# MACROGENICS®

Developing Breakthrough Biologics, Life-changing Medicines™

# **Corporate Presentation**

March 2020

# Legal Notices

The information in this slide deck is current as of March 1, 2020, unless otherwise noted, and is qualified in its entirety by reference to MacroGenics' Annual, Quarterly and Current Reports filed with the SEC. MacroGenics undertakes no obligation to update any of the information herein.

#### **Cautionary Note on Forward-Looking Statements**

Any statements in these materials about future expectations, plans and prospects for MacroGenics ("Company"), including statements about the Company's strategy, future operations, clinical development of the Company's therapeutic candidates, milestone or opt-in payments from the Company's collaborators, the Company's anticipated milestones and future expectations and plans and prospects for the Company and other statements containing the words "subject to", "believe", "anticipate", "plan", "expect", "intend", "estimate", "project", "may", "will", "should", "would", "could", "can", the negatives thereof, variations thereon and similar expressions, or by discussions of strategy constitute forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: the uncertainties inherent in the initiation and enrollment of future clinical trials, expectations of expanding ongoing clinical trials, availability and timing of data from ongoing clinical trials, expectations for the timing and steps required in the regulatory review process, expectations for regulatory approvals, the impact of competitive products, our ability to enter into agreements with strategic partners and other matters that could affect the availability or commercial potential of the Company's product candidates and other risks described in the Company's filings with the Securities and Exchange Commission. In addition, the forward-looking statements included in this presentation represent the Company's views only as of the date hereof. The Company anticipates that subsequent events and developments will cause the Company's views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, the Company specifically disclaims any obligation to do so, except as may be required by law. These forward-looking statements should not be relied upon as representing the Company's views as of any date subsequent to the date hereof.

#### **Trademarks**

DART, TRIDENT, MacroGenics, the MacroGenics logo, "Breakthrough Biologics, Life-Changing Medicines" and "Developing Breakthrough Biologics, Life-Changing Medicines" are trademarks or registered trademarks of MacroGenics, Inc. The Incyte logo is a registered trademark of Incyte Corporation. The Zai Lab logo is a registered trademark of Zai Lab, Limited. The I-Mab logo is a registered trademark of I-Mab Biopharma.

#### **Investigational Agents**

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

March 1, 2020



Late-stage immuno-oncology company	<ul> <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> <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> <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> <li>\$216M cash, cash equivalents and marketable securities at 12/31/19</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 Mar	ket Rights
Margetuximab	HER2+ Breast					Greater China
(HER2)	HER2+ Gastric/GEJ (+MGA012/MGD013)		zaiuab			
Flotetuzumab	AML					
(CD123 × CD3)	AML (+MGA012)					
<b>MGA012</b> (PD-1)	Solid Tumors					(Incyte) <sup>(b)</sup>
Enoblituzumab (B7-H3)	SCCHN (+MGA012/MGD013)					Greater China
<b>MGD013</b> (PD-1 × LAG-3)	Solid Tumors & Heme Malignancies					Greater China
<b>MGD019</b> (PD-1 × CTLA-4)	Solid Tumors					
<b>MGC018</b> (B7-H3) <sup>(a)</sup>	Solid Tumors				MACROGENICS	

MGD = DART MGA = Antibody MGC = ADC

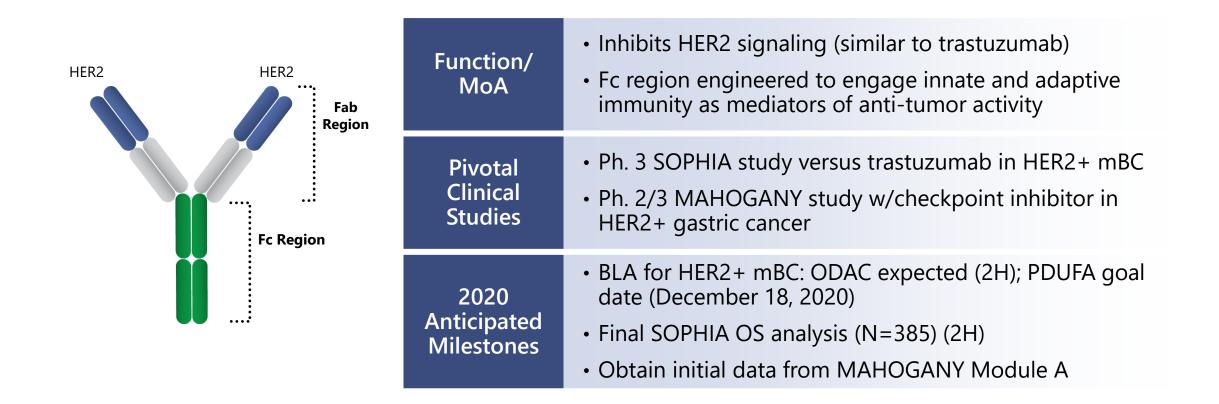
(a) MGC018 is an antibody-drug conjugate (ADC) based on a duocarmycin payload with cleavable peptide linker that was licensed from Synthon Biopharmaceuticals.

(b) MacroGenics retains rights to develop its pipeline assets in combination w/MGA012 (INCMGA0012) and to manufacture a portion of global clinical and commercial supply needs of MGA012. 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

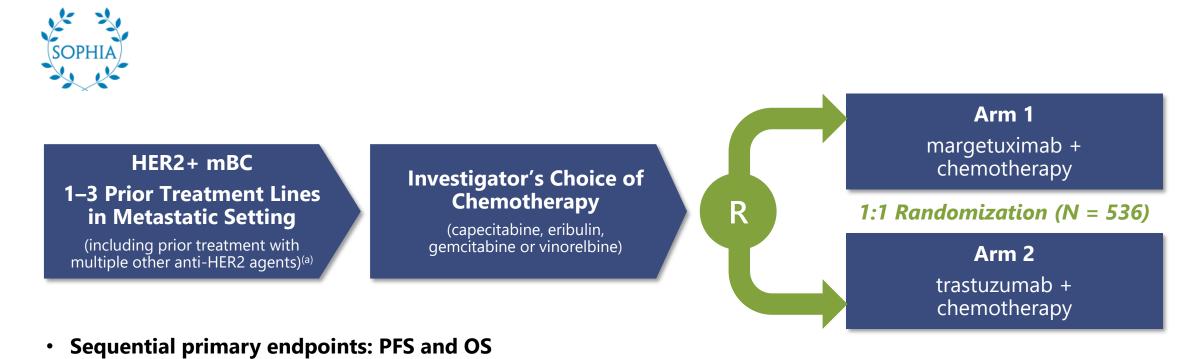
December 2020 PDUFA goal date for BLA for HER2+ metastatic breast cancer (mBC)



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



PFS (N=257, HR=0.67,  $\alpha$ =0.05, power=90%) OS (N=385, HR=0.75,  $\alpha$ =0.05, power=80%)

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

Patients carrying CD16A (FcyRIIIa) 158F allele

were pre-specified exploratory subpopulation

•

### Primary PFS Endpoint: Margetuximab Demonstrated Superiority to Trastuzumab

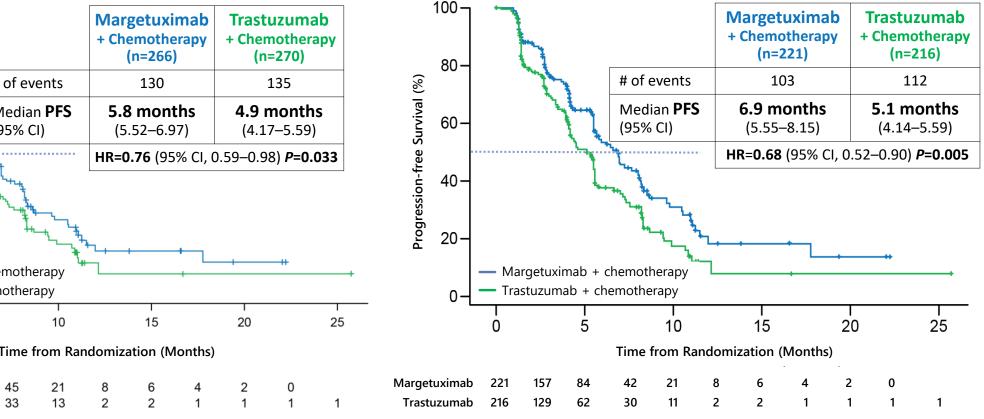
#### **PFS Primary Endpoint (ITT Population):** 24% Risk Reduction of Disease Progression 100-100 Margetuximab Trastuzumab + Chemotherapy + Chemotherapy (n=266) (n=270) 80-80 Progression-free Survival (%) # of events # of events 130 135 5.8 months 4.9 months Median **PFS** 60-60 (95% CI) (95% CI) (5.52 - 6.97)(4.17 - 5.59)HR=0.76 (95% CI, 0.59-0.98) P=0.033 40-40 20-20 Margetuximab + chemotherapy Margetuximab + chemotherapy Trastuzumab + chemotherapy Trastuzumab + chemotherapy Λ 0 20 25 5 10 15 Ω 10 0 5

Time from Randomization (Months)

Margatuyingah	266	171	04	45	24	0	6	4	2	0	
Margetuximab	200	174	94	45	21	0	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



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).

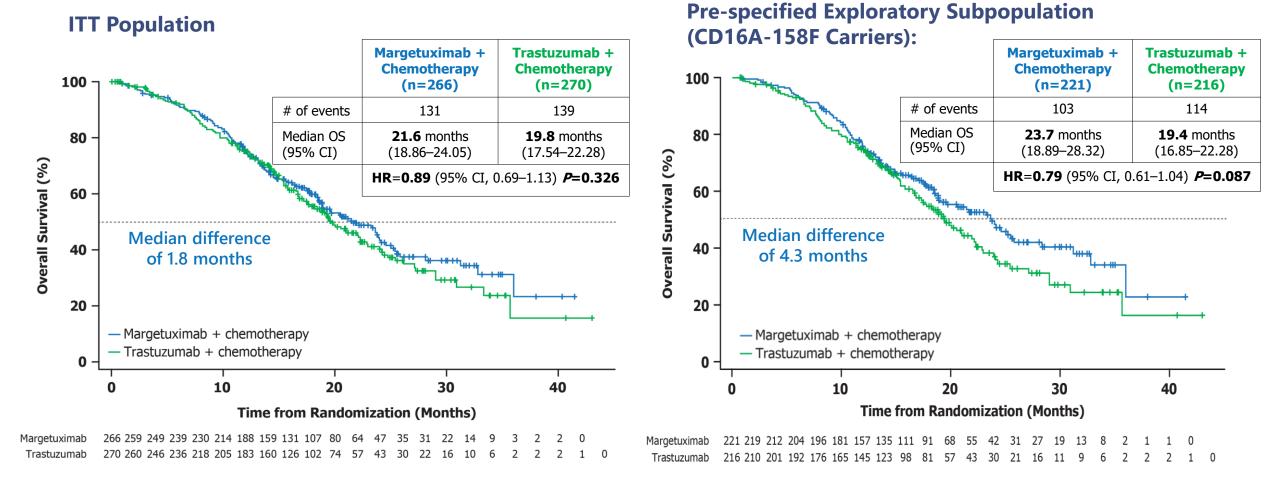
#### Rugo, et al., ASCO 2019



Progression-free Survival (%)

# Second Interim Overall Survival Analysis: Trend Favored Margetuximab

#### Final analysis expected 2H20

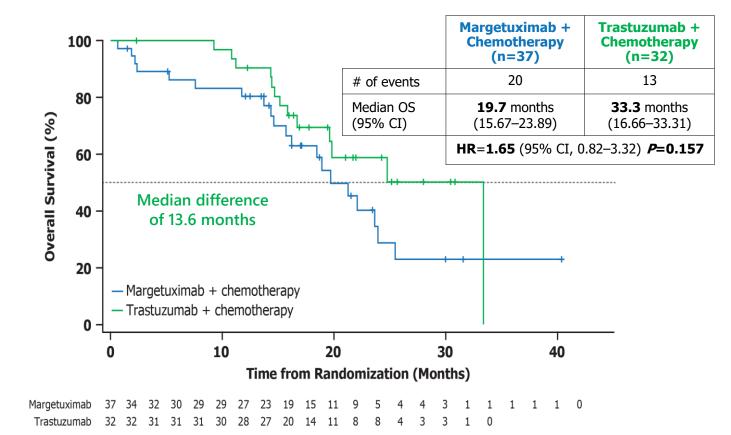


September 2019 data cut-off after 270 events in ITT population. Median follow-up: 15.6 months. ITT=Intent to Treat population: N=536. CD16A 158F Carriers=FF or FV Genotype. CI=confidence interval. HR=Hazard Ratio (ITT by stratified Cox model; F Carriers by unstratified Cox model).

#### Rugo, et al., SABCS 2019

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

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



Unbalanced patient characteristics

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

Less favorable

Rugo, et al., SABCS 2019

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).



#### **Overall Safety Profiles Similar**

Adverse Events (AE)

	Margetuximab + Chemotherapy (n=264)		Trastuzumab + Chemotherapy (n=266)	
Any grade AE, n (%)	260 (	98.5)	261 (	98.1)
Any margetuximab or trastuzumab-related AE, n (%)	160 (	(60.6)	132 (	49.6)
<b>Grade ≥3 AE</b> , n (%)	142 (	(53.8)	140 (	52.6)
Grade $\geq$ 3 margetuximab or trastuzumab-related AE, n (%)	34 (	12.9)	22 (	8.3)
<b>Any SAE</b> , n (%)	43 (16.3) 49 (18.4)		18.4)	
Any margetuximab or trastuzumab-related SAE, n (%)	5 (	5 (1.9) 4 (1.5)		1.5)
AE leading to treatment <sup>a</sup> discontinuation, n (%)	8 (	(3.0) 7 (2.6)		2.6)
AEs resulting in death, <sup>b</sup> n (%)	3 (1.1) <sup>c</sup>		2 (0	).8) <sup>d</sup>
AEs of special interest, n (%)	All Grade	Grade ≥3	All Grade	Grade ≥3
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**

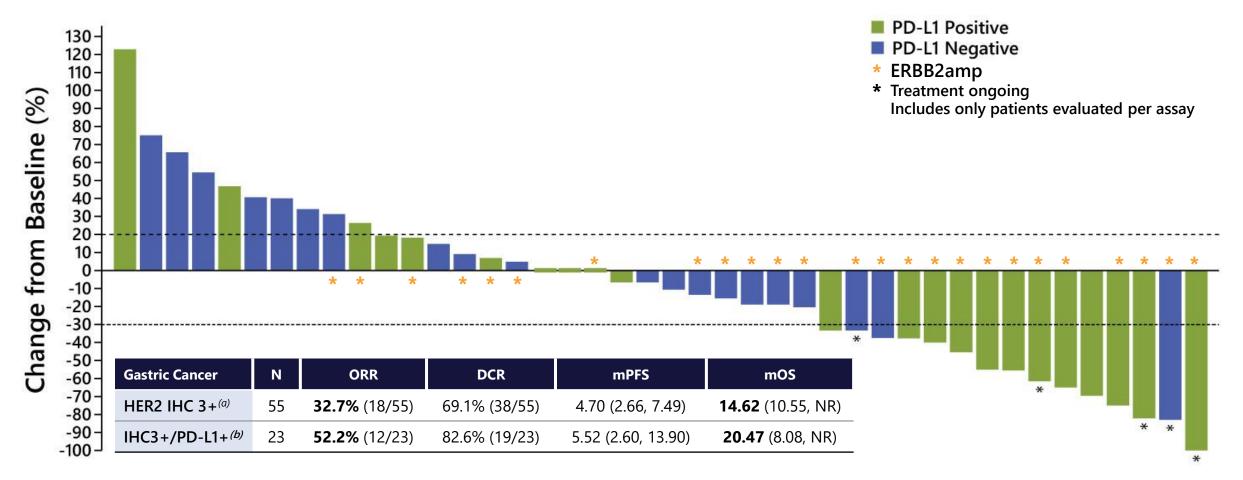
Ability to tailor treatment by selecting among four different chemotherapies **Familiarity** Side effect profile is well known and manageable CD16A exploratory analysis 85% of population are F carriers

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		2 <sup>nd</sup> Line				
	SOC	SOC	Ongoing Phase 2 Study		Failed	Ongoing Study	
Agent	Trastuzumab + Chemo <sup>(a)</sup>	Ramucirumab + Paclitaxel <sup>(b)</sup>	Margetuximab	+ Pembrolizumab <sup>(c)</sup>	Pembrolizumab <sup>(d)</sup> (KEYNOTE-61)	DS-8201 <sup>(e)</sup>	
(Study)	(TOGA)	(RAINBOW)			PD-L1+	20 0201	
ORR	47%	28%	33%	52%	15.8%	43%	
Median PFS	6.7 mos.	4.4 mos.	4.7 mos.	5.5 mos.	1.5 mos.	5.6 mos.	
Median OS	13.1 mos.	9.6 mos.	14.6 mos.	20.5 mos.	9.1 mos.	12.8 mos.	
≥ Grade 3 TRAEs	68%	Overall: N/A 41% Neutropenia 15% Hypertension 12% Fatigue		20%	14%	48%	
Gastric/GEJ Patient Mix	80/20%	80/20%	100	0%/0%	70%/30%	80%/20%	

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.

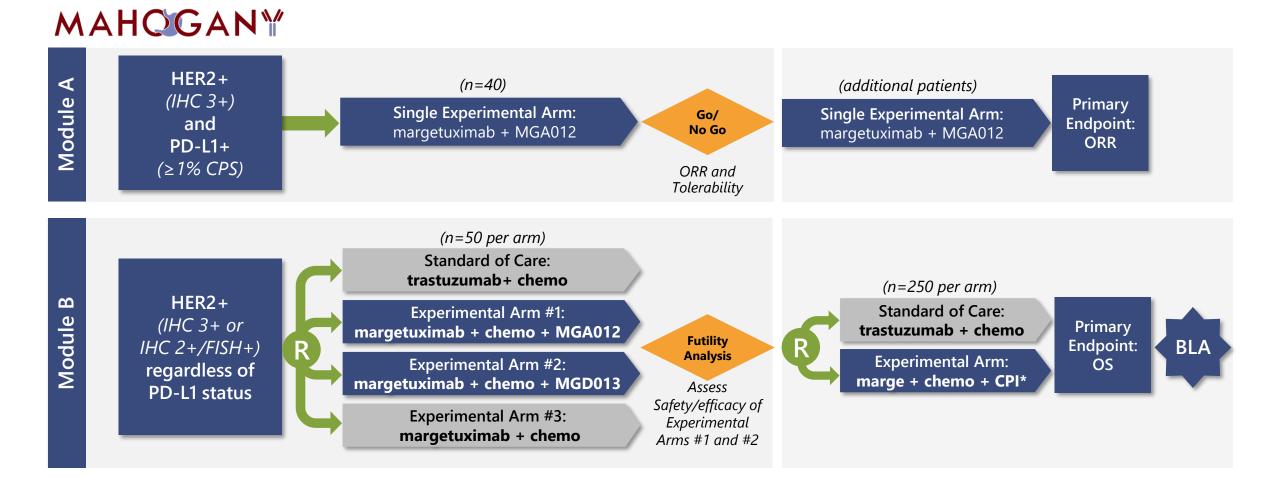
(d) Shitara, et al., 2018, Lancet;

(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



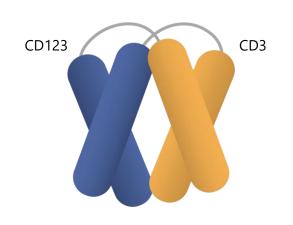
#### **MAHOGANY** (<u>Ma</u>rgetuximab in <u>H</u>ER2-p<u>o</u>sitive <u>Ga</u>stric Cancer

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



#### Flotetuzumab: CD123 × CD3 DART Molecule

Establishing leadership position among CD123-targeting bispecifics

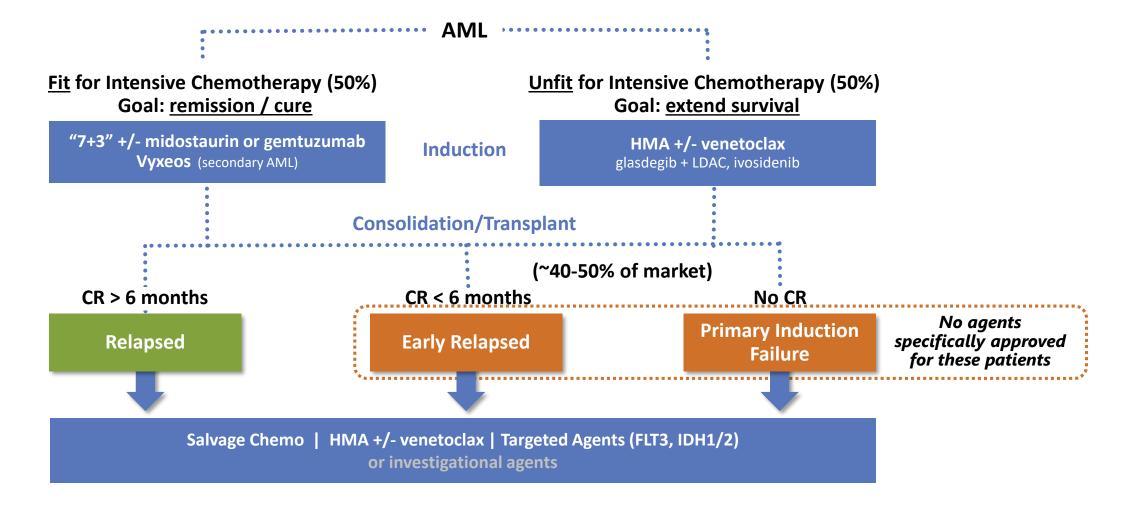


Function/ MoA	<ul> <li>Redirected T-cell killing against leukemia cells         <ul> <li>Eliminates leukemic stem cells</li> <li>Spares normal hematopoietic stem cells</li> <li>Engages any T-cell without HLA-restriction</li> </ul> </li> </ul>
Ongoing Clinical Studies	<ul> <li>Phase 1/2 study in relapsed or refractory AML</li> <li>Phase 1 study combined with MGA012 in R/R AML</li> </ul>
2020 Anticipated Milestones	<ul> <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

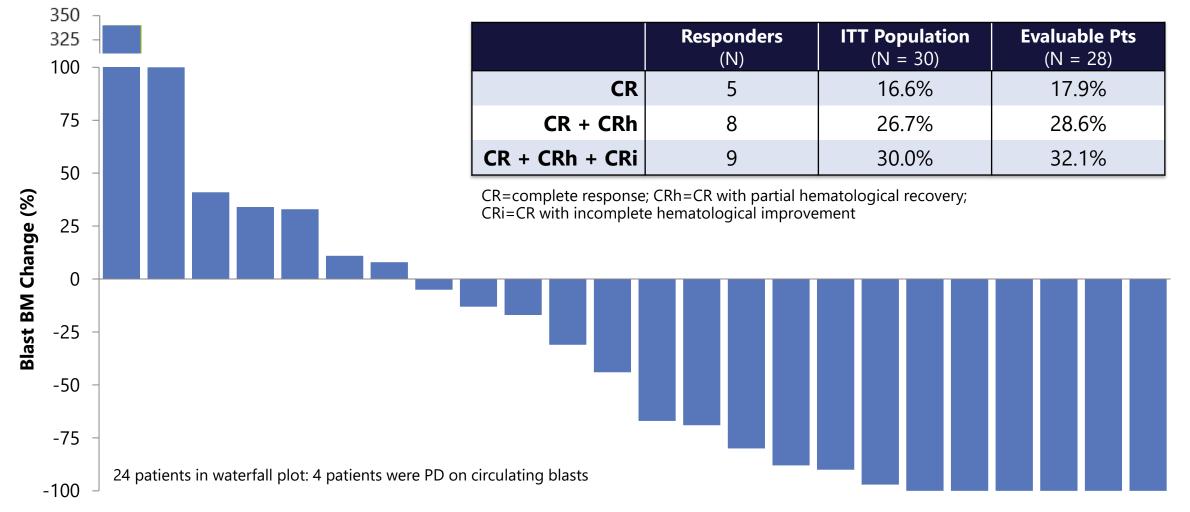
#### Expansion in primary induction failure & early relapsed AML patients

Dose Escalation		Dose Expansion				
		Data present	red at ASH 2018	Data presented at ASH 2019		
Establish Target Dose and Schedule (n=47)		Relapsed/Refractory AML at RP2D (n=50)				
			Subset Analysis of Ref Primary Induction F	fractory Population: ailure & Early Relapsed AML (n=30)		
Target Dose: 500 ng/kg/d Cycle 1: Continuous Infusion ove Cycle ≥ 2: 4 Days On / 3 Day	r 28 Days	•	ti-step, lead-in dosing care to mitigate CRS	Enriched for refractory subpopulation; Optimized lead-in dosing		
Inclusion/Exclusion Criteria	<ul> <li>Refractory population:         <ul> <li>Refractory to ≥2 induction attempts, or</li> <li>1<sup>st</sup> relapse with initial CR duration of &lt;6 months, or</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	,		essed by modified IWG formed using NanoStr	6 criteria ring® PanCancerlO 360™ assay		



### 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>

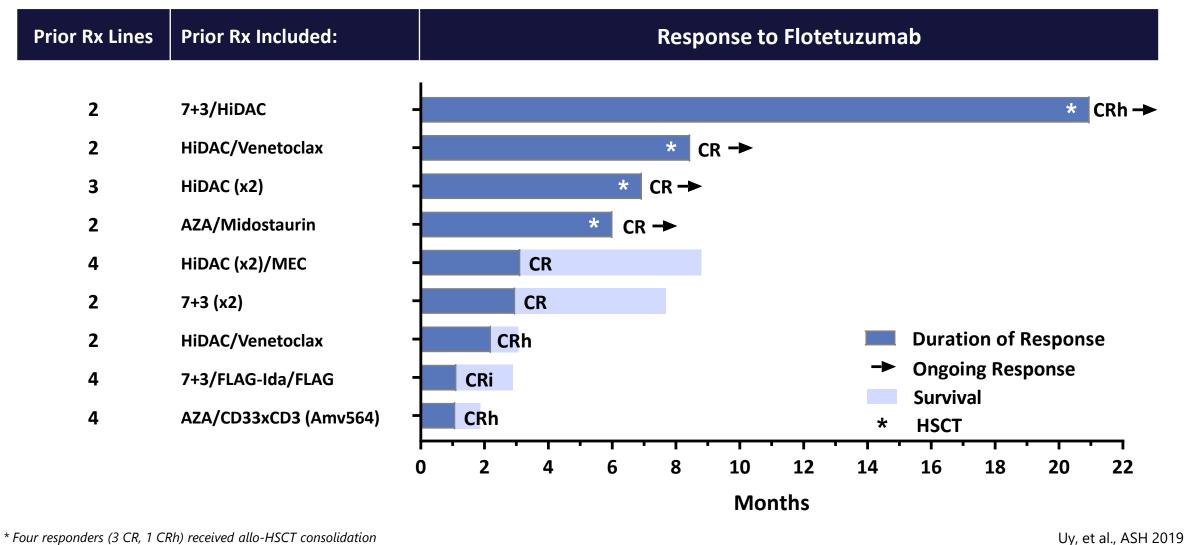


(a) Unpublished analysis of the CLASSIC I, VALOR, ADMIRAL trials and additional trials that included venetoclax, gemtuzumab-ozogamicin, and IDH1/2 inhibitors; (n=1328): CR/CRh = 12.5% [95% CI = 7.7%, 19.6%]

Uy, et al., ASH 2019



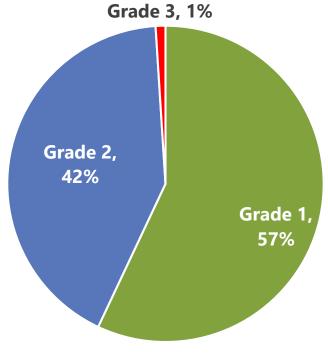
#### Flotetuzumab: Duration of Response in PIF & Early Relapsed AML Patients



# 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



20

### 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)
 Combination with MGA012 initiated

#### **Potential First Indication**

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

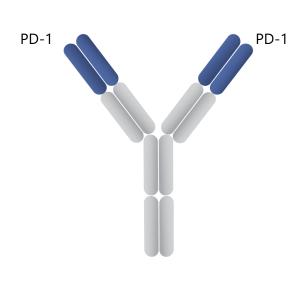
\* Pending ongoing discussions with FDA



Commercial Value

#### MGA012: Anti-PD-1 antibody

#### Global collaboration with Incyte

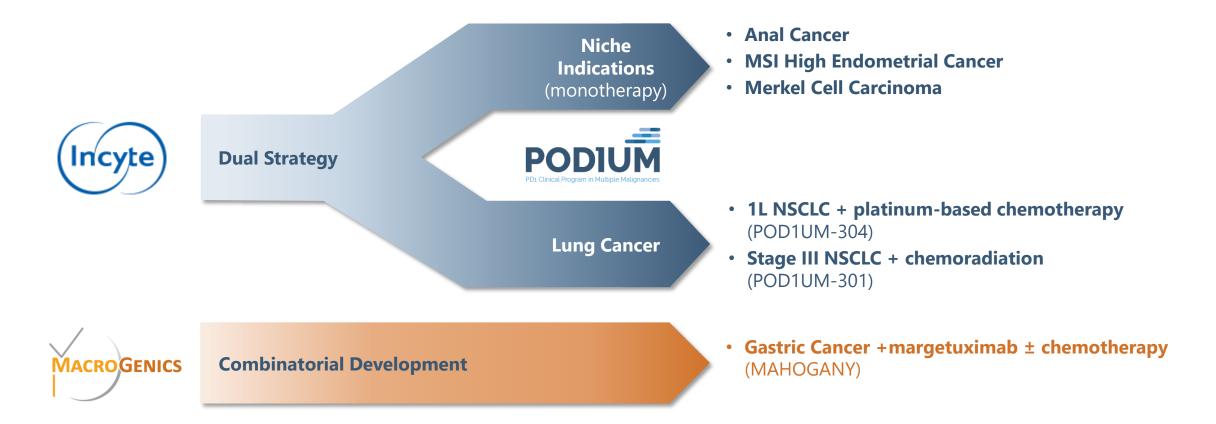


Function/ MoA	<ul> <li>Humanized, hinge-stabilized IgG4 mAb</li> <li>Inhibits PD-1</li> </ul>
Ongoing Clinical Studies	<ul> <li>Six registration-directed studies ongoing or planned in 2020 across a broad range of tumor types<sup>(a)</sup></li> </ul>
Global Incyte Transaction	<ul> <li>Up to \$750M in milestones (\$15M received to date)</li> <li>Tiered royalties of 15-24% on future MGA012 sales</li> <li>Rights to develop pipeline assets with MGA012</li> </ul>
2020 Anticipated Milestones	<ul> <li>Monotherapy data in anal cancer</li> <li>Initiation of Ph. 3 randomized studies in NSCLC</li> </ul>



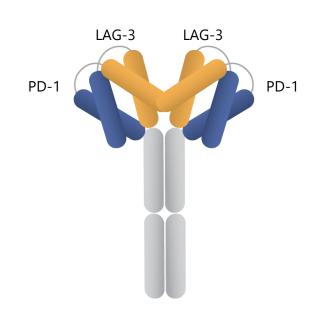
### **Comprehensive Development Plans for MGA012**

Multiple potentially registration-enabling clinical studies





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



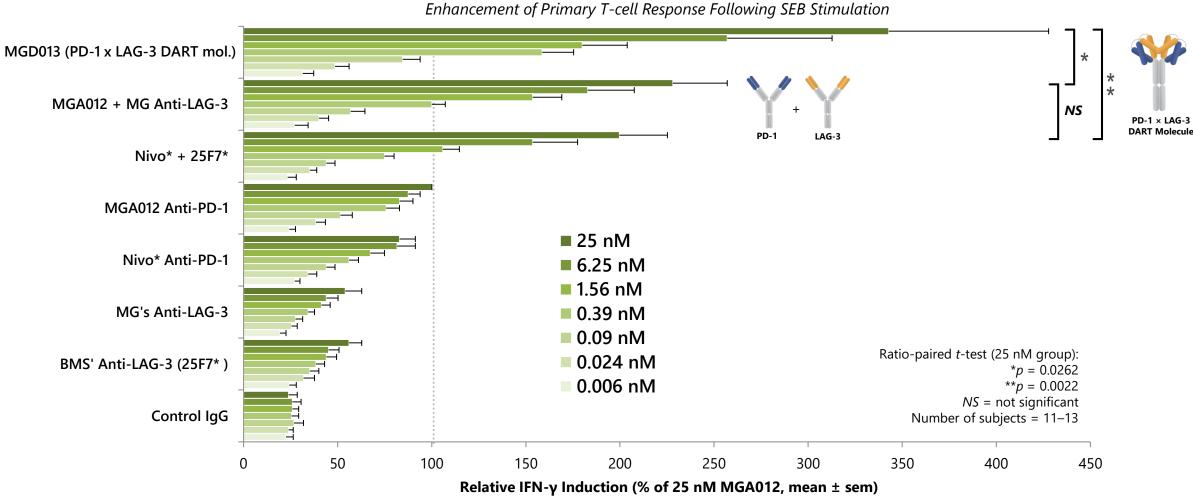
Function/ MoA	<ul> <li>Simultaneous and/or independent blockade of two checkpoint molecules</li> <li>Reactivation of exhausted T cells</li> </ul>
Ongoing Clinical Studies	<ul> <li>Ph. 1 dose expansion in nine tumor types (solid and liquid); checkpoint-naïve and checkpoint-experienced</li> </ul>
2020 Anticipated Milestones	<ul> <li>Present data from ongoing Ph. 1 at scientific conf. (1H)</li> <li>Select indications for further monotherapy development</li> <li>Planned combination studies with both margetuximab and enoblituzumab</li> </ul>



#### **MGD013**

# MGD013: Synergistic T-cell Activation

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

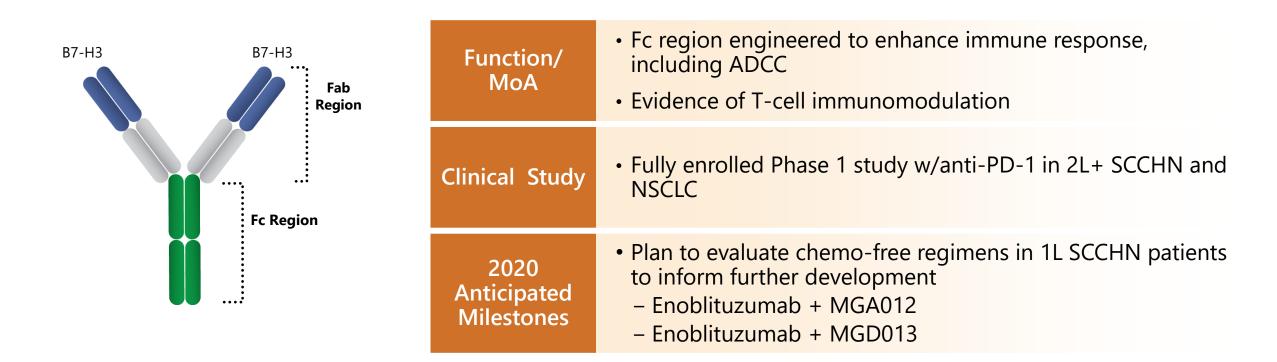


<sup>\*</sup>IFNγ release by 25 nM MGA012 = 3276±744 pg/ml.

MACRO GENICS

# Enoblituzumab: Potential Leading Anti-B7-H3 mAb

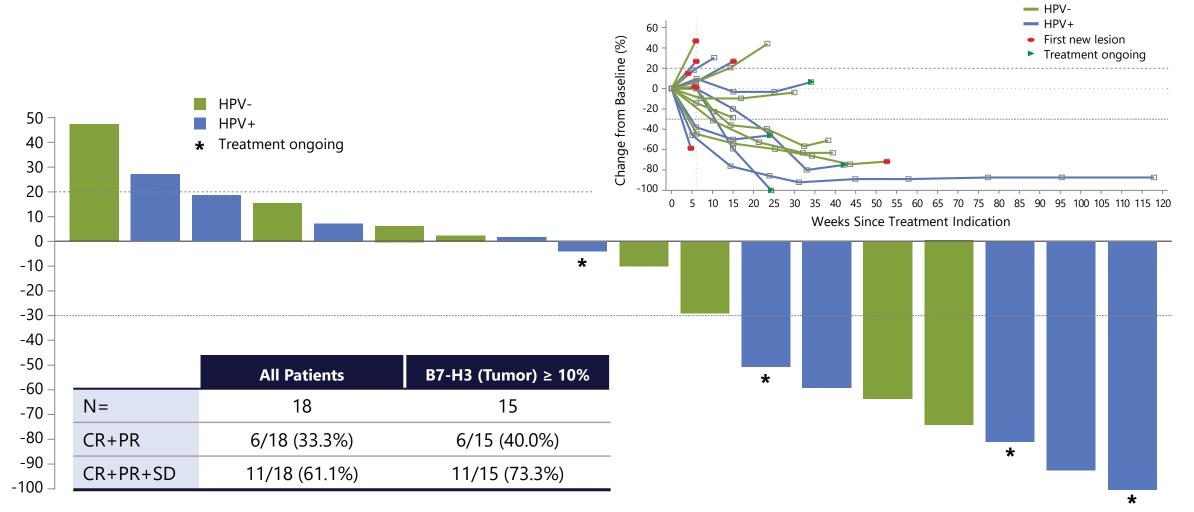
Leveraging immune modulation through Fc optimization





### 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  $\geq$ 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

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

Margetuximab

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) MGA012 (Anti-PD-1 mAb)

Per Incyte's disclosure

Incyte

MGD013 (PD-1 × LAG-3 DART molecule)

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

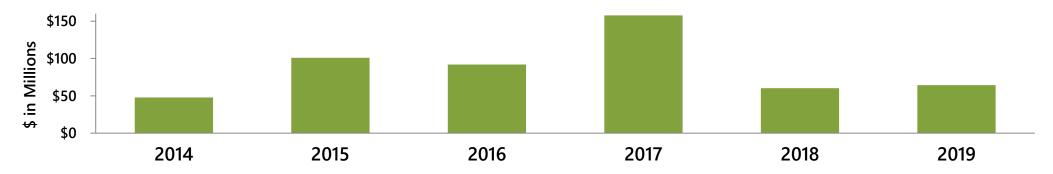


#### **Financial Overview**

- \$216M Cash, cash equivalents and marketable securities as of December 31, 2019
  - Focused on extending cash runway into 2022 via anticipated and potential collaboration payments, program prioritization and ongoing realignment of resources
- Historical financial details:

\$ in Millions	2014	2015	2016	2017	2018	2019
Total Revenues	\$48	\$101	\$92	\$158	\$60	\$64
R&D Expense	70	98	122	147	191	195
Total Operating Expenses	86	121	152	180	231	241
Cash & Investments	158	339	285	305	233	216

• Revenues from collaborative and government agreements (>\$500M since 2013 IPO):







#### Thank You!



#### **Investor Relations Inquiries:**

**Jim Karrels** – Senior Vice President, CFO 301-354-2681 | karrelsj@macrogenics.com

**Anna Krassowska, Ph.D.** – Vice President, Investor Relations and Corporate Communications 240-552-8662 | krassowskaa@macrogenics.com

#### **Business Development Inquiries:**

**Eric Risser** – Senior Vice President, Chief Business Officer 301-354-2640 | rissere@macrogenics.com



Link to our latest presentations: http://ir.macrogenics.com/events.cfm



