

# ANTENGENE INVESTOR PRESENTATION

TREATING PATIENTS BEYOND BORDERS

MARCH 2023

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# Antengene is Executing on Our Strategy to Bring Transformative Medicines to Patients Around the World



# **ANTENGENE**





# **Global Team of Industry Veterans**



# Global Management Team with Deep Local Experience and Insights Working Seamlessly Across Regions

#### **Amily Zhang Chief Medical Officer**









John F. Chin, MBA Chief Business Officer







**Eitan Liu** 

**Chief Operating Officer** 

Jasmine Sun, M.D., MPH

Tigermed MERCK



























Bo Shan, Ph.D. Chief Scientific Officer









Donald Lung, JD, MBA









Yijun Yang, Ph.D., Sc.D

Corporate Vice President, Head of Clinical Enabling Functions & Operational Excellence









Founder / Chairman / Chief Executive Officer











**Thomas Karalis** 

Corporate Vice President, Head of Asia Pacific Markets













Corporate Vice President, Biometrics & Regulatory **Enabling Functions** 















Corporate Vice President, Head of Hematology Business Unit, China





















Track Record of Antengene Management Team













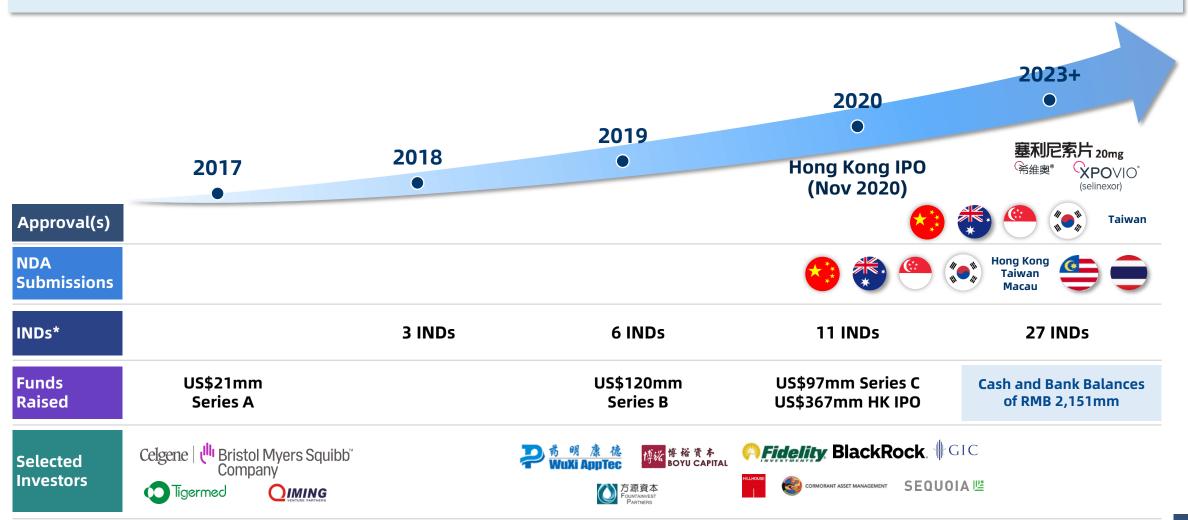




# Dual Engine of Growth Through Value-adding Partnerships and In-house Discovery



# Rich Pipeline with Commercialization Across Multiple Markets, Driven by Strong Execution Capabilities



# Antengene Has Executed and Delivered on Significant Milestones Since IPO

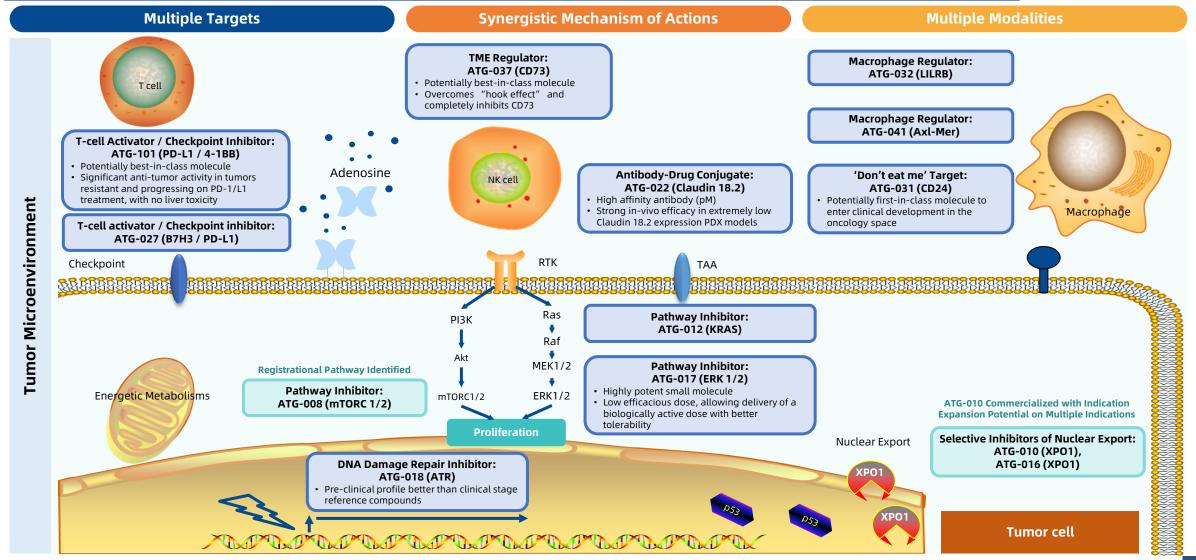


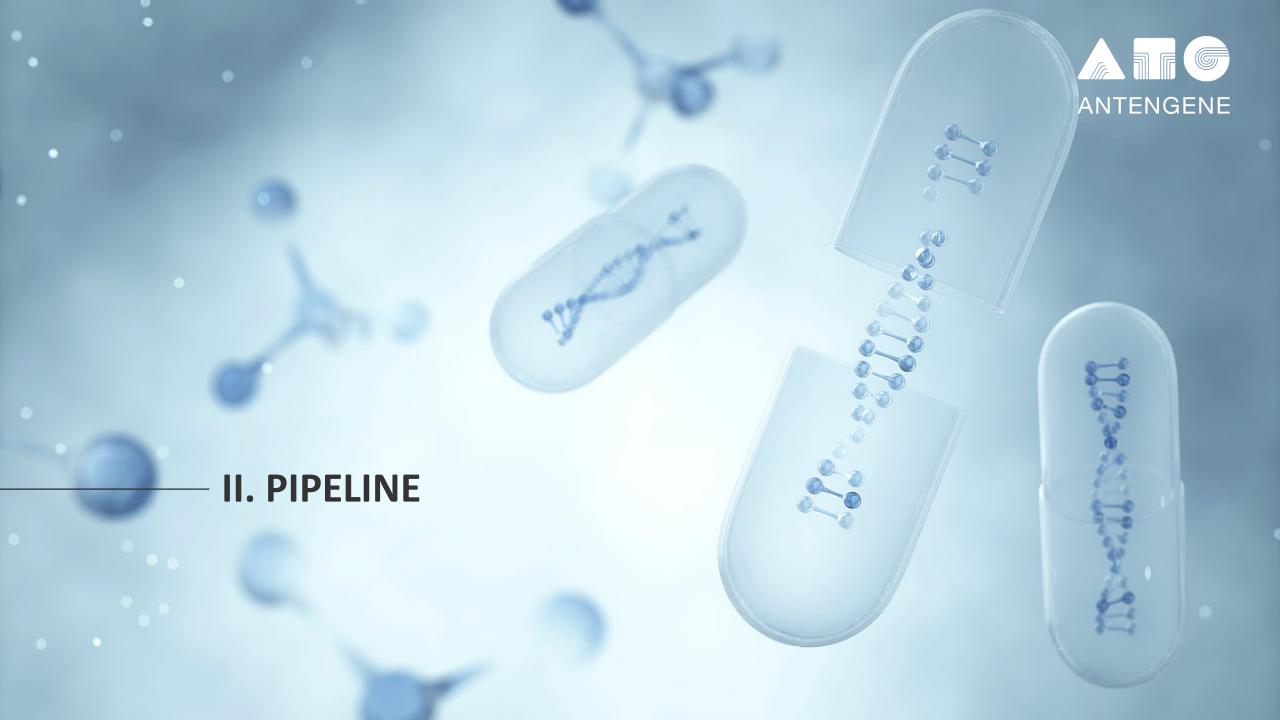
		November 20 <sup>th</sup> , 2020	November 20 <sup>th</sup> , 2022		
Commercialization	Product Approvals	0	塞利尼索片 (Selinexor) (Selinexor) (Taiwan) (Selinexor) (Taiwan) (Tai		
Registrational Trials	ATG-010 (Selinexor)	2 ongoing	4 ongoing; 1 completed		
Registrational Path	ATG-008 (Onatasertib)	No	Yes (Relapsed/Metastatic Cervical Cancer)		
Global Best-in-class Potential Assets in Clinical Stage		ATG-017 - ERK1/2 small molecule inhibitor	ATG-017 - ERK1/2 small molecule inhibitor ATG-101 - PD-L1/4-1BB bispecific antibody ATG-037 - CD73 small molecule inhibitor ATG-018 - ATR small molecule inhibitor ATG-022 - Claudin 18.2 ADC (IND submitted)		
Global First-in-class Potential Asset		0	ATG-031 - CD24 monoclonal antibody		
Cash Reserve		RMB 918 mm (immediately prior to IPO)	RMB 2,151 mm*		
Market Cap		USD 1,549 mm	USD 356 mm		

# The Antengene Pipeline Includes Multiple Novel Immuno-oncology and Targeted Products - Allowing Broad Proprietary Combinations



## **ANTENGENE**





# Pipeline of Commercial or Near NDA Stage Drugs with First-in-Class/Best-in-Class Potentials



**ANTENGENE** 

Assets	Target (Modality)	Indication	Pre-clinical	Phase I	Phase II	Phase III	NDA	Commercialization	Antengene Rights	Partner
			Combo with dexamethasone (MARCH)  Mainland China NDA approved							
			Combo with dexamethasone <i>(</i> .	STORM) - Partner's Piv	rotal Trial in the US		US, EU, SK, St	G, AU & TW NDA approved		
		R/R Multiple Myeloma	Combo with bortezomib and d	examethasone <i>(BENCI</i>	H)	*				
			Combo with bortezomib and dexamethasone (BOSTON) - Partner's Pivotal Trial in the US		US, EU, SG, AU & TW sNDA approved					
			Combo with IMID/PI/CD38 mAl	and dexamethasone	(STOMP)					<b>i</b> Karvonharm¹
ATG-010 <sup>1</sup> (Selinexor)	XPO1 (Small molecule)		Monotherapy (SEARCH)		*					Karyopharm*
		R/R Diffuse Large B-cell Lymphoma	Monotherapy <i>(SADAL) - Partne</i>	er's Pivotal Trial in the	US		US , SG	, SK & TW sNDA approved	APAC <sup>2</sup>	ANTENGENE
			Combo with R-GDP (DLBCL-036	<i>7)</i>	*					
		R/R NHL	Combo with lenalidomide + rit	uximab <i>(SWATCH)</i>						
		R/R T-cell & NK-cell Lymphoma	Combo with ICE/GemOx/tisleli	zumab <i>(TOUCH)</i>	with 💆 BeiG	ene				
		Myelofibrosis	Monotherapy <i>(MF 035)</i>		*					
ATG-016 (Eltanexor)	XPO1 (Small molecule)	R/R MDS	Monotherapy (HATCH)							
ATG-008	mTORC1/2	TORC1/2  Small molecule)	Combo with toripalimab (TORG	:H-2)*	v	vith 君实生物 TopAlliance			APAC <sup>3</sup>	Celgene ( <sup>Ill</sup> ) Bristol Myers Squibb <sup>°</sup> Company
(Onatasertib)	(Small molecule)		Combo with ATG-010 <i>(MATCH)</i>							ANTENGENE

Partner Trials<sup>5</sup>

Antengene Trials<sup>4</sup>

Registrational Trial in China

Global Trials in Collaboration with Partner

<sup>1 (</sup>s)NDA approved by US FDA, China NMPA, Australia TGA, South Korea MFDS and Singapore HSA; China Hong Kong and China Taiwan NDA submissions are completed;

<sup>&</sup>lt;sup>2</sup> Antengene has rights for Greater China (Mainland China, Hong Kong, Taiwan, Macau), Australia, New Zealand, South Korea, and the ASEAN Countries;

<sup>3</sup> Antengene has rights for Greater China, South Korea, Singapore, Malaysia, Indonesia, Vietnam, Laos, Cambodia, the Philippines, Thailand and Mongolia;

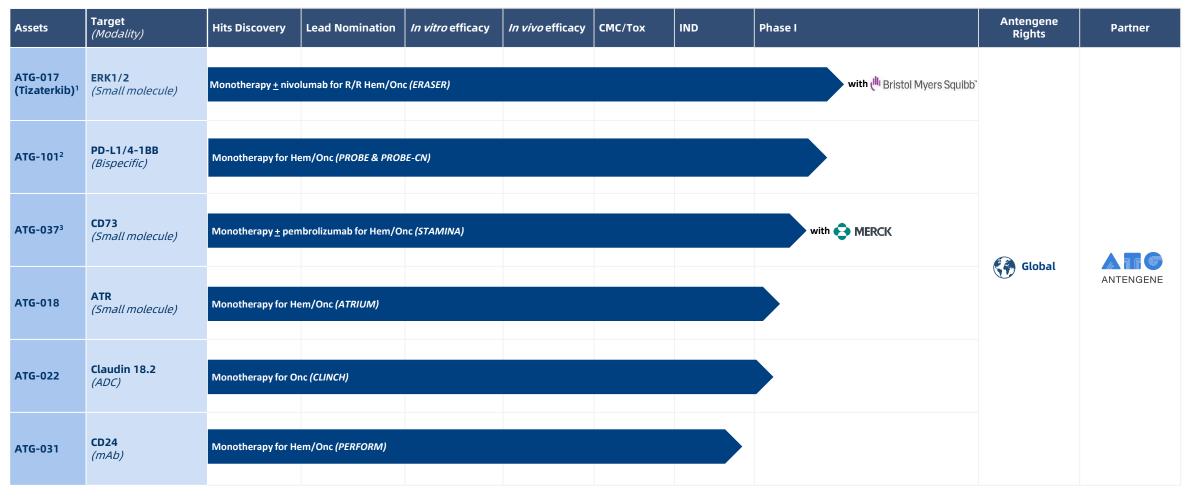
<sup>&</sup>lt;sup>4</sup> Most advanced trial status in Antengene territories and the trials are responsible by Antengene;

<sup>&</sup>lt;sup>5</sup> Most advanced trial status in partner territories in the rest of the world and the trials are conducted by our licensing partners

<sup>\*</sup> Investigator-initiated trials; R/R: relapsed/refractory; ND: newly diagnosed; MD5: myelodysplastic syndrome; CRC: colorectal cancer; PrC: prostate cancer; CAEBV: chronic active Epstein-Barr virus; NHL: non-Hodgkin lymphoma; Hem/Onc: hematological malignancies and solid tumors; R-GDP: Rituximab, Gemcitabine, Dexamethasone & Cisplain; Cisplain;

# A Clinical Stage Pipeline with Transformational Potentials





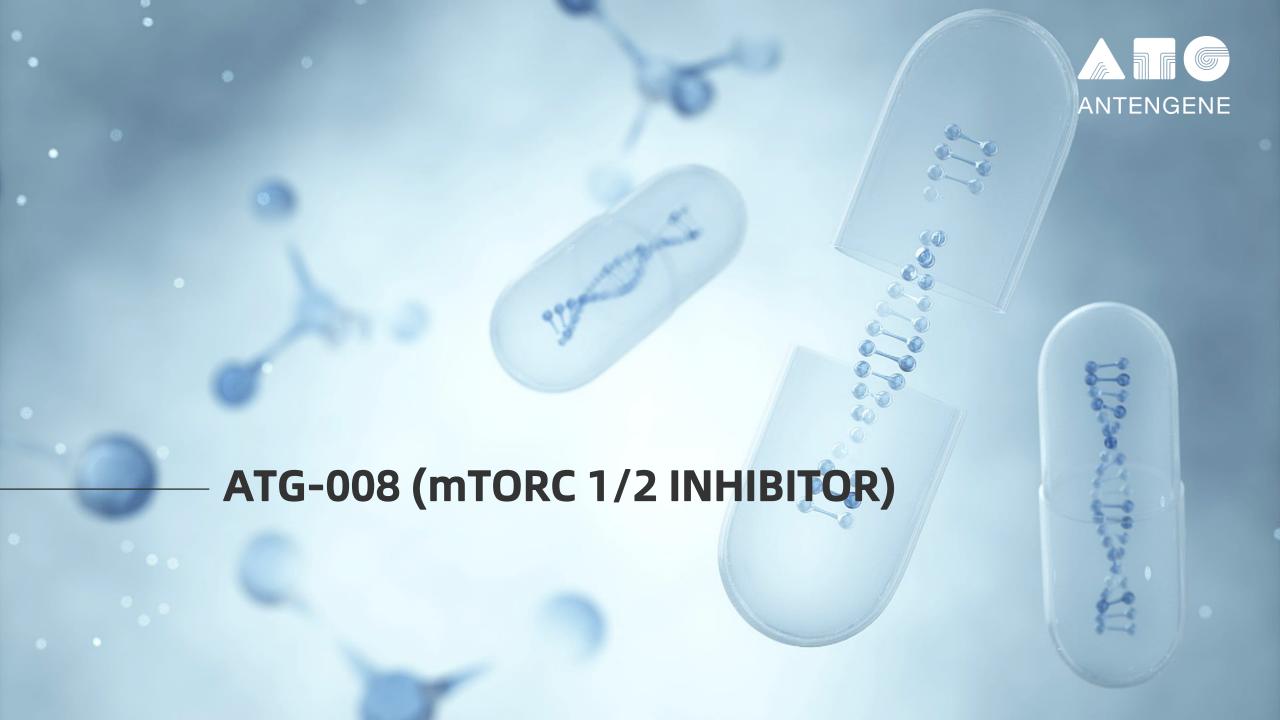
Antengene Trials

Hem/Onc = hematological malignancies and solid tumors

<sup>&</sup>lt;sup>1</sup> Licensed from AstraZeneca and Antengene has obtained exclusive global rights to develop, commercialize and manufacture ATG-017;

<sup>&</sup>lt;sup>2</sup> Licensed from Origincell and Antengene has obtained exclusive global rights to develop, commercialize and manufacture ATG-101;

<sup>&</sup>lt;sup>3</sup> Licensed from Calithera Biosciences and Antengene has obtained exclusive global rights to develop, commercialize and manufacture ATG-037



# ATG-008 (Onatasertib): A Novel Second Generation mTORC1/2 Inhibitor

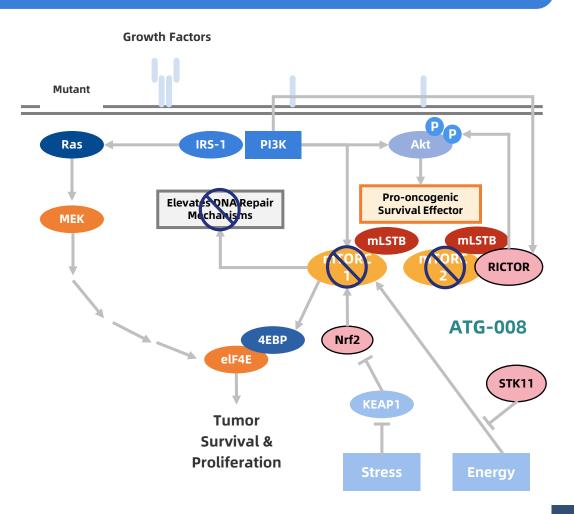


# **Summary of ATG-008 (Onatasertib)**

- Mammalian target of rapamycin (mTOR), a core component of two structurally distinct protein complexes (mTORC1 and mTORC2), regulates different cellular processes and is upregulated in multiple types of tumors
- When mTORC1 is inhibited, mTORC2 is upregulated. This increase in mTORC2 activity generates a surplus of phosphorylated PKB/AKT which, despite mTORC1 inhibition, inhibits apoptosis and promotes cell proliferation via alternative pathways
- mTORC1 and mTORC2 has to be inhibited simultaneously for good anti-tumor efficacy

### First- and Best-in-Class Potential

- Second generation mTOR inhibitor, targeting both TORC1 and TORC2
- Demonstrated comprehensive mTOR inhibition, which could minimize development of resistance due to mTORC2 upregulation
- Encouraging initial clinical data in combination with anti-PD-1 mAb in the treatment of relapsed or metastatic cervical cancer



# ATG-008 (Onatasertib) In Combination with Toripalimab

Potential Best-in-Class Treatment for 2L+ Cervical Cancer as Demonstrated in "TORCH-2"



	ATG 008 + Toripalimab (Data from "TORCH-2")	Pembrolizumab (Global Standard of Care)	AK104 (Only CPI Approved by CDE)	Sintilimab + Anlotinib
Mechanism of Action (MoA)	mTORC 1/2i + PD-1 mAb	PD-1 mAb	PD-1/CTLA-4 BsAb	PD-1 mAb + VEGFRi
Number of Patients	21 (ITT)	98 <mark>(ITT)</mark>	100 (FAS, ITT 111)	39 (EE, ITT 42)
Prior Treatment Lines	≤2 (52.4%); ≥ <b>3 (47.6%)</b>	≤2 (69.4%); ≥3 (30.6%)	≤2 (100%)	≤2 (78.6%); ≥3 (21.4%)
PD-L1	N, TPS≥1% (42.8%)	N, CPS≥1 (83.7%)	N	Y, CPS≥1 (100%)
ORR	52.4%; <b>77.8% (TPS≥1%)</b>	12.2%	33%	59%
DCR	94.4%	30.6%	52%	94.9%
PFS (months)	5.45; 9.63 (15 mg cohort)	2.1	3.75	9.4
OS (months)	NE	9.4	17.5	NE
Response in CPI treated	1/2	N/A	N/A	N/A
Response in AdCa	1/2	1/5	NE	0/6

# **Key Takeaways of ATG-008 (Onatasertib) Clinical Programs**





Encouraging initial data observed in TORCH-2 study of ATG-008 in combination with Toripalimab in treatment of relapsed or metastatic cervical cancer subgroup-Including favorable tolerability with an ORR of 52.4% (11/21), regardless of PD-L1 status



ATG-008 demonstrated single agent activity in 2L+ HBV positive hepatocellular carcinoma



The safety, efficacy and PK profiles of ATG-008 monotherapy are in line with prior results, which warrants further combination development



Pre-IND consultation with CDE planned for a pivotal study that will define the regulatory path for ATG-008, with advanced cervical cancer as the lead indication



The **TORCH-2 trial is still enrolling patients** to further evaluate the role of ATG-008 & anti-PD-1 combination in patients who have failed prior CPI treatments



# Global-Rights Pipeline Comprised of Clinical Stage and IND-Ready Assets with First and/or Best-in-Class Potential



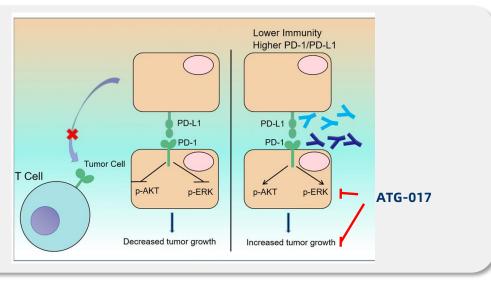
	ATG-017 (Tizaterkib)	ATG-101	ATG-037	ATG-018	ATG-022	ATG-031
Target	ERK1/2	PD-L1/4-1BB	CD73	ATR	Claudin 18.2	CD24
Modality	Small Molecule	Bispecific Antibody	Small Molecule	Small Molecule	ADC	Monoclonal Antibody
Indication	<ul> <li>RASm NSCLC, Pancreatic cancer, CRC, and Melanoma</li> <li>I/O combinations</li> </ul>	<ul> <li>Re-sensitize prior CPI responders (NSCLC, SCLC, GI, H/N SCC, melanoma)</li> <li>Disease with previously limited CPI activity</li> <li>Multiple combination opportunities</li> </ul>	<ul> <li>Monotherapy where immune suppressed TME is critical</li> <li>Broad opportunities both as monotherapy and combination with existing / future I/O</li> </ul>	Hematological Malignancies / Solid Tumors	Solid Tumors	Hematological Malignancies / Solid Tumors
Differentiation	<ul> <li>Higher potency and dual IoC and PoA activity with slow off-rate kinetics</li> <li>Lower efficacious dose with a higher max absorbable dose/dose ratio</li> <li>Broad therapeutic potential (targeting RAS/MAPK pathway)</li> <li>Multiple combination opportunities</li> </ul>	<ul> <li>✓ PD-L1 cross-linking dependent activation of 4-1BB to avoid unwanted 4-1BB signaling in normal tissue and minimize risk of hepatotoxicity</li> <li>✓ Demonstrated significant antitumor activity in animal models of resistant tumors as well as those that progressed on anti-PD-1/L1 treatment</li> <li>✓ Displayed an excellent safety profile in GLP toxicology studies</li> </ul>	<ul> <li>✓ Orally bioavailable small molecule that completely overcomes 'hook effect' common in other anti-CD73 antibodies</li> <li>✓ Tissue penetrance not achievable with mAbs</li> <li>✓ Promising preclinical efficacy as a monotherapy and strong combination potential</li> </ul>	<ul> <li>✓ Better <i>in vivo</i> efficacy compared with benchmark in preclinical CDX tumor models</li> <li>✓ Orally available</li> </ul>	<ul> <li>✓ High affinity antibody (pM); Strong in vivo efficacy pre-clinically in Claudin 18.2 low expression PDX models</li> <li>✓ Demonstrated an excellent safety profile in GLP toxicology studies</li> </ul>	<ul> <li>✓ First in class target</li> <li>✓ No clinical competitor</li> <li>✓ Showed monotherapy in vivo efficacy and synergy with chemotherapy, rituximab and CPI</li> </ul>
Status	Enrollment ongoing in Australia for continuous dosing and intermittent dosing cohorts; Combo with nivolumab to initiate enrollment in 2023	Phase 1 clinical trial "PROBE" ongoing in Australia (4 <sup>th</sup> cohort), first patient to be dosed in the US; "PROBE-CN" ongoing in China (3 <sup>rd</sup> cohort)	Phase 1 clinical trial "STAMINA" ongoing in Australia, currently enrolling for the 2 <sup>nd</sup> cohort	Phase 1 clinical trial "ATRIUM" ongoing in Australia, currently enrolling for the 3 <sup>rd</sup> cohort	Australian HREC approved in December 2022	IND planned for early Q1 2023

# ATG-017 (Tizaterkib) May Enhance the Activity of Checkpoint Inhibitors or **Reverse Resistance Mechanisms**



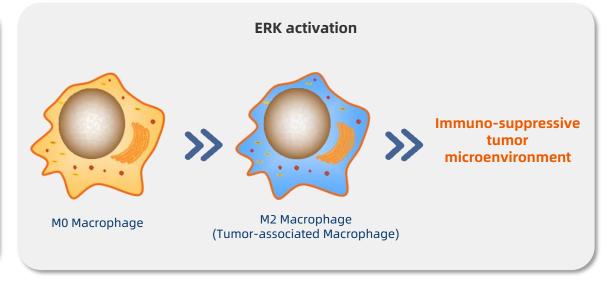
Through inhibiting ERK1/2 activity, ATG-017 may enhance the activity of checkpoint inhibitors or reverse resistance mechanisms

ERK activation contributes to hyper-progressive disease induced by anti-PD-1 therapy



- PD-1/PD-L1 expression on tumor cells inhibit tumor cell growth through deregulation of canonical signaling pathways, including the AKT and ERK1/2 pathways, and prevent the interaction with PD-1-expressing T cells
- Clinically available antibodies targeting PD-1 (blue) or PD-L1 (cyan) enhance tumor cell growth via activation of AKT and ERK1/2 in the absence of adaptive immunity, which may be associated with hyper-progressive and pseudo-progressive disease in the clinic.

ERK activation contributes to M2 macrophage polarization and immuno-suppressive tumor microenvironment



- Multiple lines of research suggests that **ERK1/2 activation** contributes to:
  - Tumor-associated macrophage infiltration and M2 macrophage polarization, causing an immunosuppressive microenvironment and reduced efficacy of anti-PD-1 therapy

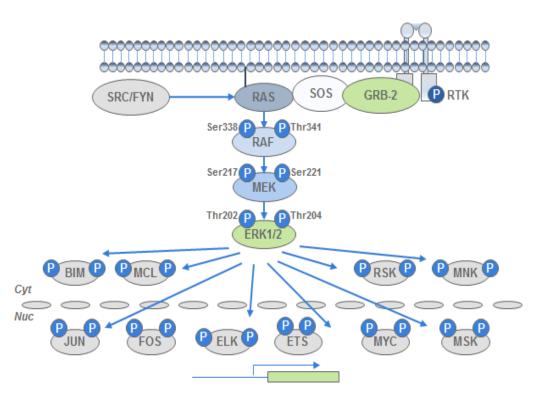
Enrollment Ongoing in Australia for Continuous Dosing and Intermittent Dosing Cohorts; Combo with Nivolumab to Initiate Enrollment in 2023

# ATG-017 (Tizaterkib): Potentially Best-in-Class ERK1/2 Inhibitor



## **Summary of ATG-017 (Tizaterkib)**

 ERK1/2: RAS/MAPK signaling pathway drives cell survival and proliferation; dysfunction in the signaling pathway is a major trigger for the development of most cancer types



#### **Best-in-Class Potential**

■ Potent and selective small molecule extracellular signal-regulated kinases 1 and 2 (ERK1/2) inhibitor with best-in-class potential

## **Leading in Clinical Development**

- First-in-human Phase I trial investigating safety and preliminary efficacy among patients with solid tumors and hematological malignancies
- Currently in the 6<sup>th</sup> cohort of monotherapy continuous dosing in solid tumors of the Phase I "ERASER" trial
- Preliminary efficacy observed in current monotherapy dose escalation study
- Combo cohort with Nivolumab planned for early 2023

## **Broad Therapeutic Potential in Cancer**

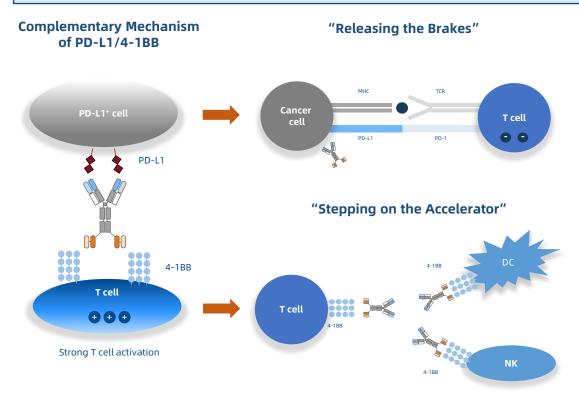
- Great clinical potential as a monotherapy or combination in multiple solid tumors and hematological malignancies that harbor activating alterations in the RAS-MAPK pathway
  - E.g. RASm NSCLC, Pancreatic, CRC, and Melanoma

# ATG-101 Has the Potential to Optimize PD-L1 Antagonism and Tumor-specific 4-1BB Agonism



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- Efficacy of PD-1/PD-L1 targeting is well-demonstrated over the past decade
- 4-1BB is a T cell co-stimulatory receptor, the benefits of which have yet to be realized in the clinic
- The concept of PD-L1×4-1BB bispecific antibody like ATG-101 has demonstrated **promising activity in early clinical trials** with an **acceptable safety profile** (GEN1046, NCT03917381)
- Novel design of ATG-101: high affinity of PD-L1 and conditional activation of 4-1BB, results in 4-1BB agonist activity only when crosslinked by PD-L1-positive tumor cells
- Biodistribution murine model confirms PD-L1 drug localization<sup>1</sup>



Enrollment Ongoing in Australia (4th Cohort) and China (3rd Cohort)

# **Excellent Safety Profile**

- High affinity of PD-L1 and conditional activation of 4-1BB results in 4-1BB agonist activity only when crosslinked by PD-L1-positive tumor cells, reducing risk of 4-1BB related liver toxicity
  - No liver toxicity observed in GLP toxicology study in cynomolgus monkeys with dose up to 100 mg/kg

#### **Broad Therapeutic Potential in Cancer**

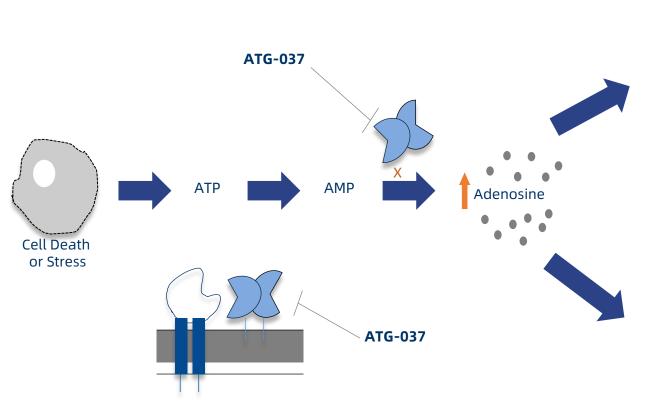
- Demonstrated potent in vivo efficacy in anti-PD-1/PD-L1 resistant and relapsed mouse tumor models
- Activates exhausted T cells in vitro, suggesting a potential in reversing T cell dysfunction and exhaustion
- Increases the infiltration, proliferation and activation of CD8+ T cells and the infiltration of Natural Killer T cells in the tumor microenvironment, thus rendering "cold" tumors "hot"

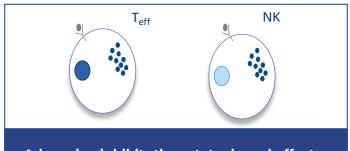
Source: 1. Prof Andrew Scott, ONJCRI, 2022

# **ATG-037 Can Reverse Adenosine-Mediated Immunosuppression**

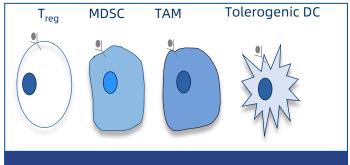


The adenosine axis plays a well-established and critical role in suppression of the immune response and ATG-037 can reverse adenosine-mediated immunosuppression





Adenosine inhibits the cytotoxic and effector function of T cell and NK cells



Adenosine induces immunosuppressive cell types and enhances their function

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# ATG-037: Orally Available Small Molecule Inhibitor of CD73 with Best-in-Class Potential



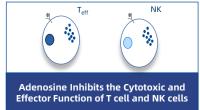
## **Summary of ATG-037**

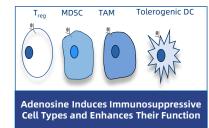
■ Functions to inhibit CD73 – the ecto-5′-nocleotidase that catalyzes the conversion of AMP to adenosine, a key immune suppressive molecule in the tumor microenvironment

#### **Best-in-Class Potential**

- Completely blocks CD73 activity and overcomes "hook effect" commonly seen in anti-CD73 antibodies
- Promising pre-clinical efficacy as monotherapy or in combination with standard of care (SoC) in both solid and liquid tumors
- Rescues T-cell functions in high AMP conditions

# ATG-037 ATP AMP Adenosine ATG-037



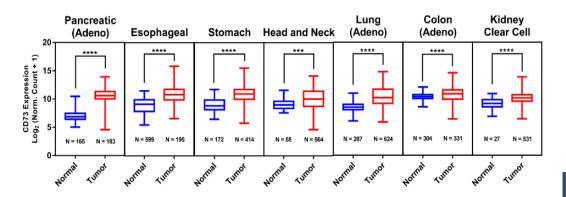


## **Excellent Safety Profile**

- No ATG-037 related toxicity identified in GLP toxicology studies
  - Potential large therapeutic window
- **No inhibition** of CD39 and other related targets (up to 10 mM)

# **Broad Therapeutic Potential in Multiple Tumor Types**

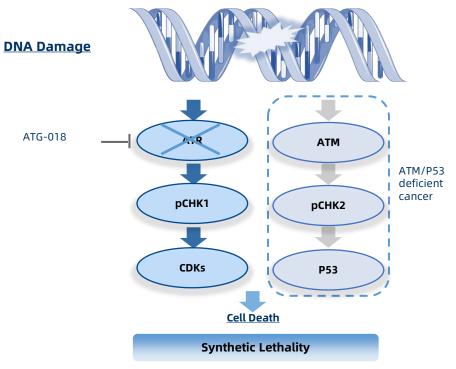
Pancreatic, esophageal, gastric, non-small cell lung, colorectal, prostate, head and neck etc.



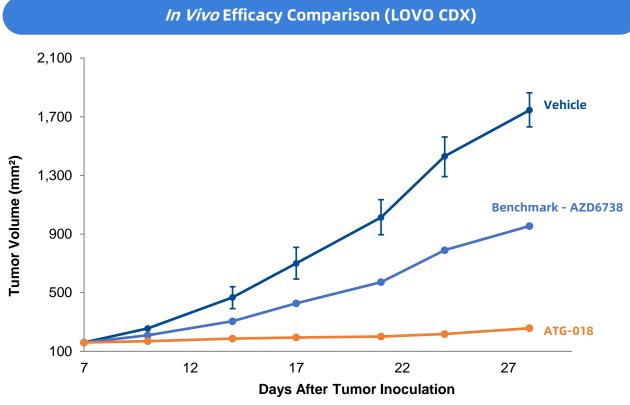
# ATG-018 is an Oral and Highly Selective Small Molecule Inhibitor of ATR that may Improve on Benchmark ATR Inhibitors



- Many patients with malignant tumors carry genetic alternations which correlate with functional loss or deregulation of key DDR proteins, most notably p53 and ATM
- These tumors **extensively rely on ATR** for DNA repair
- ATG-018 can inhibit DNA damage repair, release tumor cells from cell cycle arrest and induce synthetic lethality in ATM/p53-deficient tumor cells
- ATG-018 Demonstrated superior in vivo efficacy, compared with clinical benchmark in pre-clinical CDX models

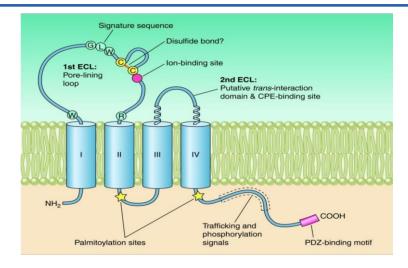


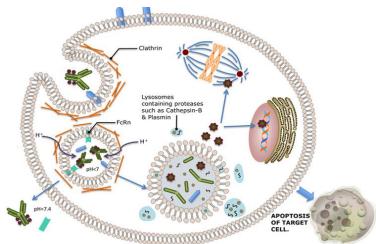
# Enrollment Ongoing in Australia (3<sup>rd</sup> Cohort)



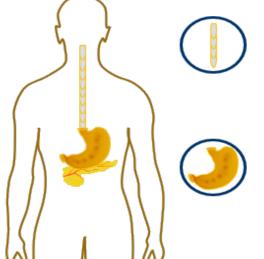
# ATG-022 is a High Affinity Anti-Claudin 18.2 ADC with Potential Activity Even in Tumors with Very Low Level Expression of the Target







## Claudin 18.2 over-expressed in multiple tumor types



## **Esophagus Cancer**

- Positive in 18.2% primary adenocarcinoma
- Positive in 17.9% regional lymph node metastasis

#### **Gastric Cancer**

- Positive in 87% primary tumors
- Positive in 80% lymph node metastasis
- Anti-Claudin 18.2 antibody, IMAB362 (zolbetuximab), demonstrated promising efficacy in human clinical trials

#### **Pancreatic Cancer**

Positive in 45%-90% ductal adenocarcinoma

# Other Tumors

 Claudin 18.2 mRNA expression was detected in multiple tumor types including NSCLC, ovarian cancer, and colorectal cancer

Australian HREC Approved in December 2022

# ATG-022: An Anti-Claudin 18.2 ADC with Potent *In Vivo* Efficacy in Claudin 18.2 Very Low-Expression Tumors



## **Summary of ATG-022**

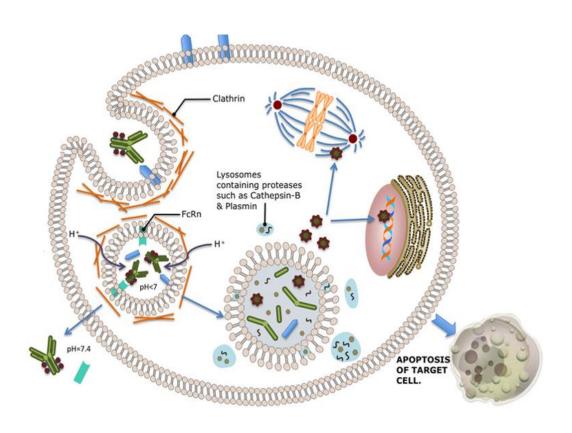
- Claudin 18.2 is a tumor-associated antigen overexpressed particularly in gastric, esophageal and pancreatic cancers, occasionally in other tumors including lung, ovarian, and head & neck malignancies
- Clinical ADC candidate with vc-MMAE as linker payload (DAR4)

#### **Best-in-Class Potential**

- High affinity antibody (pM grade) against Claudin 18.2 allows targeting of patients with low expression of Claudin 18.2
- Strong in vivo efficacy pre-clinically in PDX models with various Claudin 18.2 expression levels, including in tumors with extremely low Claudin 18.2 expression

## **Excellent Safety Profile**

- Demonstrated an excellent safety profile in GLP toxicology studies
  - Induced complete tumor regression (tumor-free) in pre-clinical PDX model without affecting the body weight of the animal
- Displayed high specificity in Retrogenix's Cell Microarray Technology Experiment
  - ATG-022 mAb specifically interacted with Claudin 18.2, the primary target, on both fixed and live cells



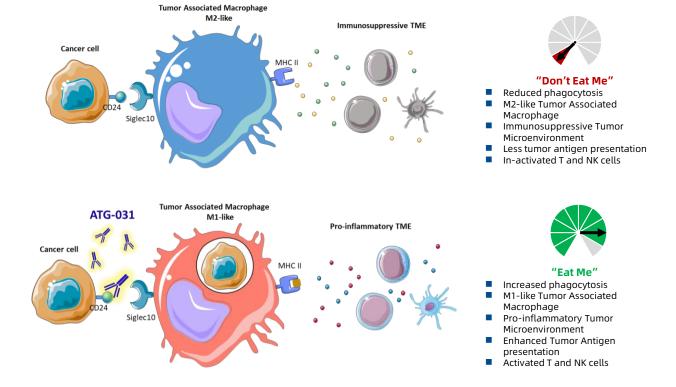
Christina Peters, Stuart Brown Antibody-drug conjugates as novel anti-cancer chemotherapeutics

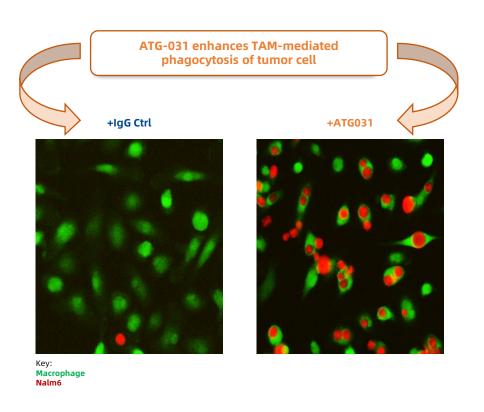
# ATG-031: First-in-Class CD24 Antibody to Inhibit the "Don't Eat Me" Signal



## **Summary of ATG-031**

- CD24 is a novel "don't eat me" target not expressed in healthy erythrocytes, thus potentially overcoming the anemia issues commonly seen in CD47
- First-in-class humanized CD24 mAb inhibits the "don't eat me" signal by blocking CD24-Siglec10 pathway and enhances macrophage-mediated phagocytosis of cancer cells
- CDx antibody successfully developed in-house for patient selection
- Potent single agent in vivo efficacy and synergy with chemotherapy or CPI

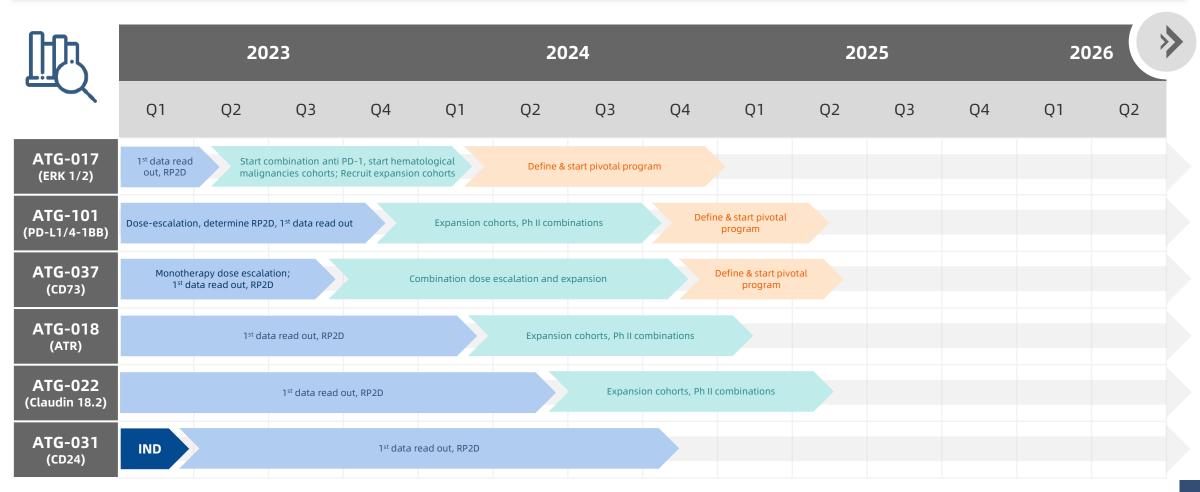




# Clinical Development Timeline Spanning 2023 to 2025 Encompassing a Series of Clinical Data Readouts



# Early data on safety, PK, PD through 2023 with ATG-017, ATG-101 and ATG-037





# 









**Approved in South Korea** July 30<sup>th</sup>, 2021

**Commercial Launch Dec 2021** 

- rrMM XPOVIO® in combination with dexamethasone (Xd)
- rrDLBCL XPOVIO® as monotherapy (X)



**Approved in Mainland China December 14th, 2021** 

**Commercial Launch May 2022** 

rrMM - XPOVIO® in combination with dexamethasone (Xd)



# **Approved in Singapore** March 1st, 2022

**Commercial Launch May 2022** 

- rrMM XPOVIO® in combination with bortezomib and dexamethasone (XVd)
- rrMM XPOVIO® in combination with dexamethasone (Xd)
- rrDLBCL XPOVIO® as monotherapy (X)



# **Approved in Australia** March 9<sup>th</sup>, 2022

**Commercial Launch May 2022** 

- rrMM XPOVIO® in combination with bortezomib and dexamethasone (XVd)
- rrMM XPOVIO® in combination with dexamethasone (Xd)



# **Approved in Taiwan** October 21st, 2022

**Expected Commercial Launch** 

2023

- rrMM XPOVIO® in combination with bortezomib and dexamethasone (XVd)
- rrMM XPOVIO® in combination with dexamethasone (Xd)
- rrDLBCL XPOVIO® as monotherapy (X)



## **Expected Approval in Hong Kong** 2023

**Expected Commercial Launch** 2023





rrMM - XPOVIO® in combination with dexamethasone (Xd)

# **ASEAN NDA Schedule**









# **Expected Approval in Malaysia** H2 2024

- rrMM XPOVIO® in combination with bortezomib and dexamethasone (XVd)
- rrMM XPOVIO® in combination with dexamethasone (Xd)
- rrDLBCL XPOVIO® as monotherapy (X)

**NDA Submission Dec 2022** 

> **NDA Approval** H<sub>2</sub> 2024

**Commercial Launch** H2 2024





# **Expected Approval in Thailand** H2 2024

- rrMM XPOVIO® in combination with bortezomib and dexamethasone (XVd)
- rrMM XPOVIO® in combination with dexamethasone (Xd)
- rrDLBCL XPOVIO® as monotherapy (X)

**NDA Submission Dec 2022** 

> **NDA Approval** H<sub>2</sub> 2024

**Commercial Launch** H2 2024





# **Expected Approval in Indonesia** H2 2024

- rrMM XPOVIO® in combination with bortezomib and dexamethasone (XVd)
- rrMM XPOVIO® in combination with dexamethasone (Xd)
- rrDLBCL XPOVIO® as monotherapy (X)

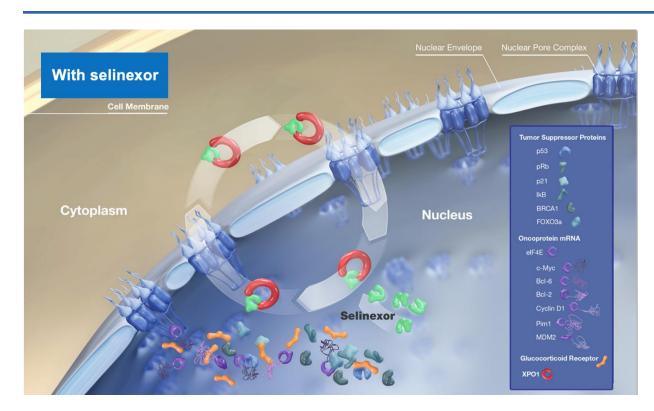
**NDA Submission** H1 2023

> **NDA Approval** H2 2024

**Commercial Launch** H2 2024

# ATG-010 (Selinexor) - First-in-class and Only-in-class SINE Compound with Unique MoA and Differentiated Profile





# **Key Highlights**

- 1<sup>st</sup> and only XPO1 inhibitor approved by FDA for treating R/R MM and R/R DLBCL
- 1<sup>st</sup> and only FDA-approved drug for the treatment of both R/R MM and R/R DLBCL
- Only single-agent, oral therapy approved by the FDA to treat R/R DLBCL
- Recommended by NCCN and CSCO guidelines for R/R MM and R/R DLBCL treatment



# **Synergy with Antengene Pipeline Assets**

■ SINE + mTORi

Selinexor + ATG-008 in diffuse large B-cell lymphoma (MATCH)

■ SINE + I/O:

Selinexor + ATG-101 in solid tumors and lymphoma

# Clinical Benefits Validated by Selinexor's Completed and Ongoing Studies in Multiple Myeloma and DLBCL



# **ANTENGENE**



# **BOSTON**

(SVd)

#### Selinexor Dosage: 100mg QW

- 1-3 prior therapies
- ORR: 76% (SVd) vs. 62% (Vd)
- CR rate: **17%** (SVd) vs. 10% (Vd)
- mPFS: 13.93 mos (SVd) vs. 9.46 mos (Vd)
- mDOR: 20.3 mos (SVd) vs. 12.9 mos (Vd)
- Improved efficacy achieved when receiving 40% less bortezomib and 25% less dexamethasone

# **STOMP**

(SVd/SPd/SRd/SKd/etc.)

- 11 combinations
- ORR (study arm vs, benchmark data):
  - SKd: **78%** vs. 23% (Kd)
  - SDd: **73%** vs. 29% (D)
  - SPd: **65**% (pts dosed at RP2D) vs. 29% (Pd)
  - SRd: 92% vs. 67% (Rd)

# **STORM**

(Sd)

#### Selinexor Dosage: 80mg BIW

- mOS (≥MR): 15.6 mos
- Penta refractory (median # of prior therapies: 8)
  - ORR: 25%
- mPFS: 3.7 mos
- mOS: 8.6 mos

# SADAL

(5)

## Selinexor Dosage: 60mg BIW

- 2-5 prior lines
- ORR: **29**%
- CR rate: 13%
- mDOR: 9.3 mos
- mOS: 9.0 mos
- mOS (≥MR): Not reached
- mOS (SD): 18.3 mos

**FDA Approved** 

**FDA Approved** 

**FDA Approved** 





Diffuse Large B-cell Lymphoma



Source: Dimopoulos M, et al. ASCO 2020. Abstract 8501; Gasparetto C, et al. ASH 2020. Abstract 1366.; Gasparetto C, et al. ASCO 2020. Abstract 8510.; Chen C, et al. ASH 2020. Abstract 726.; White D, et al. ASH 2020. Abstract 1393.; Kyprolis Package Insert; Study PX-171-003 A1; Lonial et al. Lancet 2016.; Pomalyst Package Insert.; Stewart et al. NEJM 2015.; Revilimid\* (lenalidomide), Pomalyst\* (pomalidomide), Velcade\* (bortezomib), Kyprolis\* (cartilizomib) or Darzalex\* (daratumumabl.; Chira N, Vogi DT, Dimopoulos M, et al. Results of the Pivotal STORM Study (Part 2) in Penta-Aberfactor 2020 Multiple Myeloma (MM): Deep and Durable Responses with Oral Selinexor Plus Low Doos Dexamethasorne in Patients with PentaMMs, Blood 2018: The Haematolkage vice and publication expected in the Torss and Tor

# Multiple Selinexor Containing Regimens Recommended by NCCN, ESMO, CSCO, and CMDA-CMA Guidelines









#### 1-3 Prior Therapies

- SVd QW
- SDd
- SPd
- SKd
- > 3 Prior Therapies (whose disease is refractory to at Least Two Pls, IMIDs, and an anti-CD38 mAb)
- Sd

#### **Diffuse Large B-cell Lymphoma**

3L+ (including patients with disease progression after transplant or CAR T-cell therapy)

S monotherapy



European Society for Medical Oncology

#### **Multiple Myeloma**

#### **2L Option After VRD**

- R sensitive (SVd)
- R refractory (SVd)
- V sensitive (SVd)

## **2L Option After DaraRD**

- R sensitive (SVd)
- R refractory (SVd)

#### **2L Option After DaraVMP or DaraVTD**

V sensitive (SVd)

#### Second or Subsequent Relapse

- R refractory and PI sensitive (SVd)
- Triple-class refractory (Sd)



## **Multiple Myeloma**

# Relapsed/Refractory

- SVd Upgraded to Level 1 Recommendation
- SPd
- SDd **New Inclusions**
- SKd

## Diffuse Large B-cell Lymphoma

#### Relapsed/Refractory

S monotherapy — Upgraded to Level 2 Recommendation





**Chinese Medical Doctor Association Chinese Medical Association** 

# **Multiple Myeloma**

## Relapsed/Refractory

- SVd
- SPd **New Inclusions** SDd
- SKd

<sup>\*</sup> Some of the information in this presentation is from third-party studies and only provided to medical research professionals for academic purpose. Antengene is not responsible for the contents published by such external sources.

<sup>\*\*</sup> Approved for RRMM by the US FDA, European EMA, Chinese NMPA, Korean MFDS, Singaporean HSA, Australian TGA, and Taiwan TFDA. Approved for RRDLBCL by the US FDA, Korean MFDS, Singaporean HSA, and Taiwan TFDA. As of Nov 14, 2022. \*\*\* Indications for Selinexor undergoing clinical trial / planned study include: PTCL, NKTL, AML, MDS, MF

# Dose Reduction can be Used to Manage Patients, while Optimizing Outcomes with PFS of 16.6 Months



# The median dosage of XPOVIO in the BOSTON trial was 80 mg (range: 30-137 mg) taken once weekly<sup>1</sup>

## Key efficacy endpoints for patients (N=195) with and without XPOVIO dose restrictions in the BOSTON trial<sup>2</sup>

	ITT Patient Population	Patients with Dose Reduction	
Patient population	N = 195	n=126	
% of ITT arm	100	65	
mPFS, mo	13.9 (95% CI: 11.7, NE)	16.6 (95% CI: 12.9, NE)	
ORR, %	76.4	81.7	
≥VGPR, %	44.6	51.6	
mDOR, mo	20.3 months (95% CI: 12.6, NE)	Not evaluable (95% CI: 13.8, NE)	

#### **Limitation of Subgroup Analyses:**

- This post hoc analysis was exploratory in nature, not included in the study objectives, and does not control for type 1 error
- This post hoc analysis was not powered or adjusted for multiplicity to assess PFS across other prespecified subgroups
- This post hoc analysis was underpowered to detect clinically meaningful differences in treatment effect

65% of patients in the XVd arm had an XPOVIO dose reduction (126/195 patients) vs 35% of those without a dose reduction (65/195 patients)<sup>2</sup>

Source: Karyopharm Investor Presentation dated December 8th, 2021

<sup>1.</sup> XPOVIO. Prescribing information. Karyopharm Therapeutics Inc; 2021. 2. Jagganath, et al. ASH 2021

<sup>\*</sup>Response was evaluable in 125 of 126 patients receiving a dose modification for selinexor and 66 of the 69 patients who did not receive a dose modification for selinexor. Overall response rate is the proportion of patients who achieve a partial response or better, before IRC-confirmed progressive disease or initiating a new MM treatment or crossover. Cl=confidence interval, IRC=independent review committee; ITT=intent to treat; mDOR=median duration of response; mo=month; mPFS=median progression-free survival; NE=not evaluable; ORR=overall response rate; VGPR=very good partial response.

<sup>\*\*</sup> Some of the information in this presentation is from third-party studies and only provided to medical research professionals for academic purpose. Antengene is not responsible for the contents published by such external sources.

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\*\*\*\* Indications for Selinexor undergoing clinical trial / planned study include: PTCL, NKTL, AML, MDS, MF

# **XPOVIO Evolving into a Standard of Care with Dose and Schedule Redefined Over Time to Improve Efficacy and Patient Experience**



From the STORM trial to the BOSTON trial to the STOMP trial, XPOVIO dosing has been continually refined to help optimize the patient experience

**US FDA Approval Date: Dec 2020** 

2<sup>nd</sup> approval in MM

Dose: 100mg, once weekly

**US FDA Approval Date: July 2019** 

**Ongoing/Completed** 

1<sup>st</sup> approval in MM Dose: 160mg (80 mg, twice weekly)

 $\mathsf{Xd}$ 

**STORM** 

XVd **BOSTON**  SPd, SKd, SDd **STOMP** 

Phase 1/2 study in MM

Dose Range: 60-100mg, once weekly

Phase 1/2, open-label, multi-center study Patients with RRMM

Phase 3, 2-arm, active comparatorcontrolled, open-label, multi-center study After at least 1 prior therapy in MM

(dose escalation/expansion)

Phase 2b, single-arm, open-label, multi-center study

Patients with penta-refractory RRMM

**Once Weekly** (previously twice weekly)

**Lower Dose** (previously a higher dose) **XPOVIO-based Triplets** 

(previously a doublet)

**Earlier Lines** 

(previously only in later lines)

**Supportive Care** 

(active symptom management)

Source: Karyopharm Investor Presentation dated February 8th, 2022

<sup>\*</sup> STOMP was designed to study selinexor in combination with other MOAs across multiple triplet and quadruplet regimens, including XVd. MM=multiple myeloma; MOA=mechanism of action; RRMM=relapsed or refractory multiple myeloma.

<sup>\*\*</sup> Combinations other than XVd and Xd are not promoted by Karyopharm, but may be considered for future indication updates.

<sup>\*\*\*</sup> Combinations other than Xd are not promoted by Antengene, but may be considered for future indication updates

<sup>\*\*\*\*</sup> Some of the information in this presentation is from third-party studies and only provided to medical research professionals for academic purpose. Antengene is not responsible for the contents published by such external sources.

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<sup>\*\*\*\*\*\*\*</sup> Indications for Selinexor undergoing clinical trial / planned study include: PTCL, NKTL, AML, MDS, MF

# Broad and Deep Potential for Selinexor / SINE Beyond Multiple Myeloma



Incidence / Prevalence China (APAC)		Global Pivotal Study Ongoing
19,600 / 68,600 (1,900) / (8,740)	MF	
49,000 / 57,937 (3,100) / (9,300)	MDS	Signal Detection Studies/IITs in Preparation in China
84,000 / 116,280 (3,200) / (3,520) (AML)	Leukemia	Signal Detection Studies/IITs in Preparation in China
86,000 / 204,910 (9,100) / (53,000)	Endometrial Cancer	<ol> <li>Global Study</li> <li>Partner in the US announced top-line results in Phase III Study</li> <li>Potentially first solid tumor indication for Selinexor</li> </ol>
50,585 84,463 (9,199) / (34,658) (DLBCL + TCL)	Lymphoma (i.e., DLBCL, TCL)	<ol> <li>Approved in the US for 3L DLBCL; pivotal study ongoing in China</li> <li>Recommended by NCCN and CSCO guidelines</li> <li>Multiple studies (SADAL, SEARCH, XPORT-030, SWATCH, TOUCH, RWD)</li> </ol>
21,000 / 54,800 (6,000) / (23,500)	Multiple Myeloma	<ol> <li>Approved in the US for 2L+ MM and approved in China for rrMM</li> <li>Recommended by NCCN, ESMO, CSCO, CMPA-CMA guidelines as 2L+ therapy</li> <li>Multiple studies (BOSTON, BENCH, STORM, STOMP, MARCH, RWD)</li> </ol>
Total: Total: 310,185 / 586,990		

Source: Antengene research

(32,499)

(132,718)

<sup>\*</sup> Investigator Initiated Trials (IIT)

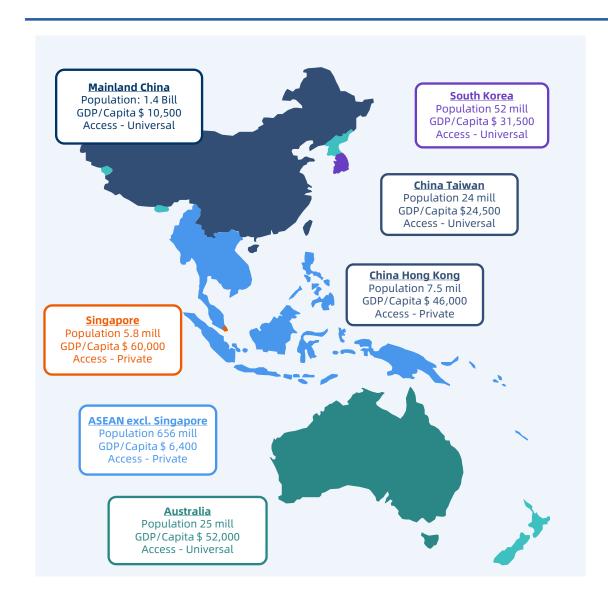
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<sup>\*\*\*\*</sup> Indications for Selinexor undergoing clinical trial / planned study include: PTCL, NKTL, AML, MDS, MF

# **Antengene is Focused on Markets with Greatest Commercialization Potential**







Commercialization strategy focuses on selection of 6 core stage 1 markets defined by 3 parameters for success:

- High unmet need
- Reimbursed markets
- High GDP/capita



Initial focus is to build Antengene presence in the core markets



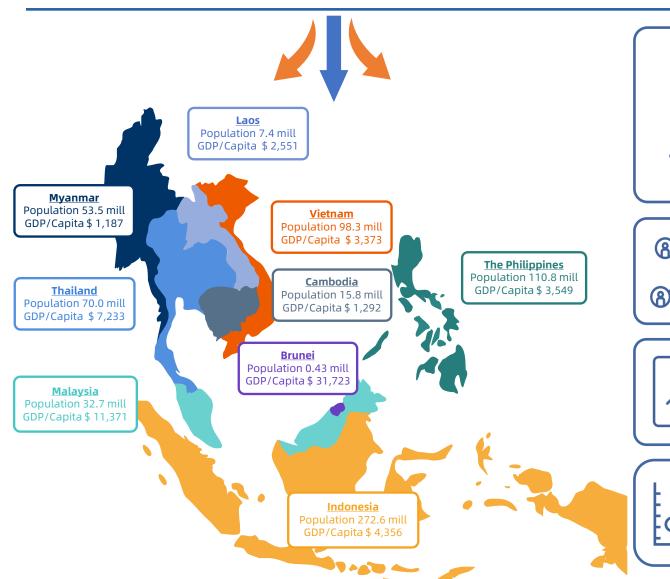
Ensure successful commercial launch of Xpovio®



Expand portfolio in core markets and expand Antengene presence to other stage 2 ASEAN markets

# Antengene is Expanding into Stage 2 ASEAN Markets with Significant Future Commercialization Potential







Tiered commercialization strategy in ASEAN market expansion countries:

Tier 1: Indonesia, Malaysia, Thailand

Tier 2: Vietnam, The Philippines



Already launched in high profile APAC markets such as Australia, South Korea, Singapore etc.



Seasoned commercial team with strong track record in block buster drugs in APAC



Strong growth pipeline with FIC and BIC potential assets

# **Building XPOVIO® Launch Momentum with Regulatory Approvals Across Core Markets**





# Commercial Team with a Proven Track Record of Success



#### **Commercialization Strategy**



John F. Chin

■ 30+ years of experience in the pharmaceutical industry, instrumental involvement in the commercial launch and lifecycle management of REVLIMID®, one of the industry's most successful oncology products globally

#### **Commercialization in China**



Lixin Yu

#### ■ 30+ years of experience in commercialization for Oncological **Products in China**

Successful launch cases in hematological, global-local products in Multiple Myeloma, Lymphoma and Leukemia

#### **Commercialization in APAC**



- Thomas Karalis
- 30+ years of experience in the pharmaceutical industry, achieved multiple regulatory and reimbursement milestones in APAC
- Successful launches of REVLIMID®, POMALYST® and ABRAXANE® in APAC markets

Track record of Antengene commercial team in hematology:













#### **China Marketing**



Frank Sun Director, Marketing and Commercial Channels, Hematology BU China

Deep industry experience in hematology product launch in Mainland China, market development and team management

#### **China Sales**



Chen Wei National Director, Hematology BU China

Deep industry experience in commercializing hematology products in Mainland China

#### **China Medical Affairs**



Executive Director, Medical, China Seasoned experience in Hematology & Skin Cancer, proven track record for the launch of a series of novel medicines, including Zelboraf, Hemlibra, Gazyva and Polivy, as well as the expansion of new indications



Austin Wang Associate Director, MSL, China Extensive experience in working with key KOLs, deep medical insights in CN Hema, market and landscape

#### **AU/NZ Commercialization**



AU, US and EU Commercial, Govt Affairs and Market Access leadership roles in Hematology, Oncology and Specialty Therapeutics

Michele Robbins

#### **APAC Medical Affairs**



Affairs leadership roles. Extensive clinical/translational research background in Hematology and Oncology

AU, US and Global Medical

#### **GM** of South Korea



ISPEN KR.30+ years of industry experience in new product launch, market development and team management Minyoung Kim

Former Country GM at

#### **APAC Commercialization**

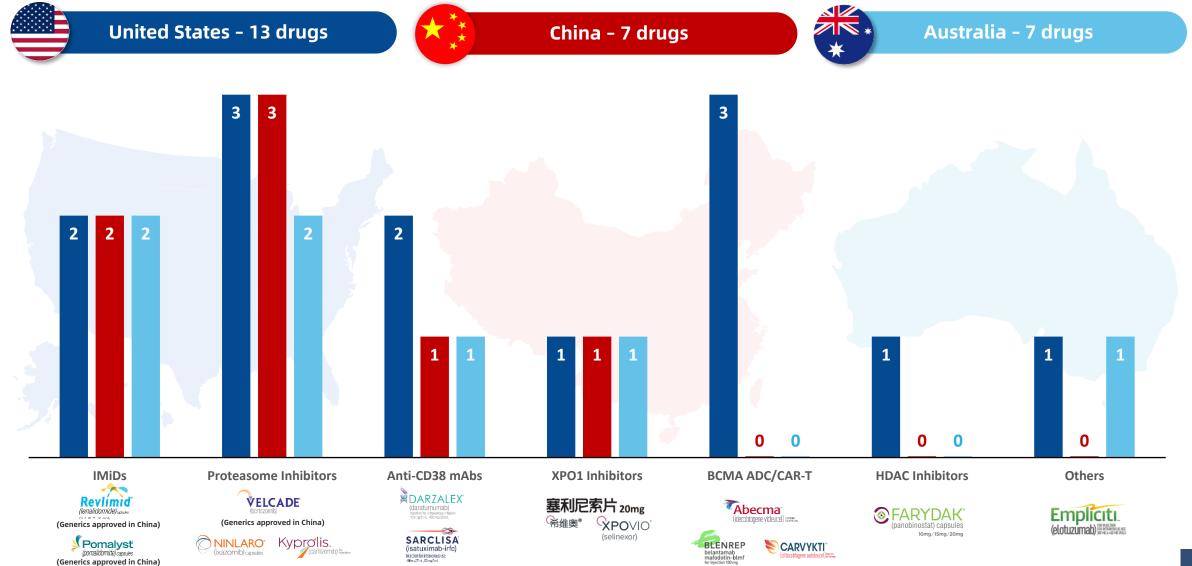


APAC commercial experience including Global Marketing CAR T Launch and strong background in Sathya Walisinghe Hematology & Oncology

Extensive ANZ, US and

# Fewer Multiple Myeloma Medicines Approved in China/Reimbursed in Australia Compared to the US - Launching with Less Competition Outside the US





# Successful Commercial Launch of XPOVIO® in Mainland China



# 塞利尼索片 20mg......





#### **Approved Indication:**

 XPOVIO® in combination with dexamethasone (Xd) in Relapsed / Refractory Multiple Myeloma (rrMM)

#### **Treatment Guideline Recommendations in China**

- R/R Multiple Myeloma:
  - CSCO Guidelines for the Diagnosis and Treatment of Hematologic Malignancies 2022
  - CMDA & CMA Guidelines for the Diagnosis and Management of Multiple Myeloma in China (2022 revision)
- R/R Diffuse Large B-cell Lymphoma:
  - CSCO Guidelines for the Diagnosis and Treatment of Lymphomas 2022



Official Commercial Launch 13<sup>th</sup> May, 2022

600 Hospitals



**100+ DTP Pharmacies** 



30+ Provinces, Autonomous Regions & Municipalities



6 Selinexor Containing Regimens Recommended by Treatment Guidelines Globally



Multiple Inclusions into Local Government Supported / Guided Commercial Insurance



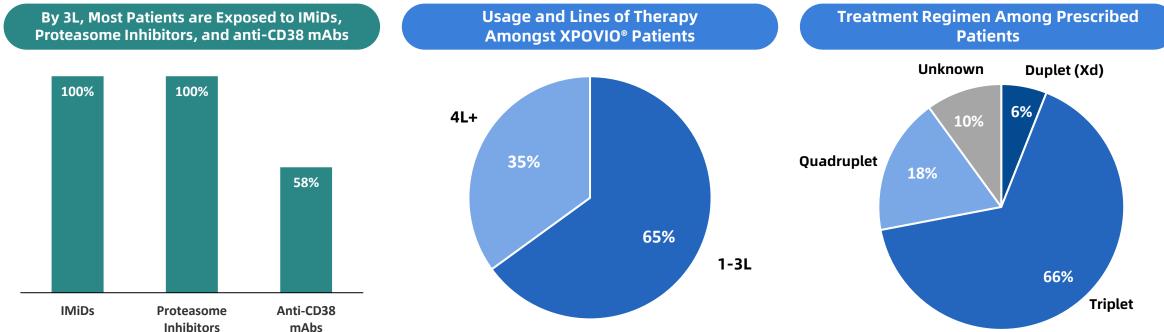
H1 2022 Revenue RMB 54.0 million

170+ Staff Commercialization Team Across Mainland China



# Initial Observations for XPOVIO® Launch in China Market - XPOVIO® Being Prescribed in Earlier Lines of Therapy in a Range of Combination Regimens





## Physician Testimonials Highlighting XPOVIO's Differentiated Profile

"MARCH, BOSTON trial data indicates that Selinexor combo regimens bring more innovative therapeutic options and better treatment outcomes for relapsed/refractory, multidrug resistance, metastasis and/or high-risk MM patients."

KOL, Dr. Jun Ma, Chief Supervisor of CSCO, Harbin Hematology and Oncology Institute "Selinexor is more convenient and likely leads to higher compliance because it is an **oral regimen**. The efficacy of Selinexor is proven in a number of clinical trials. Besides being used as a monotherapy, Selinexor could also be **combined with a number of drugs such as chemo, target therapy, I/O, etc.**"

KOL, Dr. Zhiming Li, Sun Yat-sen University Cancer Center

# **Asia Pacific Markets - Executing on XPOVIO® Launch Plans**



# **Reimbursement Timelines**



# **Excellent Launch Trajectory**



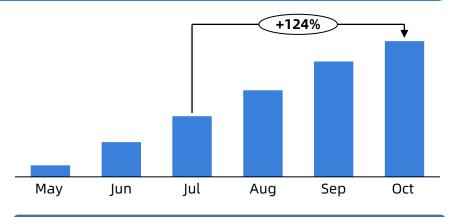
## **Australia**

- Total number of XPOVIO® treated patients **doubled in 3 months** (between July to October)
- First multiple myeloma indication (Xd regimen) included for reimbursement on 1st September
  - XPOVIO<sup>®</sup> achieved that in 180 days; whereas oncology medicines are listed in 496 days on average
- Xd achieved >50% new patient share of available penta-refractory patients
- Reimbursement of XVd regimen anticipated in H1 2023



# **Other Asia Pacific Markets**

- Reimbursement anticipated in Taiwan and South Korea in 2024
- Building of KOL advocacy and XPOVIO® experience:
  - >250 patients treated with XPOVIO® via pre approval access program
  - o Pre-reimbursement Patient Familiarization Program activated
- ASEAN markets expansion commencing with NDA submissions in Thailand and Malaysia in
   2022, and Indonesia in H1 2023



Limited Availability of Reimbursed Triplet Regimens in APAC
Markets Compared to the US



**3 Regimens** 

DVd, PVd and ERd



2 Regimens

KRd and NRd



3 Regimens

DVd, DRd and IRd



# **Steady Stream of Catalysts Continue to Drive Value for Investors**



# Focused on Execution and Key Priorities to Drive Value for Investors in 2023



#### **Continued Revenue Generation Across China and APAC markets**

• Starting with 2 disease areas with multiple indication expansion / untapped opportunities with an only-in-class asset in unique markets



## **Broad and Deep Pipeline of Differentiated Global Rights Assets**

 10 global rights assets with highly-differentiated, combinational and synergistic mechanism of action with series of upcoming data read outs



#### **Forming Value Creating and Synergistic Partnerships**

 Continued BD discussions on assets, clinical collaborations, in/out-licensing and value-creating partnerships



#### **Efficiently Utilizing Cash Provided by Our Strong Base of Global Shareholders**

• RMB2,151mm of cash and bank balances as of 30<sup>th</sup> June 2022



ANTENGENE CORPORATION LIMITED (SEHK: 6996.HK)

MARCH 2023

# THANK YOU

TREATING PATIENTS BEYOND BORDERS