mg/kg)	Placebo	MGTA-145 + plerixafor (0.015 - 0.15 mg/kg)	Plerixafor	MGTA-145 + plerixafor (0.03 - 0.07 mg/kg)	Plerixafor	MGTA-145 + plerixafor (0.015 - 0.03 mg/kg)
	n=24 n (%)	n=12 n (%)	n=38 n (%)	n=14 n (%)	n=8 n (%)	n=2 n (%)	n=8*** n (%)
Subjects with any drug related TEAE*	19 (79.2)	-	31 (81.6)	8 (57.1)	6 (75.0)	-	8 (88.9)
Diarrhea	-	-	6 (15.8)	5 (35.7)	1 (12.5)	-	1 (11.1)
Nausea	-	-	7 (18.4)	2 (14.3)	1 (12.5)	-	4 (44.4)
Abdominal discomfort/pain	-	-	5 (13.2)	4 (28.6)	-	-	3 (33.3)
Vomiting	-	-	3 (7.9)	1 (7.1)	-	-	1 (11.1)
Back pain / Musculoskeletal pain**	19 (79.2)	-	24 (63.2)	2 (14.3)	4 (50.0)	-	3 (33.3)
Dizziness / Lightheadedness	-	-	5 (15.6)	1 (7.1)	-	-	4 (44.4)
Headache	-	-	4 (10.5)	1 (7.1)	2 (25.0)	-	2 (22.2)
Dysgeusia	-	-	-	2 (14.3)	-	-	-
Paraesthesia	-	-	2 (5.3)	-	1 (12.5)	-	1 (11.1)

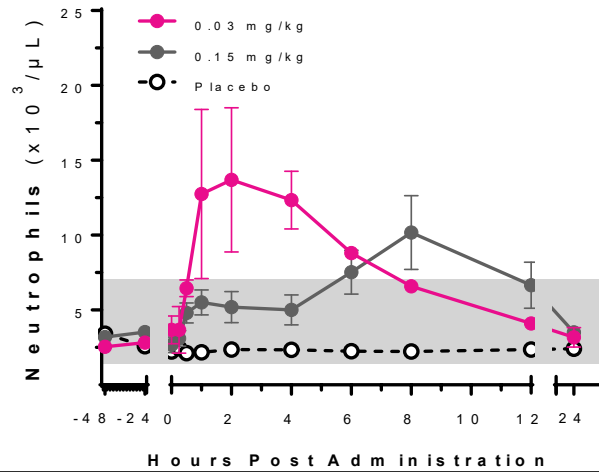
*There was no dose response in AEs; data are aggregated.

**Back pain was transient (<20 minutes).

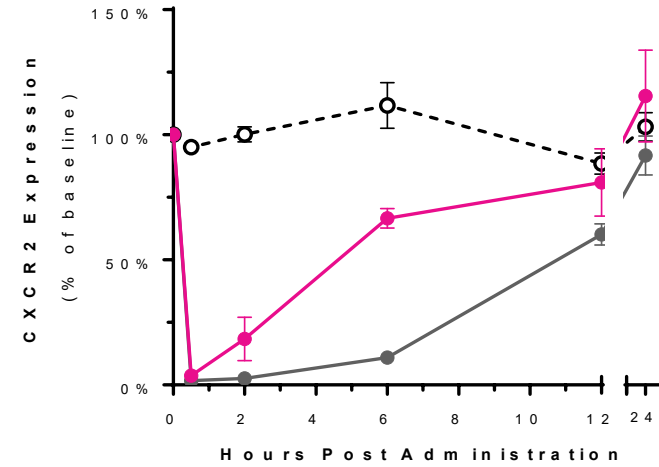
***A 9th subject enrolled in Part D but did not undergo leukapheresis.

MGTA-145 has Rapid On-Target Neutrophil PD with Minimal Activation

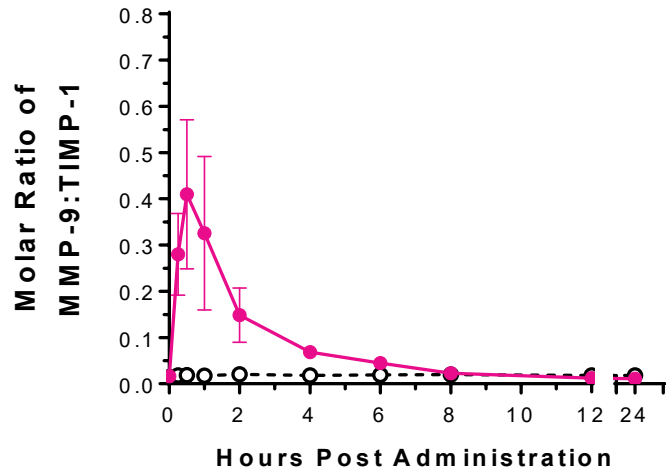
NEUTROPHIL MOBILIZATION



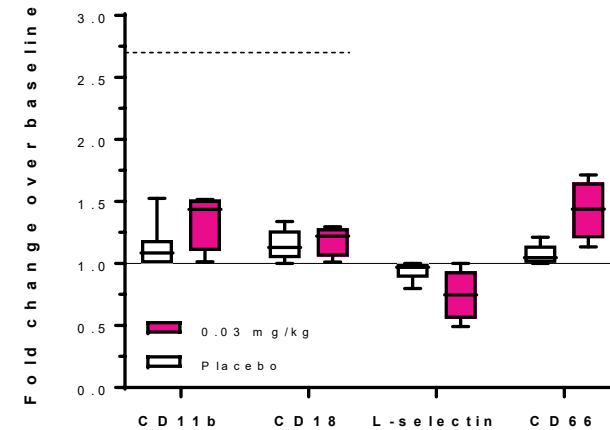
CXCR2 TARGET DOWN-MODULATION



MMP-9 RELEASE



MINIMAL NEUTROPHIL ACTIVATION



Dotted line represents the anticipated effect of 5 days of G-CSF [Falanga *et al.*, *Blood*. 1999]

MGTA-145 Enables Reliable Collection of $>2 \times 10^6$ CD34⁺ Cells in One Day

Part B: Mobilization at 0.015 versus 0.03 mg/kg, 2h stagger

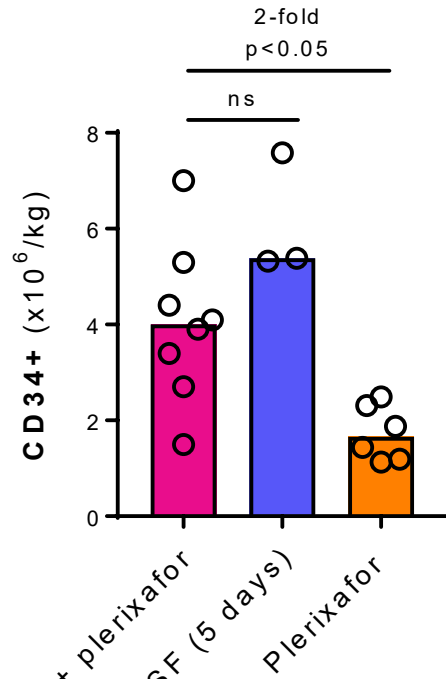
Mobilization Regimen	MGTA-145 dose (mg/kg)	Subjects (n)	Peak CD34 ⁺ (#/μL) Median (range)	% ≥ 20 / μL	% ≥ 40 / μL
MGTA-145 + Plerixafor	0.015	6	35 (17-78)	83% (5/6)	33% (2/6)
	0.03	6	40 (18-63)	83% (5/6)	50% (3/6)
Plerixafor	0	14	26 (13-78)	64% (9/14)	21% (3/14)

Part D: Apheresis Collection at 0.015 versus 0.03 mg/kg dose, 2h stagger

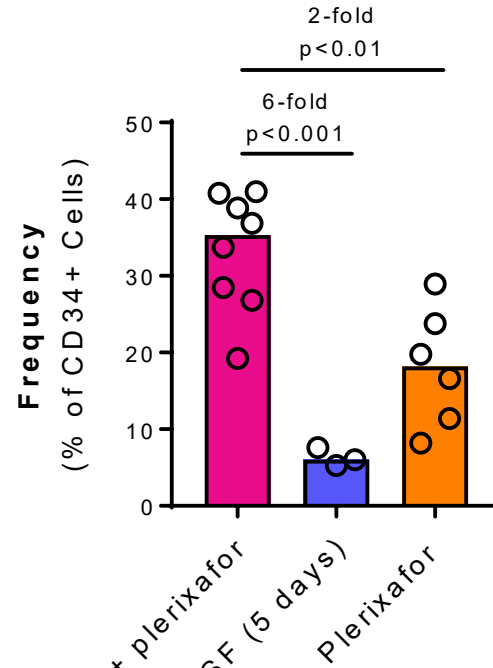
MGTA-145 dose (mg/kg)	Subjects (n)	Total CD34 ⁺ Yield ($\times 10^6$) Median (range)	CD34 ⁺ / kg ($\times 10^6$)		
			Mean	Median	Range
0.015	4	310 (118-525)	4.0	3.7	1.5 - 7.0
0.03	4	321 (239-500)	4.1	4.3	2.7 - 5.3

MGTA-145 + Plerixafor Enables Greater Collection of HSCs after Apheresis in a Phase 1 Healthy Volunteer Study

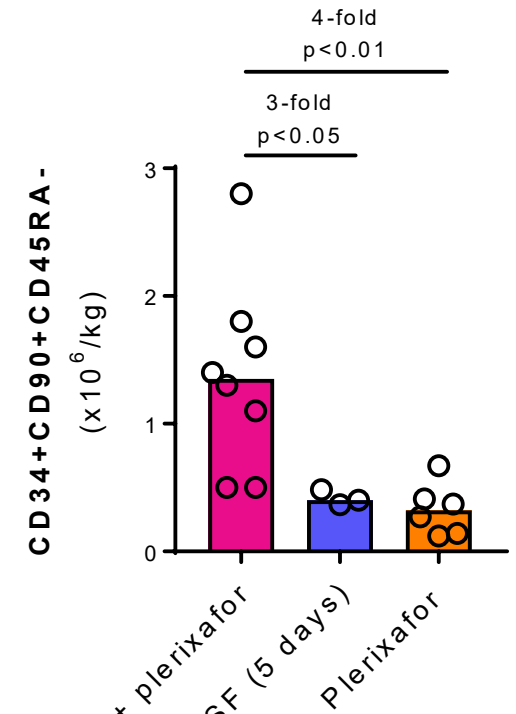
CD34+ NUMBER



CD34+CD90+CD45RA- FREQUENCY



CD34+CD90+CD45RA- NUMBER



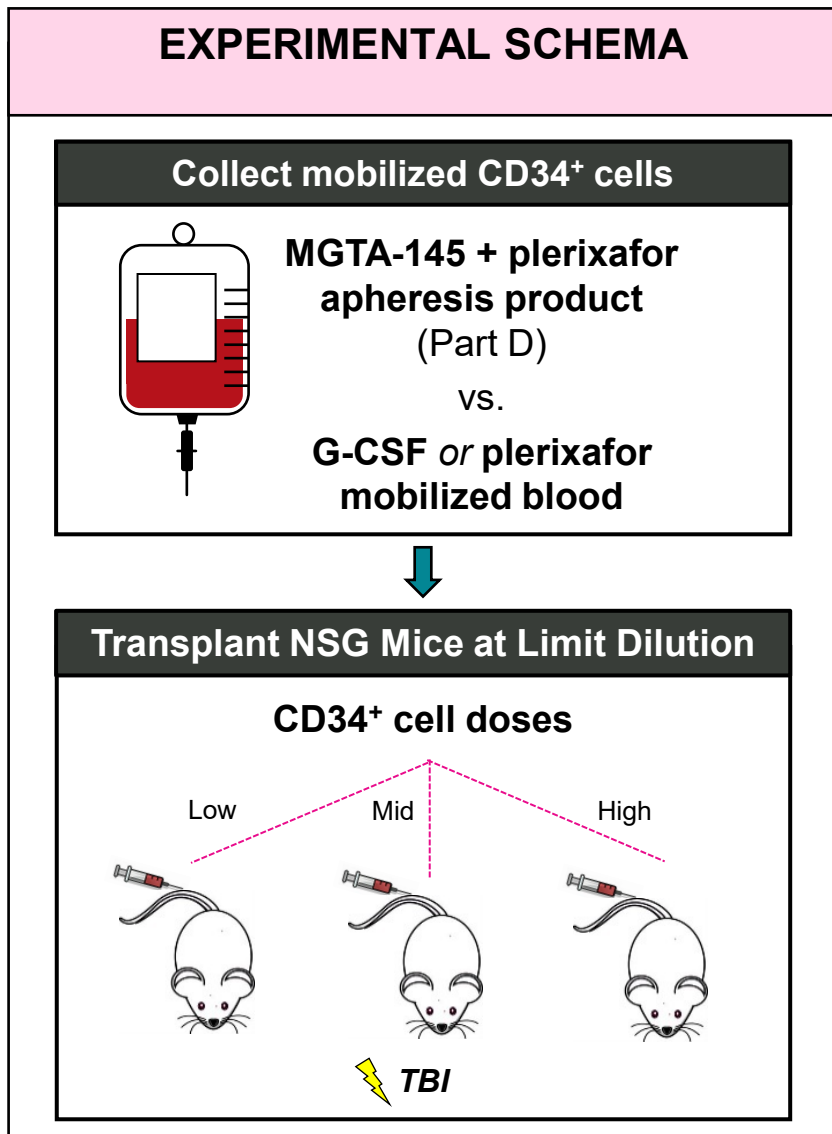
Bars represent median
Symbols represent individual donor

MGTA-145 + plerixafor: n=7 donors (mobilized with 0.015 or 0.03 mg/kg MGTA-145)

G-CSF: n=3 donors

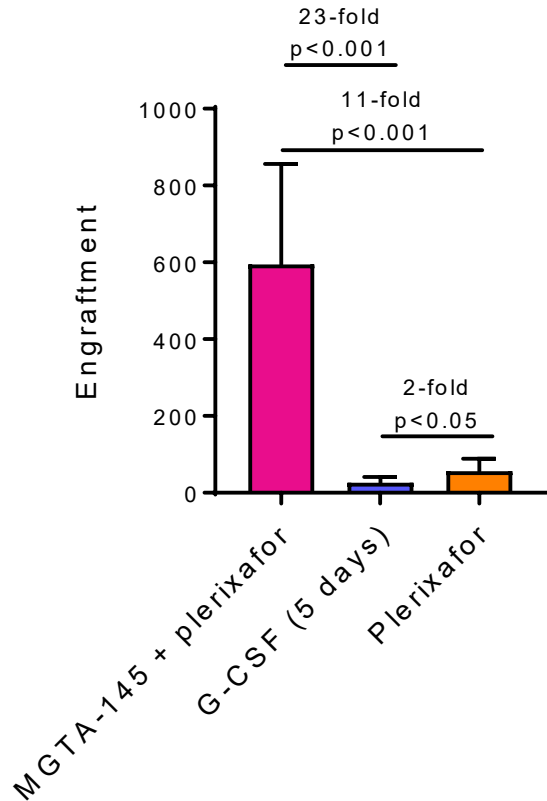
Plerixafor: n=6 donors

Determination of Engraftment Kinetics of MGTA-145 + Plerixafor Mobilized CD34+ Cells from Phase 1 Healthy Volunteer Study in NSG Mice



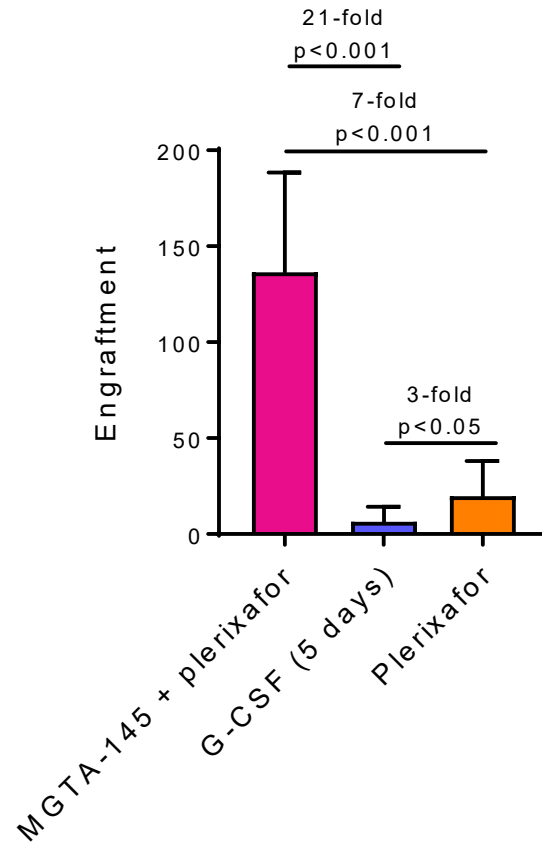
MGTA-145 + Plerixafor CD34+ Cells from Phase 1 Healthy Volunteer Study Show Higher Multilineage Engraftment Compared to G-CSF and Plerixafor Mobilized CD34+ Cells in Primary and Secondary NSG Mouse Transplants

WEEK 16 ENGRAFTMENT PRIMARY NSG RECIPIENTS

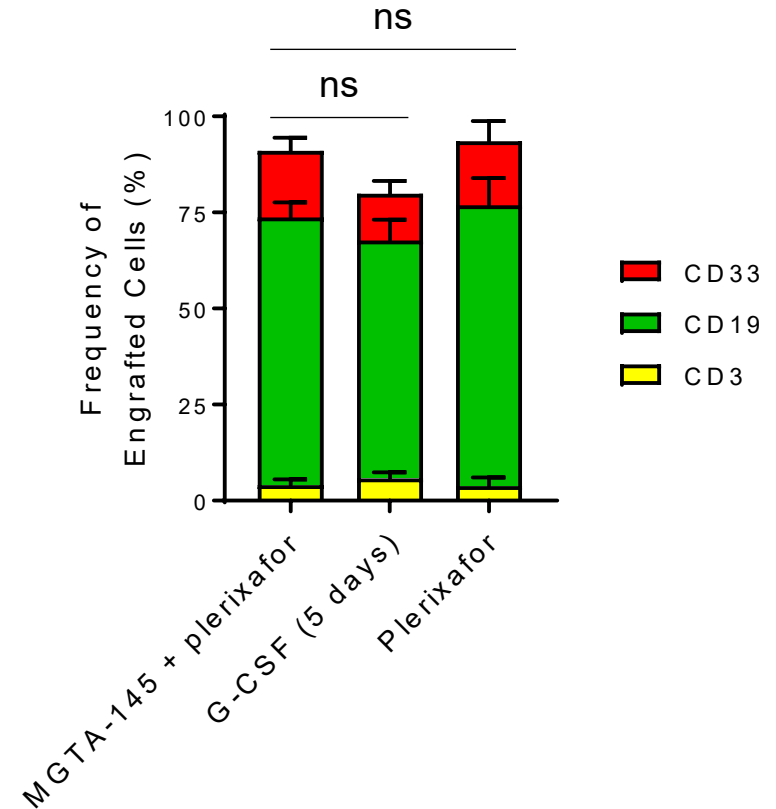


SRC per 1×10^6 cells \pm 95% CI
 n=3-4 donors
 n=7-8 mice per cell dose

WEEK 16 ENGRAFTMENT SECONDARY NSG RECIPIENTS



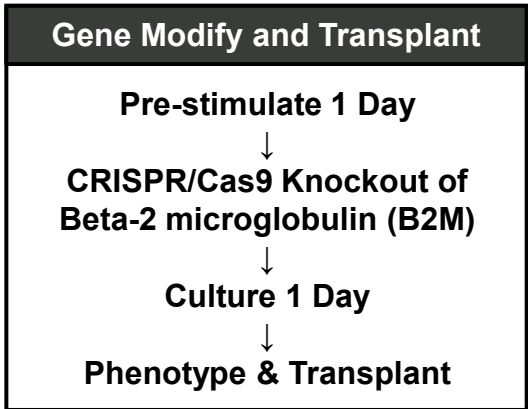
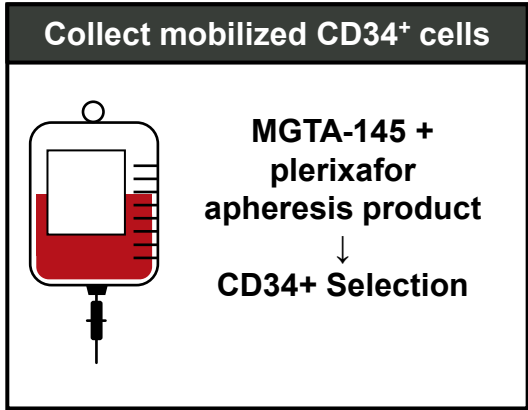
WEEK 16 LINEAGE COMPOSITION SECONDARY NSG RECIPIENTS



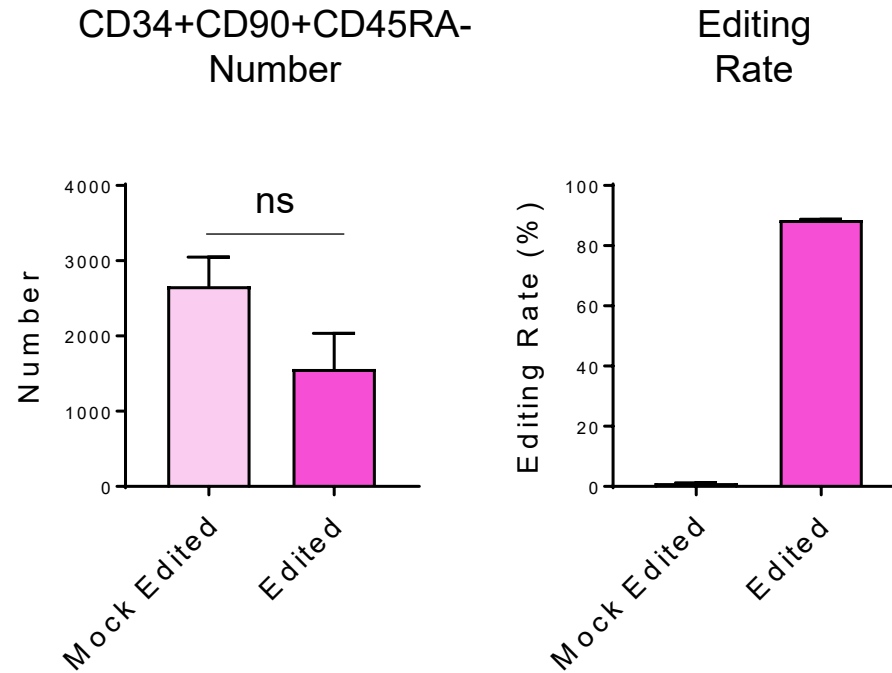
Mean \pm SEM
 n=3-4 donors
 n=7-8 mice per donor

MGTA-145 + Plerixafor CD34+ Cells from Phase 1 Healthy Volunteer Study Can Be Efficiently Gene Modified and Engraft in NSG Mice

EXPERIMENTAL SCHEMA

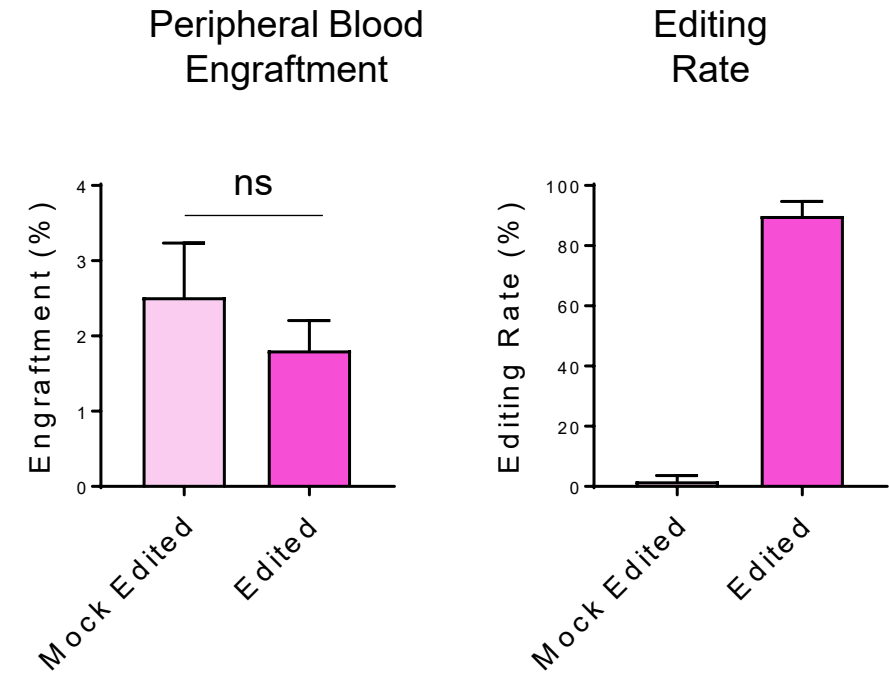


IN VITRO GENE EDITING



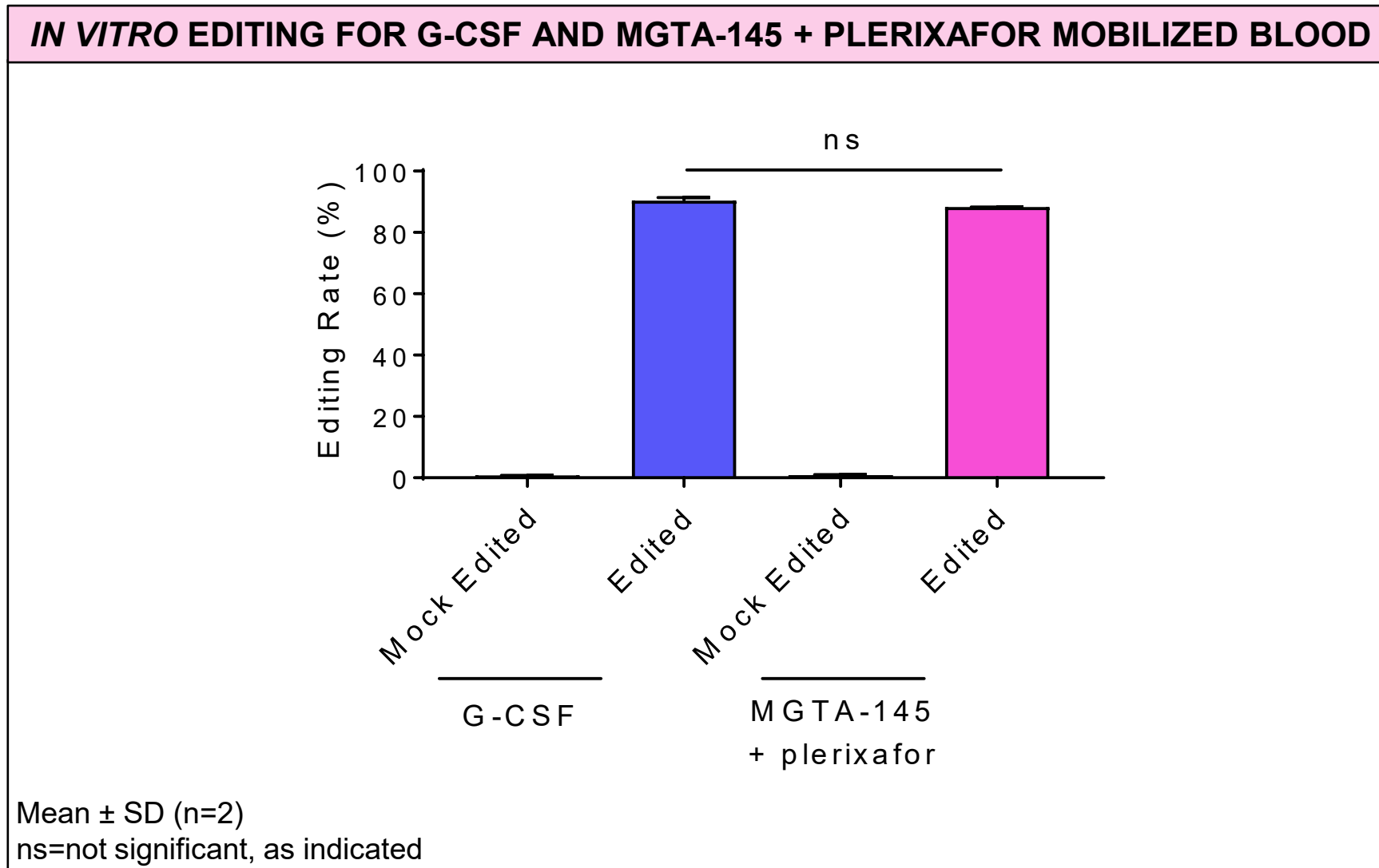
Mean ± SD (n=2)

WEEK 16 NSG ENGRAFTMENT



n=7-8 mice

MGTA-145 + Plerixafor Mobilized Blood Can Be Gene-Modified at the Same Rate as G-CSF Mobilized Blood



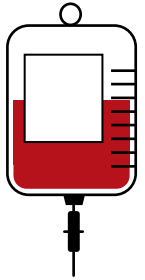
MGTA-145 + Plerixafor Grafts Are Enriched for Hematopoietic Stem/Progenitor Cells

	145-HV-101 Part D	Devine <i>et al.</i> , Blood 2008	
	MGTA-145 + plerixafor n=7	plerixafor n=24	G-CSF n=8
	Median (range)	Median (range)	Median (range)
CD34+ (x10 ⁶ /kg)	4.1 (1.5-7.0)	2.9 (1.2-6.3)	4.2 (2.5-18.7)
CD3+ (x10 ⁸ /kg)	4.0 (3.3-6.2)	4.6 (1.5-7.8)	1.3 (1.2-6.8)
CD4+ (x10 ⁸ /kg)	3.7 (3.0-5.0)	3.2 (1-5.7)	1.1 (0.7-3.2)
CD8+ (x10 ⁸ /kg)	0.2 (0.0-0.6)	1.3 (0.4-3.4)	0.4 (0.3-3.4)
CD19+ (x10 ⁸ /kg)	1.8 (1.1-1.9)	1.0 (0.2-2.4)	-
CD56+ (x10 ⁸ /kg)	0.5 (0.2-1.0)	0.3 (0.1-1.0)	0.2 (0.1-0.5)

MGTA-145 + Plerixafor Grafts From Phase 1 Healthy Volunteer Study Are Immunosuppressive in a Xenograft Mouse Model

EXPERIMENTAL SCHEMA

Collect PBMCs



**MGTA-145 + plerixafor
apheresis product
(Part D)**

vs.

**G-CSF or plerixafor
mobilized blood**

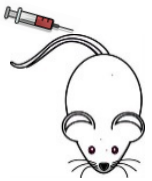
vs.

unmobilized blood



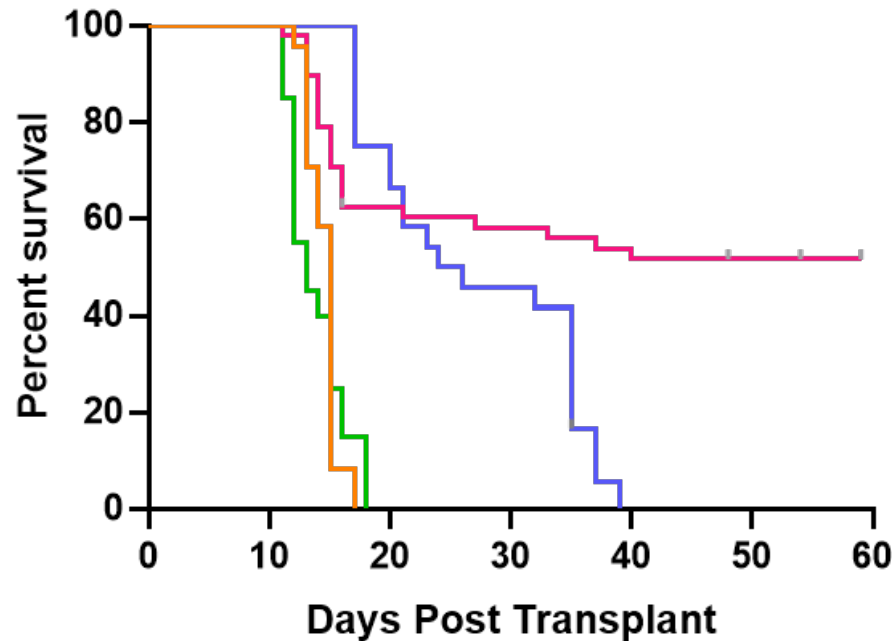
Transplant NSG Mice

6×10^6 PBMCs per recipient



TBI

SURVIVAL AFTER XENOTRANSPLANT OF MOBILIZED BLOOD



	Median Survival (Days)
Whole Blood	13
G-CSF	25
Plerixafor alone	15
145-p	60+

LOG RANK TEST

145-p vs G-CSF: $p < 0.01$

145-p vs plerixafor: $p < 0.001$

Unmobilized: $n=3$ donors, $n=6-7$ mice/donor
Mobilized: $n=3-6$ donors per regimen, $n=8$ mice/donor

MGTA-145 + Plerixafor Mobilizes a Graft with High Numbers of Functional HSCs and the Potential for Reduced GvHD

- MGTA-145 is well-tolerated in 79 subjects as monotherapy and in combination with plerixafor.
- MGTA-145 engages CXCR2 on neutrophils to mobilize CD34⁺ cells into peripheral blood.
- MGTA-145 administration is safe, as monotherapy or in combination with plerixafor, and leads to robust CD34⁺ cell mobilization.
- Ph1 graft characterization of MGTA-145 + plerixafor mobilized blood demonstrates:
 - Collection of high numbers of CD34⁺ and CD34⁺CD90⁺ cells
 - Significantly higher multilineage engraftment compared to G-CSF or plerixafor mobilized CD34⁺ cells in primary and secondary NSG mouse recipients
 - Efficient gene modification and NSG engraftment of MGTA-145 + plerixafor CD34⁺ cells
 - Potent immunosuppression compared to G-CSF or plerixafor mobilized blood in a xenotransplant mouse model

Summary

	G-CSF	MGTA-145 + plerixafor
Mechanism of action	Bone remodeling	Chemokine cell migration
Time to mobilize and collect	5+ days	<1 day
Tolerability	Majority with bone pain, headache, myalgia, and/or fatigue (up to 1+ week) ^a	Majority with transient, grade 1 back pain (most <20 minutes)
Efficacy ($\geq 2 \times 10^6$ CD34 ⁺ /kg)	78% ^b	88% (7/8)
Quality of CD34 ⁺ (% CD90 ⁺ Median Yield)	6%	35%
Function of CD34 ⁺	-	Up to 23x increased engraftment

^a Pulsipher *et al*, *Blood*. 2009; ^b Holig, *Transfus Med Hemother*. 2013.



Day
injection



Same-day
blood draw



Same-day
apheresis

Based on the high number of functional hematopoietic stem cells mobilized by **MGTA-145 + plerixafor**, a Phase II study in multiple myeloma is enrolling patients (NCT04552743) and Magenta plans to initiate two Phase II trials in sickle cell disease with bluebird bio and in allogeneic transplant with Be the Match in 2021

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