



BeiGene

# BeiGene Early Development Pipeline and Research

Thursday, July 9, 2020 – 9:00 a.m. ET

# Today's Participants



**Xiaodong Wang, Ph.D.**

*Chairman of Scientific Advisory Board & Co-Founder*



**John V. Oyler**

*Chairman, Co-Founder, & CEO*



**Lai Wang, Ph.D.**

*SVP, Head of Global Research & APAC Clinical Development*



**Eric Hedrick, M.D.**

*Chief Advisor*



**Jane Huang, M.D.**

*Chief Medical Officer, Hematology*



**Yong (Ben) Ben, M.D.**

*Chief Medical Officer, Immuno-Oncology*



**Howard Liang, Ph.D.**

*CFO & Chief Strategy Officer*



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# Agenda

Howard Liang, Ph.D.

*CFO and Chief Strategy Officer*

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# Agenda

- **Introduction** – Howard Liang
- **Opening Remarks** – Xiaodong Wang  
BeiGene's research foundation
- **BeiGene's Drug Discovery Engine** – Video Presentation  
People, capabilities, and facilities
- **Research and Internally Developed Assets** – Lai Wang  
TIGIT, Bcl-2, OX40, and HPK1
- **In-Licensed Programs** – Eric Hedrick  
Sotorasib (AMG 510), Sitravatinib, and Zanidatamab (ZW25)
- **Concluding Remarks** – John V. Oyler
- **Q&A**





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# Opening Remarks

Xiaodong Wang, Ph.D.

*Chairman of Scientific Advisory Board, Co-Founder and Member of Board of Directors*

# Founded with the Goal of the Best Medicine for the Most People

## The founding of a science-based company 10 years ago in China

- Why in China?

## Our philosophy: BeiGene believes the path to the best medicine is following the science

- Believe in a core research principle to follow the science: evidence and logic, not hearsay or portfolio decoration
- Pursue programs with best-in-class differentiation
- Be unafraid to terminate subpar programs at any time

## BeiGene's research team is productive and has delivered

- **Two** drugs approved and a **third** one at the filing stage, all with clinically differentiated properties
- **11** internally developed molecules advanced into the clinic, all with pre-clinically differentiated properties



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# BeiGene's Drug Discovery Engine Video Presentation





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# The Discovery Engine

Lai Wang, Ph.D.

*SVP, Head of Global Research and APAC Clinical Development*

# Executive Summary

## **BeiGene has built an exceptional research organization with broad capabilities & scope**

- Strong organization built over last decade and attracted outstanding talent
- Broad capabilities exist in this team to attack cancer through many modalities and targets

## **This team has shown proven internal research track record of success**

- 11 molecules delivered to the clinic in the first 10 years
- Two of these approved and one at the filing stage
  - Outstanding clinical data demonstrated for each

## **We have created a robust early clinical pipeline**

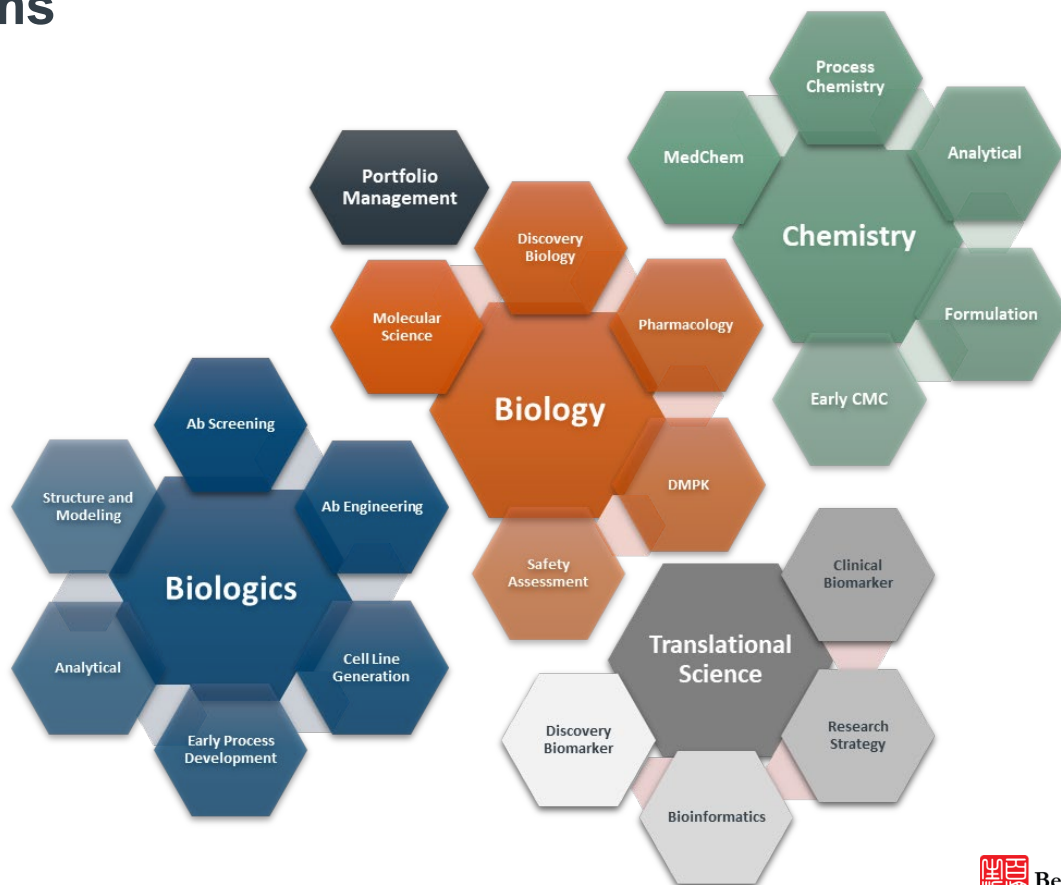
- Potentially differentiated compounds against TIGIT, Bcl-2, OX40
- Potentially first-in-class program in HPK1
- Compelling internal combination opportunities
- Planning to accelerate TIGIT program into Phase 3

# The Discovery Engine

- **Research Organization, Capabilities**
- Proven Internal Research Track Record
- Robust Promising Pipeline

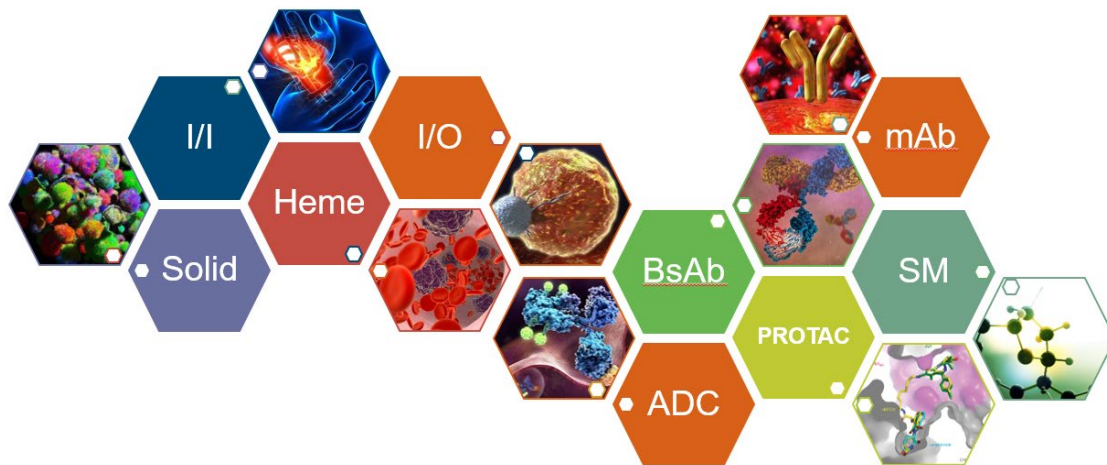
# Integrated Research Capabilities Offer Opportunities to Address Wide Range of Biological Problems

- Comprehensive small molecule and biologics discovery engine
- Efficient portfolio management
- Striving for seamless transition to manufacturing and clinical development



# Full Suite of Tools Applied Across Oncology and Beyond

- Moving beyond oncology to areas such as I/I
- Cutting-edge tools such as PROTAC, bispecific Ab, and ADC
- Pursuing 10+ potentially best-in-class and first-in-class projects with the plan to double that in one year



# Expansion of BeiGene Research



• 2011–2018

• TODAY

• PLANNED IN ONE YEAR

## Beijing Research Center

(ONLY 1<sup>ST</sup> AND 2<sup>ND</sup> FLOOR)

- Team size <200
- 6-8 preclinical programs

## Beijing Research Center

- Team size 350+
- ~12 preclinical programs

## Beijing Research Center Shanghai Research Center

- Team size 650+
- Capability for ~24 preclinical programs

# The Discovery Engine

- Research Organization, Capabilities
- **Proven Internal Research Track Record**
- Robust Promising Pipeline

# Proven Internal Research Track Record

## Two approved products, with a third at filing stage

- BRUKINSA (zanubrutinib) approved in US and China
  - First China-discovered compound to be approved by the FDA and granted Breakthrough Therapy Designation
  - Highly selective, complete and sustained target inhibition in tumor tissue
  - Improved safety profile shown in Phase 3 head to head trial despite missing the primary efficacy endpoint
- Tislelizumab approved in China for 2 indications, with 3 additional indications under review
  - Differentiated MOA by completely removing Fc function, thus avoiding macrophage mediated T-cell elimination
  - High complete response rate in lead indication cHL
- Pamiparib at filing stage in China
  - Demonstrated brain penetration in preclinical models, potential for treating brain tumor and brain metastasis
  - Not a drug pump substrate, preventing a potential resistance mechanism that has been reported for other PARPi in clinic

## 11 molecules discovered in-house and advanced into clinic in the last 10 years

- Broad range of I/O programs including differentiated OX-40, TIGIT
- Compelling and challenging Bcl-2 program



# The Discovery Engine

- Research Organization, Capabilities
- Proven Internal Research Track Record
- **Robust Promising Pipeline**

# Internal Capabilities and Collaborations Create Robust Pipeline

25+ assets, 8 with global rights

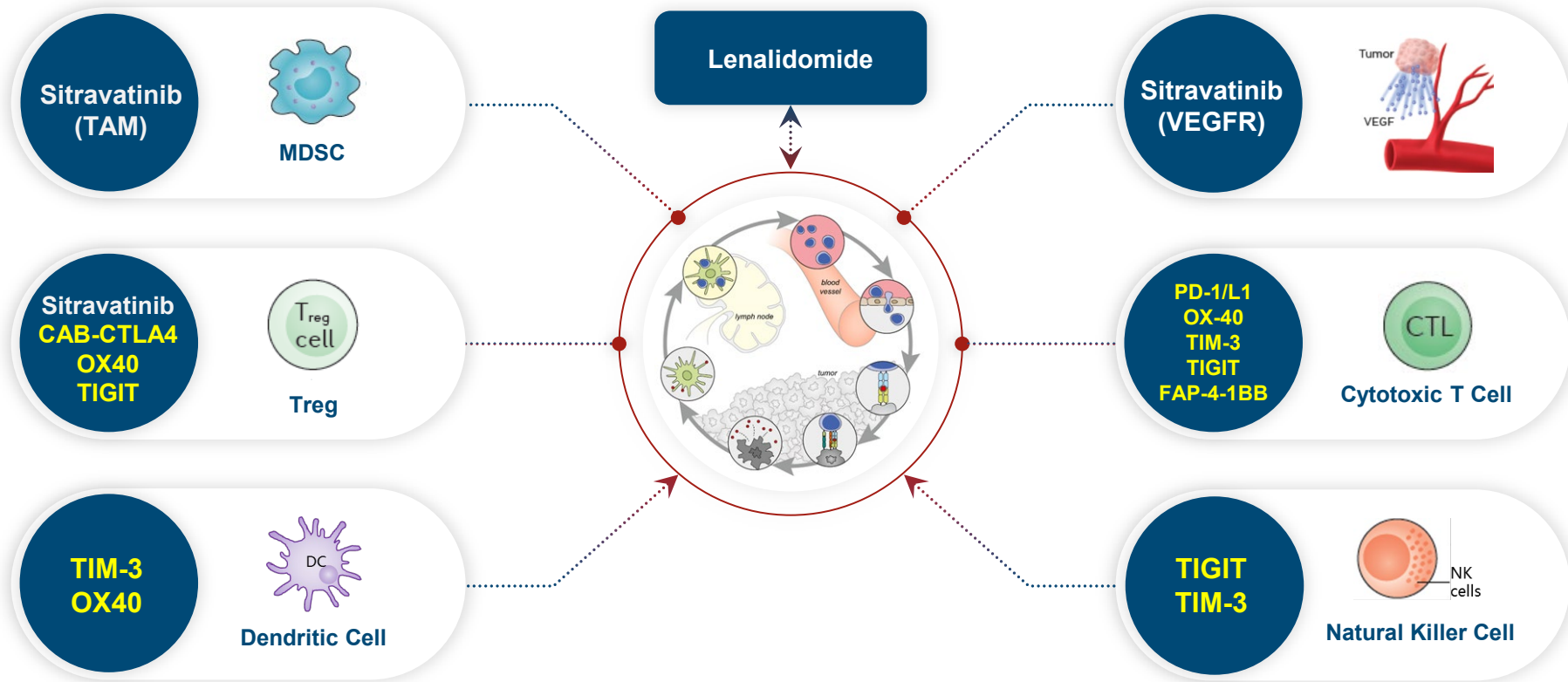
COMPOUND	(TARGET) / PROGRAM	DOSE ESC.		DOSE EXPANSION		PIVOTAL		COMMERCIAL RIGHTS	PARTNER
		PH1a	PH1b	PH2*	PH2**	PH3			
BGB-A1217	(TIGIT) + tislelizumab	Solid tumors						Global	
BGB-A445	(OX40) + tislelizumab	Solid tumors						Global	
BGB-A425	(TIM-3) Mono, + tislelizumab	Solid tumors						Global	
BGB-A333	(PD-L1) Mono, + tislelizumab	Solid tumors						Global	
BGB-11417	(Bcl-2) Mono, + zanubrutinib	B-cell malignancies		Phase 1 study startup ongoing				Global	
BGB-15025	(HPK1) Mono, + tislelizumab	IND Enabling studies ongoing						Global	
BGB-10188	(PI3Kδ) Mono, + tislelizumab, + zanubrutinib	B-cell + solid malignancies						Global	
lifirafenib	(RAF dimer)	B-Raf/K-RAS/N-RAS mut. solid tumors						Global	
BA3017	(CTLA4) Mono, + tislelizumab	Phase 1 study startup ongoing						Global	BioAtla
AMG 510	(KRAS G12C)	Solid Tumors, NSCLC, CRC							
AMG 701 <sup>^^</sup>	(BCMA)	MM							
AMG 176	(Mcl-1, SM (i.v.))	Hematologic malignancies							
AMG 397	(Mcl-1, SM (oral))	Hematologic malignancies							
AMG 330 <sup>^</sup>	(CD33)	Myeloid malignancies							
AMG 673 <sup>^^</sup>	(CD33)	AML							
AMG 427 <sup>^^</sup>	(FLT3)	AML						China	Amgen
AMG 562 <sup>^^</sup>	(CD19)	NHL							
AMG 596 <sup>^</sup>	(EGFRvIII)	Glioblastoma							
AMG 757 <sup>^^</sup>	(DLL3)	SCLC							
AMG 160 <sup>^^</sup>	(PSMA)	Prostate cancer							
AMG 506	(FAP x 4-1BB, DARPin®)	Solid Tumors							
AMG 199 <sup>^^</sup>	(MUC17)	GC/GEJC							
Sitravatinib	(multi-kinase inhibitor) + tislelizumab	NSCLC, RCC, OC, MEL						Asia ex-Japan, AU, NZ	Mirati
	Mono, + tislelizumab	HCC, GC/GEJC							
Zanidatamab†	(HER2, bispecific antibody)	Breast cancer, GEA						Asia ex-Japan, AU, NZ	Zymeworks
ZW49	(HER2, bispecific ADC)	Planned (in Ph1 ex-China by Zymeworks)						Asia ex-Japan, AU, NZ	Zymeworks
BGB-3245	(B-RAF)	Solid tumors						Asia ex-Japan	SpringWorks <sup>1</sup>
SEA-CD70	(anti-CD70)	Planned (starting Ph.1 ex-Asia by Seattle Genetics)						Asia ex-Japan, AU, NZ	Seattle Genetics
DKN-01	(DKK1) + tislelizumab ± chemo	Trials in GC/GEJ planned						Asia ex-Japan, AU,NZ	Leap Therapeutics

†Addition compounds from Amgen collaboration not yet disclosed

\* Some indications will not require a non-pivotal Ph2 clinical trial prior to beginning pivotal Ph2 or Ph3 clinical trials. \*\*Confirmatory clinical trials post approval are required for accelerated approvals. <sup>^</sup> BITE, <sup>^^</sup> HLE BITE, <sup>†</sup> ZW25, AML: acute myeloid leukemia, HLE BITE: Half-life extended Bi-specific T-cell engagers, GC/GEJ: gastric cancer/gastroesophageal junction, HCC: hepatocellular carcinoma, IND: Investigational New Drug, MEL: melanoma, MM: multiple myeloma, NHL: non-Hodgkin's lymphoma, N/SCLC: non-/small cell lung cancer, OC: ovarian cancer, RCC: renal cell carcinoma, SM: small molecule; 1. By MapKure, a JV with SpringWorks

# Cancer Immunotherapy

Small Molecule  
Biologics

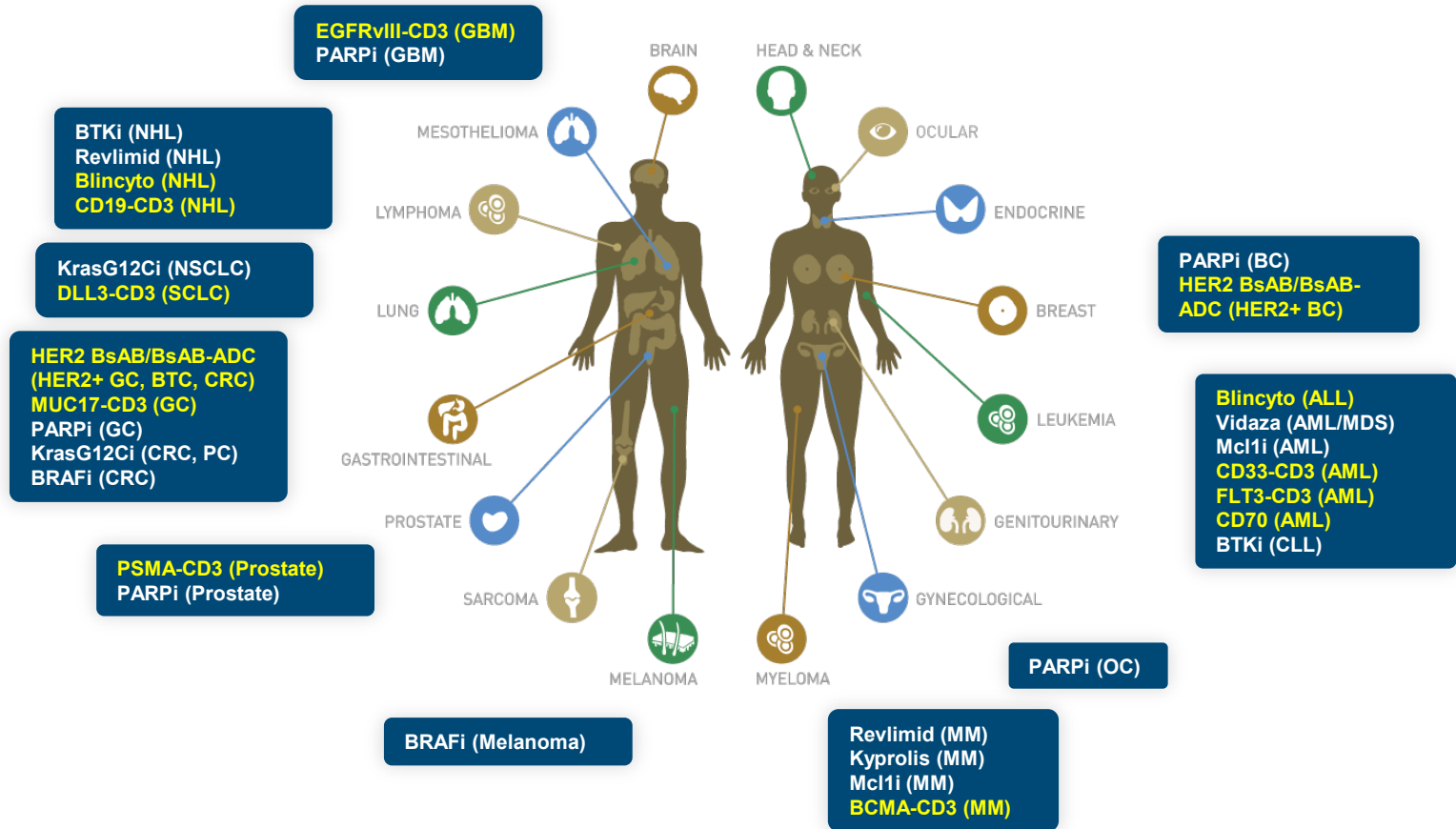


Source: Modified from Daniel S. Chen, *Immunity*, 2013; CAB=Conditional Active Biologics

# Tumor-Targeted Therapy

Small Molecule

Biologics



# Robust Promising Pipeline

- **BGB-A1217 (TIGIT Antibody)**
- BGB-11417 (Bcl-2 Inhibitor)
- BGB-A445 (Non Ligand-Competing OX40 Antibody)
- BGB-15025 (HPK1 Inhibitor)

# Executive Summary: TIGIT Program

## Encouraging POC data on tiragolumab/atezolizumab (Roche) at ASCO 2020

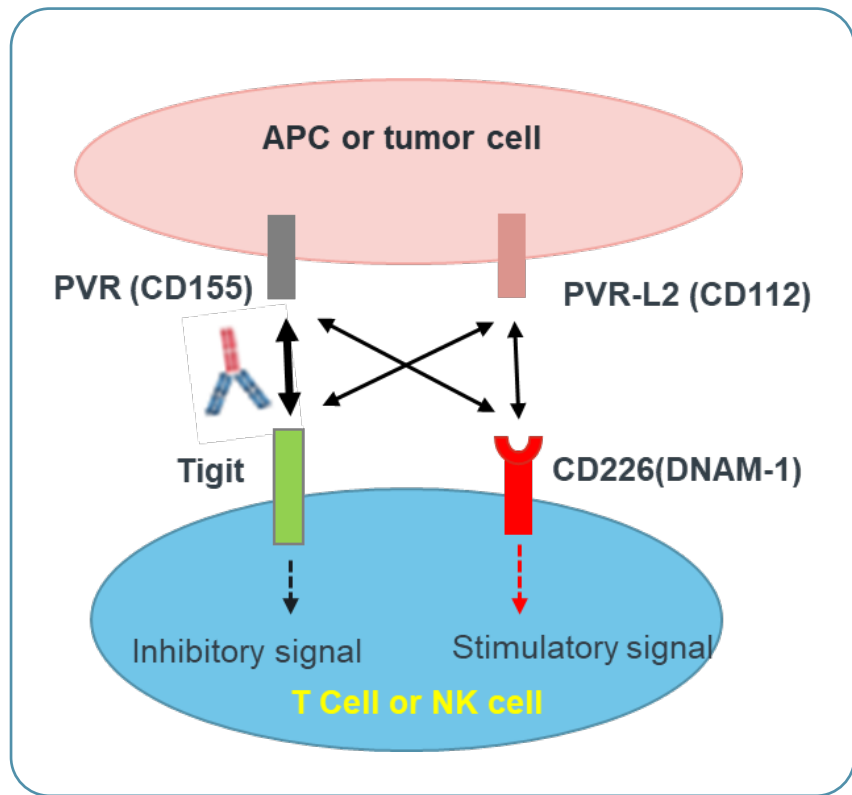
### **BGB-A1217 (TIGIT mAb) is one of the three most advanced TIGIT antibodies with full Fc function and RP2D for PD-(L)1 combination**

- ~4x more potent than tiragolumab in preclinical studies
- Competent Fc required for efficacy based on preclinical data
- Combination with tislelizumab generally well-tolerated, no DLT, recommended Phase 2 dose (RP2D) identified<sup>1</sup>

### **Potential to compete globally, possibly transformative**

- Registrational program being planned

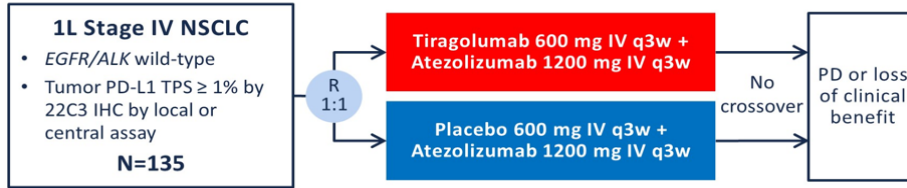
# TIGIT Ab Activates T/NK Cells by Blocking TIGIT and Ligand Interaction



- TIGIT shares its ligand PVR (CD155) and PVR-L2 (CD112) with the activating receptor CD226 (DNAM-1)
- BGB-A1217 blocks the binding of PVR/PVR-L2 to TIGIT and reactivates T effector cells and NK cells by:
  - Suppressing TIGIT-mediated inhibitory signaling
  - Increasing ligand availability for CD226 co-stimulatory receptor

# ASCO Update: Roche's TIGIT (Tiragolumab) plus PD-L1 (Atezolizumab) Combo Demonstrated Promising Activity in 1L PD-L1+ NSCLC

## Study Design (CITYSCAPE)



### Stratification Factors:

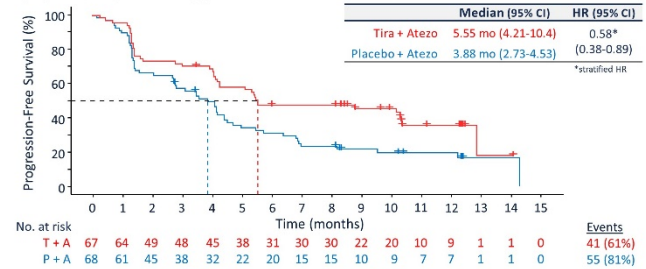
- PD-L1 TPS (1-49% vs ≥ 50%)
- Histology (Non-Squamous vs Squamous)
- Tobacco use (yes vs no)

- **Co-Primary Endpoints:** ORR and PFS
- **Key Secondary Endpoints:** Safety, DOR, OS, Patient-reported outcomes (PROs)
- **Exploratory Endpoints:** Efficacy analysis by PD-L1 status

## Results:

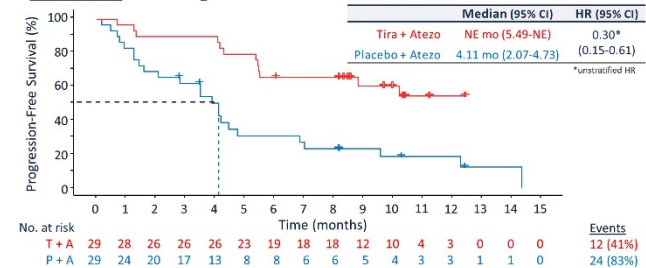
	ITT (TPS≥1%) N=135		PD-L1 high (TPS≥50%) n=58		PD-L1 low (TPS<1-49%) n=77	
	Tiragolumab +Tecentriq	Placebo +Tecentriq	Tiragolumab +Tecentriq	Placebo +Tecentriq	Tiragolumab +Tecentriq	Placebo +Tecentriq
ORR % (Follow-up 10.9 months)	37	21	66	24	16	18
mPFS, months (Follow-up 10.9 months)	5.55	3.88	NE	4.11	4.04	3.58
	0.58 (0.38-0.89)		0.3 (0.15-0.61)		0.89 (0.53,1.49)	

### Updated Investigator-Assessed PFS: ITT



ITT = intention-to-treat; P+A = placebo + atezolizumab; T+A = tiragolumab + atezolizumab Follow data cutoff: 02 December 2019

### Updated Investigator-Assessed PFS: PD-L1 TPS ≥ 50%

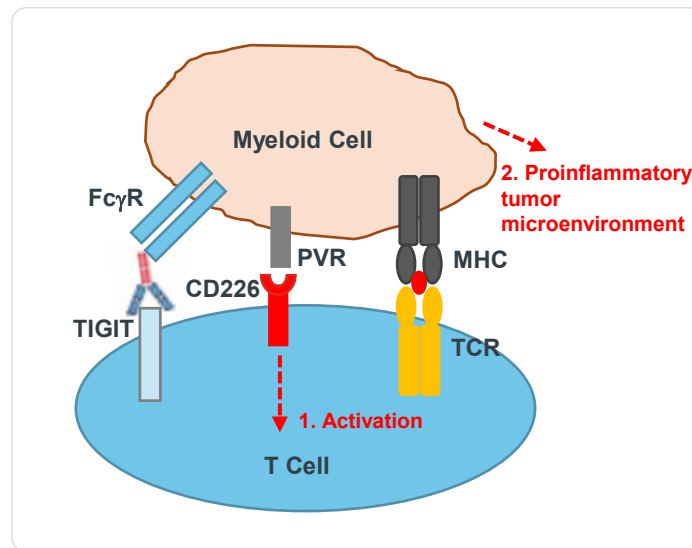
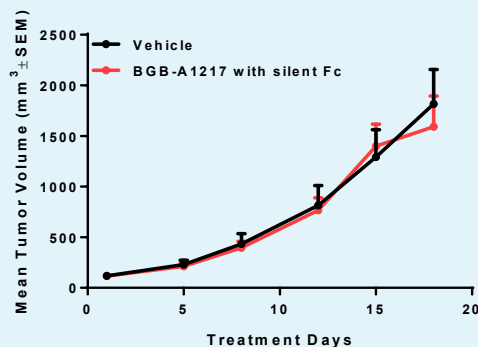
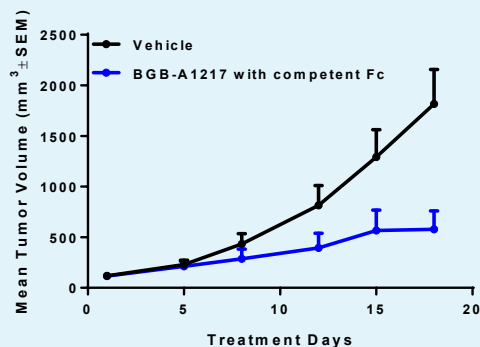


NE = non-evaluable; P+A = placebo + atezolizumab; T+A = tiragolumab + atezolizumab; TPS = tumor proportion score Follow data cutoff: 02 December 2019



# Fc Effector Function Appears Critical for Anti-Tumor Activity of TIGIT Ab

## Competent Fc is required for BGB-A1217 in CT26 model



## Multiple MOA may exist for competent Fc

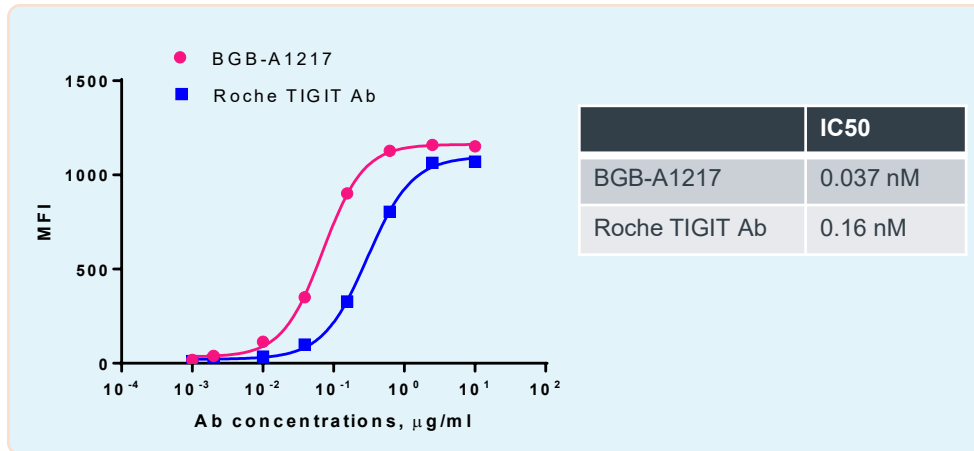
1. Fc/Fc $\gamma$ R co-engagement enhances T cell responsiveness by enhancing the quality of immune synapse
2. Fc/Fc $\gamma$ R engagement on myeloid cell creates proinflammatory TME by activating myeloid cells

# TIGIT Competitive Landscape

FORMAT	HYPOTHESIS	DRUG NAME	COMPANY	COMBO DOSE	STATUS
WT IgG1	WT IgG1 required for maximal efficacy based on preclinical studies	Tiragolumab	Roche	600 mg Q3W	Ph1 initiated in May 2016 Ph2 in cervical cancer planned in Jun 2020 Ph3 in SCLC initiated in Feb 2020 Ph3 in NSCLC initiated in Mar 2020
		Vibostolimab	Merck	Not disclosed	Ph1 initiated in Dec 2016 Ph1/2 in melanoma planned in Apr 2020 Ph2 in NSCLC initiated in Jan 2020
		Etigilimab	OncoMed/Mereo	NA	Ph1 initiated in May 2017
		BGB-A1217	BeiGene	Not disclosed	Ph1 initiated in Aug 2019 with combo escalation from beginning
		TSGN-TG	Seattle Genetics	NA	Ph1 initiated in Apr 2020
		EOS-884448	iTeos	NA	Ph1 initiated in Feb 2020
Mutant IgG1	Less effective	AB-154	Arcus/Gilead	NA	Ph1 initiated in Aug 2018 Ph2 in NSCLC initiated in Jan 2020
		BMS-986207	BMS	NA	Ph1 initiated in Nov 2016
WT IgG4	Less effective	ASP-8374	Astellas/Potenza	NA	Ph1 initiated in Sep 2017
		COM902	Compugen	NA	Ph1 initiated in Mar 2020
Not Disclosed		IBI-939	Innovent	NA	Ph1 planned in May 2020

# BGB-A1217 Program Moving Aggressively Towards Registration Trial

- Four-fold more potent than tiragolumab (Roche)<sup>1</sup>
- BGB-A1217 Phase 1 combination with tislelizumab ongoing in advanced solid tumors
- Generally well-tolerated, no DLT, **combination recommended phase 2 dose has been determined**
- Full target occupancy was observed in PBMCs at lowest dose level
- Moving aggressively towards registration trial



# Robust Promising Pipeline

- BGB-A1217 (TIGIT Antibody)
- **BGB-11417 (Bcl-2 Inhibitor)**
- BGB-A445 (Non Ligand-Competing OX40 Antibody)
- BGB-15025 (HPK1 Inhibitor)

# Executive Summary: Bcl-2 Program

## BGB-11417 is a potential best-in-class Bcl-2 inhibitor

- **Potent Bcl-2 inhibitor, with potential to overcome resistance to venetoclax**
- Ability to be dosed high if needed, e.g. for solid tumor indications
- More selective than venetoclax for Bcl-2 relative to Bcl-xL
- NOAEL in animal GLP tox studies with exposure close to 30-fold higher than predicted human therapeutic exposure<sup>1</sup>
- Well-positioned to be combined with zanubrutinib, BeiGene's potentially best-in-class BTK inhibitor

## BGB-11417 FIH study ongoing

- Dose escalation initiated early this year, currently at 80 mg QD, which is predicted to be equivalent to 400 mg of venetoclax
- Combination trial with zanubrutinib planned to be initiated H2 2020

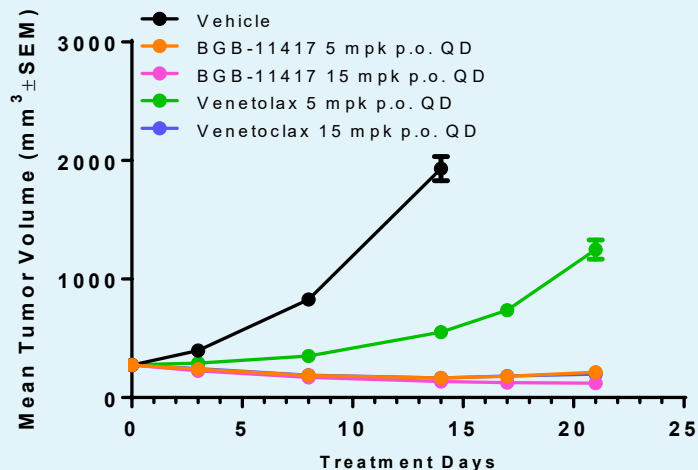
# BGB-11417 Was More Potent and Selective than Venetoclax in Biochemical and Cellular Assays

	BGB-11417	Venetoclax	Potency Improvement (Fold, BGB-11417/Venetoclax)
Bcl-2 WT (Biochemical IC50, nM)	0.035	1.3	37
Bcl-2 G101V (Biochemical IC50, nM)	0.28	34	121
Bcl-2 WT (Cell Proliferation IC50, nM)	0.42	3.4	8.1
Bcl-2 G101V (Cell Proliferation IC50, nM)	4.6	75	16.3
Fold selectivity (TF-FRET assay) Bcl-xL; Mcl-1; Bcl-w; Bcl-2A1	>1000; >1000; >1000; >1000	325; >1000; >1000; >1000	

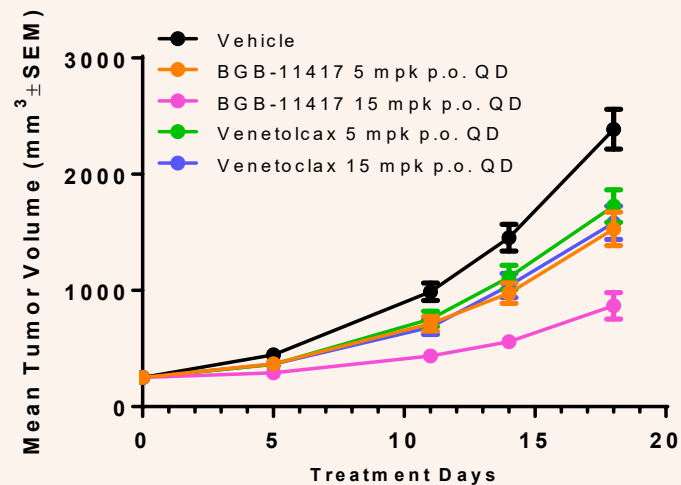
Bcl-2 G101V mutation emerged as resistance to Venetoclax in clinic

# BGB-11417 Was More Efficacious than Venetoclax in Both Wild-Type and Bcl-2-G101V Xenograft Models

## BGB-11417 is more efficacious in RS4:11 model



## BGB-11417 is efficacious in RS4:11-G101V model



# Bcl-2 Inhibitors Demonstrated Activity in Solid Tumors

## Breast cancer

- Bcl-2 is overexpressed in approximately 80% of primary ER+ breast cancer<sup>1,2</sup>. Bcl-2 is often expressed at high levels in poorer-prognosis luminal B tumors, as well as good-prognosis luminal A tumors<sup>3</sup>.
- Combining venetoclax with endocrine therapy had a tolerable safety profile and elicited notable activity in ER and Bcl-2-positive metastatic breast cancer. For 24 patients treated at the RP2D, the confirmed radiologic response rate was 54% and the clinical benefit rate was 75%<sup>4</sup>.
- Venetoclax 800 mg/day was selected as the RP2D in combination with tamoxifen; no higher doses were explored due to the potential “pill burden”, while BGB-11417 may not have this issue.
- Dual targeting of CDK4/6 and Bcl-2 pathways augmented tumor response in ER+ breast cancer. The effect was associated with increased apoptosis<sup>5</sup>.

## SCLC

- Dual Bcl-2 and Bcl-xL inhibitor, navitoclax (ABT-263) showed preliminary clinical benefit in SCLC<sup>6</sup>.
- Preclinical cell line screen and PDX experiments showed high Bcl-2 expression conferred sensitivity of SCLC to venetoclax<sup>7</sup>.



## Robust Promising Pipeline

- BGB-A1217 (TIGIT Antibody)
- BGB-11417 (Bcl-2 Inhibitor)
- **BGB-A445 (Non Ligand-Competing OX40 Antibody)**
- BGB-15025 (HPK1 Inhibitor)

# Executive Summary: OX40 Program

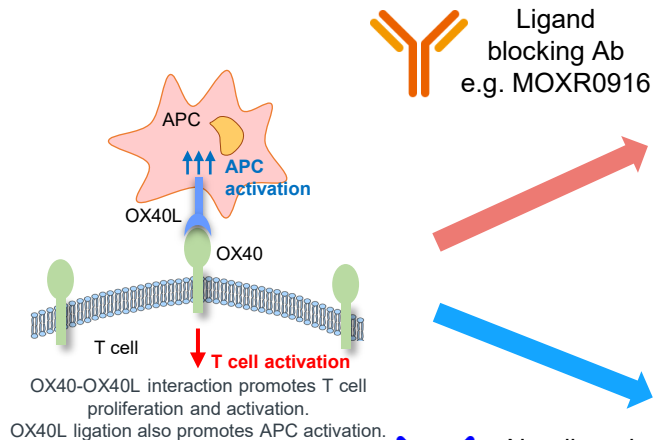
**BGB-A445 (OX40 agonist antibody) is differentiated from all other OX40 Abs in the clinic**

- **Does not disrupt OX40-OX40L engagement**
  - Retains OX40L signaling on antigen presenting cells
  - Achieves maximal OX40 activation by keeping natural ligand stimulation
- Widely efficacious as monotherapy in preclinical models, including PD-1 resistant models
- Has shown combo effect with PD-1 Ab, TLR9 agonist, PI3K $\delta$  inhibitor, sitravatinib and chemo in preclinical models

## Phase 1 clinical trial ongoing

- Monotherapy dose escalation ongoing
- Combination dose escalation trial with tislelizumab is planned to start in H2 2020

# BGB-A445 Is a Non-ligand Blocking OX40 Antibody, Differentiated from Other Clinical OX40 Antibodies





Ligand blocking Ab  
e.g. MOXR0916

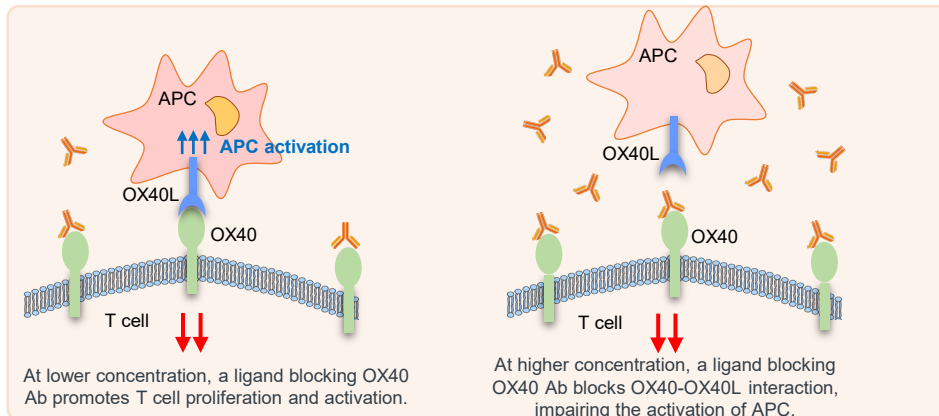


Non-ligand blocking Ab  
e.g. BGB-A445

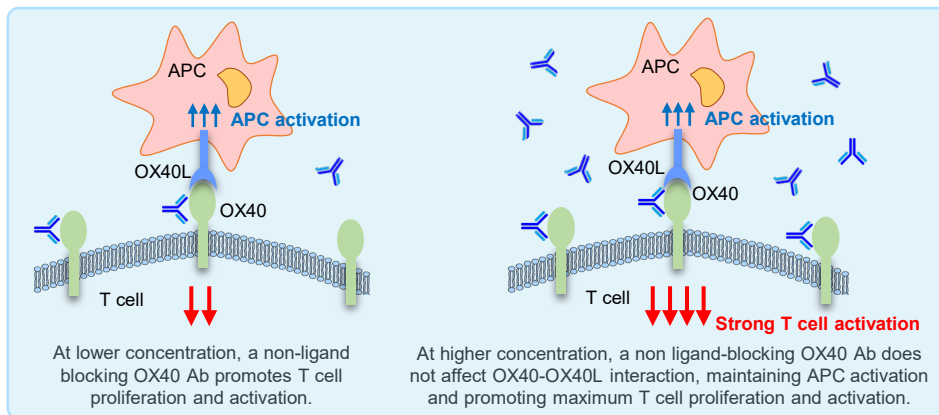


-  Agonistic, ligand blocking  $\alpha$ OX40 Ab
-  Agonistic, ligand non-blocking  $\alpha$ OX40 Ab

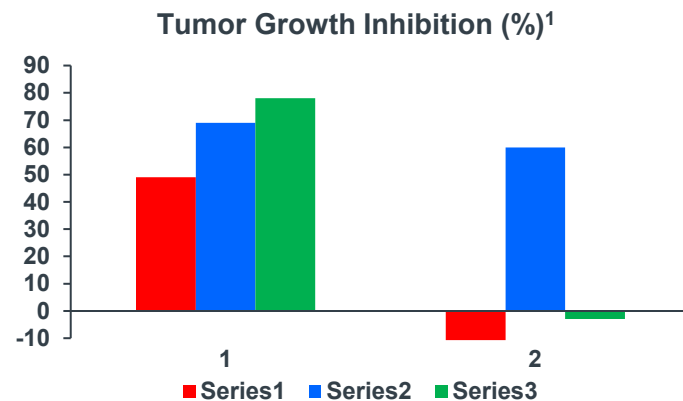
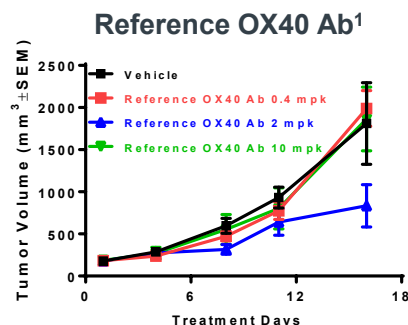
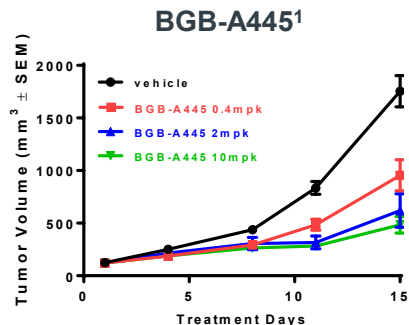
APC = antigen presenting cell



$\alpha$ OX40 Ab concentration increase



# BGB-445 Showed Dose-Response, While Competitor's OX40 Ab Showed Hook Effect in MC38 OX40 Humanized Mice Model



## Competitor OX40 Abs Showed Limited Efficacy in Clinic, Mainly at Low Dose Levels

Name	MEDI0562	MOXR0916	PF-04518600	BMS-986178	ABBV-368	GSK3174998
Company	AstraZeneca	Genentech	Pfizer	BMS	Abbvie	GSK
Dose Range	0.03-10 mg/kg (mono) 0.04-0.4 mg/kg (combo)	0.01-20 mg/kg	0.01–10 mg/kg (mono) 0.1-3 mg/kg (combo)	0.3-5 mg/kg	0.01 to 3.0mg/kg	0.003-10 mg/kg
Dose Level of Objective Responses	<b>Mono (50 pts):</b> 1 PR@0.03 mg/kg 1 PR@3 mg/kg  <b>Combo with Durva (26 pts):</b> 2 PR@0.1mg/kg 1 PR@0.4 mg/kg	<b>Mono expansion @ 5mpk (17 pts):</b> 2 PR  <b>Combo with Atezo (51 pts):</b> 1 PR@0.01 mg/kg 1 PR@0.2 mg/kg	<b>Mono (49 pts):</b> 1 PR@0.1 mg/kg 1 PR@0.3 mg/kg  <b>Combo with α4-1BB (37 pts):</b> 2 PR@0.3 mg/kg	<b>Combo with Nivo (16 pts):</b> 3 PR, 1 PR@5mg/kg; other two unknown	<b>Mono (36 pts):</b> 1 PR@0.01 mg/kg	<b>Mono (45 pts):</b> 1 PR@0.3 mg/kg  <b>Combo with Pembro (96 pts):</b> 3 CR, 5 PR; 1 CR at 0.1 mg/kg, others unknown

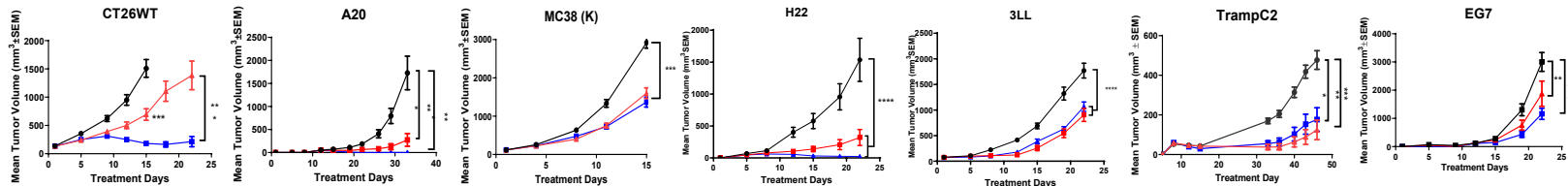
Sources: 1. Internal data 2. Glisson *et al.* ESMO 2018 (abstract 1152P). Goldman *et al.* ASCO 2020 (abstract 3003). Hansen *et al.* AACR 2016 (abstract CT097). Infante *et al.* ASCO 2016 (abstract 101). El-Khoueiry *et al.* ASCO 2017 (abstract 3027). Hamid *et al.* ESMO 2018 (abstract 1184P). Olszanski *et al.* SITC 2017 (abstract O17). Spira *et al.* ESMO 2018 (abstract 1149P). Postel-Vinay *et al.* AACR 2020 (abstract CT150).

# OX40 Competitive Landscape

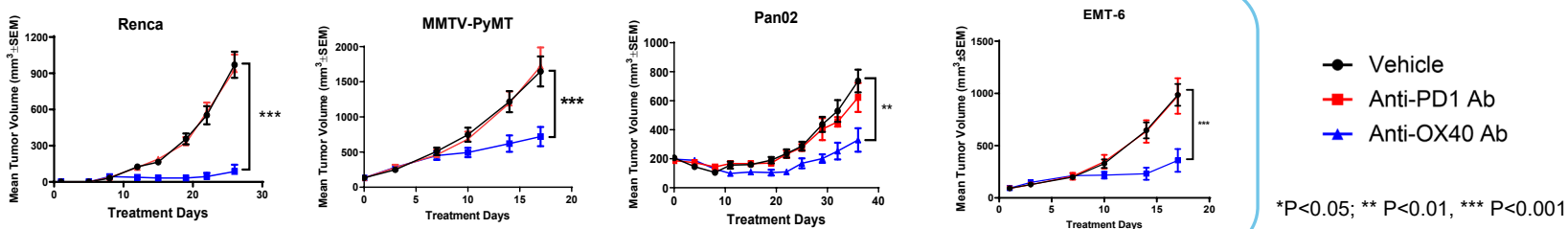
DRUG NAME	DESCRIPTION	COMPANY	DISEASE	STATUS
<b>MOXR-0916</b>	IgG1 OX40 agonist Block OX40L	Roche	Solid tumors	Ph1 initiated in Aug 2014 Development discontinued in 2017
<b>MEDI-0562</b>	IgG1 OX40 agonist Block OX40L	MedImmune/AZ	Solid tumors	Ph1 initiated in Mar 2016 Ph1b in HNSCC/melanoma initiated in Jul 2018 Ph2 in OC initiated in Jun 2018 Development discontinued in 2019
<b>PF-04518600</b>	IgG2 OX40 agonist Block OX40L	Pfizer	Solid tumors	Ph1 initiated in Apr 2015 Ph2 in RCC initiated in Sep 2017 Ph2 in TNBC initiated in Jul 2019 Development discontinued in 2019
<b>GSK-3174998</b>	IgG1 OX40 agonist Block OX40L	GSK	Solid tumors MM	Ph1 initiated in Sep 2015 Ph1 in MM initiated in Oct 2019
<b>BMS-986178</b>	IgG1 OX40 agonist Block OX40L	BMS	Solid tumors	Ph1 initiated in Jun 2016
<b>INCAGN-1949</b>	IgG1 OX40 agonist Block OX40L	Agenus/Incyte	Solid tumors	Ph1 initiated in Oct 2016
<b>ABBV-368</b>	IgG1 OX40 agonist Block OX40L	Abbvie	Solid tumors	Ph1 initiated in May 2017 Ph1b in HNSCC initiated in Jan 2020
<b>IBI-101</b>	IgG1 OX40 agonist Block OX40L	Innovent	Solid tumors	Ph1 initiated in Dec 2018
<b>INBRX-106</b>	OX40 agonist	Inhibrx/Elpiscience	Solid tumors	Ph1 initiated in Dec 2019
<b>BGB-A445</b>	IgG1 OX40 agonist <b>Does NOT block OX40L</b>	BeiGene	Solid tumors	Ph1 initiated in early 2020

# OX40 Ab Was More Efficacious than PD-1 in Mouse Syngeneic Models

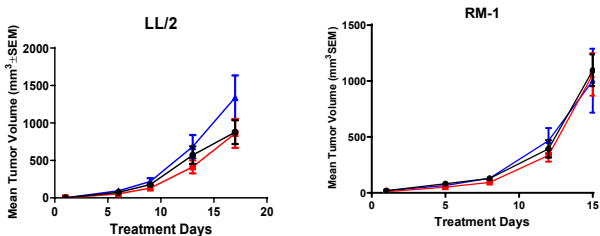
Responded to **both**  $\alpha$ OX40 and  $\alpha$ PD-1



Responded to  $\alpha$ OX40 Ab **only**

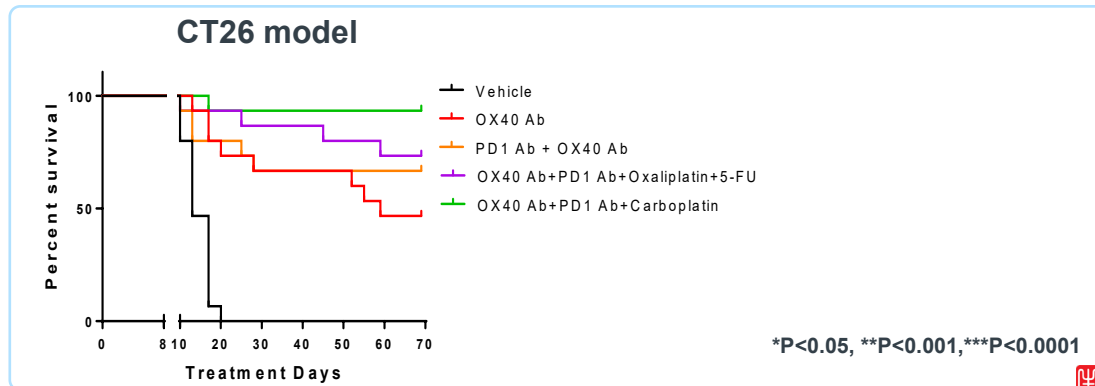
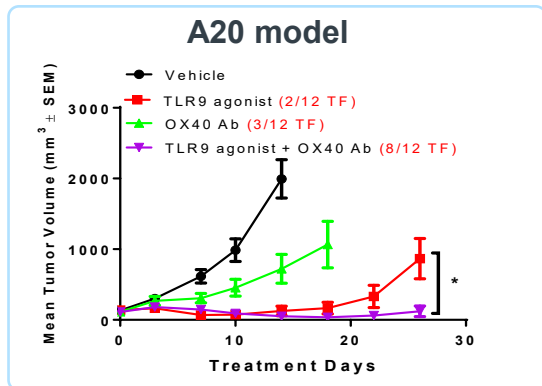
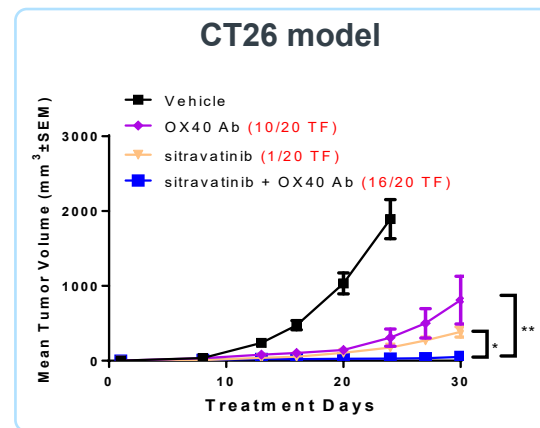
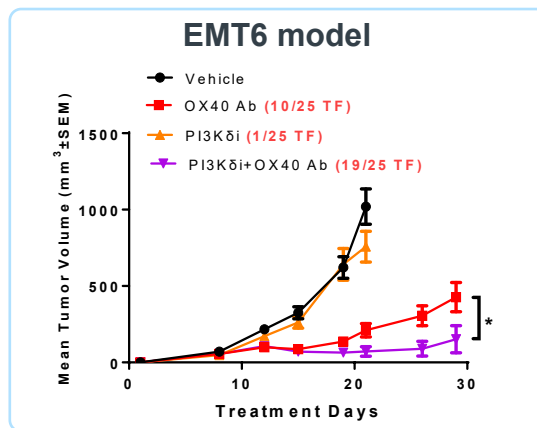
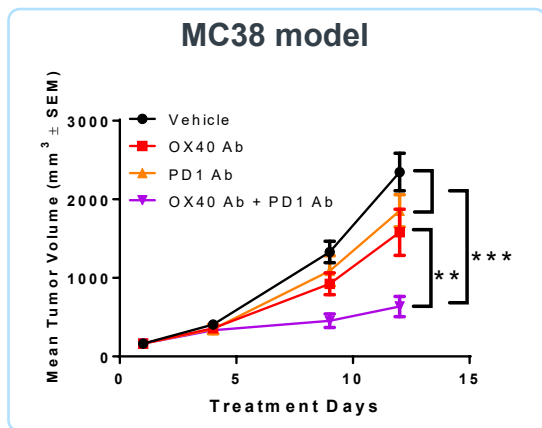


Responded to **neither**  $\alpha$ OX40 nor  $\alpha$ PD-1

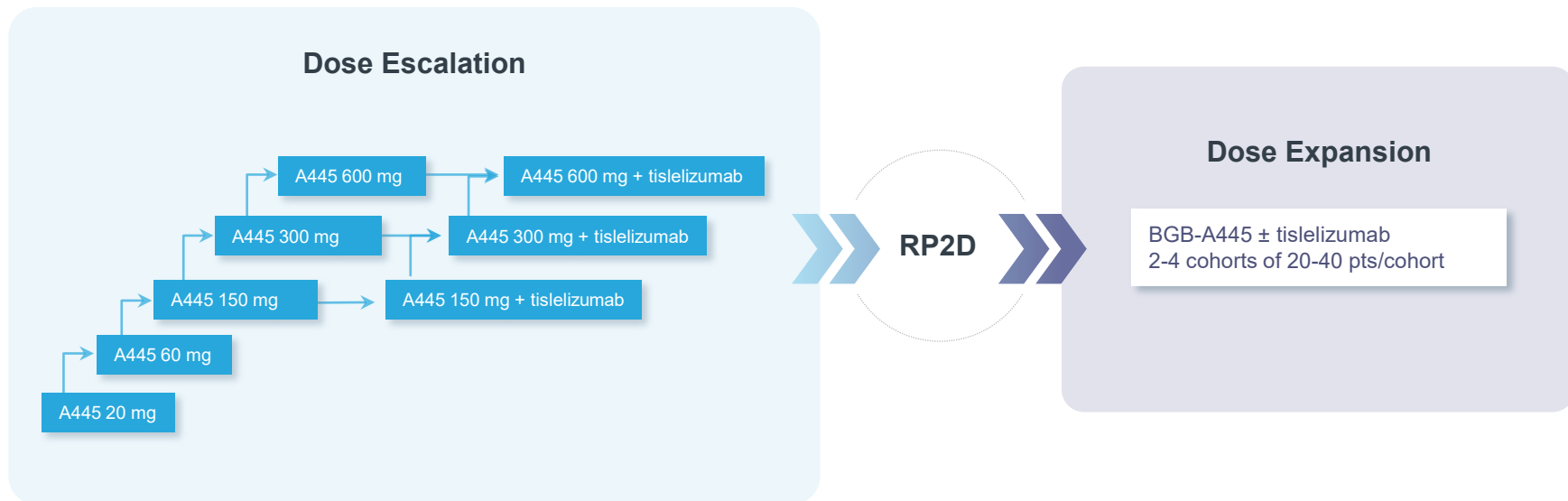


- OX40 Ab was active in 11/13 models while PD-1 Ab was only active in 7/13 models
- In most models where both agents were active, OX40 Ab showed stronger anti-tumor activity.

# OX40 Ab Has Shown Combination Activity with PD-1 Ab, PI3K $\delta$ Inhibitor, Sitravatinib, TLR9 Agonist, and Chemo



# Ph1 Study Design and Current Status of BGB-A445 (OX40 Antibody)



- Dose escalation schedule is BGB-A445 Q3W ± tislelizumab Q3W.



# Robust Promising Pipeline

- BGB-A1217 (TIGIT Antibody)
- BGB-11417 (Bcl-2 Inhibitor)
- BGB-A445 (Non Ligand-Competing OX40 Antibody)
- **BGB-15025 (HPK1 Inhibitor)**

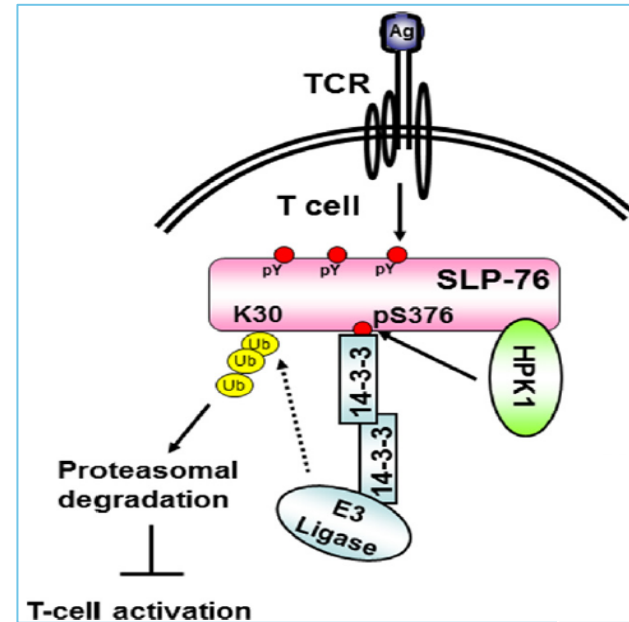
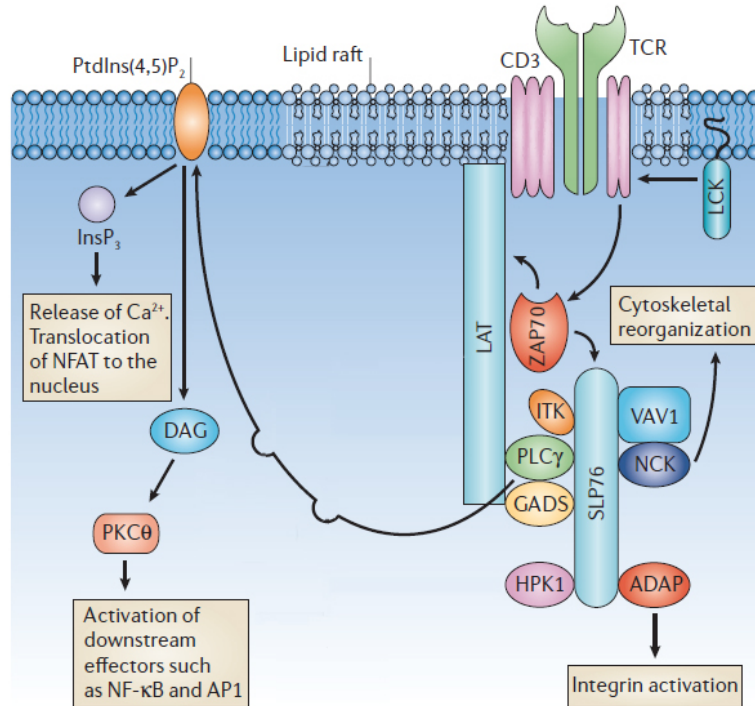
# Executive Summary: HPK1 Program

## **BGB-15025 is a potentially first-in-class HPK1 inhibitor**

- HPK1 is a key negative feedback regulator of TCR signaling; inhibition of HPK1 enhances T cell activation
- Robust combination anti-tumor activity with PD-1 Ab in preclinical animal models<sup>1</sup>
- Preliminary tox study suggests wide therapeutic window (~20-50 fold)

## **IND submission expected Q4 2020**

# HPK1 Negatively Regulates T-cell Receptor Signaling

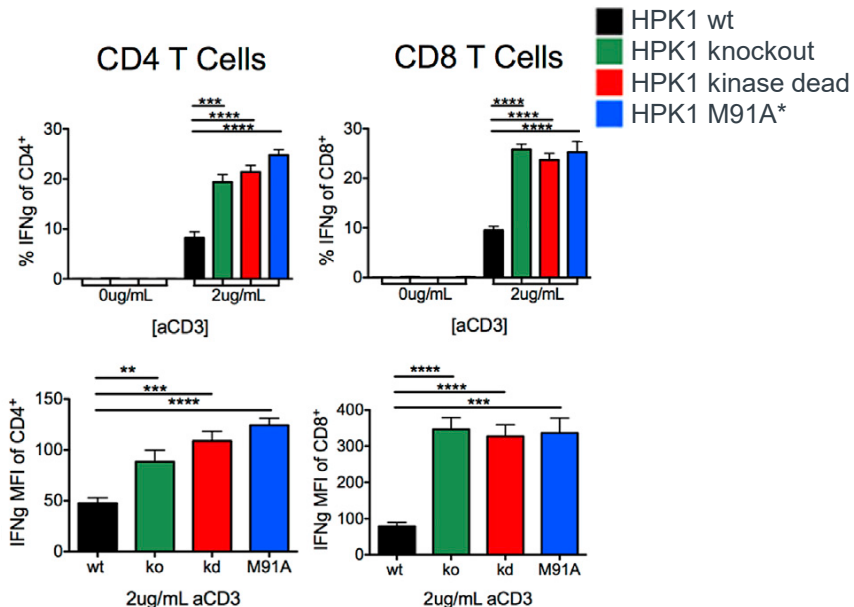


Sairy Hernandez et al, Cell Reports 25, 80–94, 2018

Phosphorylation of the adaptor SLP-76 by HPK1 leads to degradation of SLP-76 which is crucial for T-cell activation.

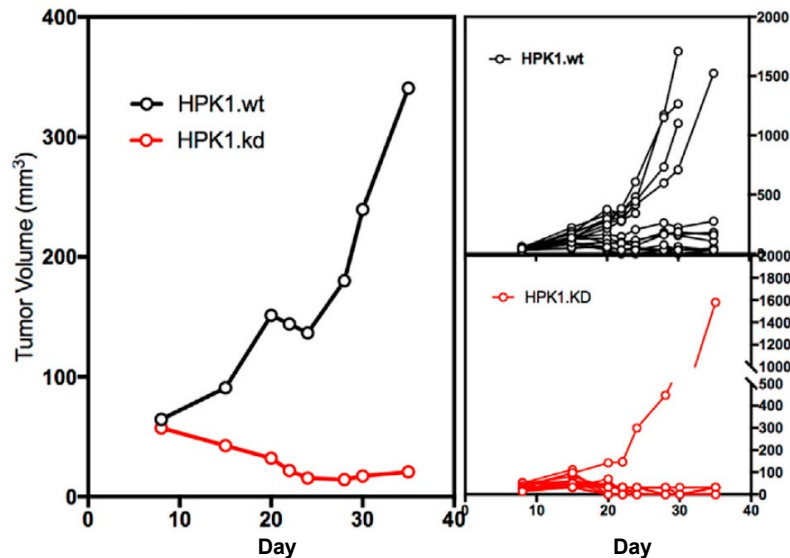
# Strong Scientific Evidence Supports Critical Role for HPK1 in T-Cell Activation and Anti-Tumor Immunity

T-cells with reduced HPK1 catalytic activity show enhanced activation upon  $\alpha$ CD3 treatment



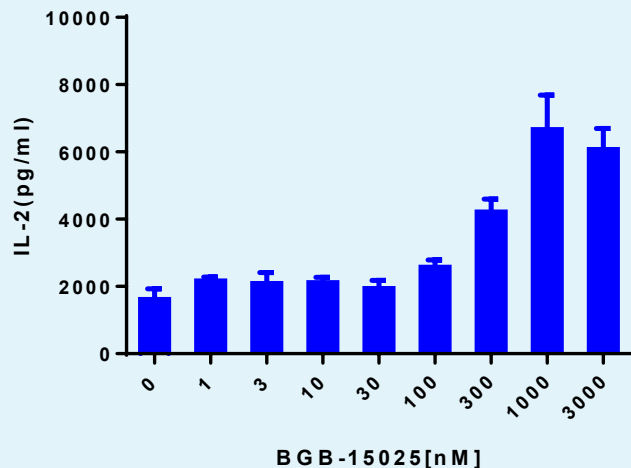
\*M91A mutation reduces HPK1 kinase activity by ~50% in T cells.  
 \*P<0.05, \*\* P<0.01, \*\*\* P<0.001, \*\*\*\* P<0.001

Tumor rejection in GL261 model in HPK1 kinase dead mice

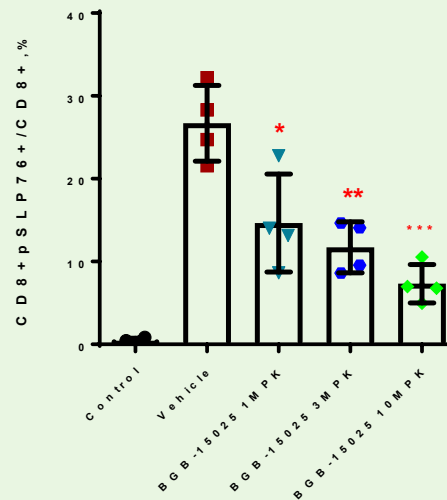


# BGB-15025 Demonstrated Significant *in Vitro* and *in Vivo* PD Effect

## BGB-15025 increased IL2 production in PBMC

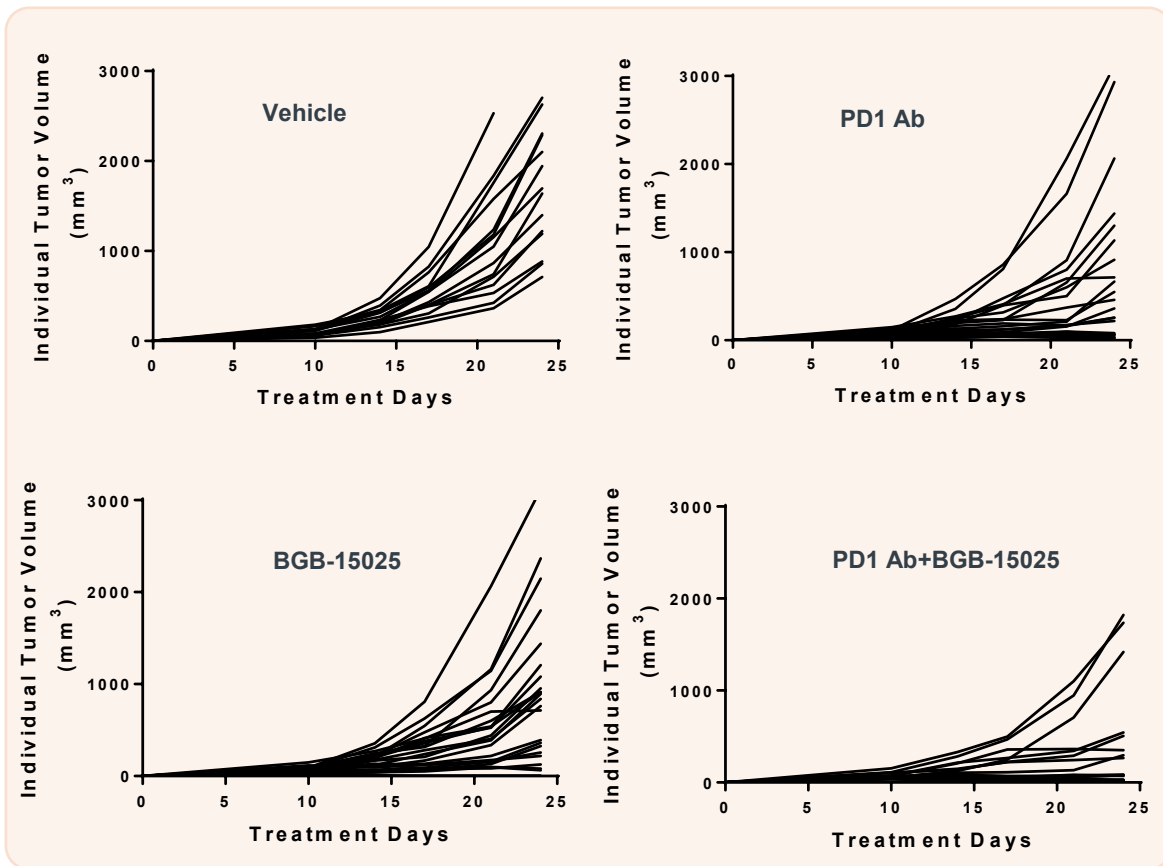


## Splenic pSLP76 PD (6hr post treatment)



\*P<0.05; \*\* P<0.01, \*\*\* P<0.001 vs. Vehicle

# BGB-15025 Showed Significant Combo Efficacy with PD-1 Antibody



Group	Dosage	Tumor-free	TV<50 mm <sup>3</sup>	TV<100 mm <sup>3</sup>
Vehicle (n=15)	-	0	0	0
PD-1 Ab (n=25)	1mpk	4%	20%	40%
BGB-15025 (n=15)	1mpk	13%	13%	13%
<b>PD-1 Ab + BGB-15025 (n=25)</b>	<b>1mpk + 1mpk</b>	<b>28%</b>	<b>52%</b>	<b>68%</b>

BGB-15025 demonstrated significant combo effects with PD-1 Ab at as low as 1 mg/kg in CT26WT syngeneic model.

# Productive Discovery Engine

**Always science driven, proven record in target selection**

**Full internal capabilities, efficient portfolio management**

**Cutting edge technologies such as PROTAC, ADC, bsAb**

**Robust early pipeline (25+ in clinical stage and 10+ in preclinical), including:**

- BGB-A1217 (TIGIT): One of three most advanced programs, Fc effector function competent, accelerating to registration trials
- BGB-11417 (Bcl-2): Potent Bcl-2 inhibitor, potentially overcomes venetoclax resistance
- BGB-A445 (OX40): The only endogenous ligand non-competing agent
- BGB-15025 (HPK1): Potentially first-in-class, prevents T-cell exhaustion



BeiGene

# In-Licensed Programs

Eric Hedrick, M.D.  
*Chief Advisor*



# Executive Summary

## External collaborations contribute significantly to our clinical pipeline:

- 25+ molecules across 9 collaborations
- Complementary with existing internal clinical and research programs
- Diversification of therapeutic modalities (e.g. Amgen BiTE platforms)
- Expansion of IO tislelizumab-based combination opportunities

## Added focus on key disease indications:

- PD-1 sensitive Asia-prevalent tumor types (lung, liver, gastric) sitravatinib, zanidatamab (ZW-25), etc.
- NSCLC: Sotorasib (AMG 510)
- HER2-expressing cancers (breast, gastric) zanidatamab/ZW49

**Anticipate several programs entering late-stage development within the next 6-18 months**

# Internal Capabilities and Collaborations Create Robust Pipeline

25+ assets, 8 with global rights

COMPOUND	(TARGET) / PROGRAM	DOSE ESC.			DOSE EXPANSION		PIVOTAL		COMMERCIAL RIGHTS	PARTNER
		PH1a	PH1b	PH2*	PH2**	PH3				
BGB-A1217	(TIGIT) + tislelizumab	Solid tumors							Global	
BGB-A445	(OX40) + tislelizumab	Solid tumors							Global	
BGB-A425	(TIM-3) Mono, + tislelizumab	Solid tumors							Global	
BGB-A333	(PD-L1) Mono, + tislelizumab	Solid tumors							Global	
BGB-11417	(Bcl-2) Mono, + zanubrutinib	B-cell malignancies			Phase 1 study startup ongoing				Global	
BGB-15025	(HPK1) Mono, + tislelizumab	IND Enabling studies ongoing							Global	
BGB-10188	(PI3Kδ) Mono, + tislelizumab, + zanubrutinib	B-cell + solid malignancies							Global	
lifirafenib	(RAF dimer)	B-Raf/K-RAS/N-RAS mut. solid tumors							Global	
BA3017	(CTLA4) Mono, + tislelizumab	Phase 1 study startup ongoing							Global	BioAtla
AMG 510	(KRAS G12C)	Solid Tumors, NSCLC, CRC								
AMG 701 <sup>AA</sup>	(BCMA)	MM								
AMG 176	(Mcl-1, SM (i.v.))	Hematologic malignancies								
AMG 397	(Mcl-1, SM (oral))	Hematologic malignancies								
AMG 330 <sup>A</sup>	(CD33)	Myeloid malignancies								
AMG 673 <sup>AA</sup>	(CD33)	AML								
AMG 427 <sup>AA</sup>	(FLT3)	AML						China		Amgen
AMG 562 <sup>AA</sup>	(CD19)	NHL								
AMG 596 <sup>A</sup>	(EGFRvIII)	Glioblastoma								
AMG 757 <sup>AA</sup>	(DLL3)	SCLC								
AMG 160 <sup>AA</sup>	(PSMA)	Prostate cancer								
AMG 506	(FAP x 4-1BB, DARPin®)	Solid Tumors								
AMG 199 <sup>AA</sup>	(MUC17)	GC/GEJC								
Sitravatinib	(multi-kinase inhibitor) + tislelizumab Mono, + tislelizumab	NSCLC, RCC, OC, MEL HCC, GC/GEJC							Asia ex-Japan, AU, NZ	Mirati
Zanidatamab†	(HER2, bispecific antibody)	Breast cancer, GEA							Asia ex-Japan, AU, NZ	Zymeworks
ZW49	(HER2, bispecific ADC)	Planned (in Ph1 ex-China by Zymeworks)							Asia ex-Japan, AU, NZ	Zymeworks
BGB-3245	(B-RAF)	Solid tumors							Asia ex-Japan	SpringWorks <sup>1</sup>
SEA-CD70	(anti-CD70)	Planned (starting Ph.1 ex-Asia by Seattle Genetics)							Asia ex-Japan, AU, NZ	Seattle Genetics
DKN-01	(DKK1) + tislelizumab ± chemo	Trials in GC/GEJ planned							Asia ex-Japan, AU,NZ	Leap Therapeutics

† Addition compounds from Amgen collaboration not yet disclosed

\* Some indications will not require a non-pivotal Ph2 clinical trial prior to beginning pivotal Ph2 or Ph3 clinical trials. \*\*Confirmatory clinical trials post approval are required for accelerated approvals. <sup>A</sup> BITE, <sup>AA</sup> HLE BITE, <sup>†</sup> ZW25, AML: acute myeloid leukemia, HLE BITE: Half-life extended Bi-specific T-cell engagers, GC/GEJ: gastric cancer/gastroesophageal junction, HCC: hepatocellular carcinoma, IND: Investigational New Drug, MEL: melanoma, MM: multiple myeloma, NHL: non-Hodgkin's lymphoma, N/SCLC: non-/small cell lung cancer, OC: ovarian cancer, RCC: renal cell carcinoma, SM: small molecule; 1. By MapKure, a JV with SpringWorks

# In-Licensed Programs

- **Sotorasib\* (AMG 510)**
- Sitravatinib
- Zanidatamab (ZW25) (HER-2 Bispecific Antibody)

\* AMG 510 (proposed INN Sotorasib)



# Executive Summary – Sotorasib\* (AMG 510) Program

## Small molecule covalent KRAS<sup>G12C</sup> inhibitor

- Historically difficult drug target; Amgen's key discovery was a surface groove on KRAS<sup>G12C</sup> exploited to optimize potency and advance into clinic
- Estimated incidence of KRAS<sup>G12C</sup> lung cancer in Chinese patients roughly equivalent to U.S.
- Encouraging clinical activity in Phase 1; Phase 2 fully enrolled in both NSCLC and CRC

**BeiGene entered collaboration with Amgen in October 2019 and is responsible for China clinical development of sotorasib (both China-specific development and China operations within Amgen global trials)**

## Clinical Program Status

- China participation in clinical trials expected to start 4Q 2020
- Global, potentially registrational Phase 2 trial in KRAS<sup>G12C</sup> NSCLC (CodeBreak 100) is ongoing<sup>1</sup>
- Global Phase 3 trial in KRAS<sup>G12C</sup> NSCLC (sotorasib vs docetaxel) initiated in June 2020<sup>2</sup>

\* AMG 510 (proposed INN Sotorasib) Source: 1. NCT03600883 2. NCT04303780

# Sotorasib (AMG 510) in NSCLC

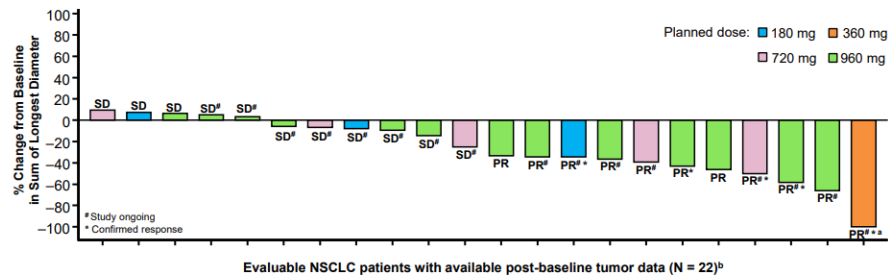
## Phase 1 data from ESMO 2019

Phase 1 Study of AMG 510, a Novel KRAS<sup>G12C</sup> Inhibitor, in Advanced Solid Tumors With KRAS p. G12C Mutation: ESMO 2019

Phase 1 Study of AMG 510, a Novel KRAS<sup>G12C</sup> Inhibitor, in Advanced Solid Tumors With KRAS p. G12C Mutation: ESMO 2019

### EFFICACY IN NSCLC

Change in Tumor Burden From Baseline



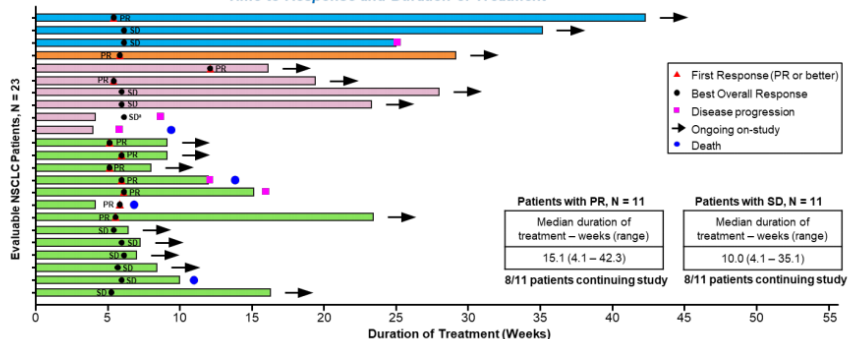
<sup>a</sup>Patient had complete response to the target lesion; <sup>1</sup>patient discontinued study due to PD prior to the 1<sup>st</sup> assessment without available post-baseline tumor burden data, and therefore is not shown on the graph.  
<sup>b</sup>Evaluable patients: patients who have been followed up for at least 6 weeks; NSCLC = non-small-cell lung cancer; PD = progressive disease; PR = partial response; SD = stable disease  
 Provided September 28, 2019, as part of an oral presentation and is qualified by such, contains forward-looking statements, actual results may vary materially; Amgen disclaims any duty to update.

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### TIME TO RESPONSE AND TREATMENT OVER TIME

Time to Response and Duration of Treatment



<sup>a</sup>The graph was plotted based on the data received from the participating sites as of the data cutoff; duration of treatment data for this patient might be missing from the study site.  
<sup>b</sup>Evaluable patients: patients who had the first 6-week scan or early progressive disease; NSCLC = non-small cell lung cancer; PR = partial response; SD = stable disease  
 Provided September 28, 2019, as part of an oral presentation and is qualified by such, contains forward-looking statements, actual results may vary materially; Amgen disclaims any duty to update.

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At 960mg RP2D N=13, PR 7 (54%), SD 6 (46), ORR 54%; Data cutoff: July 17, 2019



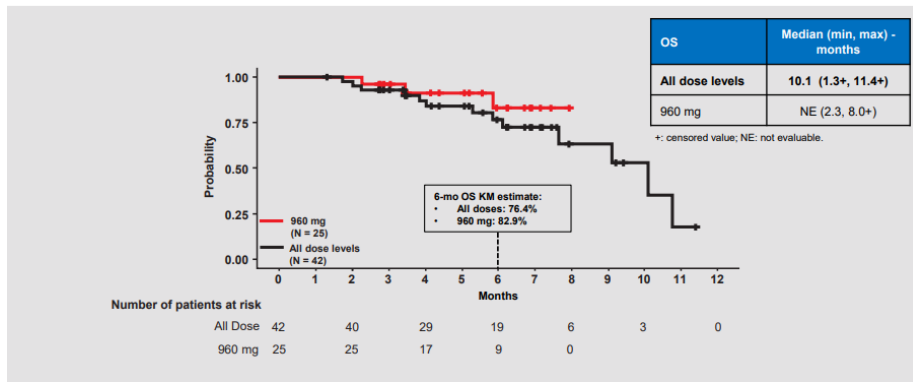
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# Sotorasib (AMG 510) in CRC

Data from ASCO 2020

## CRC: OVERALL SURVIVAL

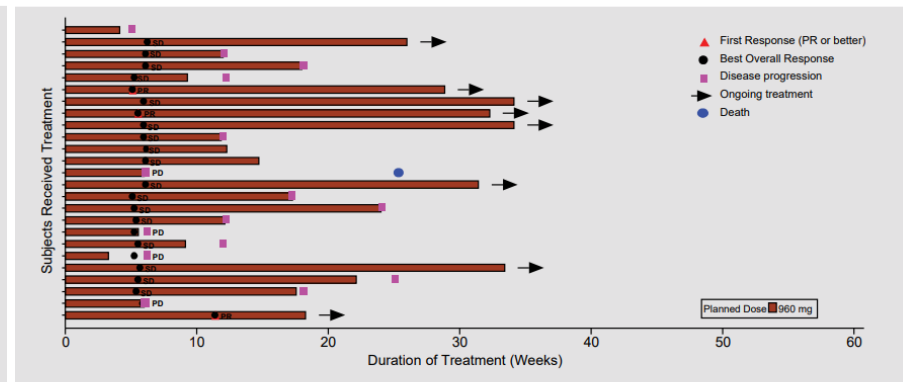


Provided May 29, 2020, as part of an oral presentation and is qualified by such, contains forward-looking statements, actual results may vary materially. Amgen disclaims any duty to update.

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## CRC: TIME TO RESPONSE AND TREATMENT OVER TIME



Provided May 29, 2020, as part of an oral presentation and is qualified by such, contains forward-looking statements, actual results may vary materially. Amgen disclaims any duty to update.

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At 960mg RP2D N=12, PR 1 (8%), SD 10 (83), ORR 8%; Data cutoff: July 17, 2019



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# In-Licensed Programs

- Sotorasib\* (AMG 510)
- **Sitravatinib**
- Zanidatamab (ZW25) (HER-2 Bispecific Antibody)

# Executive Summary - Sitravatinib Program\*

## Sitravatinib: small molecule multi-kinase inhibitor

- In addition to being a potent inhibitor of VEGFR, sitravatinib is also a potent inhibitor of: Axl, Tyro3, and MerTK
- These kinases are involved in tumor-associated macrophage activities (polarization and efferocytosis) that appear to be critical in establishment of an immuno-tolerant state
- Proof-of-concept when combined with PD-1 in PD-1 R/R NSCLC<sup>1</sup> and UC<sup>2</sup>

## BeiGene is responsible for China development activities, including China-specific trials and China participation in global trials

### Clinical Program Status

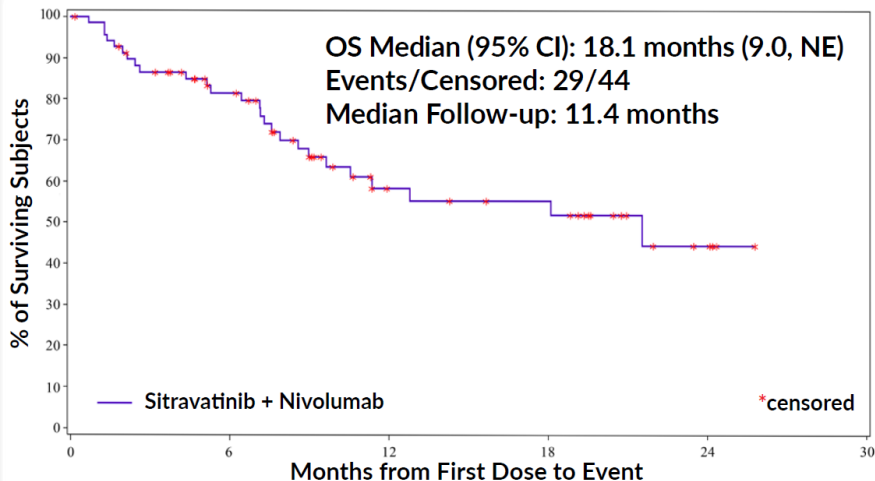
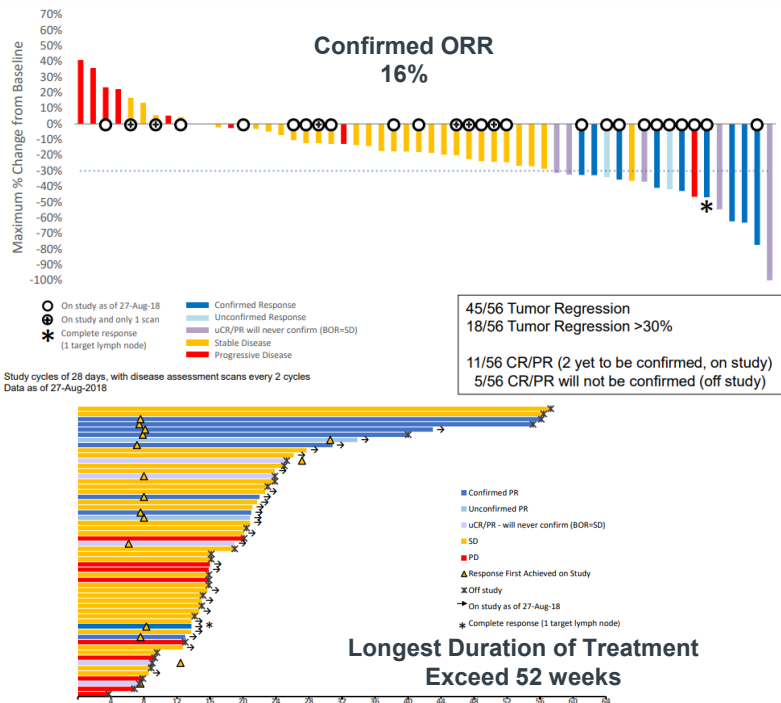
- BeiGene initiated multi-indication Phase 1b sitravatinib + tislelizumab studies in Nov 2018 in both PD-1 sensitive and insensitive tumor types (e.g. platinum resistant ovarian cancer)<sup>3</sup>
- Phase 3 registration trial in NSCLC patients with sitravatinib in combination with a PD-1 on-going

Source: 1. Leal et. al., ESMO 2018; 2. Msaouel et. al., SITC 2019; 3. Gao et. al., ESMO IO 2019; R/R: relapsed/refractory, NSCLC: non-small cell lung cancer, UC: urothelial carcinoma. \* The collaboration with BeiGene is an exclusive license agreement for the clinical development, manufacturing and commercialization of Mirati's sitravatinib in Asia (excluding Japan), Australia, and New Zealand. Mirati retains exclusive rights for the development, manufacturing and commercialization of sitravatinib for the rest of world.



# Sitravatinib/Nivolumab Combination Has Significant Clinical Activity in Patients with PD(L)-1 Refractory Tumors

## Non-squamous NSCLC



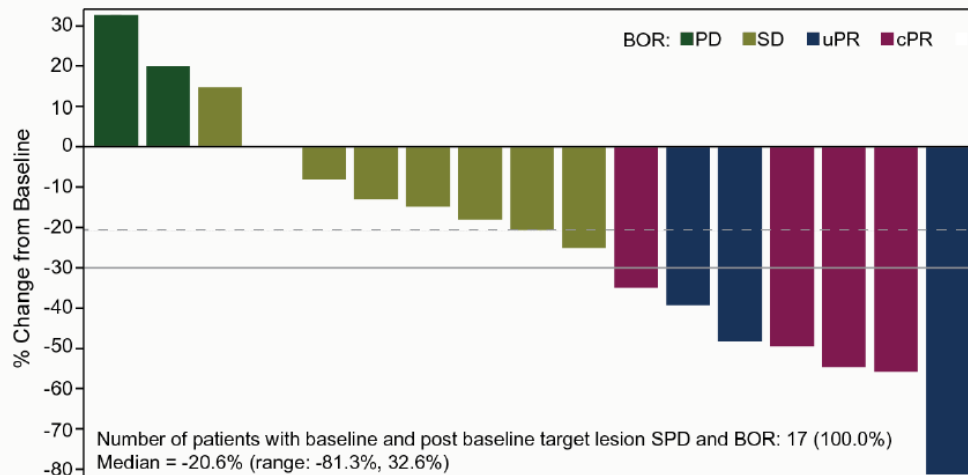
MRTX-500: Overall Survival, PCB Cohort: 1 or 2 Prior Lines of Treatment, N=73, Data as of January 30, 2020

PCB - Prior Clinical benefit (i.e., RECIST defined partial, complete response or stable disease for at least 12 weeks [-2-week window permitted for radiograph scheduling]) followed by radiographic progression of disease.

# Sitravatinib/Tislelizumab Combination Preliminary Antitumor Activity in Platinum Resistant Ovarian Cancer

## Best Response in Target Lesions

	Total (N=17)
Best Response	
Confirmed PR, n	4
Unconfirmed PR, n	3
SD, n	8
PD, n	2
Confirmed ORR, % (95% CI)	23.5 (6.8–49.9)
Median DOR, weeks (95% CI)	NR (12.29, NR)
DCR, % (95% CI)	88.2 (63.6–98.5)
Median PFS, weeks (95% CI)	18 (12.29, NR)
3-month PFS rate, % (95% CI)	88.2 (60.6–96.9)
6-month PFS rate, % (95% CI)	35.3 (9.0–63.8)



- Of 17 efficacy-evaluable patients, 7 had PR (4 confirmed PR), 8 had SD, and 2 had PD

BOR=best overall response, CI=confidence interval, cPR=confirmed partial response, DCR= disease control rate, DOR=duration of response, NR=not reached, ORR=objective response rate, PD=progressive disease, PFS=progressionfree survival, PR=partial response, PROC= platinum-resistant ovarian cancer, SD=stable disease, SPD=sum of the products of perpendicular dimensions, uPR=unconfirmed partial response

# In-Licensed Programs

- Sotorasib\* (AMG 510)
- Sitravatinib
- **Zanidatamab (ZW25) (HER-2 Bispecific Antibody)**

# Executive Summary – Zanidatamab (ZW25) Program

## Zanidatamab: bispecific antibody targeting two distinct HER2 epitopes<sup>1</sup>

- Zanidatamab biparatopic – targets extracellular domain 2: ECD2 (trastuzumab binding domain) and ECD4 (pertuzumab binding domain)
- Unique binding geometries of zanidatamab promoted increased tumor cell binding and enhanced HER2 internalization compared with trastuzumab
- Stronger anti-tumor activity compared to trastuzumab is observed in preclinical studies
- Zanidatamab, as single agent, has shown encouraging anti-tumor activity across multiple HER2-expressing tumor types (Part 1 and 2, ZWI-ZW25-101 Ph1 Study)<sup>2</sup>

**BeiGene is responsible for China development activities, including China-specific trials and China participation in global trials**

## Clinical Program Status

- Registration-enabling trial initiated in 2L HER2+ biliary tract cancer
- Ph2 combination studies are ongoing to support pivotal trials
- One registration-enabling studies are planned:
  - 1<sup>st</sup> line HER2+ gastroesophageal cancer



Zanidatamab

# Collaborations Are a Central Part of Our Comprehensive Pipeline

**Broad set of ongoing clinical collaborations that significantly augment our internal discovery, ongoing clinical development programs, and commercial products (tislelizumab and zanubrutinib)**

**Many programs planned to go to pivotal/late-stage in next 6-18 months**



BeiGene

# Concluding Remarks

John V. Oyler

*Chairman, Co-Founder & CEO*

# Summary: Research and Early Development

## Internal R&D platform generating robust, sustainable pipeline

- **Proven:** Two approved medicines (and another at the filing stage) with excellent clinical profiles
- **Cutting Edge:** Utilizing cutting edge technologies to address a wide range of biological problems
- **Impactful:** All programs potentially best-in-class or first-in-class assets such as HPK1
- **Broad and Growing:** 350+ team growing to 650+

## Built unique, sustainable competitive advantages

- **Clinical acceleration & lower cost:** 1,350+ team for China-inclusive global trials
- **Combinability with internal platform assets:** PD-1, BTK, PARP and growing
- **Science & medicine-based commercial team:** ~1,300; 6 commercial products; excellent pipeline
- **Internal manufacturing & preclinical capabilities:** Includes biologics, formulation, preclinical

## Past collaborations successful, leverage our competitive advantages, & expand our portfolio ... *and capacity exists for this to continue to be a major source of growth*

- Deep, promising collaboration pipeline
- Each competitive advantage has been demonstrated in collaborations
- Amgen collaboration provides further validation

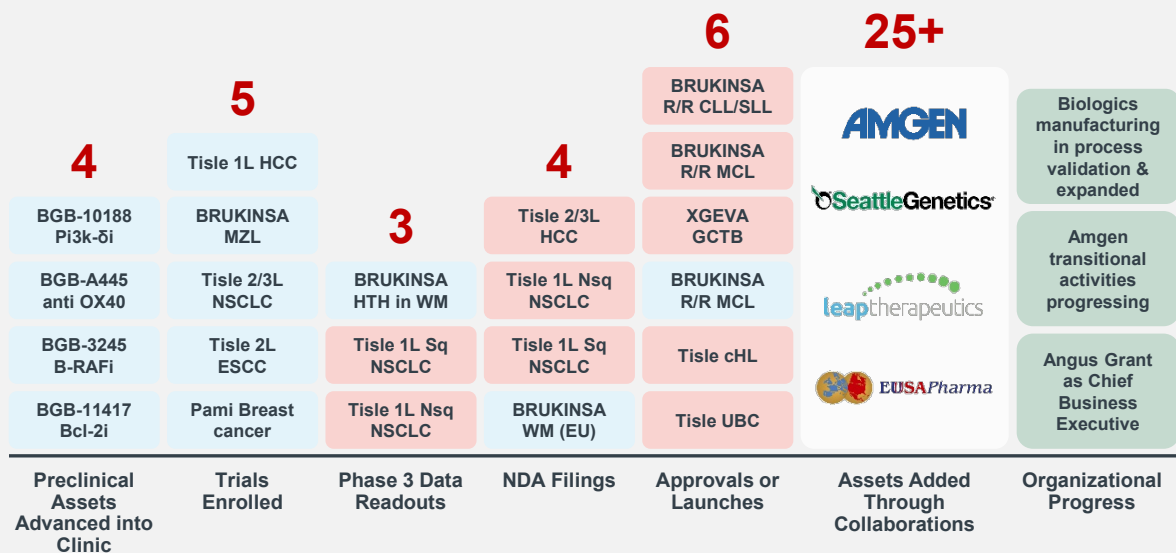
## Well positioned to act quickly & capture future internal & external breakthroughs



# Recent Accomplishments and Upcoming Milestones

China  
Global

## Past 10 Months (From 4Q19 – YTD)



## Disclosed Milestones Over Next 18 Months



\* Phase 3 or registrational enabling trials



## Future Vision

**Once in a lifetime period of transformation in our industry, which creates opportunities for smaller players to become leaders**

**BeiGene is one of the best positioned companies for this opportunity**

**On this journey, BeiGene is striving to**

- Become an oncology and scientific leader
- Expand beyond oncology into other areas of need
- Continue to build sustainable competitive advantages
- Become the best global clinical organization – addressing the biggest issue of the industry
- Transform the industry to bring better medicine to more patients more affordably

**Thank You!**



BeiGene

## Q&A

### Participants:

- Xiaodong Wang, Ph.D.
- John V. Oyler
- Howard Liang, Ph.D.
- Lai Wang, Ph.D.
- Eric Hedrick, M.D.
- Yong (Ben) Ben, M.D.
- Jane Huang, M.D.



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Thank You