



Developing  
**Breakthrough Biologics,**  
Life-changing Medicines™

## Corporate Presentation

May 2020



# Legal Notices

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## **Investigational Agents**

All Company product candidates described or mentioned herein are investigational and have not yet been approved for marketing by any regulatory authority.











# Building a Leadership Position in Immuno-Oncology

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Late-stage immuno-oncology company	<ul style="list-style-type: none"><li>• December 2020 PDUFA goal date for most advanced product candidate</li><li>• Three additional ongoing or anticipated registration-directed studies</li></ul>
Proprietary platform technologies	<ul style="list-style-type: none"><li>• Bispecific DART® platform technology that exploits multiple mechanisms</li><li>• Fc-engineering to enhance innate and adaptive immunity</li></ul>
Deep and differentiated pipeline	<ul style="list-style-type: none"><li>• Unique immune-based mechanisms</li><li>• Retain major market rights for 6 of 7 clinical assets</li></ul>
Funded to execute on plan	<ul style="list-style-type: none"><li>• \$171M cash, cash equivalents and marketable securities at 3/31/20</li><li>• Multiple 2020 inflection points</li></ul>



# Deep and Differentiated Immuno-Oncology Pipeline

Program (Target)	Potential Indication(s)	First-in-Human (Phase 1)	Proof-of-Concept (Phase 2)	Pivotal (Phase 3)	Major Market Rights
<b>Margetuximab</b> (HER2)	HER2+ Breast				 
	HER2+ Gastric/GEJ (+retifanlimab/MGD013)				
<b>Flotetuzumab</b> (CD123 × CD3)	AML				
<b>Retifanlimab</b> (PD-1)	Solid Tumors				 <sup>(b)</sup>
<b>Enoblituzumab</b> (B7-H3)	SCCHN (+retifanlimab/MGD013)				 
<b>MGD013</b> (PD-1 × LAG-3)	Solid Tumors & Heme Malignancies				 
<b>MGD019</b> (PD-1 × CTLA-4)	Solid Tumors				
<b>MGC018</b> (B7-H3) <sup>(a)</sup>	Solid Tumors				
MGD = DART	MGA = Antibody	MGC = ADC			

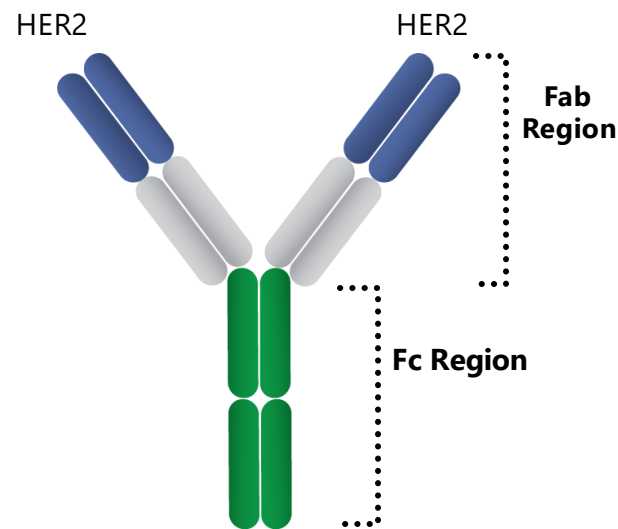
(a) MGC018 is an antibody-drug conjugate (ADC) based on a duocarmycin payload with cleavable peptide linker that was licensed from Synthon Biopharmaceuticals.

(b) MacroGenics retains rights to develop its pipeline assets in combination w/retifanlimab (MGA012) and to manufacture a portion of global clinical and commercial supply needs of retifanlimab.

**All Company product candidates described or mentioned herein are investigational and have not yet been approved for marketing by any regulatory authority.**

# Margetuximab: Anti-HER2 mAb Engineered to Enhance Activity of Immune System

*December 2020 PDUFA goal date for BLA for HER2+ metastatic breast cancer (mBC)*

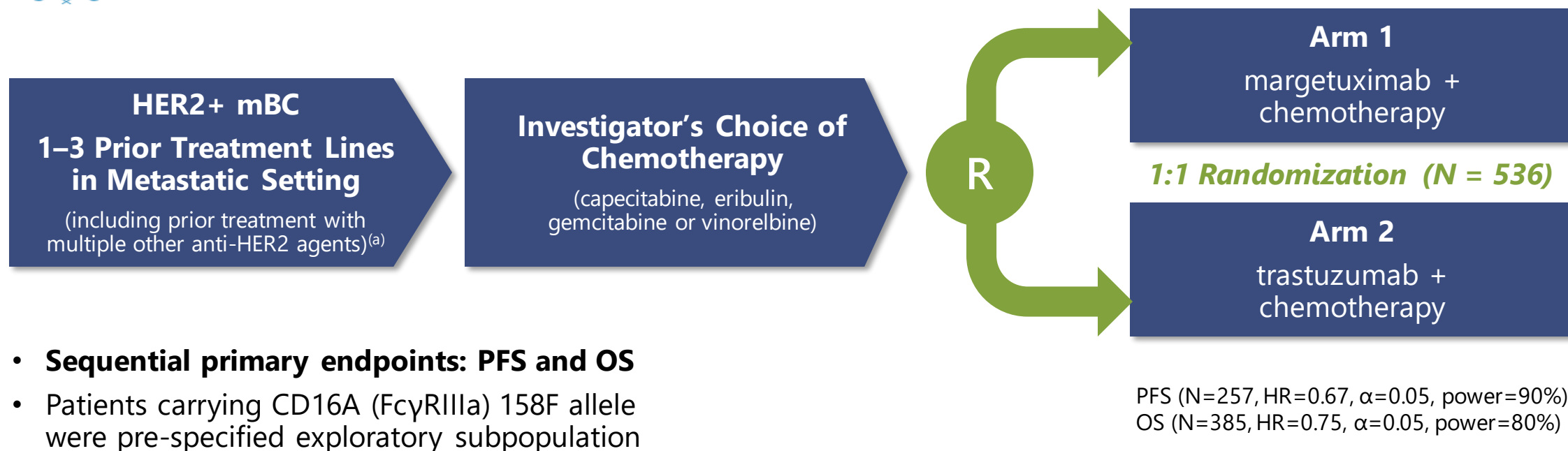


Function/ MoA	<ul style="list-style-type: none"> <li>Inhibits HER2 signaling (similar to trastuzumab)</li> <li>Fc region engineered to engage innate and adaptive immunity as mediators of anti-tumor activity</li> </ul>
Pivotal Clinical Studies	<ul style="list-style-type: none"> <li>Ph. 3 SOPHIA study versus trastuzumab in HER2+ mBC</li> <li>Ph. 2/3 MAHOGANY study w/checkpoint inhibitor in HER2+ gastric cancer</li> </ul>
2020 Anticipated Milestones	<ul style="list-style-type: none"> <li>BLA for HER2+ mBC: ODAC expected (2H); PDUFA goal date (December 18, 2020)</li> <li>Final SOPHIA OS analysis (N=385) (2H)</li> <li>Obtain initial data from MAHOGANY Module A</li> </ul>

*Margetuximab is investigational and has not yet been approved for marketing by any regulatory authority*

# Phase 3 SOPHIA Study Comparing Margetuximab to Trastuzumab

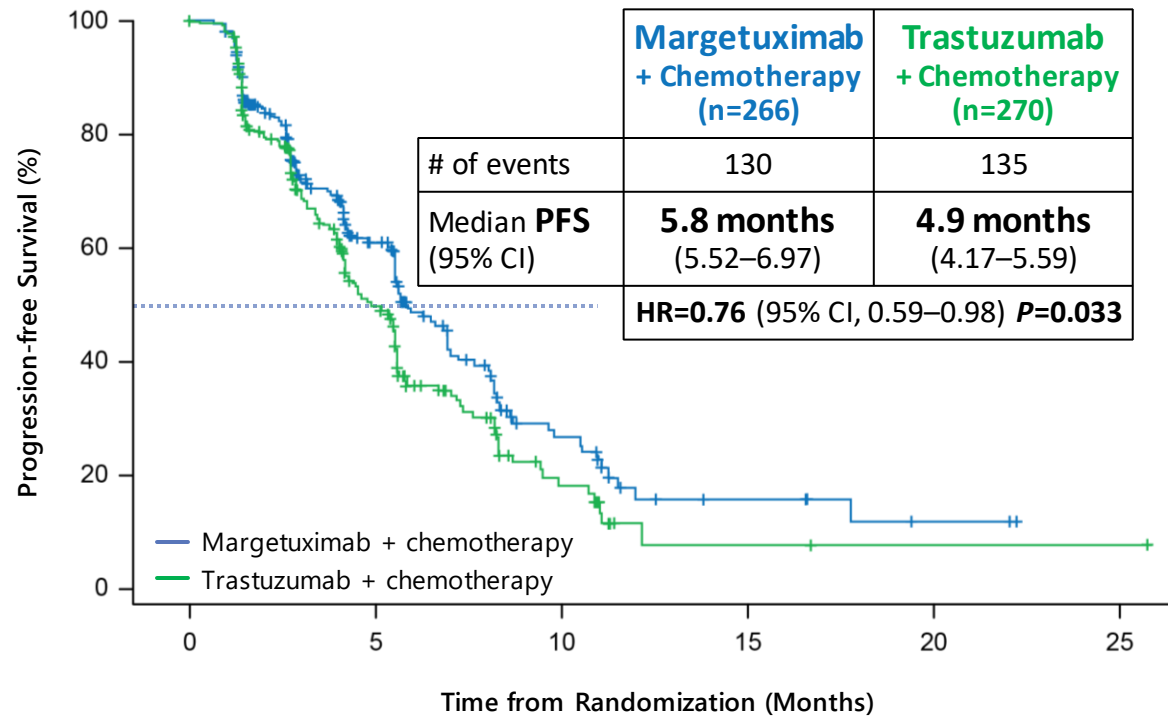
*Designed to support registration in 3rd/4th line HER2+ metastatic breast cancer*



(a) All study patients had previously received trastuzumab and pertuzumab, and approximately 90% had previously received ado-trastuzumab emtansine.

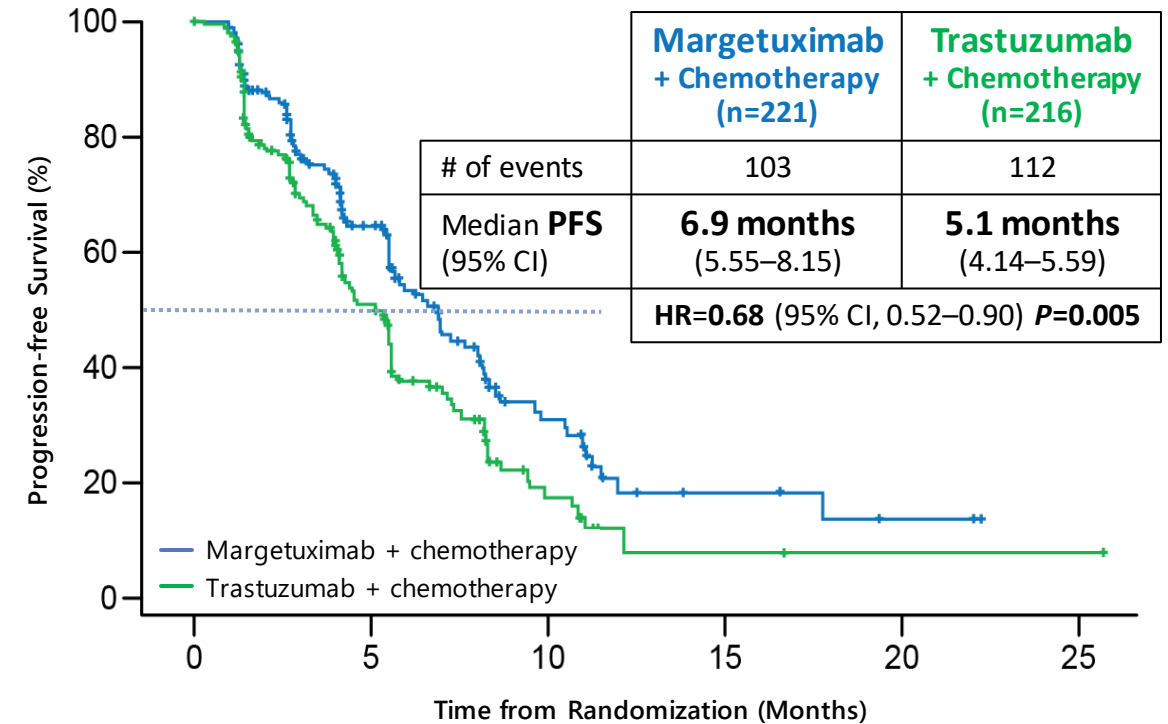
# Primary PFS Endpoint: Margetuximab Demonstrated Superiority to Trastuzumab

## PFS Primary Endpoint (ITT Population): 24% Risk Reduction of Disease Progression



Margetuximab	266	174	94	45	21	8	6	4	2	0	
Trastuzumab	270	158	74	33	13	2	2	1	1	1	1

## Pre-specified Exploratory Subpopulation (CD16A-158F Carriers): 32% Risk Reduction of Disease Progression



Margetuximab	221	157	84	42	21	8	6	4	2	0	
Trastuzumab	216	129	62	30	11	2	2	1	1	1	1

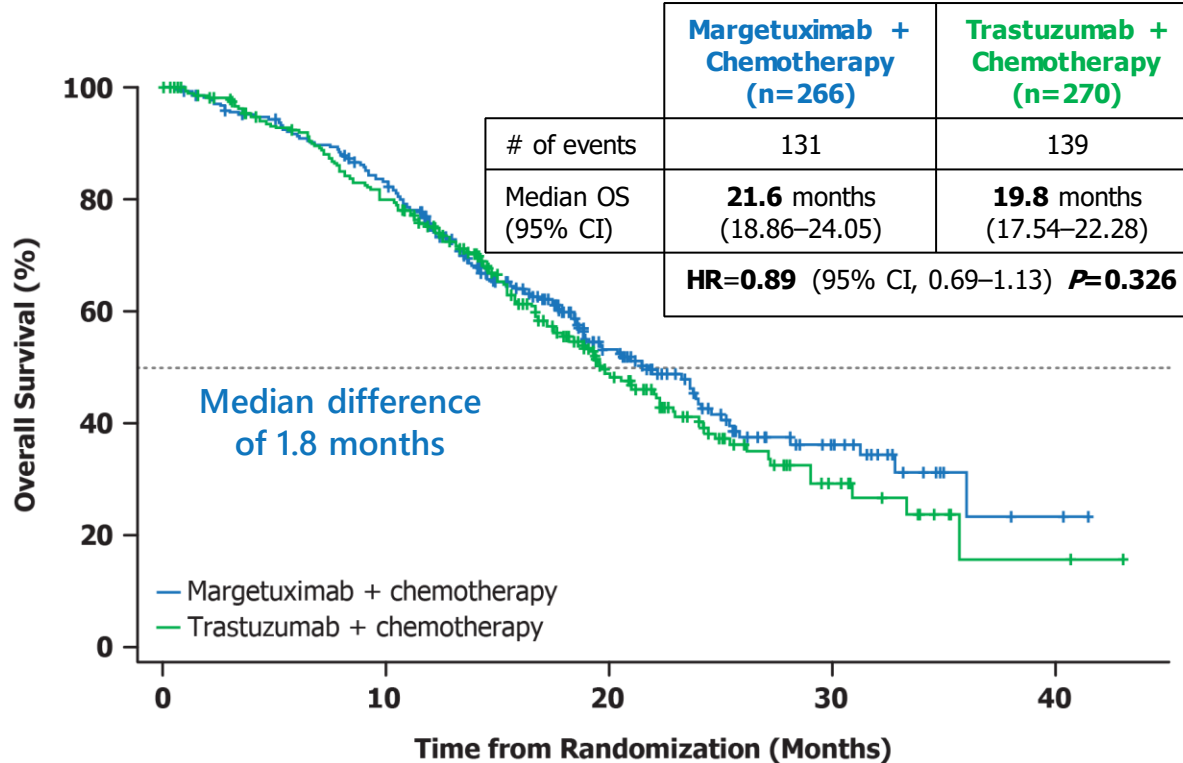
October 2018 data cut-off after 265 PFS events in ITT population.  
CI=confidence interval. ITT=Intent to Treat population: N=536. CD16A 158F Carriers=FF or FV Genotype.  
HR=Hazard Ratio (ITT by stratified Cox model; F Carriers by unstratified Cox model).

Rugo, et al., ASCO 2019

# Second Interim Overall Survival Analysis: Trend Favored Margetuximab

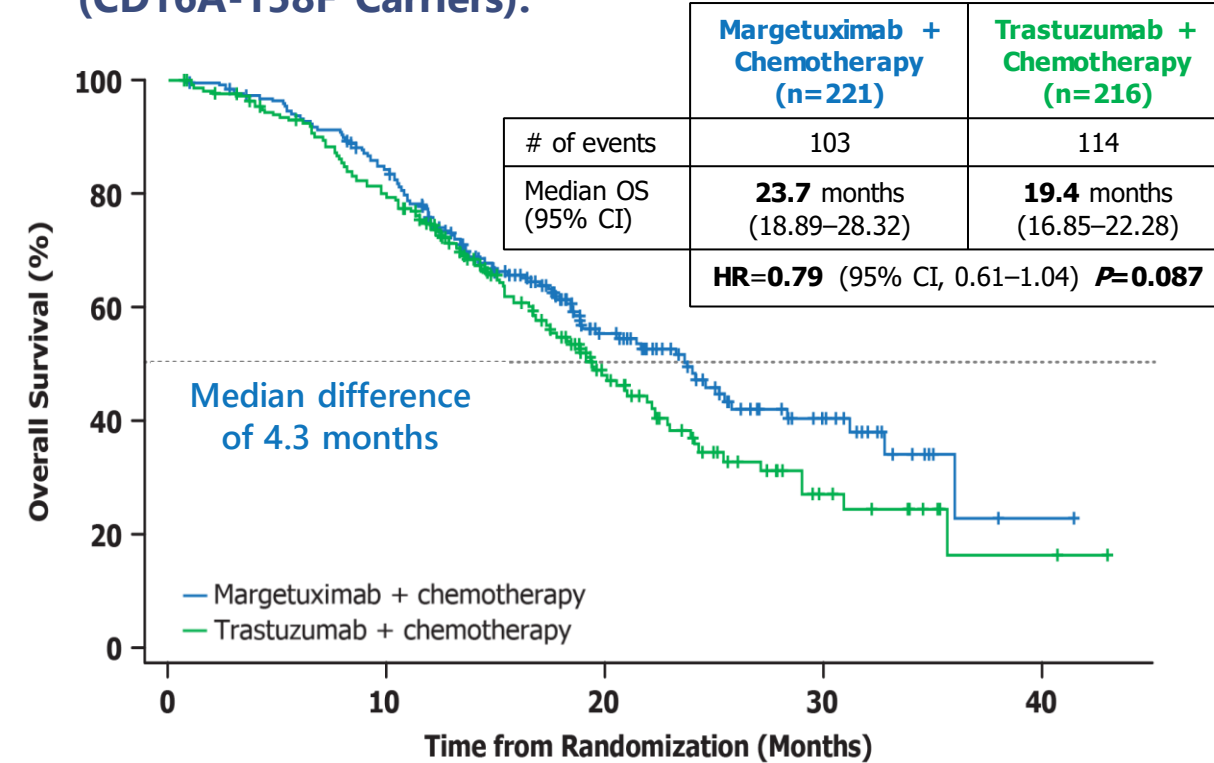
Final analysis expected 2H20

## ITT Population



Margetuximab 266 259 249 239 230 214 188 159 131 107 80 64 47 35 31 22 14 9 3 2 2 0  
Trastuzumab 270 260 246 236 218 205 183 160 126 102 74 57 43 30 22 16 10 6 2 2 2 1 0

## Pre-specified Exploratory Subpopulation (CD16A-158F Carriers):



Margetuximab 221 219 212 204 196 181 157 135 111 91 68 55 42 31 27 19 13 8 2 1 1 0  
Trastuzumab 216 210 201 192 176 165 145 123 98 81 57 43 30 21 16 11 9 6 2 2 2 1 0

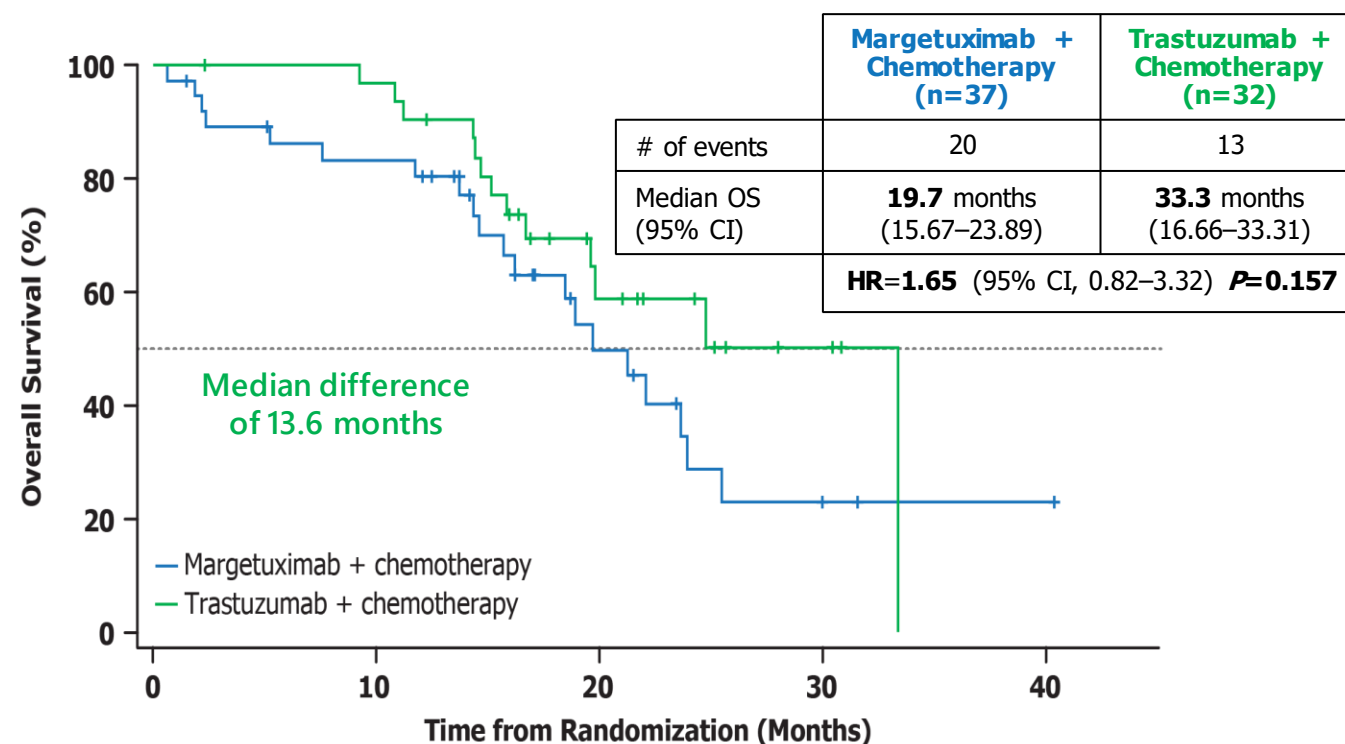
September 2019 data cut-off after 270 events in ITT population. Median follow-up: 15.6 months.  
ITT=Intent to Treat population: N=536. CD16A 158F Carriers=FF or FV Genotype.  
CI=confidence interval. HR=Hazard Ratio (ITT by stratified Cox model; F Carriers by unstratified Cox model).

Rugo, et al., SABCS 2019



# Pre-specified Exploratory OS in CD16A-158 VV Homozygotes

*VV subpopulation represents 33 events (270 events in ITT population)*



Margetuximab 37 34 32 30 29 29 27 23 19 15 11 9 5 4 4 3 1 1 1 1 0  
Trastuzumab 32 32 31 31 31 30 28 27 20 14 11 8 8 4 3 3 1 0

September 2019 data cut-off after 270 events in ITT population. Median follow-up: 15.6 months.  
CI=confidence interval. HR=Hazard Ratio (by unstratified Cox model).

## Unbalanced patient characteristics

Baseline Characteristic	Margetuximab + Chemotherapy (n=37)	Trastuzumab + Chemotherapy (n=32)
Cancer disease history		
Brain, n (%)	8 (22%)	3 (9%)
Breast, n (%)	10 (27%)	5 (16%)
Liver, n (%)	16 (43%)	10 (31%)
Lung, n (%)	11 (30%)	13 (41%)
Lymph node, n (%)	21 (57%)	16 (50%)
HER2 IHC 3+, n (%)	19 (51%)	18 (56%)
Hormone receptor +, n (%)	23 (62%)	18 (56%)
ECOG PS 1, n (%)	14 (38%)	16 (50%)
>60 years of age, n (%)	16 (43%)	5 (16%)
>2 prior metastatic lines of therapy, n (%)	15 (41%)	9 (28%)

Less favorable

Rugo, et al., SABCS 2019

# Overall Safety Profiles Similar

## Adverse Events (AE)

	Margetuximab + Chemotherapy (n=264)		Trastuzumab + Chemotherapy (n=266)	
<b>Any grade AE, n (%)</b>	260 (98.5)		261 (98.1)	
<b>Any margetuximab or trastuzumab-related AE, n (%)</b>	160 (60.6)		132 (49.6)	
<b>Grade ≥3 AE, n (%)</b>	142 (53.8)		140 (52.6)	
<b>Grade ≥3 margetuximab or trastuzumab-related AE, n (%)</b>	34 (12.9)		22 (8.3)	
<b>Any SAE, n (%)</b>	43 (16.3)		49 (18.4)	
<b>Any margetuximab or trastuzumab-related SAE, n (%)</b>	5 (1.9)		4 (1.5)	
<b>AE leading to treatment<sup>a</sup> discontinuation, n (%)</b>	8 (3.0)		7 (2.6)	
<b>AEs resulting in death,<sup>b</sup> n (%)</b>	3 (1.1) <sup>c</sup>		2 (0.8) <sup>d</sup>	
<b>AEs of special interest, n (%)</b>	<b>All Grade</b>	<b>Grade ≥3</b>	<b>All Grade</b>	<b>Grade ≥3</b>
Infusion-related reaction (IRR)	35 (13.3)	4 (1.5)	9 (3.4)	0
Discontinuation due to IRRs, n (%)	2 (0.6)	0	0	0
LV dysfunction leading to dose delay or discontinuation, n (%)	4 (1.5)	0	6 (2.3)	0

Safety Population (randomized patients who received any study treatment): N=530. April 2019 cut-off.

(a) Including both anti-HER2 study therapy and chemotherapy. (b) No AEs resulting in death were considered related to anti-HER2 study therapy.

(c) Pneumonia (n=2), pneumonia aspiration (n=1). (d) Pneumonia (n=1), acute kidney injury (n=1). LV=left ventricular; SAE=serious AE.

Rugo, et al., SABCS 2019

# Margetuximab's Potential Role in Treatment of HER2+ mBC

**Need remains for additional therapies in later lines**

Patients will progress on other HER2-directed therapies

**PFS improvement  
vs. trastuzumab  
in clinical study**

Superiority in  
head-to-head trial

**Flexibility**

Ability to tailor  
treatment by  
selecting among  
four different  
chemotherapies

**Familiarity**

Side effect profile  
is well known  
and manageable

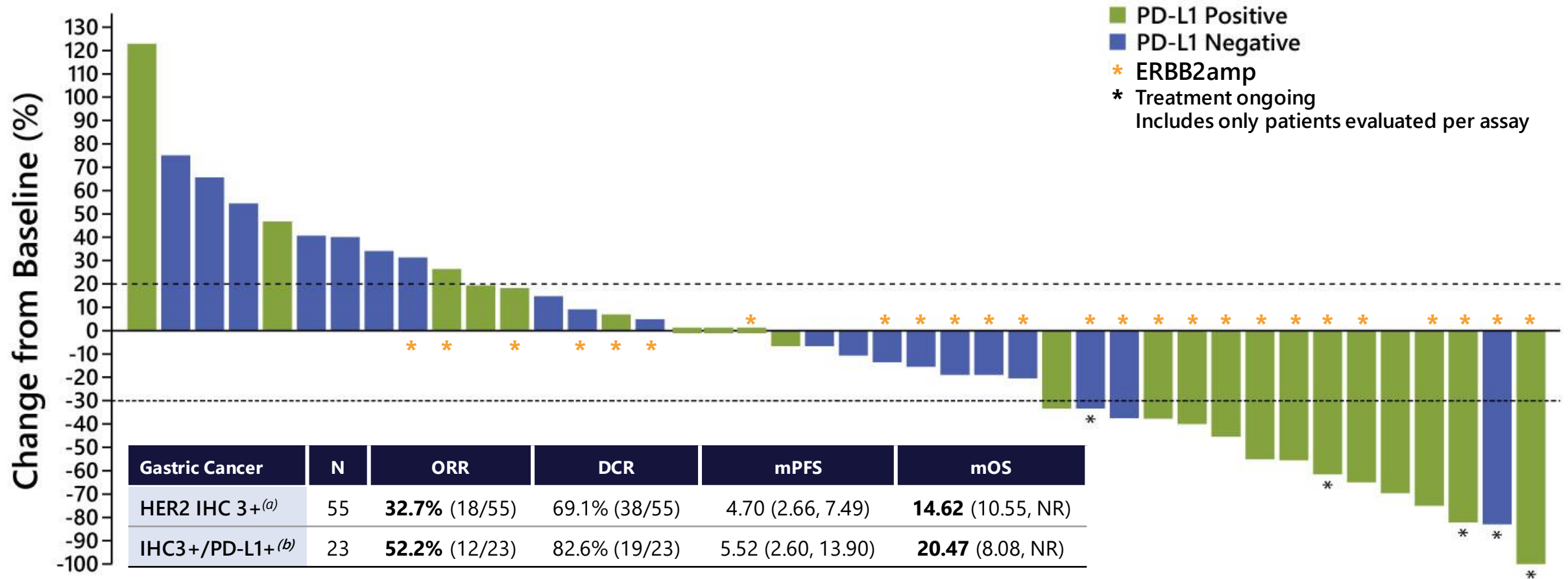
**CD16A  
exploratory  
analysis**

85% of population  
are F carriers

*Margetuximab is investigational and has not yet been approved for marketing by any regulatory authority*

# Promising Activity in Advanced Gastric Cancer Patients in Phase 2 Study

33% ORR in HER2 3+ gastric cancer previously treated with chemotherapy and trastuzumab



Data cut-off July 10, 2019. Includes patients who received  $\geq 1$  margetuximab and pembrolizumab dose in expansion phase, and had baseline measurable disease and  $\geq 1$  post-baseline disease assessment.

(a) Immunohistochemistry (IHC) test gives score of 0 to 3+ that measures amount of HER2 receptor protein on surface of cells in cancer tissue sample. Score of 0 to 1+ is called "HER2 negative", score of 2+ is called "borderline", score of 3+ is called "HER2 positive."

(b) "PD-L1 Positive" reflects Combined Positive Score (per standard FDA approved assay)  $\geq 1\%$  (PD-L1 tested on archival tissue by IHC; clone 22C3 pharmDx).

Catenacci, et al., ESMO 2019

# Gastric Cancer as Follow-on Indication

*Data from 2L margetuximab + anti-PD-1 mAb presents opportunity to advance to 1L*

## HER2+ gastric cancer benchmarks

	1st Line	2nd Line			3rd Line
	SOC	SOC	Ongoing Phase 2 Study	Failed	Ongoing Study
Agent (Study)	Trastuzumab + Chemo <sup>(a)</sup> (TOGA)	Ramucirumab + Paclitaxel <sup>(b)</sup> (RAINBOW)	<b>Margetuximab + Pembrolizumab<sup>(c)</sup></b>		Pembrolizumab <sup>(d)</sup> (KEYNOTE-61) PD-L1+
			IHC 3+	IHC 3+/PD-L1+	
ORR	47%	28%	33%	52%	15.8%
Median PFS	6.7 mos.	4.4 mos.	4.7 mos.	5.5 mos.	1.5 mos.
Median OS	<b>13.1 mos.</b>	9.6 mos.	<b>14.6 mos.</b>	<b>20.5 mos.</b>	9.1 mos.
≥ Grade 3 TRAEs	<b>68%</b>	Overall: N/A 41% Neutropenia 15% Hypertension 12% Fatigue	20%		14%
Gastric/GEJ Patient Mix	80/20%	80/20%	100%/0%		70%/30%

SOC = Standard of Care

(a) Data from Herceptin package insert; Bang, et al., Lancet, 2010;

(b) Data from Cyramza package insert; Wilkes, et al., Lancet Oncology, 2014;

(c) Data presented at ESMO 2019; Grade 3 TRAE includes all GC and GEJ patients.

(c) Data presented at ESMO 2019; Grade 3 TRAE includes all GC and GEJ patients.

(d) Shitara, et al., 2018, Lancet;

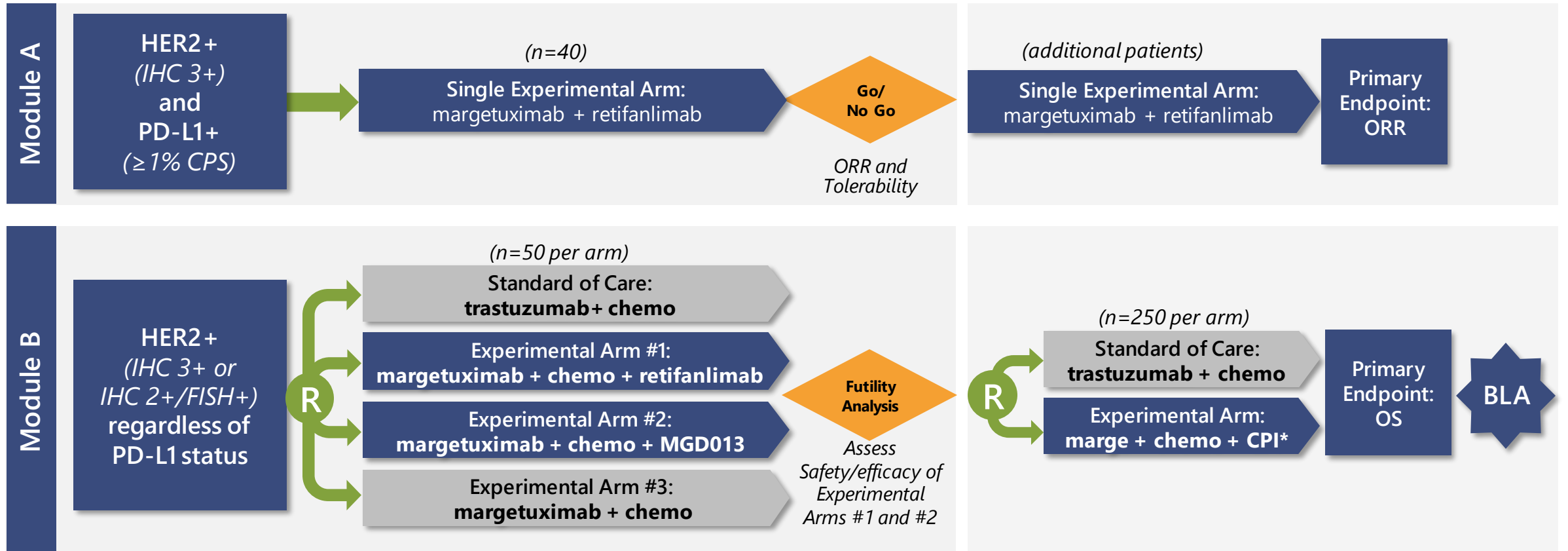
(e) Shitara, et al., 2019, Lancet Oncol.



# MAHOGANY Phase 2/3 Study: Registration Path in 1L Gastric & GEJ Cancer

*Module A has potential for U.S Accelerated Approval of chemotherapy-free regimen*

## MAHOGANY



MAHOGANY (Margetuximab in HER2-positive Gastric Cancer

\* Pending chronic tox study (if regimen with MGD013 is selected).

# Flotetuzumab: CD123 × CD3 DART Molecule

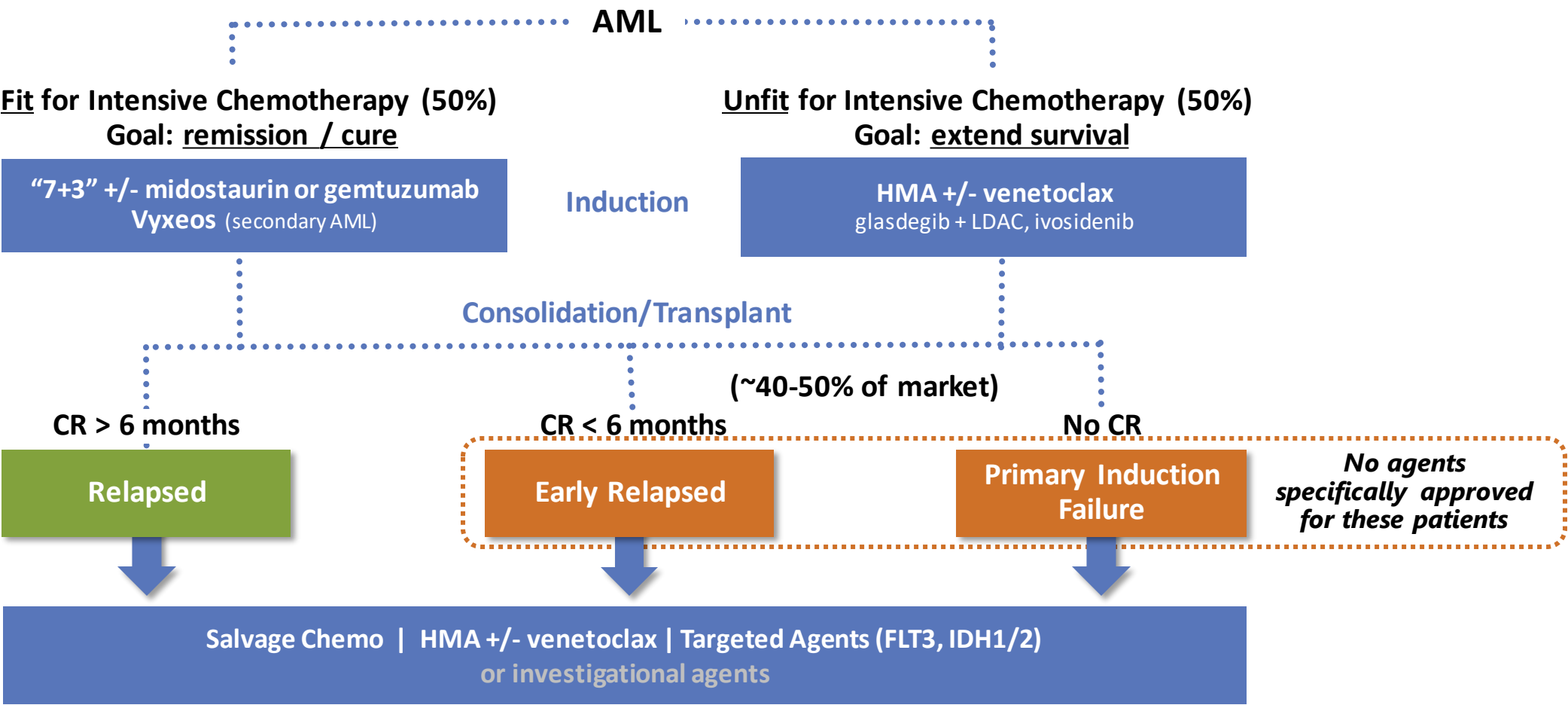
*Establishing leadership position among CD123-targeting bispecifics*



Function/ MoA	<ul style="list-style-type: none"><li>• Redirected T-cell killing against leukemia cells<ul style="list-style-type: none"><li>– Eliminates leukemic stem cells</li><li>– Spares normal hematopoietic stem cells</li><li>– Engages any T-cell without HLA-restriction</li></ul></li></ul>
Clinical Studies	<ul style="list-style-type: none"><li>• Phase 1/2 study in relapsed or refractory AML</li><li>• Phase 1 combination with retifanlimab in R/R AML ex-U.S. (paused)</li></ul>
2020 Anticipated Milestones	<ul style="list-style-type: none"><li>• Define potential registration path in primary induction failure (PIF) AML pending FDA discussions (1H)</li></ul>

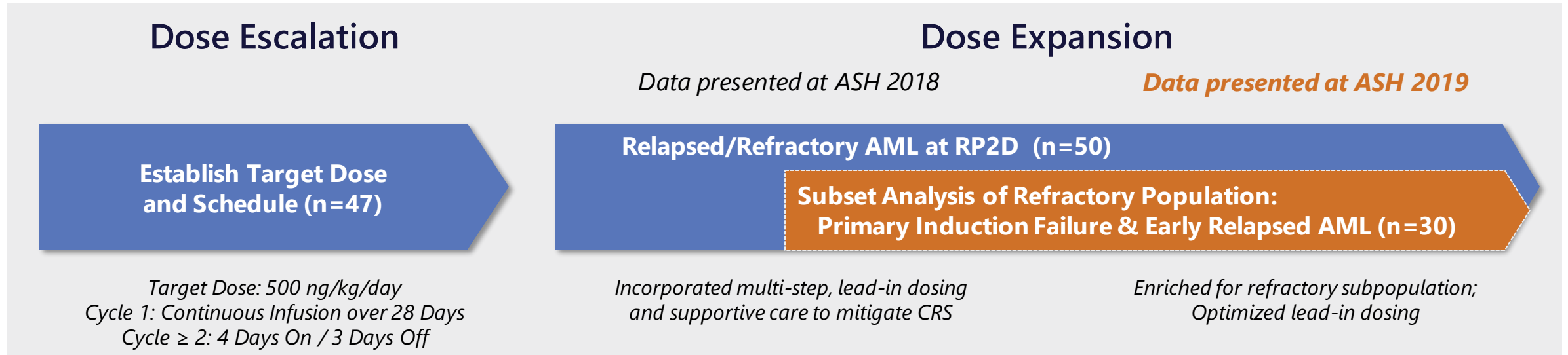
# Primary Induction Failure & Early Relapsed AML: Significant Unmet Need

50% of patients have no known targetable mutation; flotetuzumab is mutation-agnostic



# Phase 1/2 Development in AML

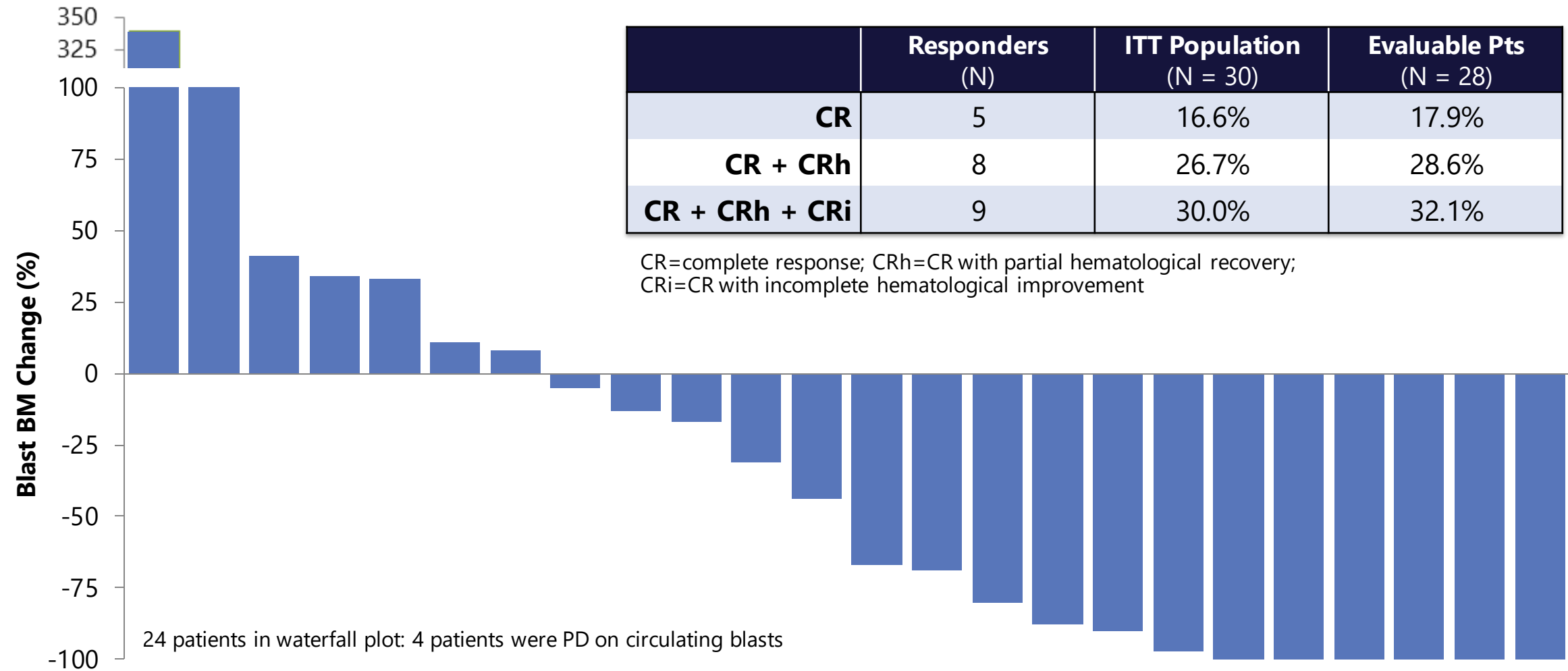
*Expansion in primary induction failure & early relapsed AML patients*



Inclusion/Exclusion Criteria	<ul style="list-style-type: none"> <li>• Refractory population: <ul style="list-style-type: none"> <li>– Refractory to ≥2 induction attempts, <u>or</u></li> <li>– 1<sup>st</sup> relapse with initial CR duration of &lt;6 months, <u>or</u></li> <li>– HMA failure to ≥4 cycles</li> </ul> </li> <li>• Relapsed population (initial CR &gt;6 months)</li> <li>• No prior allogeneic hematopoietic cell transplant</li> </ul>
Endpoints	<ul style="list-style-type: none"> <li>• Safety and disease status assessed by modified IWG criteria</li> <li>• Gene expression profiling performed using NanoString® PanCancerIO 360™ assay</li> </ul>

# Flotetuzumab is Active in Primary Induction Failure & Early Relapsed AML Patients

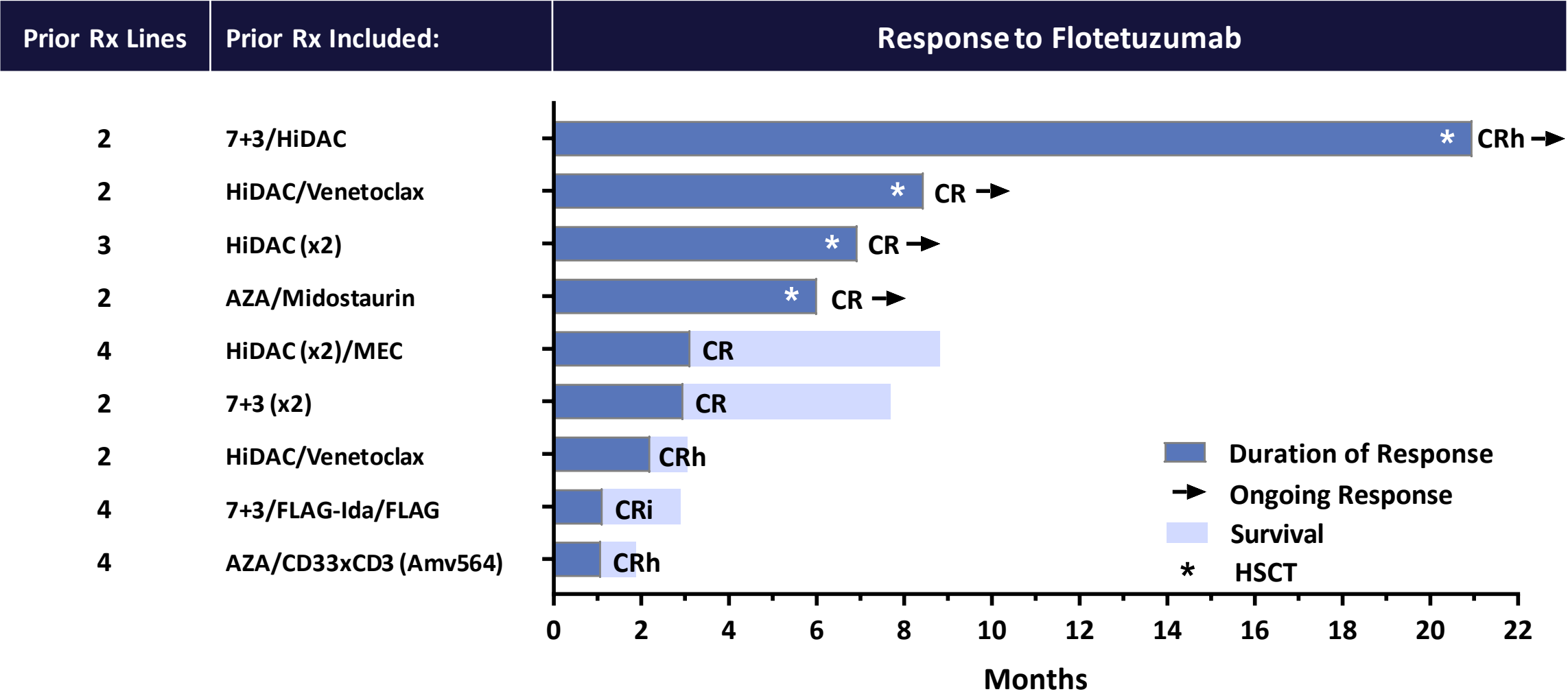
Benchmark analysis suggests historical CR+CRh rates in this setting of ~12.5%<sup>(a)</sup>



(a) Unpublished analysis of the CLASSIC I, VALOR, ADMIRAL trials and additional trials that included venetoclax, gemtuzumab-ozogamicin, and IDH1/2 inhibitors; (n=1328): CR/CRh = 12.5% [95% CI = 7.7%, 19.6%]



# Flotetuzumab: Duration of Response in PIF & Early Relapsed AML Patients



\* Four responders (3 CR, 1 CRh) received allo-HSCT consolidation

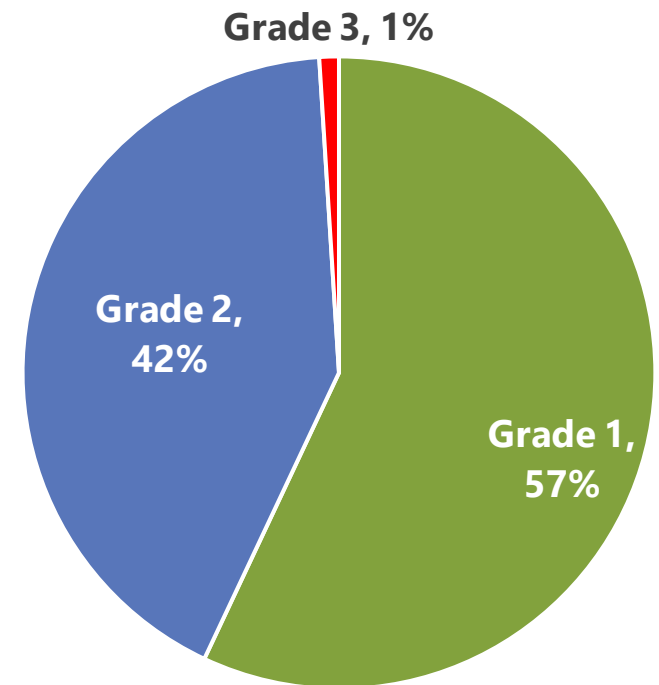
Uy, et al., ASH 2019

# Mitigating Cytokine Release Syndrome Associated With T Cell Engagers

*Decreased CRS severity and increased total flotetuzumab dose intensity*

- Infusion-related reaction /cytokine release syndrome (IRR/CRS) occurred in all (30/30) patients:
  - Mild to moderate (grade 1 or 2) in severity; only one grade 3 event reported in one patient
  - Most events observed were of short duration (Median: Grade 1=1 day; Grade 2=2 days; Grade 3=3 days)
- CRS mitigation strategies:
  - Lead-in dosing schedule for flotetuzumab
  - Early use of tocilizumab as supportive care
  - Short half-life molecule can be “switched-off” (Continuous infusion advantageous for managing exposure)

**Distribution of CRS Events by Grade**



There were no grade 4 events

Uy, et al., ASH 2019

# Capturing Full Potential of Flotetuzumab and CD123 × CD3 Bispecific Molecules

## Future Development Opportunities

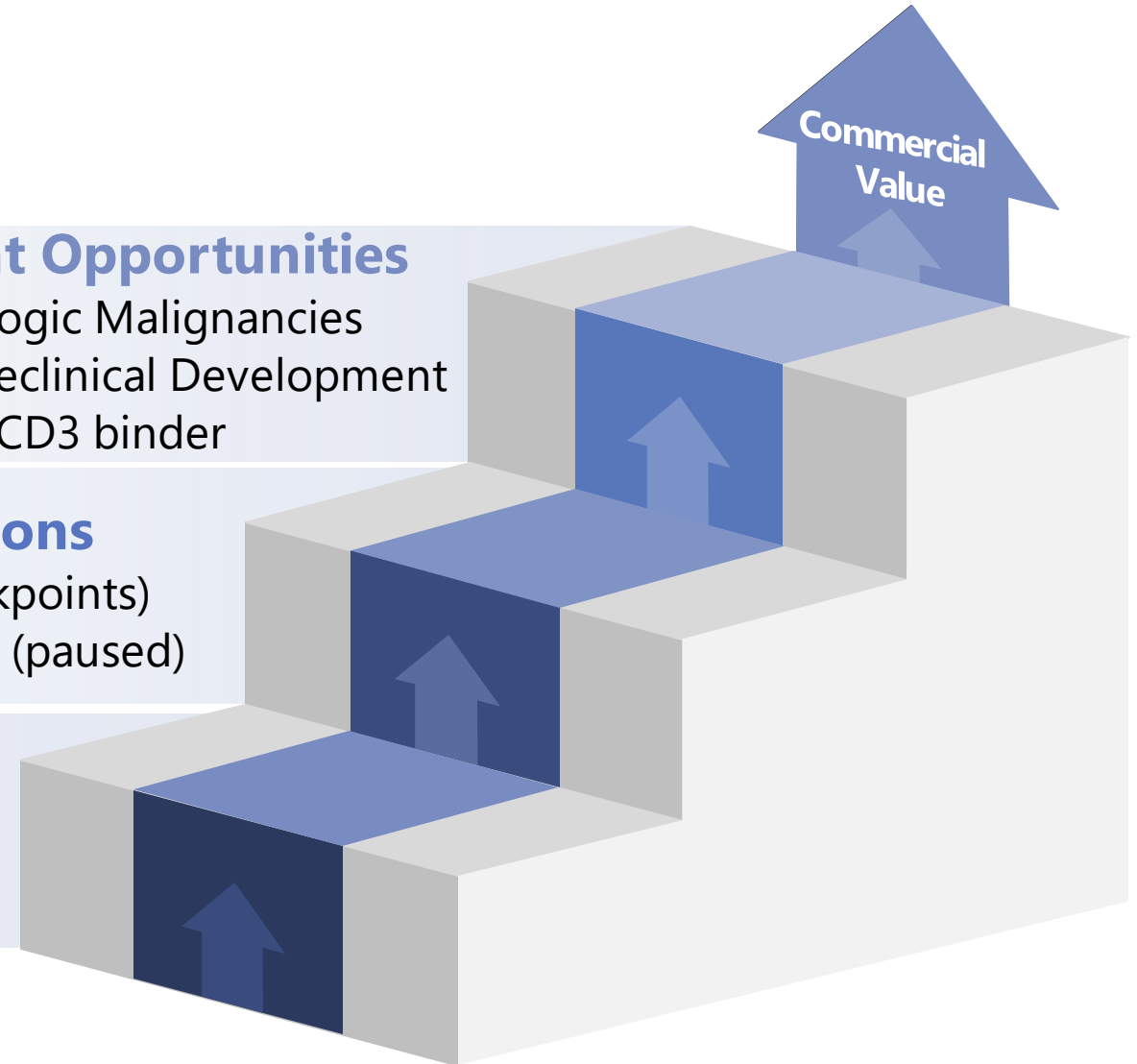
- Other CD123+ Hematologic Malignancies
- 2nd Gen. Molecule in Preclinical Development
  - Fc-bearing; alternate CD3 binder

## Expand Through Combinations

- Relapsed/Refractory AML (w/checkpoints)
  - Combine w/retifanlimab ex-U.S. (paused)

## Potential First Indication

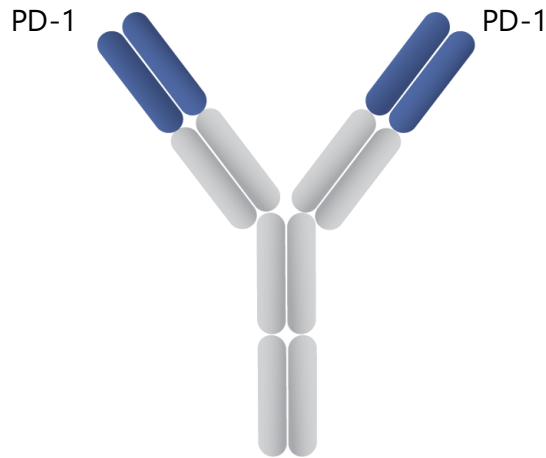
- Primary Induction Failure/Early Relapsed AML
  - Pivotal monotherapy study being planned\*




\* Pending ongoing discussions with FDA

# Retifanlimab (MGA012): Anti-PD-1 antibody

## Global collaboration with Incyte

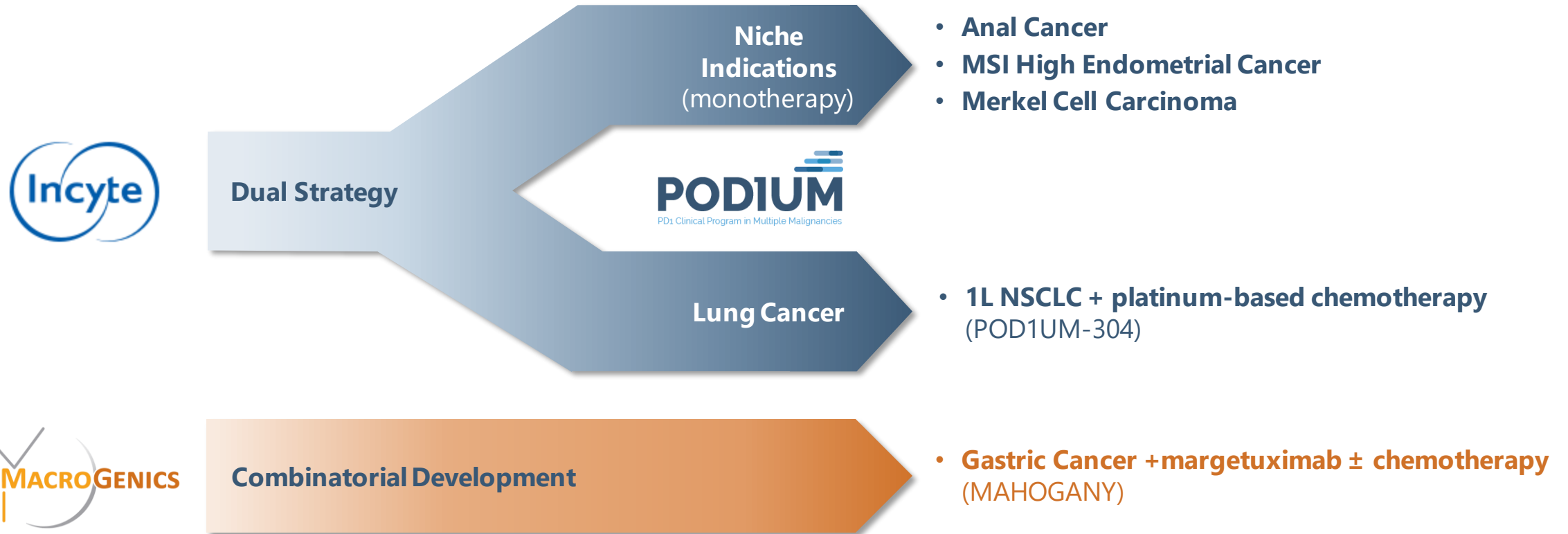


Function/ MoA	<ul style="list-style-type: none"> <li>Humanized, hinge-stabilized IgG4 mAb</li> <li>Inhibits PD-1</li> </ul>
Clinical Studies	<ul style="list-style-type: none"> <li>Five registration-directed studies ongoing or planned in 2020 across a broad range of tumor types<sup>(a)</sup></li> </ul>
Global Incyte Transaction 	<ul style="list-style-type: none"> <li>Up to \$750M in milestones (\$15M received to date)</li> <li>Tiered royalties of 15-24% on future retifanlimab sales</li> <li>Rights to develop pipeline assets with retifanlimab</li> </ul>
2020 Anticipated Milestones	<ul style="list-style-type: none"> <li>Monotherapy data in anal cancer</li> <li>Initiation of Ph. 3 randomized study in NSCLC by Incyte</li> </ul>

(a) ClinicalTrials.gov referenced May 4, 2020

# Comprehensive Development Plans for Retifanlimab

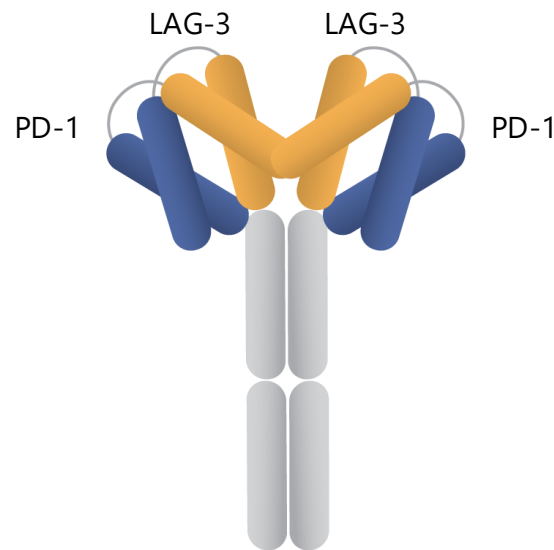
*Multiple potentially registration-enabling clinical studies*



ClinicalTrials.gov referenced May 4, 2020



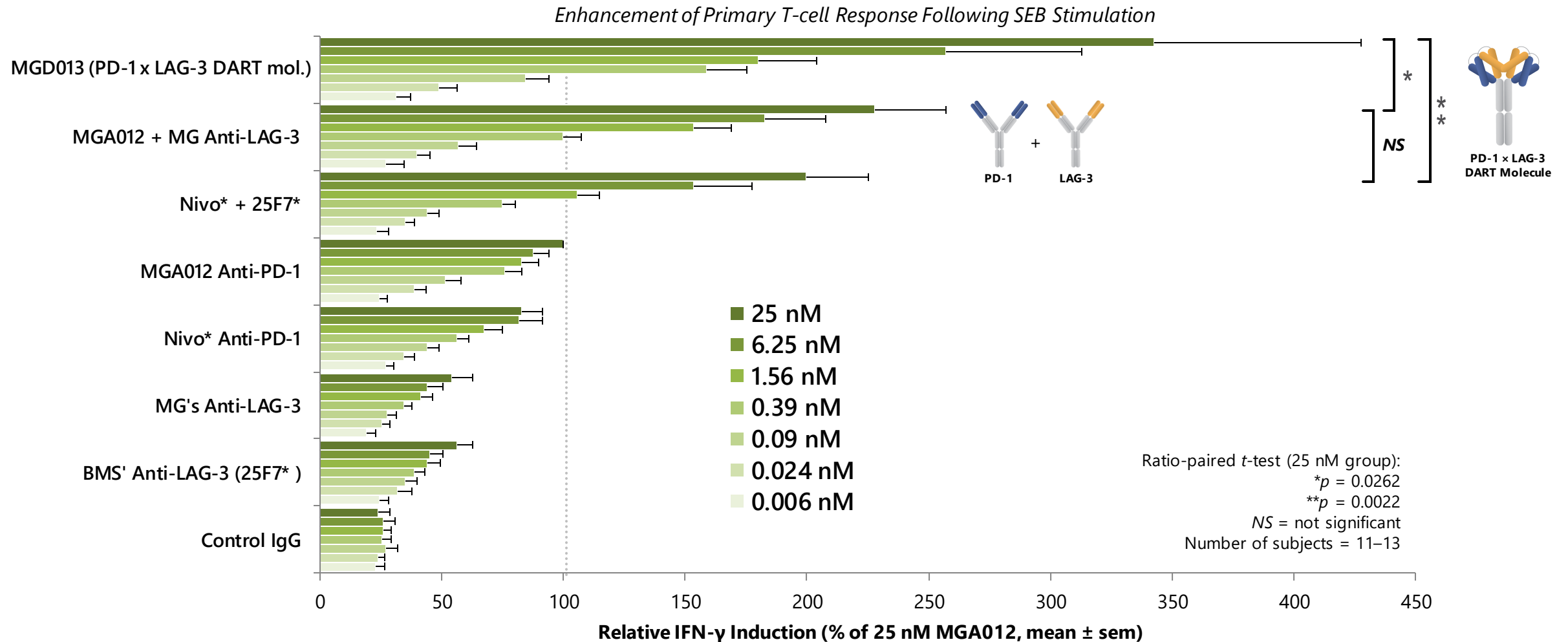
# MGD013 (PD-1 × LAG-3): First Bispecific Checkpoint Molecule in Clinical Trials



Function/ MoA	<ul style="list-style-type: none"> <li>• Simultaneous and/or independent blockade of two checkpoint molecules</li> <li>• Reactivation of exhausted T cells</li> </ul>
Clinical Studies	<ul style="list-style-type: none"> <li>• Ph. 1 dose expansion in: <ul style="list-style-type: none"> <li>– Nine tumor types (solid and liquid); checkpoint-naïve and checkpoint-experienced</li> <li>– Combination with margetuximab in HER2+ tumors</li> </ul> </li> </ul>
2020 Anticipated Milestones	<ul style="list-style-type: none"> <li>• Present data from ongoing Ph. 1 at ASCO (1H)</li> <li>• Select indications for further monotherapy development</li> <li>• Potential combination studies with both margetuximab and enoblituzumab</li> </ul>

# MGD013: Synergistic T-cell Activation

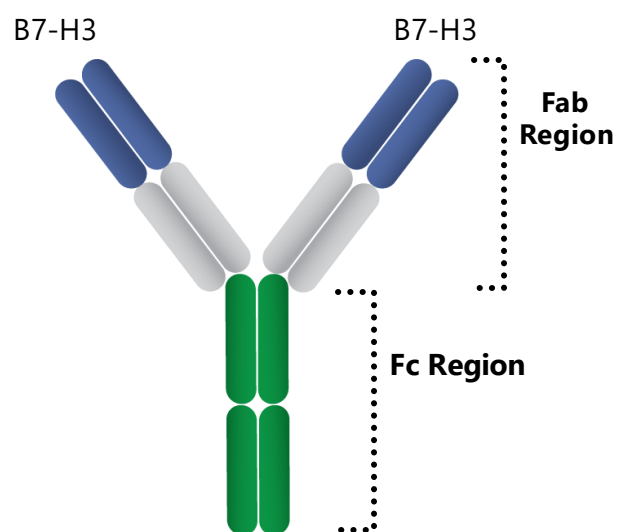
*DART molecule construct enhances T-cell activation vs. anti-PD-1 + anti-LAG-3 mAbs in vitro*



\*IFN $\gamma$  release by 25 nM MGA012 = 3276 $\pm$ 744 pg/ml.

# Enoblituzumab: Potential Leading Anti-B7-H3 mAb

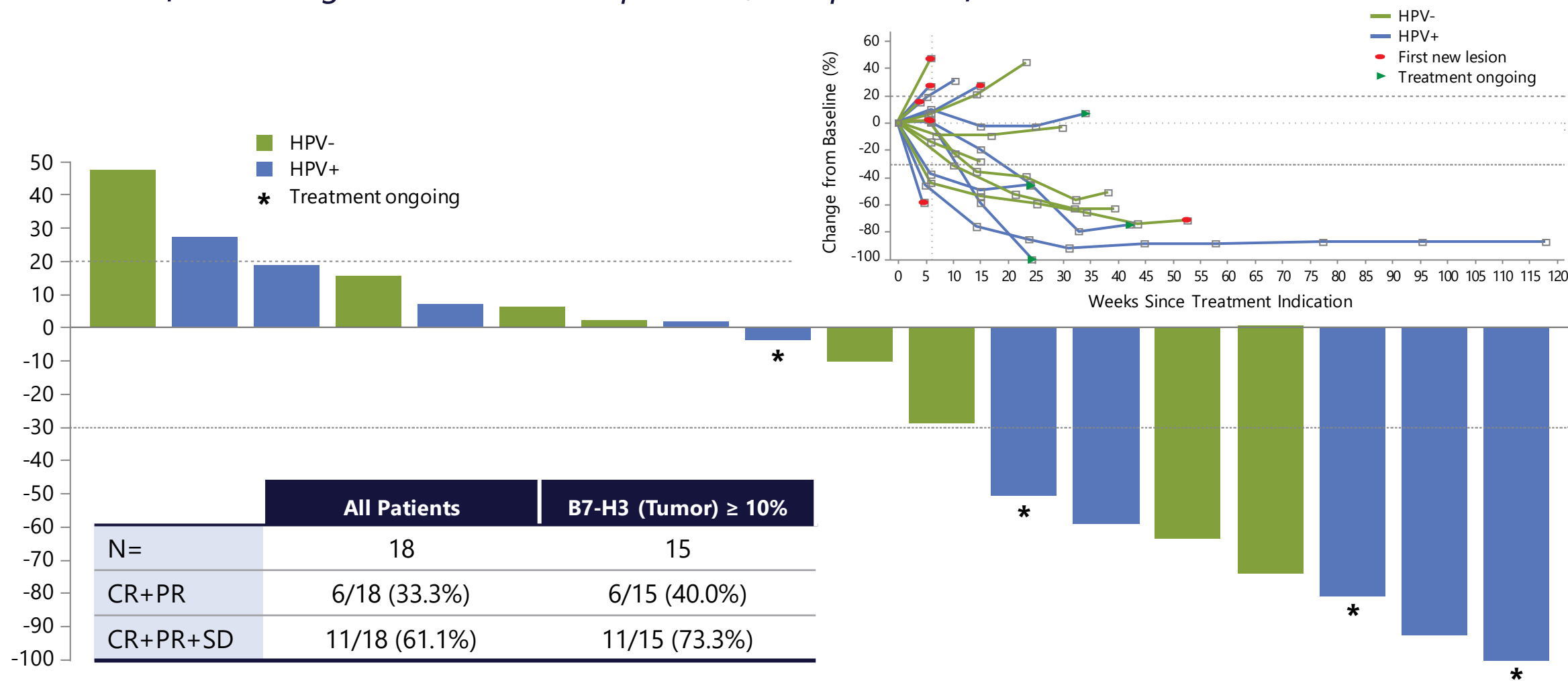
*Leveraging immune modulation through Fc optimization*



Function/ MoA	<ul style="list-style-type: none"><li>• Fc region engineered to enhance immune response, including ADCC</li><li>• Evidence of T-cell immunomodulation</li></ul>
Clinical Study	<ul style="list-style-type: none"><li>• Phase 1 study w/anti-PD-1 in 2L+ SCCHN and NSCLC</li></ul>
2020 Anticipated Milestones	<ul style="list-style-type: none"><li>• Update on timing to initiate study of enoblituzumab with retifanlimab or MGD013 as chemo-free regimens in 1L SCCHN</li></ul>

# Antitumor Activity in SCCHN Patients (*Anti-PD-1/PD-L1 Naïve*) + anti-PD-1 mAb

*Induction of tumor regression in SCCHN patients, irrespective of HPV status*



Data cut-off date: October 12, 2018. Received ≥1 prior line of chemotherapy and TKI treatment. B7-H3 testing was retrospective.

Aggarwal, et al., SITC 2018

# Encouraging Data from 2L+ Enoblituzumab plus Anti-PD-1 mAb

*Opportunity to advance to 1L SCCHN*

Agent (Study)	Study Results in Checkpoint-naïve Patients				
	<b>Enoblituzumab + Pembrolizumab</b>	Nivolumab (CHECKMATE-141) <sup>(a)</sup>	Pembrolizumab (KEYNOTE-012) <sup>(b)</sup>	Pembrolizumab (KEYNOTE-040) <sup>(c)</sup>	<i>Pembrolizumab +chemotherapy (KEYNOTE-048)<sup>(d)</sup></i>
Line	<b>2L+</b>	2L	2L+	2L	1L
N	<b>18</b>	240	174	247	281
ORR	<b>33.3%</b>	13%	16%	15%	36%

(a) Ferris, et al., 2016, N Eng J Med

(b) Keytruda® package insert

(c) Cohen, et al., 2017, ESMO LBA45; Cohen, et al., 2019, The Lancet

(d) Burtness, et al., 2018, ESMO

# Core Product Candidates with Key Milestones Anticipated in 2020

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## Margetuximab

*(Anti-HER2 mAb)*

### Breast Cancer

- ✓ BLA filing acceptance (1Q)
- ❑ Final OS (2H)
- ❑ ODAC expected (2H)
- ❑ PDUFA date (12/18/2020)

### Gastric/GEJ Cancer

- ❑ Initial data MAHOGANY Module A (2H)

## Flotetuzumab

*(CD123 × CD3 DART molecule)*

- ❑ Define registration path for PIF/ER AML (1H)

## Retifanlimab

*(Anti-PD-1 mAb)*

Per Incyte's disclosure



## MGD013

*(PD-1 × LAG-3 DART molecule)*

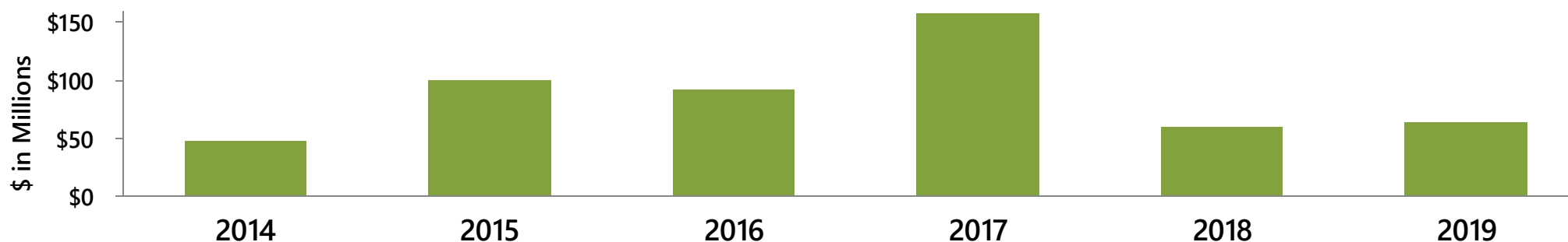
- ❑ Present data from ongoing Phase 1 (ASCO)
- ❑ Select indications for further development

# Financial Overview

- \$171M Cash, cash equivalents and marketable securities as of March 31, 2020
  - Cash runway into 2022 via anticipated and potential collaboration payments
- Historical financial details:

\$ in Millions	2014	2015	2016	2017	2018	2019	1Q Ended March 31,	
							2020	2019
Total Revenues	\$48	\$101	\$92	\$158	\$60	\$64	\$14	\$10
R&D Expense	70	98	122	147	191	195	49	47
Total Operating Expenses	86	121	152	180	231	241	59	57
Cash & Investments	158	339	285	305	233	216	171	320

- Revenues from collaborative and government agreements (>\$525M since 2013 IPO):





# Thank You!

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