ANTENGENE 2022 R&D DAY

TREATING PATIENTS BEYOND BORDERS

NOVEMBER 2022

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A GLOBAL, MULTI-PRODUCT BIOPHARMA MAKING TRANSFORMATIVE IMPACT IN HEMATOLOGY/ONCOLOGY

Antengene: Treating Patients Beyond Borders

ANTENGENE

Leading Commercial-stage R&D-driven Global Biopharmaceutical Company Focused on the Discovery, Development, Manufacturing and Commercialization of Innovative First-in-class / Best-in-class Therapeutics for the Treatment of Hematologic Malignancies and Solid Tumors

Our Vision

Developing innovative cancer medicines to treat patients beyond borders worldwide.

Our Mission

Building fully-integrated capabilities in discovery, clinical development, manufacturing and commercialization to foster the rapid clinical adoption of innovative medicines from around the world for the benefit of broad patient populations.

15 Innovative Drug Candidates

10 Assets with Global Rights

3 In-house R&D Centers

2 Manufacturing Sites

1 Product – XPOVIO® Approved in 5 Markets

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

ANTENGENE

2017 — Began Operations

2018

2019

2020 — Hong Kong IPO

2021 — Transition into a Commercial Stage Across Asia (Hong Kong, Taiwan)

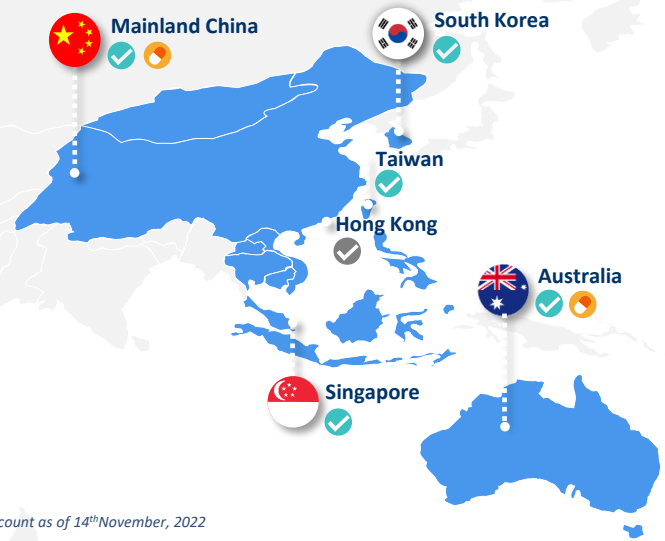
2022 — Multiple Global Rights Assets in Development

2023 – 2024 — Key Priorities:
1. Commercial revenue growth across regions
2. Key data readouts of first/best-in-class global rights portfolio
3. Value creating partnerships or collaborations

2025 — Multi-product Biopharma

Partnerships/ Research Collaboration:

- 2017: Celgene
- 2018: Karyopharm Therapeutics
- 2019: AstraZeneca, 君实生物 TopAlliance
- 2021: Bristol Myers Squibb, CALITHERA, LCB LegoChemBio
- 2022: BeiGene, celularity



15 Assets in Portfolio

德琪医药 ANTENGENE

400+ Employees Globally

17 Ongoing Trials in Mainland China, Australia, and the US

4 Ongoing Registrational Trials In Mainland China

- Regions in Antengene Markets where XPOVIO® is Approved
- Regions Expecting Selinexor Approval in 2023
- Regions with Ongoing Clinical Trials

** Employee count as of 14th November, 2022*

APAC Rights Portfolio – Enablers for Antengene with Key Milestones Achieved

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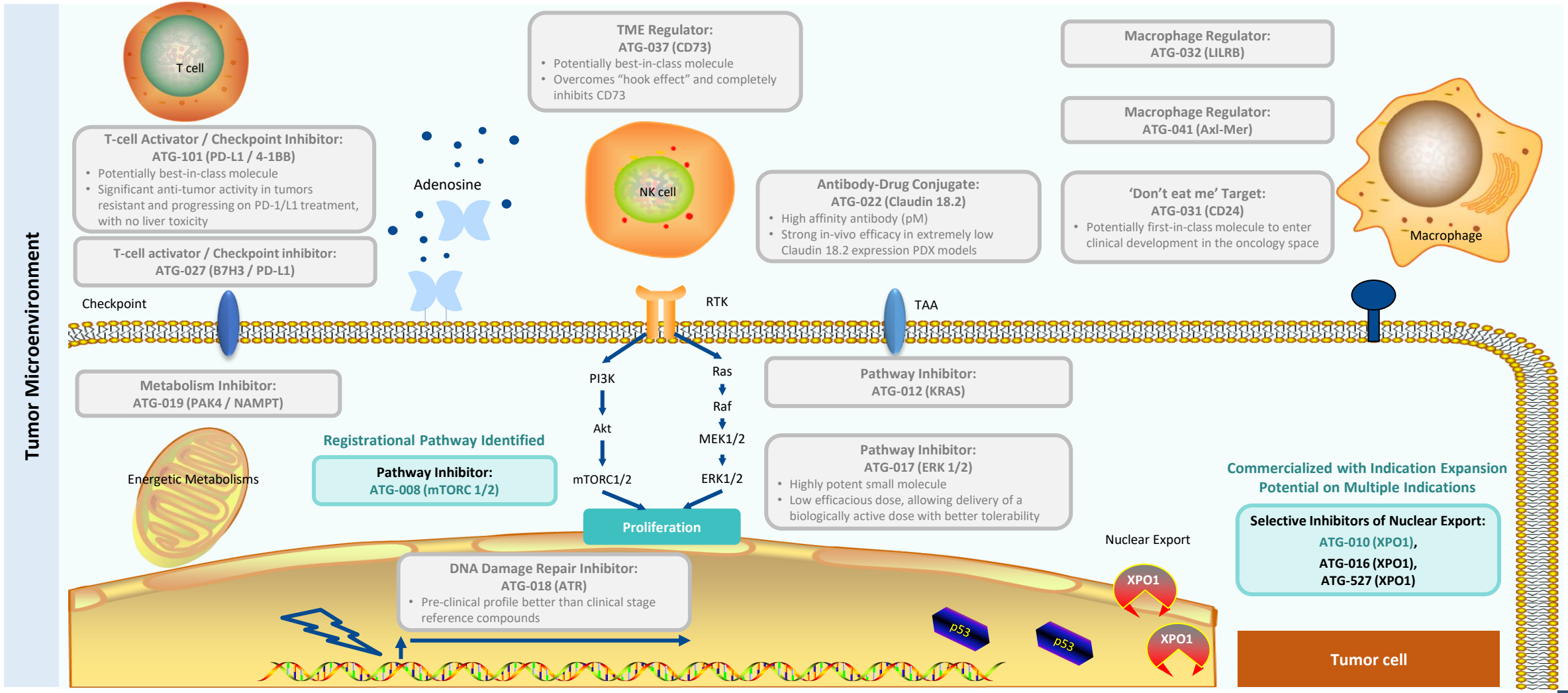
Multiple Targets

Synergistic Mechanism of Actions

Multiple Modalities



Assets with Global rights

Assets with APAC rights

Global Rights Portfolio with Globally First/Best-in-class Potential

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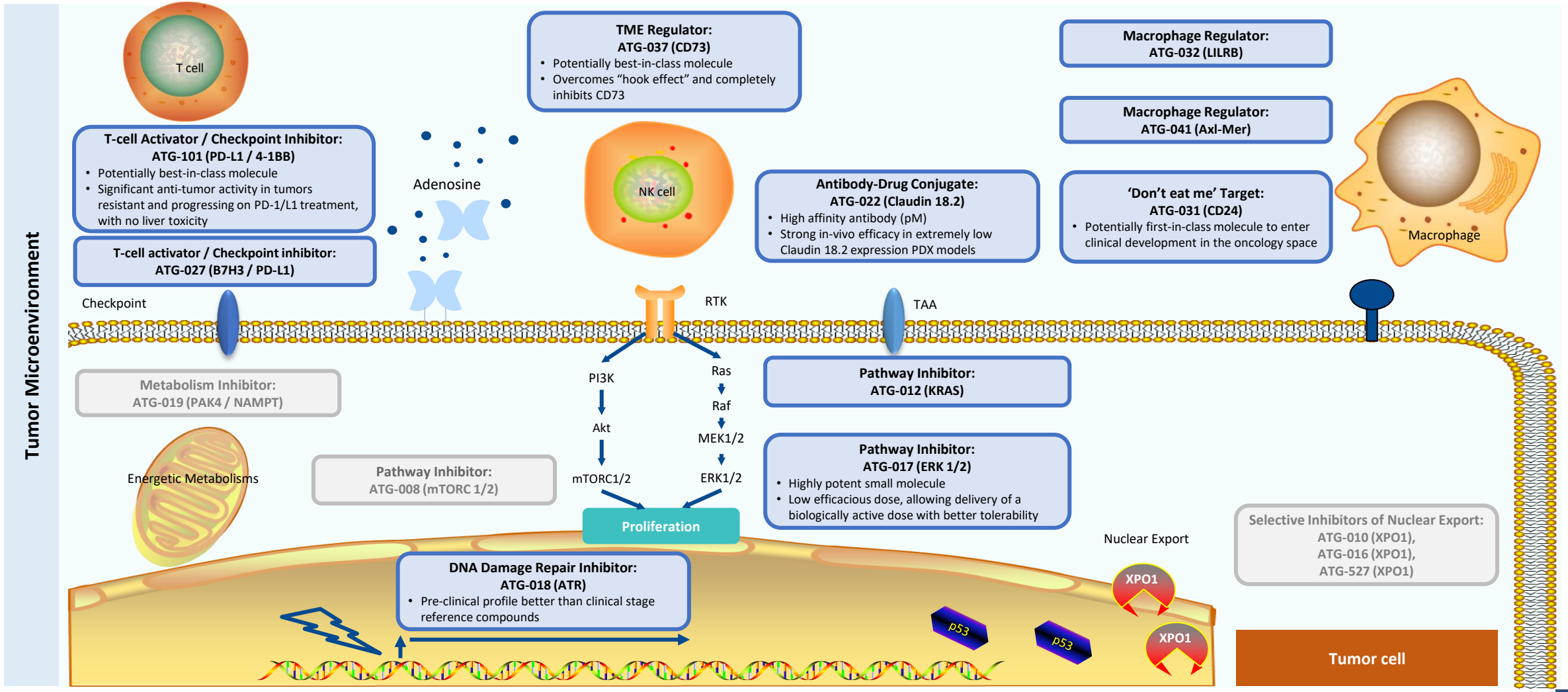
Multiple Targets

Synergistic Mechanism of Actions

Multiple Modalities



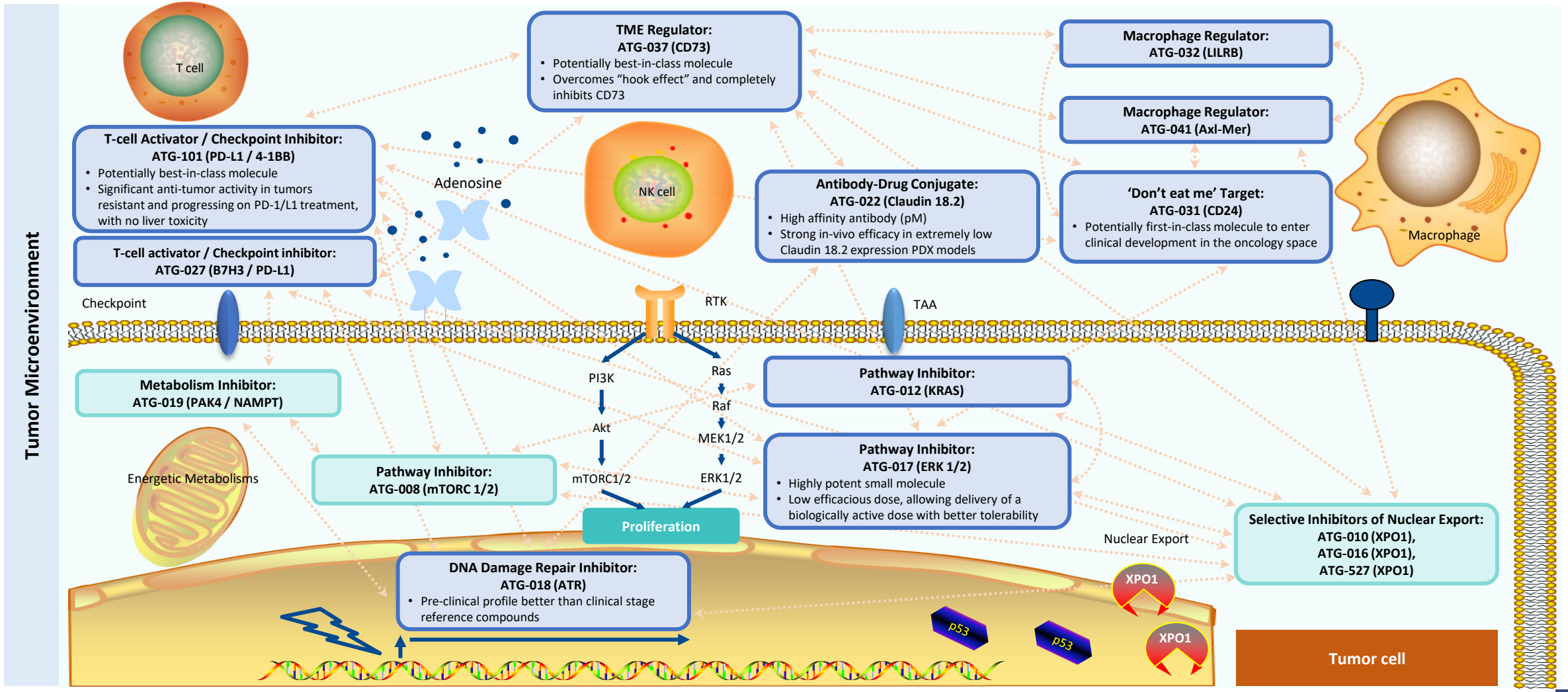
Assets with Global rights

Assets with APAC rights

Combined Portfolio – Unique Portfolio with Synergistic Mechanisms of Action

ANTENGENE

Multiple Targets | **Synergistic Mechanism of Actions** | **Multiple Modalities**



Assets with Global rights Assets with APAC rights

Key Highlights for Today – Portfolio with APAC Rights

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Data Readouts

ATG-008 (Onatasertib)

- **Phase I/II "TORCH-2" Study – In Combination with Toripalimab in Advanced Solid Tumors**
  - Encouraging efficacy observed in relapsed/metastatic cervical cancer patients, demonstrating an **ORR of 52.4% (11/21)** regardless of PD-L1 status
  - ORR for PD-L1 positive patients was **77.8% (7/9)**
  - Identified potential **registrational path** for ATG-008
- **Phase II "TORCH" Study – Monotherapy in 2L+ HBV+ Hepatocellular Carcinoma (HCC)**
  - Demonstrated **single agent activity** in HCC patients, including in patients with prior checkpoint inhibitor treatment (ORR of 16.7%)

Clinical Trial Updates

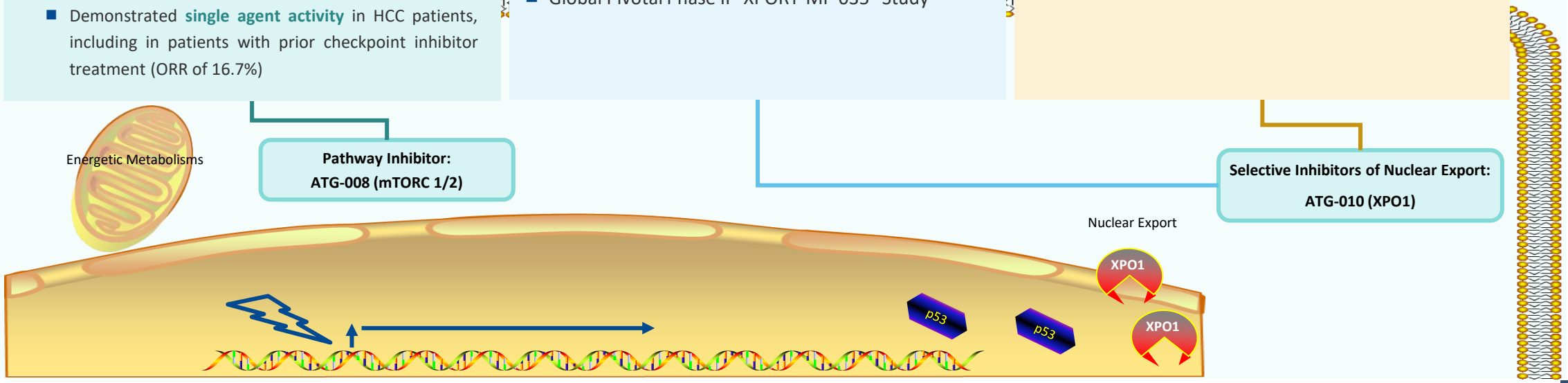
ATG-010 (Selinexor)

- Phase I/II "TOUCH" Study – Data to be presented at ASH 2022
- Pivotal Phase III "BENCH" Study
- Pivotal Phase II "SEARCH" Study
- Global Pivotal Phase II/III "XPORT-DLBCL-030" Study
- Phase Ib "MATCH" Study
- Phase I/II "SWATCH" Study
- Global Pivotal Phase II "XPORT-MF-035" Study

Commercialization Updates

ATG-010 (Selinexor)

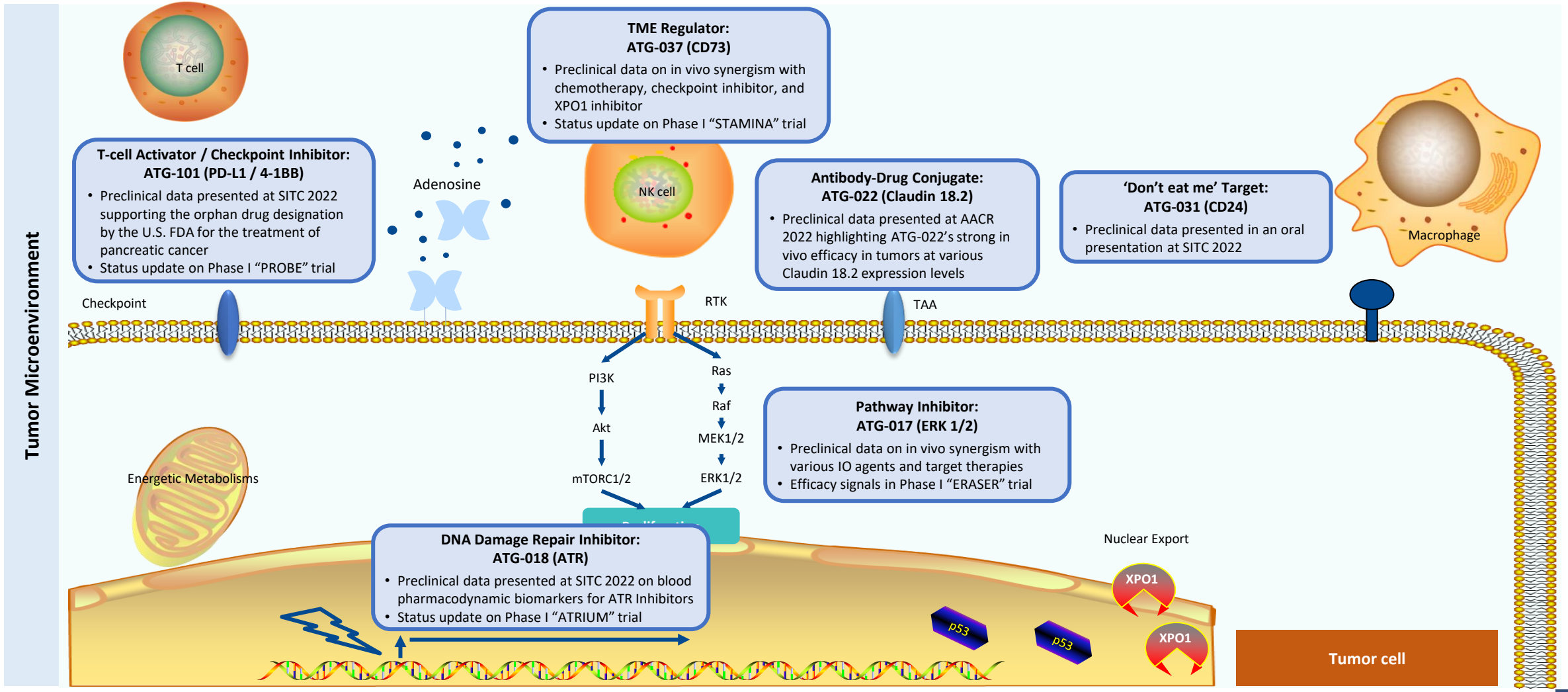
- Continued execution of XPOVIO®'s defined strategy in China and APAC region
- Launch updates with regulatory approvals across 5 core markets
- Future untapped opportunities
- Initial observations from China/APAC launch
- 2023 core priorities



Key Highlights for Today – Portfolio with Global Rights

ANTENGENE

Multiple Targets | **Synergistic Mechanism of Actions** | **Multiple Modalities**



R&D PHILOSOPHY, DIRECTION AND PROGRAM HIGHLIGHTS

Cancer Remains a Huge Challenge Globally

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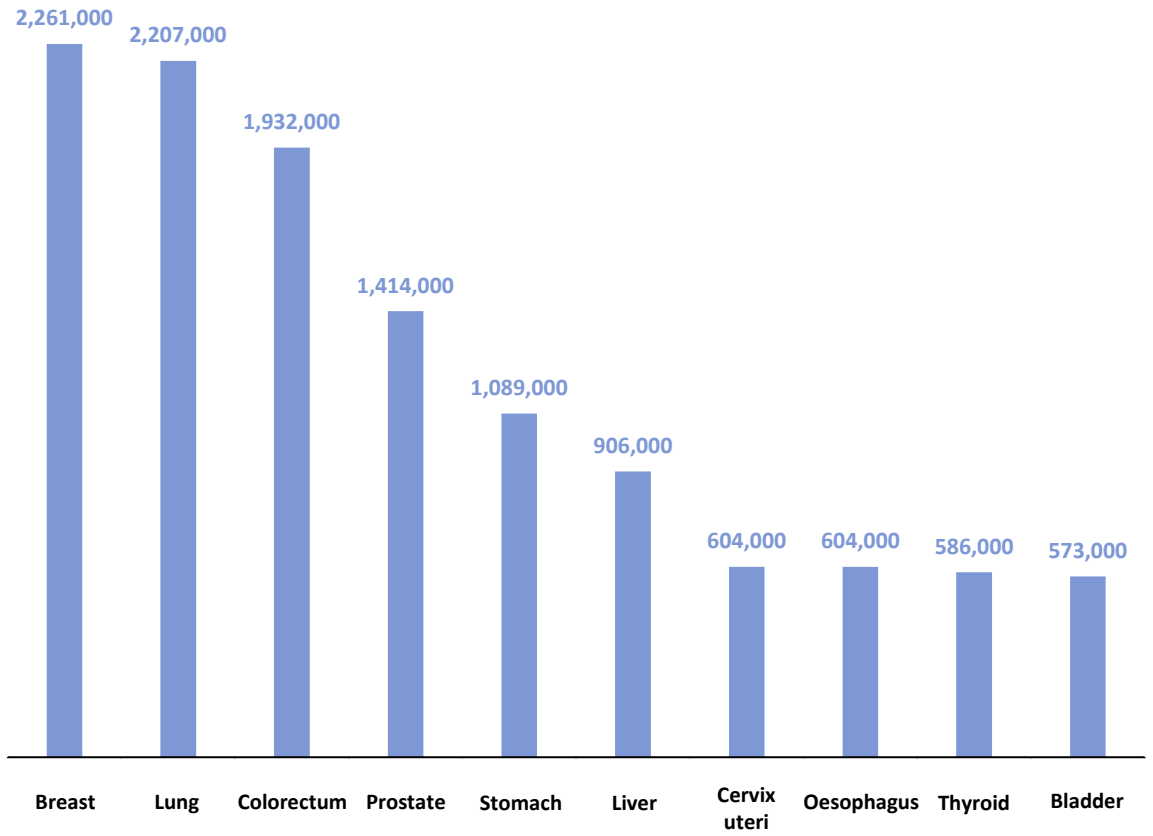
19+ Million
New Cancer Cases Each Year

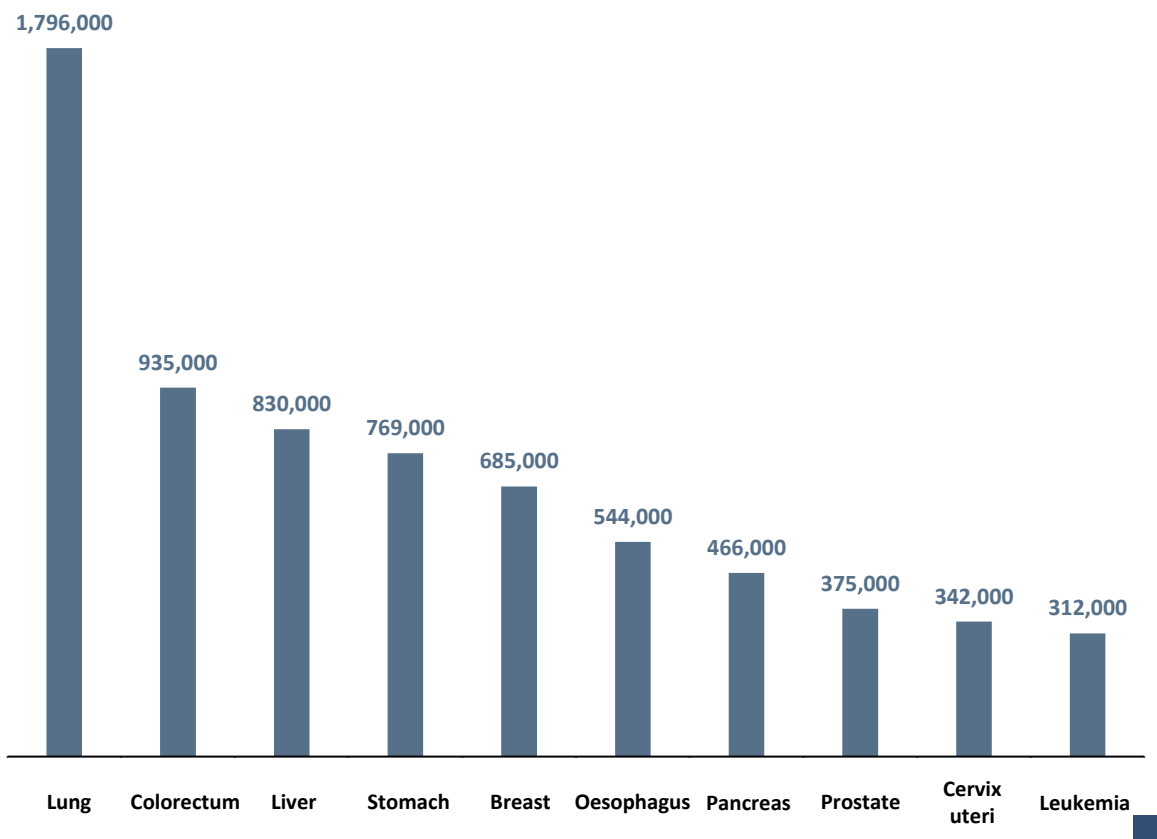
50+ Million
People Living with Cancer Worldwide

10+ Million
Cancer-related Deaths

Global Top 10 Cancer Types by Incidence in 2020

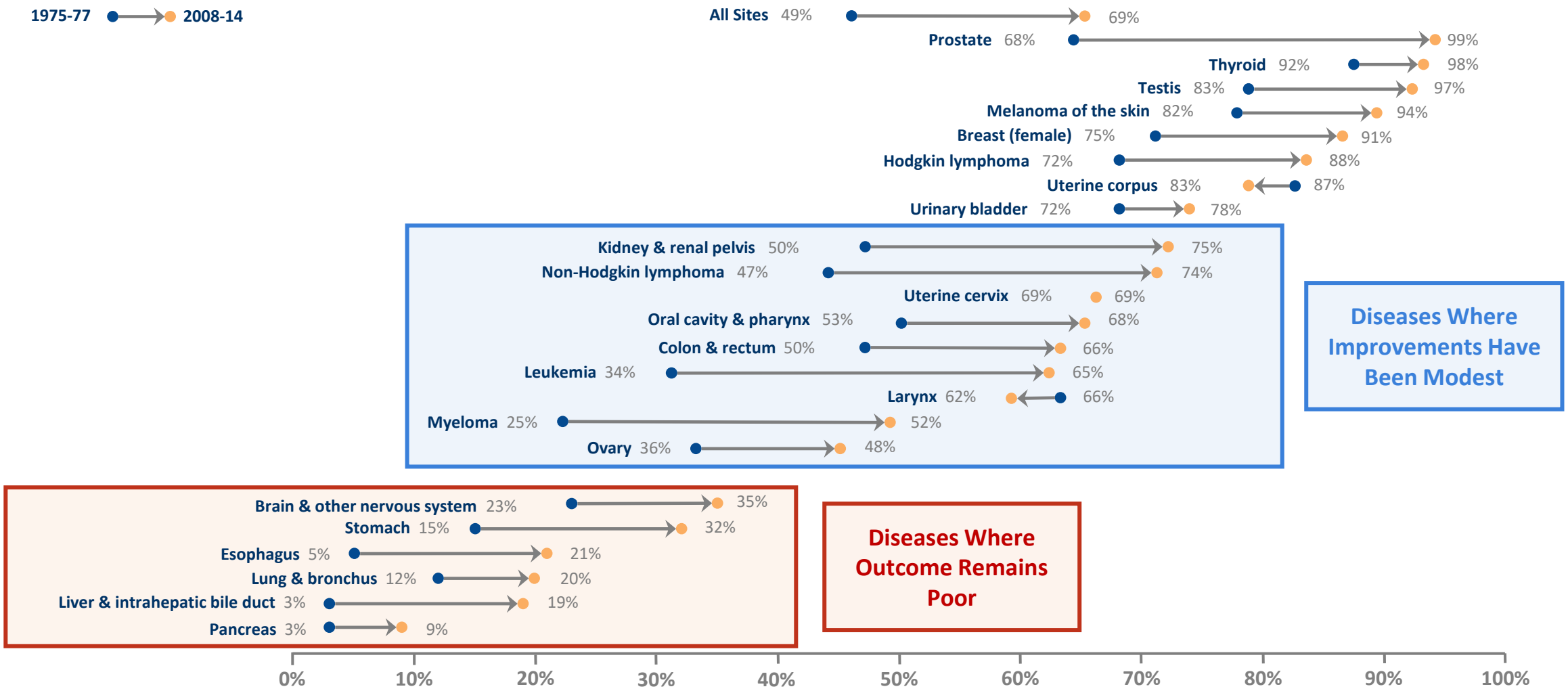


Global Top 10 Cancer Types by Mortality in 2020



Source: Globalcan

Improvements in Five-year Survival Rates (USA): Major Unmet Needs Remain, Giving Opportunity for Novel Treatments



Rates are adjusted for normal life expectancy and are based on cases diagnosed in the 9 oldest SEER registry areas from 1975 to 1977 and 2008 to 2014, respectively.
SEER: Surveillance, Epidemiology, and End Results (SEER)

Source: Literature Review, Frost & Sullivan analysis

Cancer Outcomes are Geographically Inconsistent

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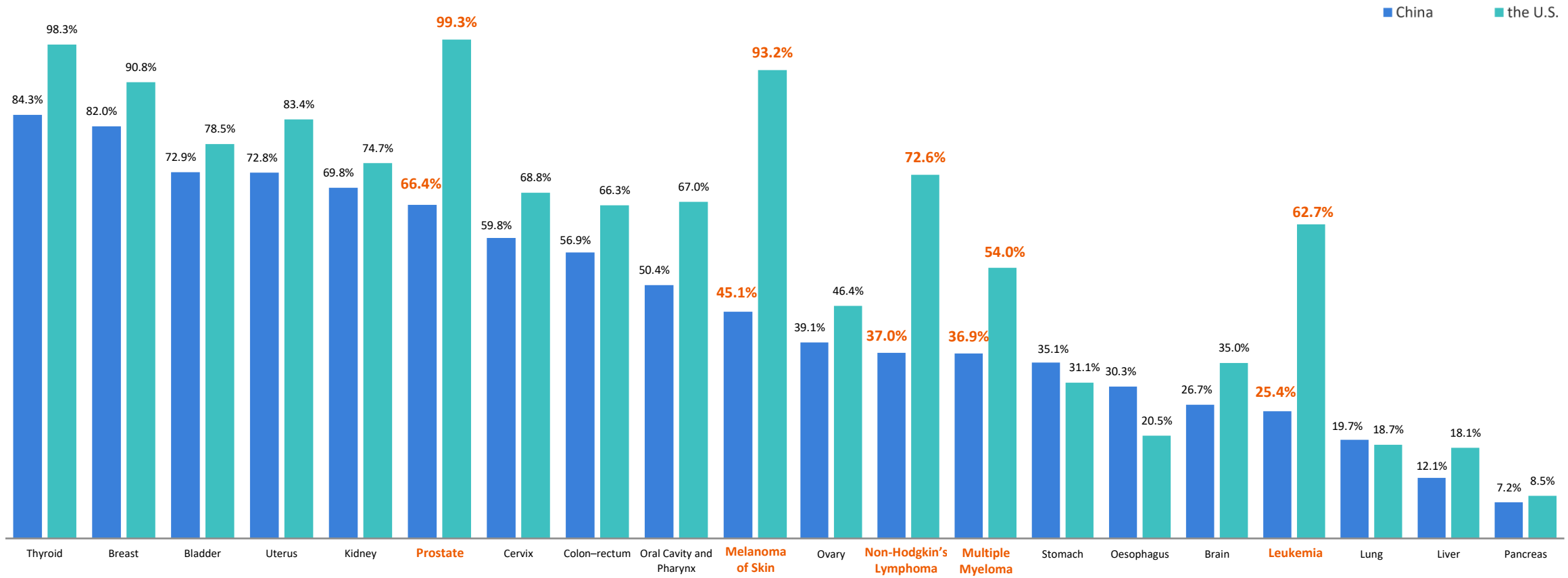
China's 5-year survival rate lags substantially behind the U.S. in prostate cancer, melanoma, non-Hodgkin's lymphoma, and leukemia

5-year Survival Rate of Cancers in China and the U.S.



Source: Globalcan, ACS, NCCR, Frost & Sullivan analysis

China Has Become a Major Contributor to Oncology Drug Development and Approval

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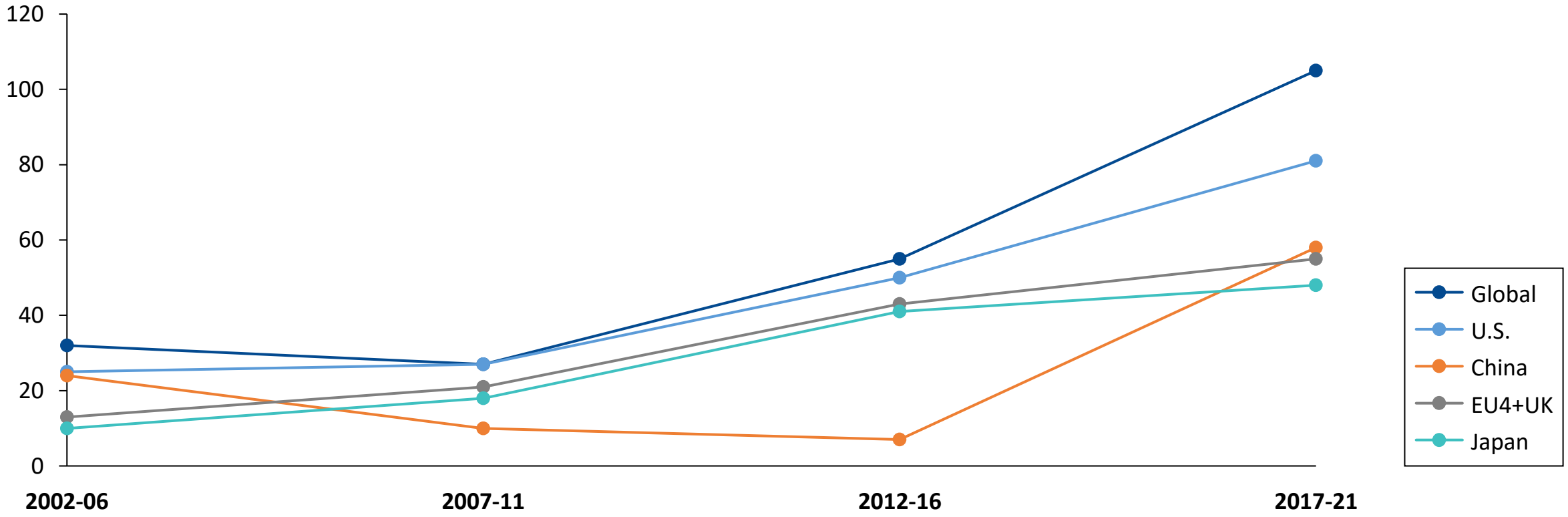
The number of novel oncology drugs from China that were launched in the last 5 years is second only to the United States

Number of Oncology Novel Drugs Launched Globally and in Selected Countries



Source: IQVIA

Global Oncology Drug Market is Outgrowing Other Therapeutic Areas

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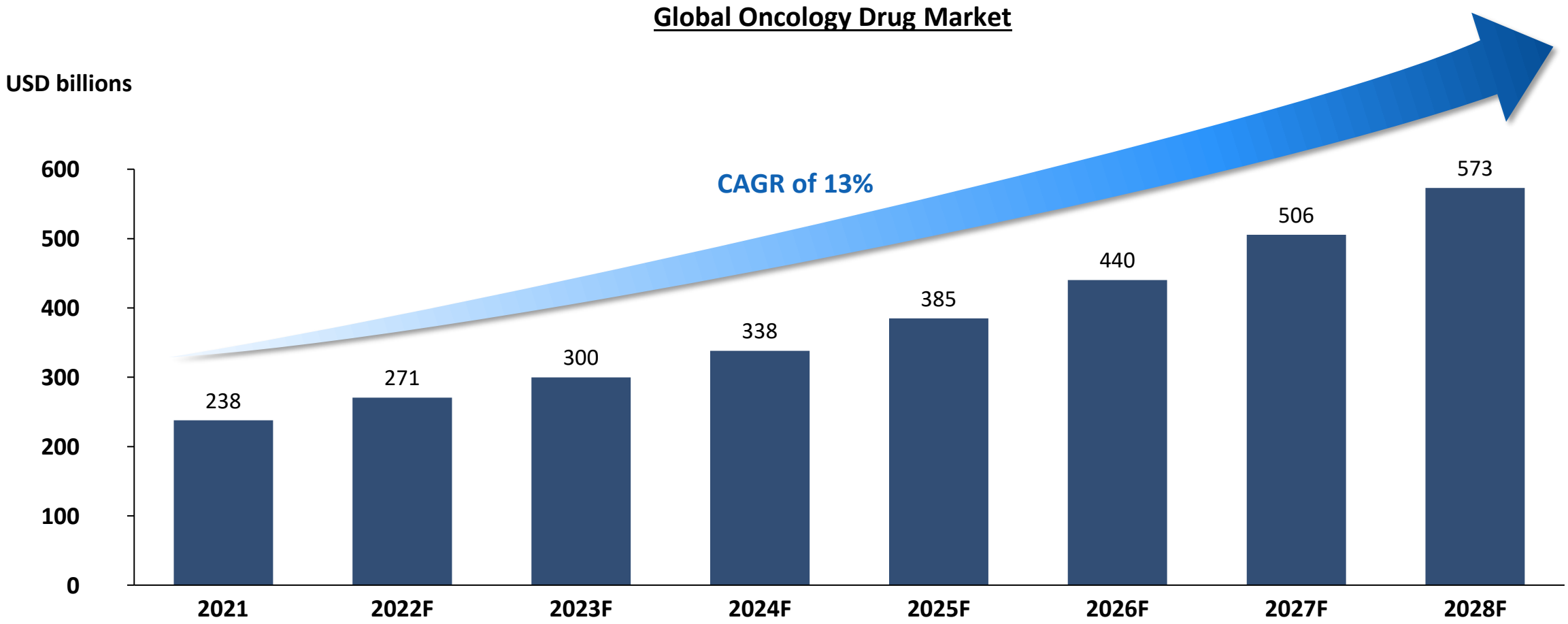
- Global oncology market size is over **$200 billion** and is expected to grow with a **CAGR of 13%**
  - The growth will be supported by continuous efforts in oncology drug R&D, increasing healthcare related spending, and drug accessibility
- Global oncology market is shifted more towards immunotherapy drugs, followed by targeted drugs in terms of size in the future



Source: GlobalData

Use of Immune Checkpoint Inhibitors Continues to Grow Dramatically in Most Geographies and Has Become a Standard of Care in Many Indications

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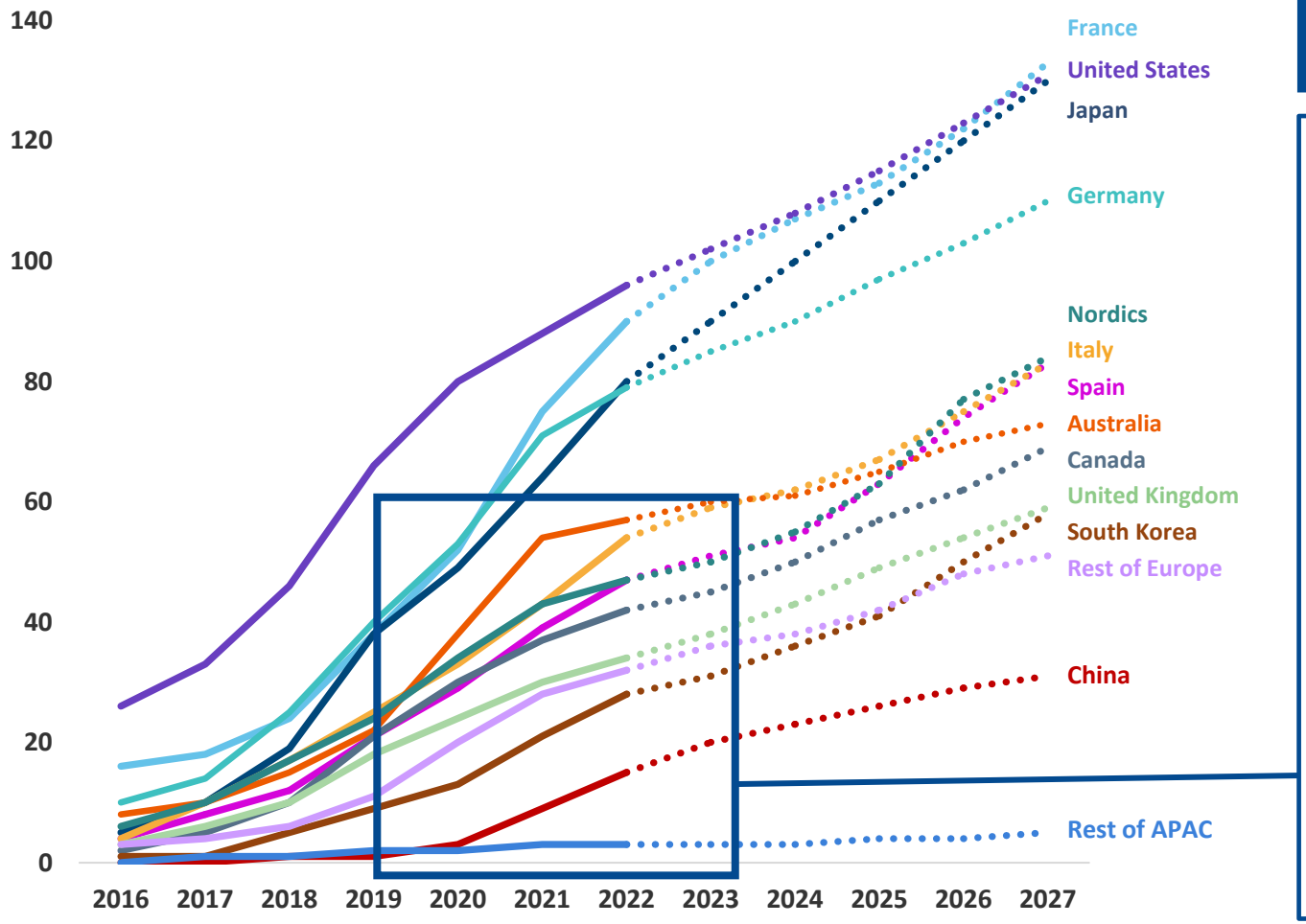
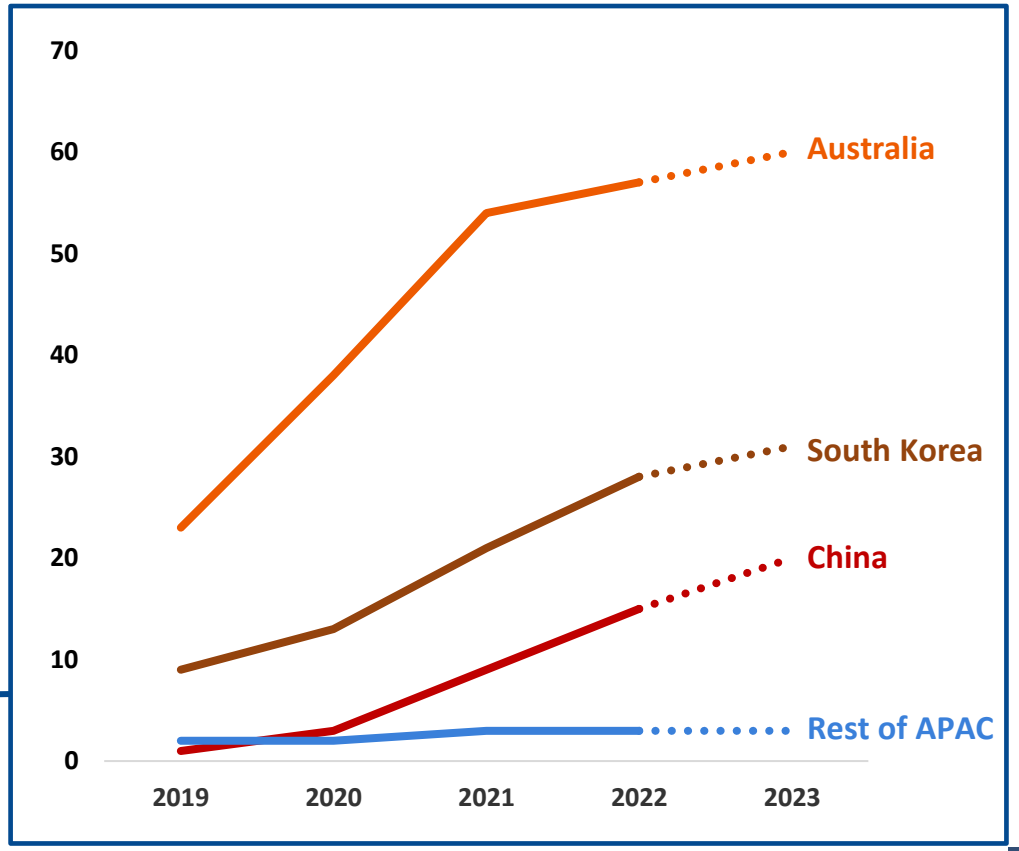
The global immuno-oncology checkpoint inhibitor markets has been growing rapidly



China and APAC (excl. Japan) use of checkpoint inhibitors continues to grow rapidly



Dotted lines are forecasts

Source: IQVIA, World Bank Population Estimates

Global Oncology Drug Market will be Dominated by I/O and Targeted Therapies

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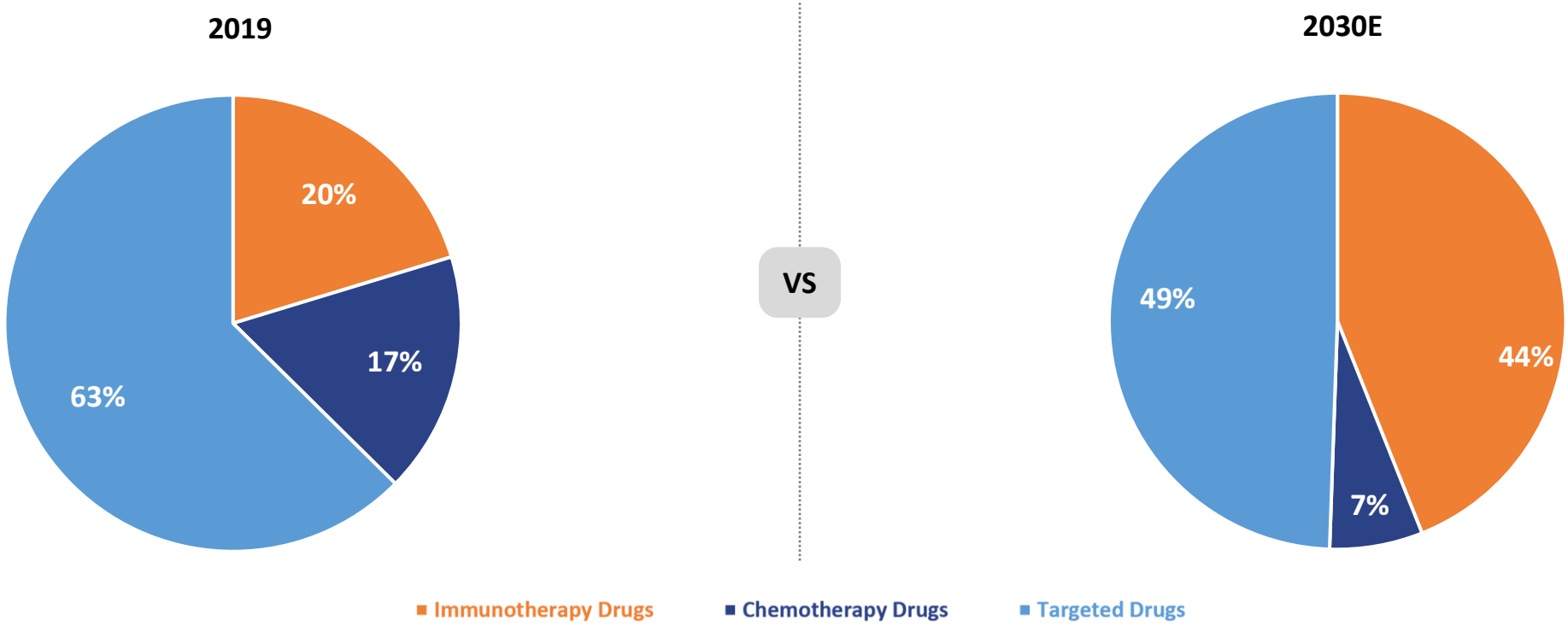
- Oncology is at the vanguard of precision medicine: more than 160 oncology biomarkers were approved in 2019, and more than 90% of pivotal trials are against molecular targets*
- Companies transforming oncology treatment will be those with a portfolio embracing novel targeted and immuno-oncology therapies

Breakdown of Global Oncology Drug Market**



* Table of pharmacogenomic biomarkers in drug labelling, Food and Drug Administration, updated December 2019, fda.gov
** Based on sales revenue

Source: Frost & Sullivan analysis

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

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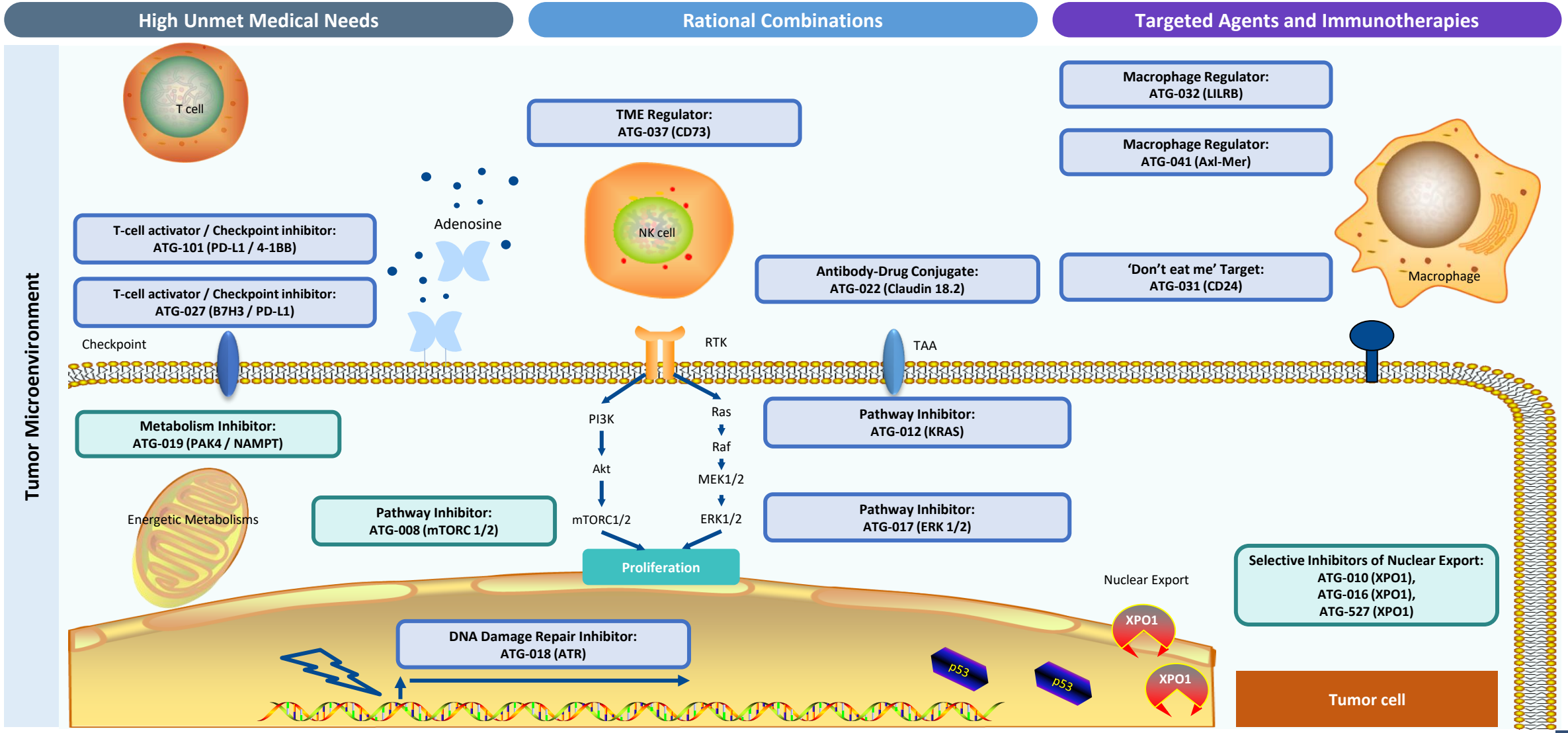

Assets with Global rights

Assets with APAC rights

Which Malignant Diseases Remain a Focus for Antengene?

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High Unmet Medical Needs

Non-small Cell Lung Cancer

ATG-008 (mTORC1/2)	ATG-017 (ERK1/2)
ATG-101 (PD-L1/4-1BB)	ATG-037 (CD73)
ATG-018 (ATR)	ATG-031 (CD24)

Pancreatic Cancer

ATG-017 (ERK1/2)	ATG-101 (PD-L1/4-1BB)
ATG-018 (ATR)	ATG-022 (Claudin 18.2)

Gastroesophageal Cancer

ATG-101 (PD-L1/4-1BB)	ATG-037 (CD73)
ATG-022 (Claudin 18.2)	

Gynecologic Cancers

ATG-008 (mTORC1/2)	ATG-101 (PD-L1/4-1BB)

Non-Hodgkin Lymphoma

ATG-010 (XPO1)	ATG-101 (PD-L1/4-1BB)

Myelodysplastic Syndromes

ATG-016 (XPO1)

Opportunity in China/APAC

Hepatocellular Carcinoma

ATG-008 (mTORC1/2)

Nasopharyngeal Carcinoma

ATG-008 (mTORC1/2)	ATG-101 (PD-L1/4-1BB)

Head and Neck Squamous Cell Carcinoma

ATG-101 (PD-L1/4-1BB)	ATG-037 (CD73)

Upper Gastrointestinal Cancers

ATG-101 (PD-L1/4-1BB)	ATG-037 (CD73)
ATG-022 (Claudin 18.2)	

Melanoma

ATG-017 (ERK1/2)	ATG-101 (PD-L1/4-1BB)

Extranodal NK/T cell Lymphoma

ATG-010 (XPO1)

Strong Biological Rationale

Targeting Specific Mutations

ATG-008 (mTORC1/2)	ATG-016 (XPO1)
ATG-017 (ERK1/2)	ATG-018 (ATR)
ATG-022 (Claudin 18.2)	

Multiple Myeloma

ATG-010 (XPO1)	ATG-037 (CD73)

Myelofibrosis

ATG-010 (XPO1)

“Don’t Eat Me” Signaling

ATG-031 (CD24)

Critical Questions That Inform Antengene Drug Discovery and Development Strategies

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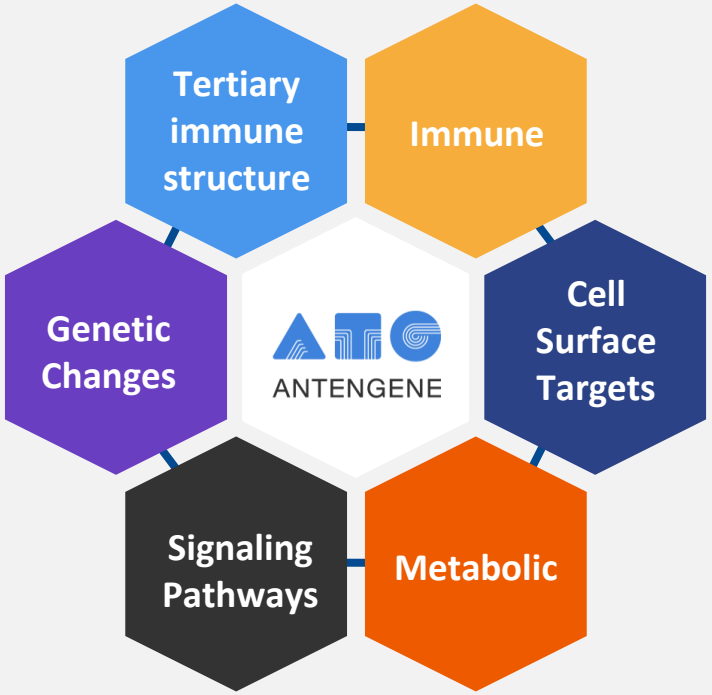
Huge potential for portfolio synergies and efficiencies via rational in-house drug combinations

- **How can we regulate the tertiary structure of the immune microenvironment?**
- **What genetic changes drive resistance?**
- **What signaling pathways are activated and targetable?**



- **How do cancer cells hide from the immune system?**
- **Are there additional immune regulators that can be modulated?**
- **What cell surface targets drive cancer invasion and metastasis?**
- **Are there critical metabolic changes that contribute to immunosuppression?**

- These are questions that **we cannot answer alone**
- It is a critical part of our development philosophy that we **build and extend existing relationships with key institutions and investigators worldwide**
- We are establishing **multi-disciplinary partnerships** with these institutions, including collaborations across **preclinical, clinical and translational research** disciplines

Factors Leading to Treatment Resistance

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Drug Resistance

Metabolic Changes

- Immunosuppressive metabolic environment
- Suppression of glycolytic capacity
- Metabolic switch to pro-survival

Genetic Alterations

- Signaling pathway activation
- Additional mutations
- Epigenetic silencing

Tumor Microenvironment

- ‘Cold’ or ‘Hot’
- Tertiary structure changes

Immune Down-regulation

- T-cell exhaustion
- Immune cell changes (e.g. TAMs, “don’t eat me”)
- Alternate immune CP activation
- Inhibitory cytokines

Antengene Drugs Targeting Each Factor Driving Resistance

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Drug Resistance

Metabolic Changes

- Immunosuppressive metabolic environment
- Suppression of glycolytic capacity
- Metabolic switch to pro-survival

ATG-037 (CD73)
ATG-019 (PAK4/NAMPT)
ATG-008 (mTOR1/2)

Genetic Alterations

- Signaling pathway activation
- Additional mutations
- Epigenetic silencing

ATG-017 (ERK1/2) **ATG-012** (KRAS)
ATG-008 (mTORC1/2) **ATG-018** (ATR)
ATG-022 (CLDN18.2) **ATG-010** (XPO1)
ATG-016 (XPO1)

Tumor Microenvironment

- 'Cold' or 'Hot'
- Tertiary structure changes

Immune Down-regulation

- T-cell exhaustion
- Immune cell changes (e.g. TAMs, "don't eat me")
- Alternate immune CP activation
- Inhibitory cytokines

ATG-101 (PD-L1/4-1BB)
ATG-027 (B7H3/PD-L1)
ATG-031 (CD24)
ATG-032 (LILRB)
ATG-041 (Alx-Mer)

Exploring Rational Combinations with Immuno-oncology Therapies

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Combinations may offer the greatest chance of success in the next advances in cancer treatments

Cancer treatment regimens with direct or indirect immune-mediated effects

Conventional Cytotoxics

Induce lymphodepletion-associated bystander immune stimulation

Pathway Inhibitors

Reverse suppressive environmental signaling

Metabolic Controllers

Turn off metabolic drive, reverse immunosuppression

Immuno-oncology Drugs

Utilize both “break” and “accelerator”

ADCs, mAbs, Oncolytic Viruses

Cancer cell disruption, make a ‘cold’ tumor ‘hot’

ATG-017 (ERK1/2 Small Molecule Inhibitor)

ATG-037 (CD73 Small Molecule Inhibitor)

ATG-022 (Claudin 18.2 Antibody-drug Conjugate)

ATG-101 (PD-L1/4-1BB Bispecific Antibody)

ATG-018 (ATR Small Molecule Inhibitor)

ATG-031 (CD24 Monoclonal Antibody)

Highlighting Our First-in-Human Portfolio

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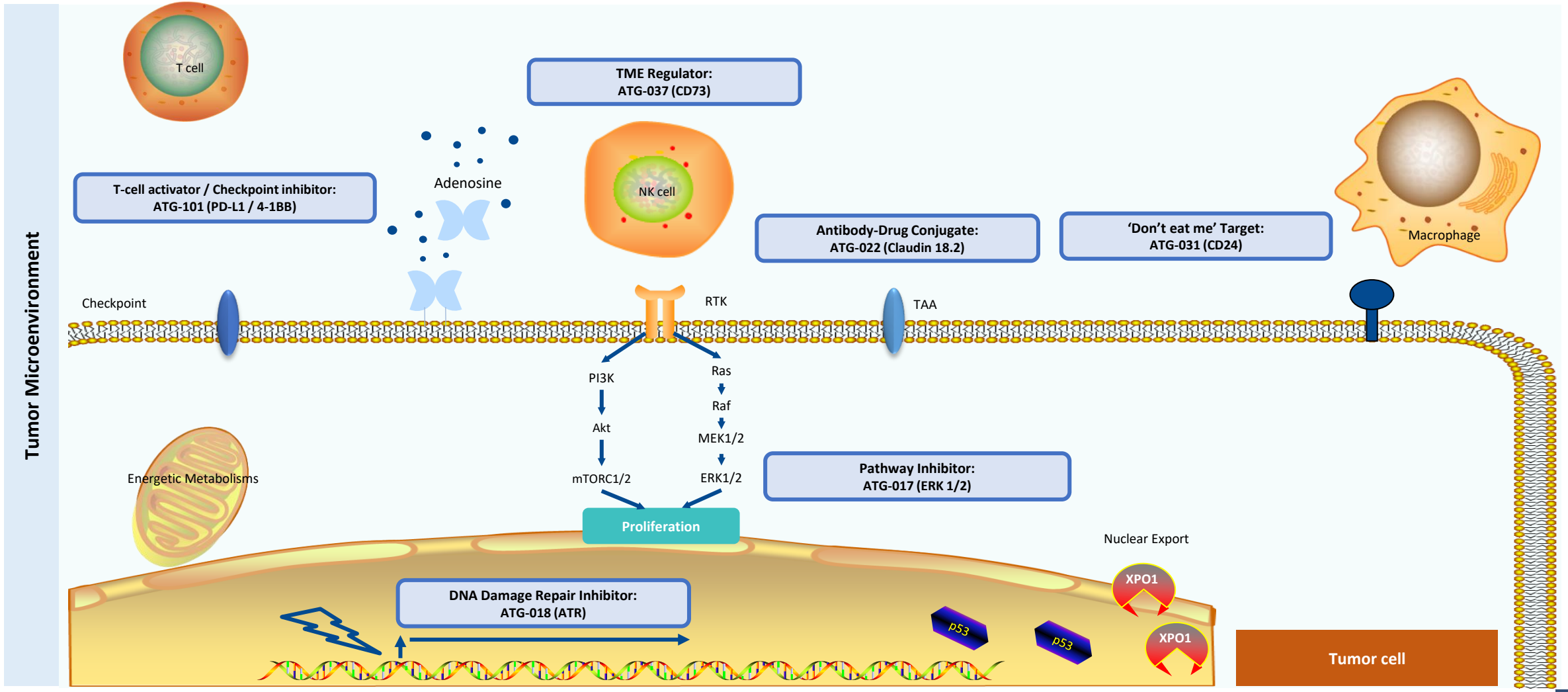
High Unmet Medical Needs | **Rational Combinations** | **Targeted Agents and Immunotherapies**



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

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	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	■ RASm NSCLC, Pancreatic cancer, CRC, and Melanoma ■ I/O combinations	■ Re-sensitize prior CPI responders (NSCLC, SCLC, GI, H/N SCC, melanoma) ■ Disease with previously limited CPI activity ■ Multiple combination opportunities	■ Monotherapy where immune suppressed TME is critical ■ Broad opportunities both as monotherapy and combination with existing / future I/O	Hematological Malignancies / Solid Tumors	Solid Tumors	Hematological Malignancies / Solid Tumors
Differentiation	✓ **Higher potency** and dual IoC and PoA activity with slow off-rate kinetics ✓ Lower efficacious dose with a higher max absorbable dose/dose ratio ✓ **Broad therapeutic potential** (targeting RAS/MAPK pathway) ✓ Multiple **combination** opportunities	✓ PD-L1 cross-linking dependent activation of 4-1BB to avoid unwanted 4-1BB signaling in normal tissue and minimize risk of hepatotoxicity ✓ Demonstrated significant anti-tumor activity in animal models of **resistant tumors as well as those that progressed on anti-PD-1/L1 treatment** ✓ Displayed an **excellent safety profile** in GLP toxicology studies	✓ Orally bioavailable small molecule that completely **overcomes 'hook effect'** common in other anti-CD73 antibodies ✓ **Tissue penetrance not achievable with mAbs** ✓ Promising preclinical efficacy as a monotherapy and strong combination potential	✓ Better **in vivo efficacy** compared with benchmark in pre-clinical CDX tumor models ✓ Orally available	✓ **High affinity antibody (pM)**; Strong in vivo efficacy pre-clinically in Claudin 18.2 low expression PDX models ✓ Demonstrated an excellent safety profile in GLP toxicology studies	✓ **First in class target** ✓ No clinical competitor ✓ Showed **mono-therapy in vivo efficacy and synergy** with chemotherapy, rituximab and CPI
Status	Currently in the 6th cohort in solid tumors of "ERASER" trial, dosing in BID; combo with nivolumab planned for late 2022	Phase 1 clinical trial "PROBE" ongoing in Australia (4th cohort), first patient to be dosed in the US; "PROBE-CN" ongoing in China (3rd cohort)	Phase 1 clinical trial "STAMINA" ongoing in Australia, currently in 2nd cohort	Phase 1 clinical trial "ATRIUM" ongoing in Australia, currently enrolling for the 3rd cohort	EC submitted in October 2022	IND planned for H1 2023

ATG-017 May Enhance the Activity of Checkpoint Inhibitors or Reverse Resistance Mechanisms

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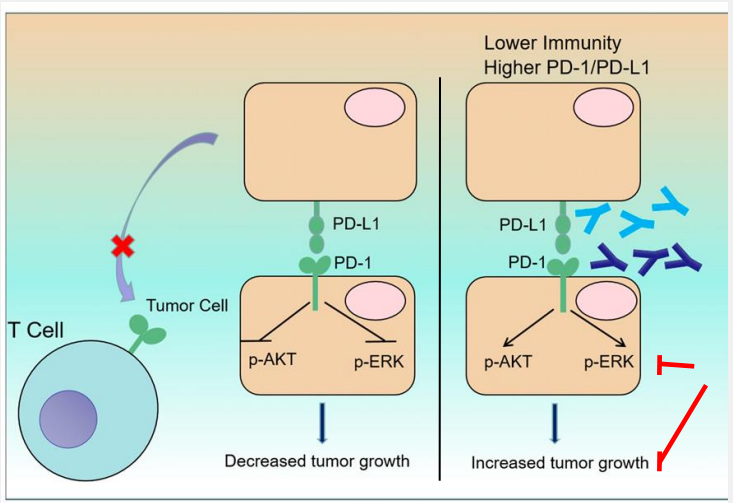
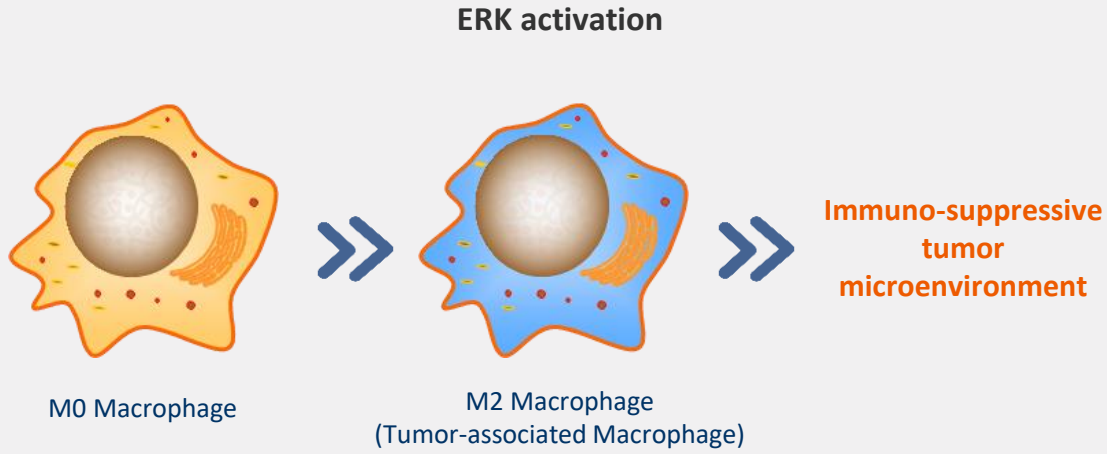
Through inhibiting ERK1/2 activity, ATG-017 may enhance the activity of checkpoint inhibitors or reverse resistance mechanisms

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

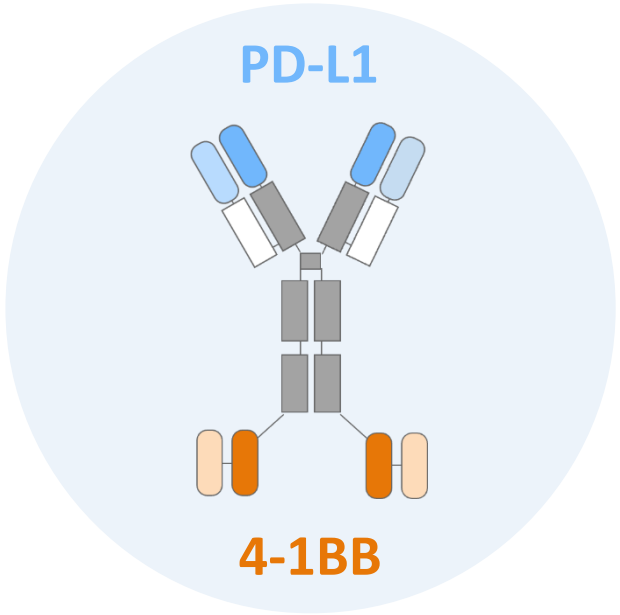
Enrollment ongoing in Australia (cohort 6)

Source: Cheng et al., 2018; Lailler et al., 2019; Mu et al., 2018; Wang et al., 2020

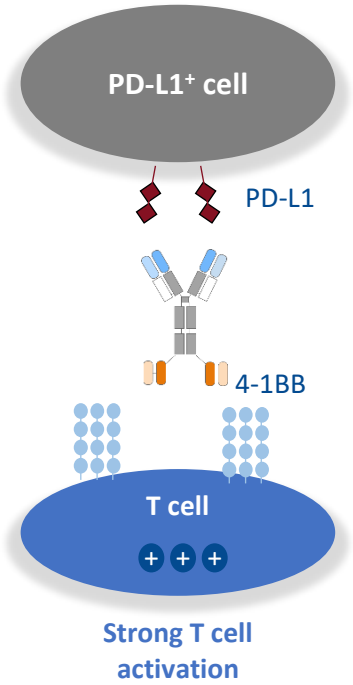
ATG-101 Has the Potential to Optimize PD-L1 Antagonism and Tumor-specific 4-1BB Agonism

ANTENGENE

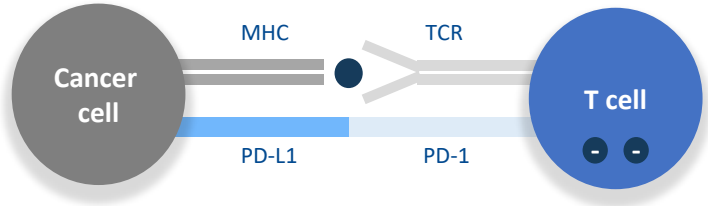
- Efficacy of PD-1/PD-L1 targeting is **well-demonstrated over the past decade**
- 4-1BB is a T cell co-stimulatory receptor, **the benefits of which have yet to be realized in the clinic**
- The concept of PD-L1×4-1BB bispecific antibody like ATG-101 has demonstrated **promising activity in early clinical 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**[1]



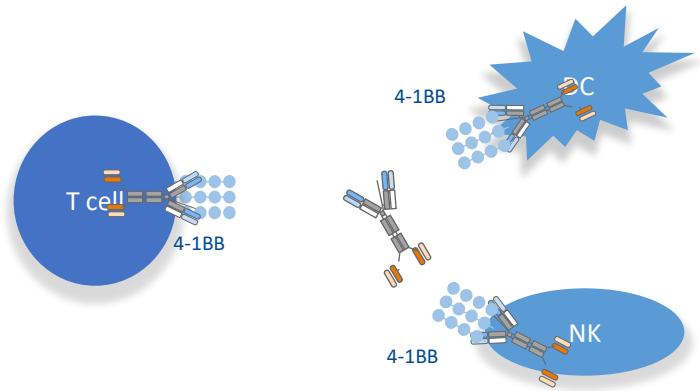
Complementary Mechanism of PD-L1/4-1BB



"Releasing the Brakes"



"Stepping on the Accelerator"

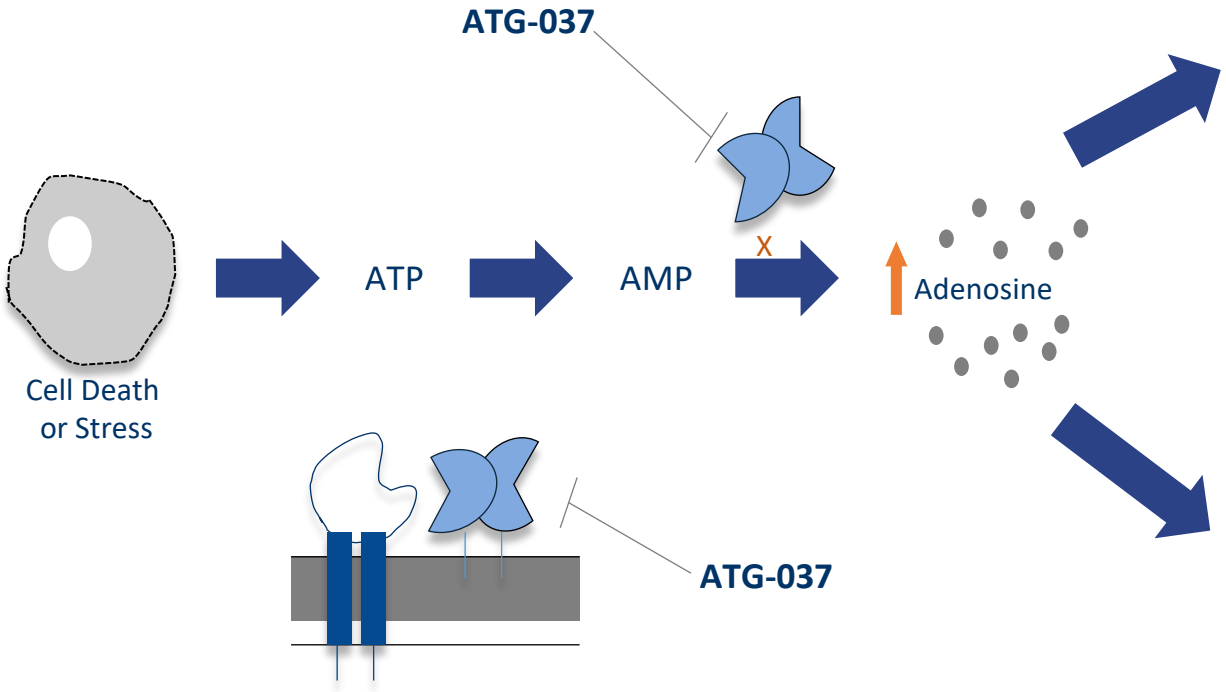


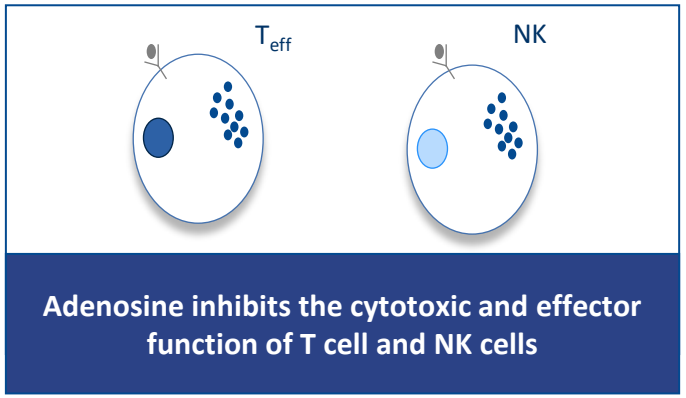
Enrollment ongoing in Australia (cohort 4) and China (cohort 3)

Source: 1. Prof Andrew Scott, ONJCRI, 2022

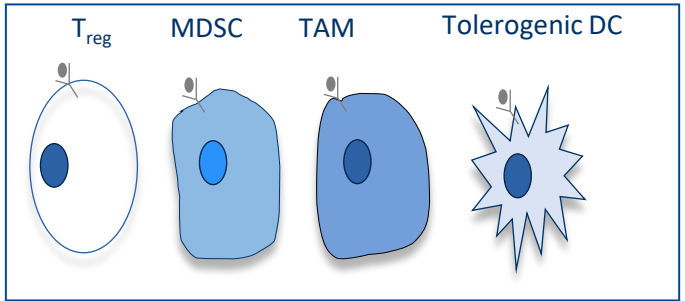
ATG-037 Can Reverse Adenosine-Mediated Immunosuppression

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



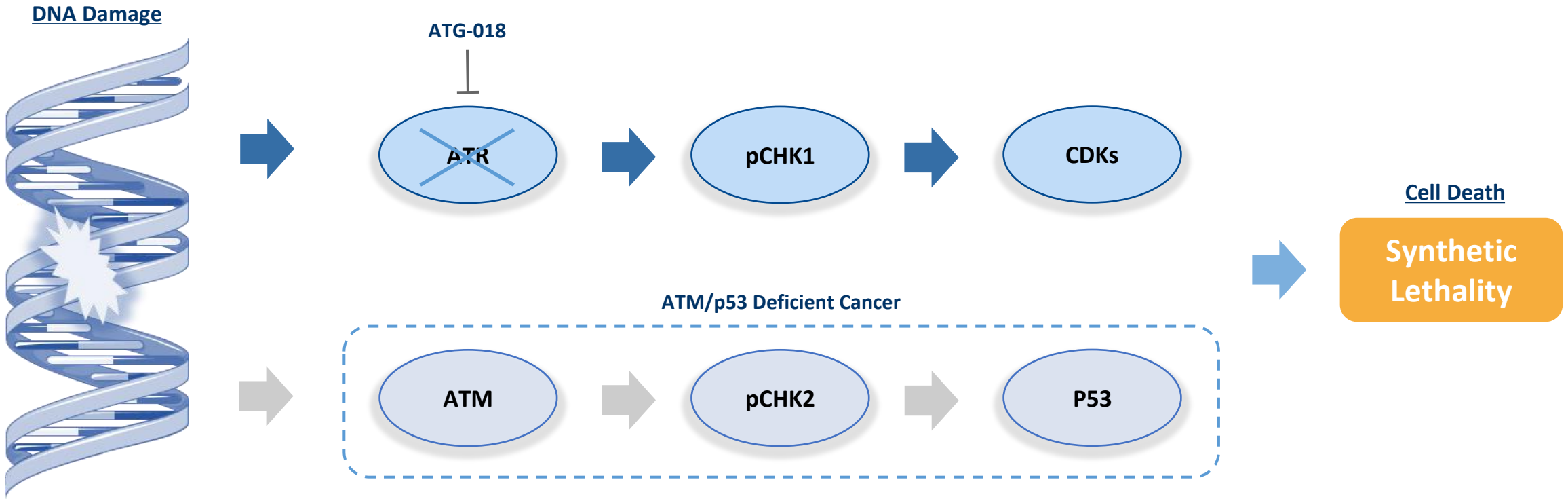
Adenosine induces immunosuppressive cell types and enhances their function

First patient enrollment in Australia – June 2022

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

ANTENGENE

- 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

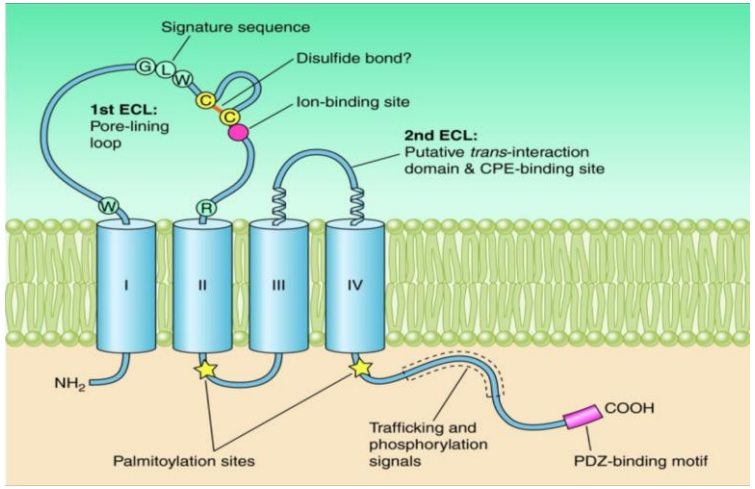


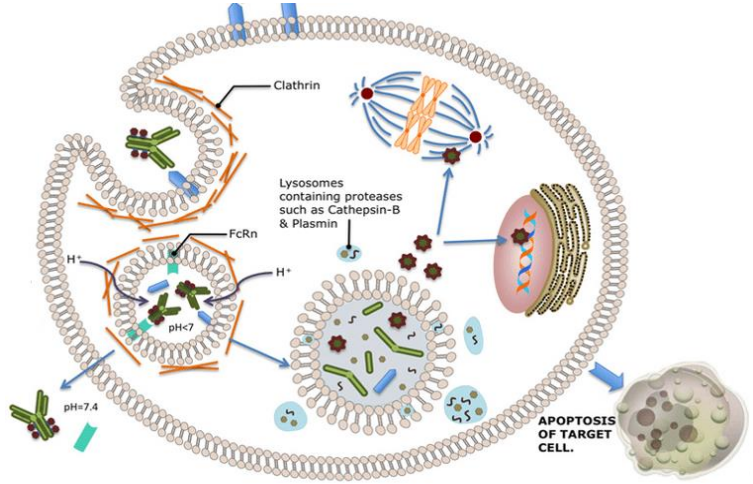
Enrollment to cohort 2 complete and starting cohort 3

ATM: ataxia–telangiectasia mutated; CDKs: cyclin-dependent kinases; pCHK1: phosphor-checkpoint kinase 1; pCHK2: phosphor-checkpoint kinase 2.

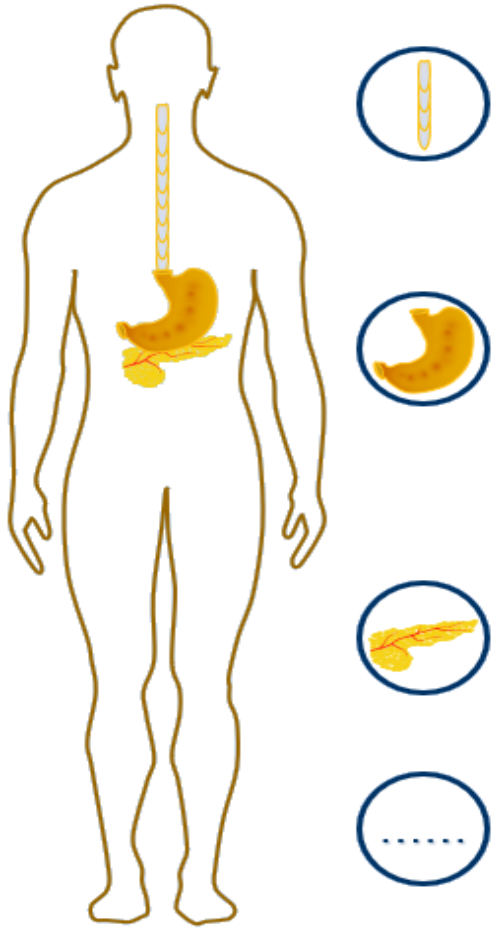
ATG-022 is a High Affinity Anti-Claudin 18.2 ADC with Potential Activity Even in Tumors with Very Low Level Expression of the Target

ANTENGENE





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
- Expressed in **34%** of metastatic lesions

Other Tumors

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

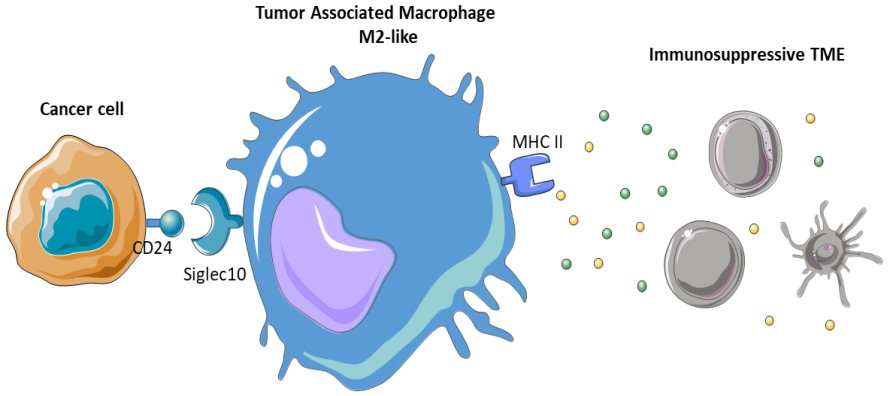
Australian HREC submission completed in October 2022

Source: Gunzel & Yu, 2013; Moentenich, 2020; Peters & Brown, 2015; Rohde, 2019; Türeci, 2019; Zhu, 2019

ATG-031 is a First-in-Class Anti-CD24 Monoclonal Antibody that should Enhance TAM-Mediated Phagocytosis and Represent a New Class of I/O Drug

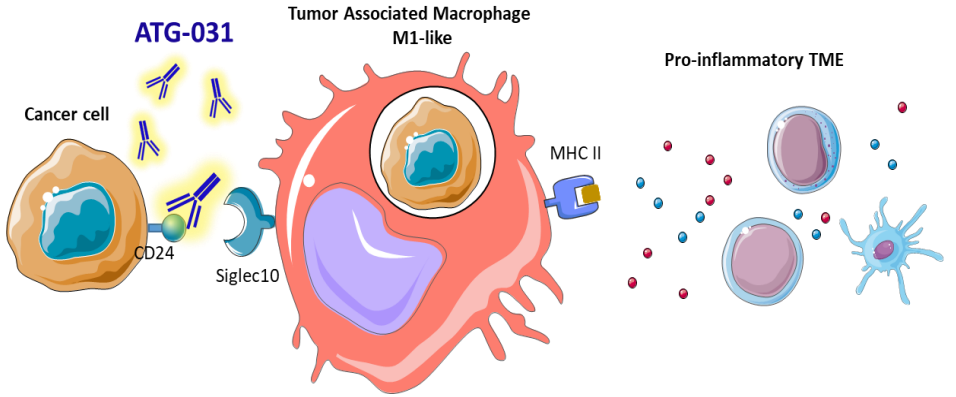
ANTENGENE

- CD24 is a **novel "don't eat me" target**, a **tumor-associated antigen** for multiple solid tumors and B cell malignancies, and a **marker for cancer stem cell**
- Blocking CD24 by ATG-031 **enhances macrophage-mediated phagocytosis of cancer cells**
- Potent **single agent** in vivo efficacy and **synergy with chemotherapy or CPI**



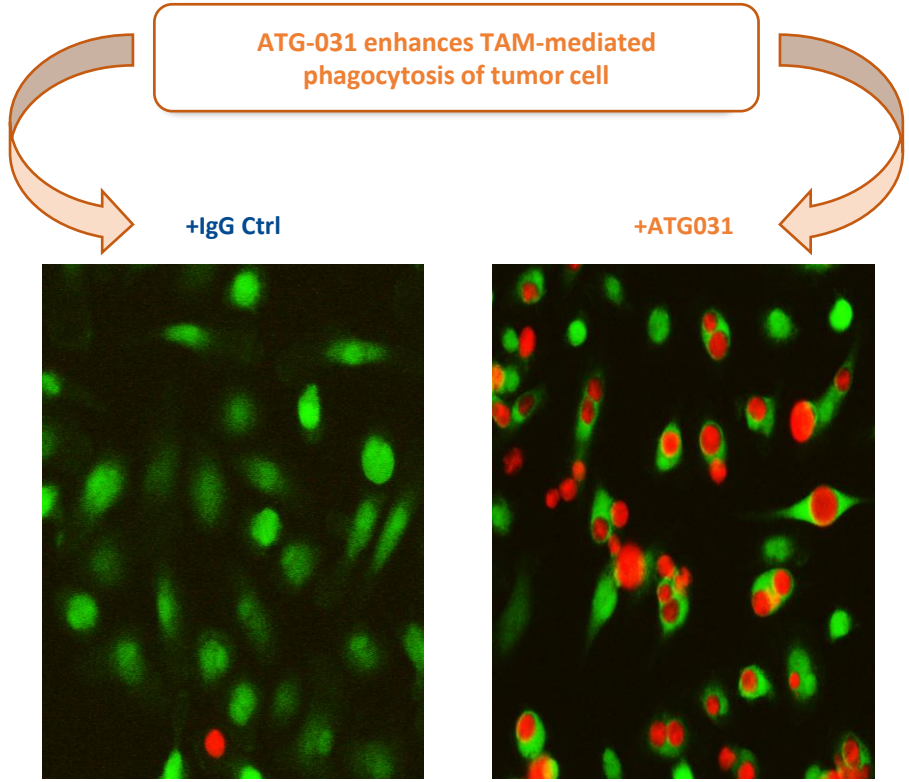
"Don't Eat Me"

- Reduced phagocytosis
- M2-like Tumor Associated Macrophage
- Immunosuppressive Tumor Microenvironment
- Less tumor antigen presentation
- In-activated T and NK cells



"Eat Me"

- Increased phagocytosis
- M1-like Tumor Associated Macrophage
- Pro-inflammatory Tumor Microenvironment
- Enhanced Tumor Antigen presentation
- Activated T and NK cells



Pipeline of Near-to-midterm Drug Candidates with First-in-class / Best-in-class Potential

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Assets	Target *(Modality)*	Indication	Pre-clinical / Phase I / Phase II / Phase III / NDA / Commercialization	Antengene Rights	Partner
ATG-010[1] (Selinexor)	XPO1 *(Small molecule)*	R/R Multiple Myeloma	Combo with dexamethasone *(MARCH)* — *Mainland China NDA approved*	APAC[2]	Karyopharm Therapeutics; ANTENGENE
			Combo with dexamethasone *(STORM) – Partner's Pivotal Trial in the US* — *US, EU, SK, SG, AU & TW NDA approved*		
			Combo with bortezomib and dexamethasone *(BENCH)* ★		
			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 mAb and dexamethasone *(STOMP)*		
		R/R Diffuse Large B-cell Lymphoma	Monotherapy *(SEARCH)* ★		
			Monotherapy *(SADAL) – Partner's Pivotal Trial in the US* — *US , SG, SK & TW sNDA approved*		
			Combo with R-GDP *(DLBCL-030)* ★		
		R/R NHL	Combo with lenalidomide + rituximab *(SWATCH)*		
		R/R T-cell & NK-cell Lymphoma	Combo with ICE/GemOx/tislelizumab *(TOUCH)* with BeiGene		
		Myelofibrosis	Monotherapy *(MF 035)* ★		
ATG-016 (Eltanexor)	XPO1 *(Small molecule)*	R/R MDS	Monotherapy *(HATCH)*		
			Monotherapy *(KCP-8602-801)*		
ATG-008 (Onatasertib)	mTORC1/2 *(Small molecule)*	2L+ HBV+ Hepatocellular Carcinoma	Monotherapy *(TORCH)*	APAC[3]	Celgene; Bristol Myers Squibb Company; ANTENGENE
		Cervical Cancer and Other Advanced Solid Tumors	*Combo with toripalimab (TORCH-2)** with 君实生物 TopAlliance		
		R/R Diffuse Large B-cell Lymphoma	Combo with ATG-010 *(MATCH)*		

Antengene Trials[4] | Partner Trials[5] | Global Trials in Collaboration with Partner | ★ Registrational Trial in China

[1] (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;
[2] Antengene has rights for Greater China (Mainland China China, Hong Kong, Taiwan, Macau), Australia, New Zealand, South Korea, and the ASEAN Countries;
[3] Antengene has rights for Greater China, South Korea, Singapore, Malaysia, Indonesia, Vietnam, Laos, Cambodia, the Philippines, Thailand and Mongolia;
[4] Most advanced trial status in Antengene territories and the trials are responsible by Antengene;
[5] Most advanced trial status in partner territories in the rest of the world and the trials are conducted by our licensing partners

* Investigator-initiated trials; R/R: relapsed/refractory; ND: newly diagnosed; MDS: 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 &Cisplatin;

AU: Australia; EU: Europe; SG: Singapore; SK: South Korea; TW: Taiwan; US: United States;

An Early-stage In-house Pipeline with Transformational Potential

ANTENGENE

	Assets	Target (Modality)	Hits Discovery	Lead Nomination	In vitro efficacy	In vivo efficacy	CMC/Tox	IND	Phase I	Antengene Rights	Partner
Clinical/IND Stage	ATG-017 (Tizaterkib)[1]	ERK1/2 (Small molecule)	Monotherapy ± nivolumab for R/R Hem/Onc *(ERASER)*						with Bristol Myers Squibb	Global	ANTENGENE
	ATG-101[2]	PD-L1/4-1BB (Bispecific)	Monotherapy for Hem/Onc *(PROBE & PROBE-CN)*								
	ATG-037[3]	CD73 (Small molecule)	Monotherapy ± IO for Hem/Onc *(STAMINA)*								
	ATG-018	ATR (Small molecule)	Monotherapy for Hem/Onc *(ATRIUM)*								
	ATG-022	Claudin 18.2 (ADC)	Monotherapy for Onc *(CLINCH)*								
	ATG-031	CD24 (mAb)	Monotherapy for Hem/Onc				*IND submission 2023*				
Discovery Stage	ATG-012	KRAS (Small molecule)	Monotherapy for Onc								
	ATG-027	B7H3/PD-L1 (Bispecific)	Monotherapy for Hem/Onc								
	ATG-032	LILRB (mAb)	Monotherapy for Hem/Onc								
	ATG-041	Axl-Mer (Small molecule)	Monotherapy for Hem/Onc								

Antengene Trials

[1] *Licensed from AstraZeneca and Antengene has obtained exclusive global rights to develop, commercialize and manufacture ATG-017;*
[2] *Licensed from Origincell and Antengene has obtained exclusive global rights to develop, commercialize and manufacture ATG-101;*
[3] *Licensed from Calithera Biosciences and Antengene has obtained exclusive global rights to develop, commercialize and manufacture ATG-037*
** ATG-037 IND equivalent in Australia = institutional scientific and ethics review before governmental notification*
Hem/Onc = hematological malignancies and solid tumors

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LATER-PHASE CLINICAL PROGRAMS UPDATE

Overview of Clinical Portfolio

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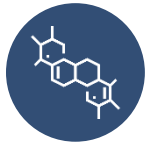
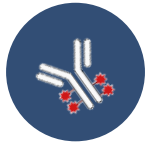
	Early Pipeline/First-in-Human	Phase Ib/Phase II	Pivotal/Phase III
 **Small Molecule Inhibitor**	• **ATG-017 (ERK1/2)** – ERASER • **ATG-018 (ATR)** – ATRIUM • **ATG-037 (CD73)** – STAMINA	• **ATG-010 (XPO1)** – XPORT-030, MATCH, SWATCH, TOUCH, MF-034 (planning) • **ATG-008 (mTORC1/2)** – TORCH, TORCH-2, MATCH	• **ATG-010 (XPO1)** – BENCH – SEARCH – XPORT-030 – MF-035
 **Monoclonal Antibody**	• **ATG-031 (CD24)** – IND planned for H1 2023	**TBD**	**TBD**
 **Bispecific Antibody**	• **ATG-101 (PD-L1/4-1BB)** – PROBE & PROBE-CN	**TBD**	**TBD**
 **Antibody-Drug Conjugate**	• **ATG-022 (Claudin 18.2)** – CLINCH	**TBD**	**TBD**

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mTORC1/2 INHIBITOR

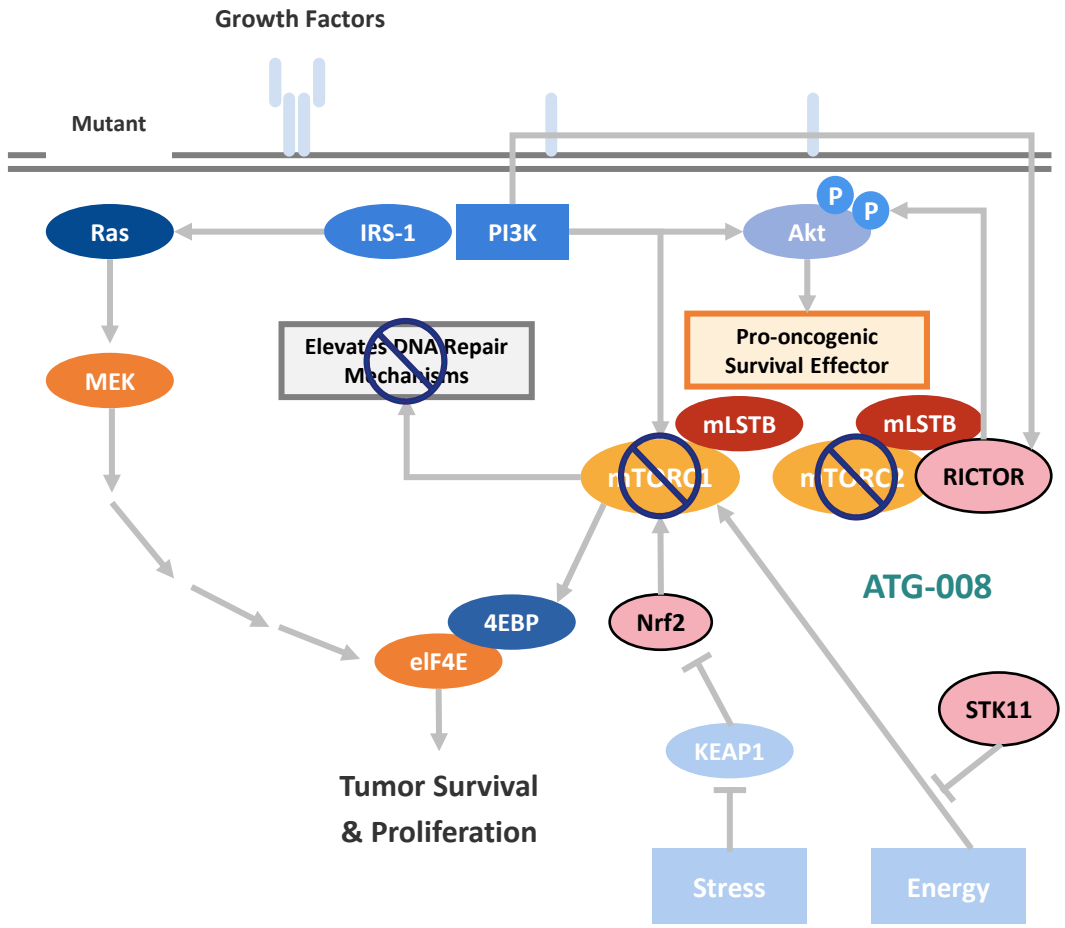
ATG-008 (Onatasertib): A Novel Second Generation mTORC1/2 Inhibitor

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**



Rationale for ATG-008 (Onatasertib) in Combination with Anti-PD-1/PD-L1 Regimen

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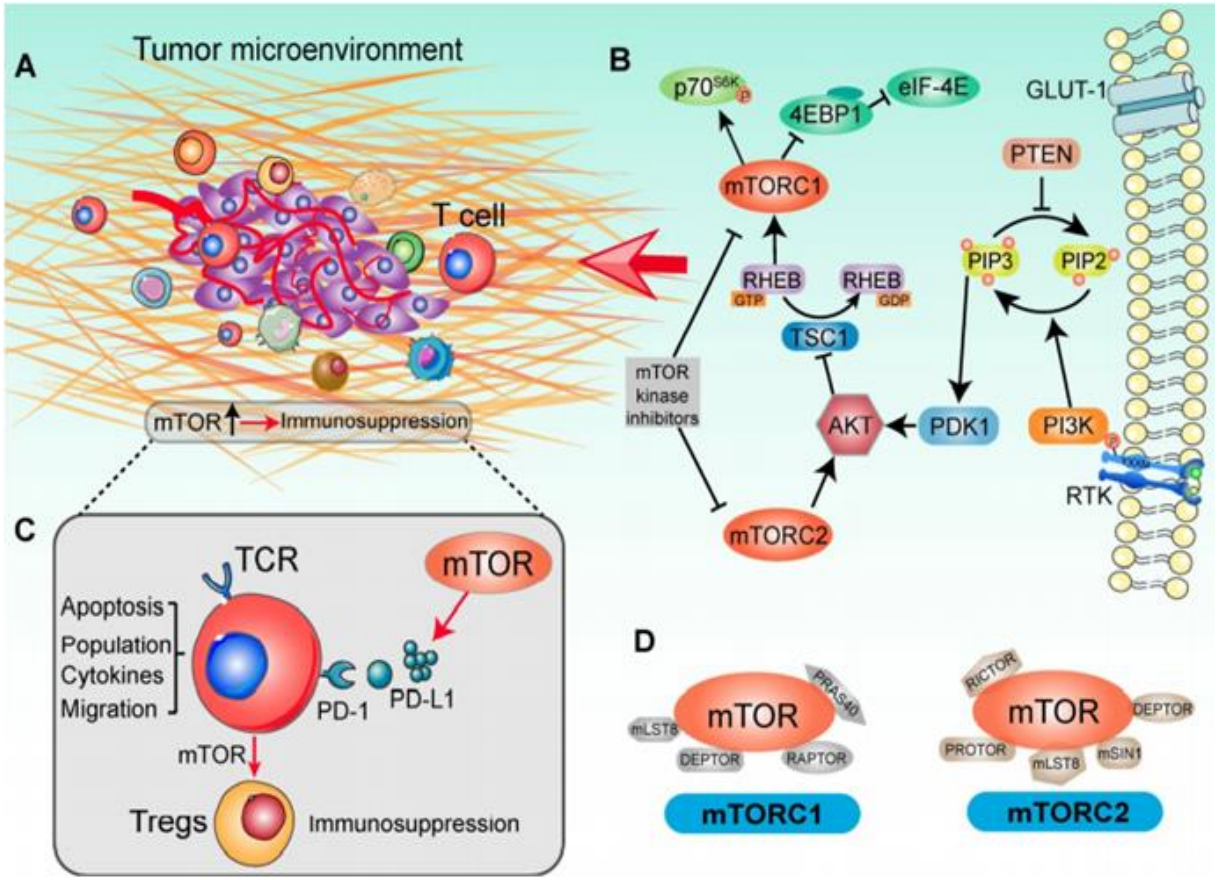
mTOR Signaling Pathway Plays Multiple Roles in Immune Cell Biology



mTORC 1 Inhibition

- Increases **effector responses**

mTORC 2 Inhibition

- Up-regulates **CD8+ T cell memory**

Blockade of PD-L1 with anti-PD-L1 mAb and Inhibiting mTOR

- Leads to the enhancement of **peripheral antigen-specific CD8+ Tumor-infiltrating lymphocytes (TILs) and/or NK cells,** thus supporting a more effective and durable control of tumors

Blockade of PD-1 with anti-PD-1 mAb and Inhibiting mTOR

- Generates **synergistic anti-tumor effects** across tumor models, including HCC, RCC, Oral SCC etc.

Source: Fabiana Conciatori et al, 2018; Kristen N et al, 2015; Ellen C. Moore et al, 2016

ATG-008 "TORCH-2" Clinical Trial Design

ANTENGENE

An Open-label, Phase I/II Dose-escalation and Expansion Study With a Dual TORC1/2 Inhibitor of ATG-008 (Onatasertib) Combined with PD-1 Antibody Toripalimab in Advanced Solid Tumors

Location: Mainland China

Key Eligibility Criteria:

- **Dose Escalation:**
  - Adv. R/R Solid tumors
  - Have not received prior immunotherapy (PD-1, PD-L1, CTLA-4. CAR-T), or mTOR/PI3K/AKT inhibitors
- **Dose Expansion:**
  - Solid tumors (incl. HCC, NET, adv. gynaecologic cancers, GBM)
  - At least 1 prior systemic therapy
  - Have not received prior mTOR/PI1K/AKT inhibitors

Phase I

Dose Escalation

ATG-008 (Onatasertib) + Toripalimab *(21-day cycle)*

Starting dose level
Onatasertib: 15 mg PO once daily
Toripalimab: 240 mg IV inf every 3 weeks

"3+3" dose escalation

Until disease progression or unacceptable toxicity (Max. 2 years therapy with Toripalimab; Onatasertib monotherapy beyond 2 years)

MTD, RP2D

Phase II

Dose Expansion

ATG-008 (Onatasertib) + Toripalimab *(21-day cycle)*

Onatasertib: RP2D PO once daily
Toripalimab: 240 mg IV inf every 3 weeks

5 cohorts (~10-12 patients each):

i. Adv. HCC
ii. NET
iii. Adv. Gynaecologic tumors
iv. Adv. Solid tumors
v. GBM

Until disease progression or unacceptable toxicity (Max. 2 years therapy with Toripalimab; Onatasertib monotherapy beyond 2 years)

Primary endpoint:
Dose escalation: MTD, RP2D
Dose expansion: ORR

Secondary endpoints:
Dose escalation: PK, ORR
Dose expansion: DOR, DCR, PFS, OS, incidence of ADA

ATG-008-HX-001
Sponsor: West China Hospital (IIT)

ADA: anti-drug antibody; Adv.: Advanced; GBM: glioblastoma multiforme; HCC: hepatocellular carcinoma; IV inf: intravenous infusion; MTD: maximum tolerated dose; NET: neuroendocrine tumour; ORR: overall response rate; PK: pharmacokinetics; PO: oral; RP2D: recommended phase 2 dose; R/R : relapsed or refractory;

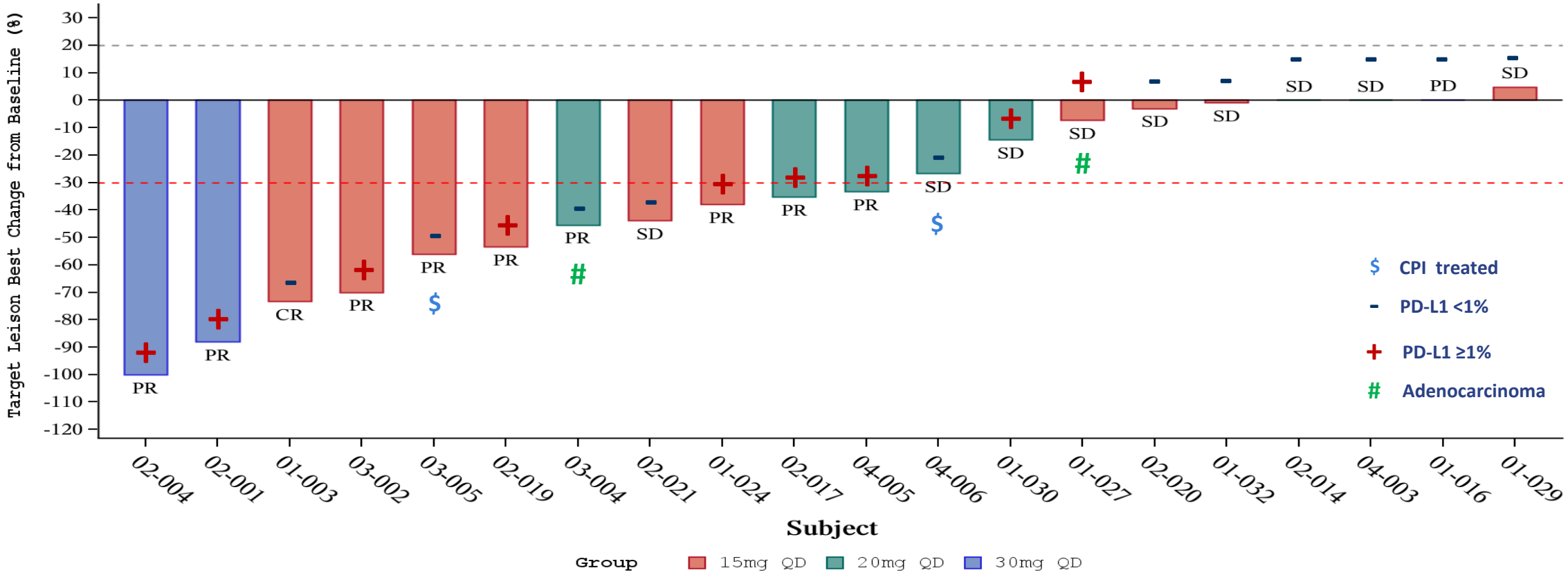
Cervical Cancer Population – "TORCH-2" Target Lesion Waterfall Plot

Deep Responses were Observed Regardless of PD-L1 Status

ANTENGENE

Preliminary Efficacy (as of October 21st, 2022)

- **21 patients** received treatment
- **ORR is 52.4%** (ITT,11/21)
  - **Efficacy Evaluable Population: ORR 55%** (11/20)
  - **PD-L1+ Population: ORR 77.8%** (7/9)

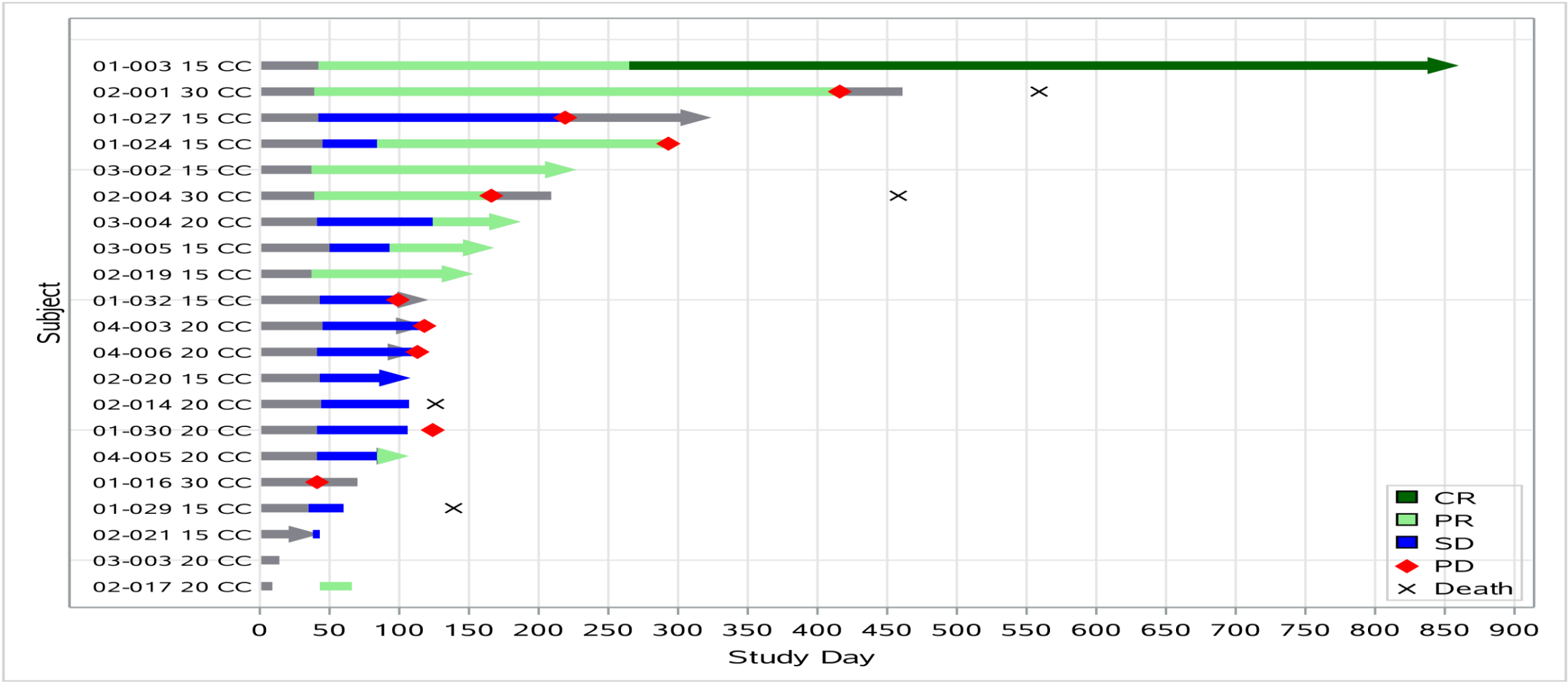


Cervical Cancer Population – "TORCH-2" Swimmer Plot

ATG-008 & Toripalimab Combination Resulted in Durable Responses

ANTENGENE

- The Median Duration of Response (mDOR) is **9.7 months**
- The Longest Treatment Duration is **850 days (Ongoing CR)** of Patient 01-003, Currently on ATG-008 Single Agent Treatment



Cervical Cancer Population – "TORCH-2" Summary of Adverse Events

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Preliminary Results (as of October 21st, 2022)

- The most common grade ≥ 3 TEAEs included:
  - **Lymphocyte count decreased (19.0%)**
  - **Rash (14.3%)**
  - **Hyperglycemia (9.5%)**

Data Cut-off Date: 21st October, 2022	15 mg QD (N=10) n (%)	20 mg QD (N=8) n (%)	30 mg QD (N=3) n (%)	Total (N=21) n (%)
Subjects with at least one TEAE	9 (90.0)	8 (100)	3 (100)	20 (100)
Serious TEAE	2 (20.0)	2 (25.0)	2 (66.7)	6 (28.6)
Grade 3 or 4 TEAE	6 (60.0)	6 (75.0)	3 (100)	15 (71.4)
TEAE Leading to Dose Modification	5 (50.0)	6 (75.0)	2 (66.7)	13 (61.9)
• TEAE leading to ATG-008 Dose Modification	5 (50.0)	6 (75.0)	2 (66.7)	13 (61.9)
• TEAE leading to Toripalimab Dose Modification	3 (30.0)	3 (37.5)	0	6 (28.6)
TEAE Leading to Dose Reduction	0	1 (12.5)	2 (66.7)	3 (14.3)
• TEAE leading to ATG-008 Dose Reduction	0	1 (12.5)	2 (66.7)	3 (14.3)
• TEAE leading to Toripalimab Dose Reduction	0	0	0	0
TEAE Leading to Dose Interruption	5 (50.0)	5 (62.5)	1 (33.3)	11 (52.4)
• TEAE leading to ATG-008 Dose Interruption	5 (50.0)	5 (62.5)	1 (33.3)	11 (52.4)
• TEAE leading to Toripalimab Dose Interruption	3 (30.0)	3 (37.5)	0	28.6
TEAE Leading to Treatment Discontinuation	0	1 (12.5)	0	1 (4.8)
TEAE Leading to Death	0	0	0	0

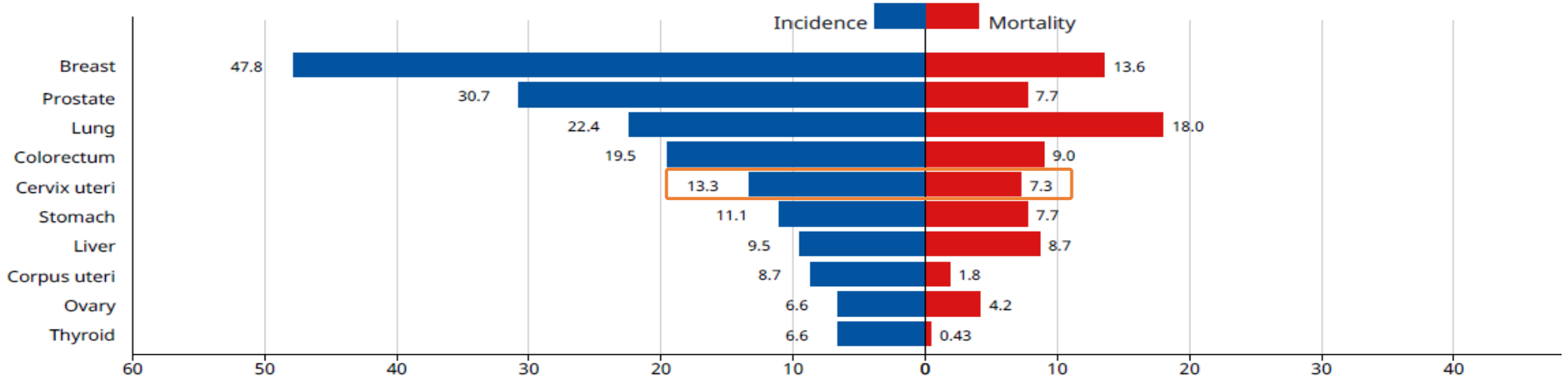
Cervical Cancer Disease Burden in 2020

ANTENGENE

- The number of cervical cancer **new cases in China** was **109,741**
- The **number of deaths** was **59,060**
- The **number of 5-year prevalence cases** was **297,278**

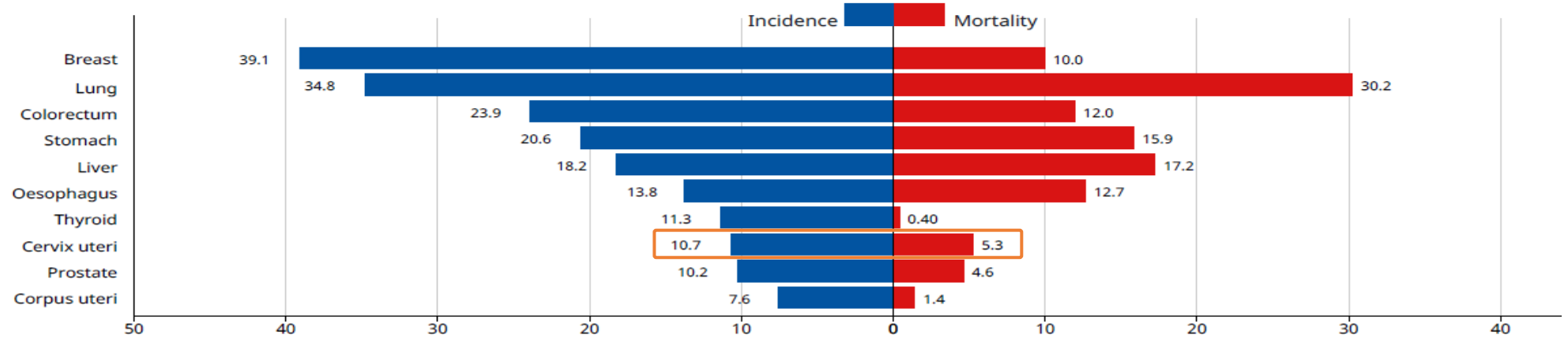
Global

Cervical cancer is a Top-10 Cancer Globally based on Age-standardized incidence and mortality rates



China

Cervical cancer is a Top-10 Cancer in China based on Age-standardized incidence and mortality rates



Source: Globalcan

ATG-008 (Onatasertib) In Combination with Toripalimab

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

ANTENGENE

	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 (ITT)	100 (FAS, ITT 111)	39 (EE, ITT 42)
Prior Treatment Lines	≤2 (52.4%); **≥3 (47.6%)**	≤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%; **77.8% (TPS≥1%)**	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

AdCa: Adenocarcinoma

Source: publications & primary research

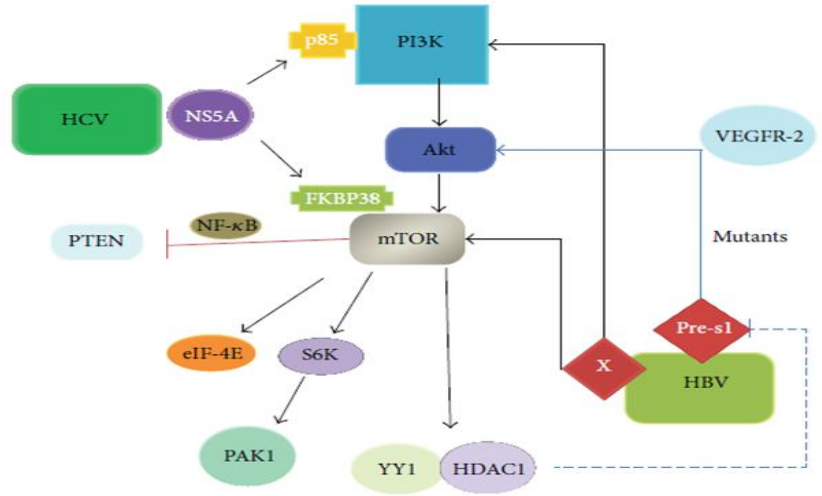
Rationale to Explore ATG-008 (Onatasertib) in HBV+ Hepatocellular Carcinoma (HCC)

ANTENGENE

Strong Rationale for the Initiation of TORCH Study

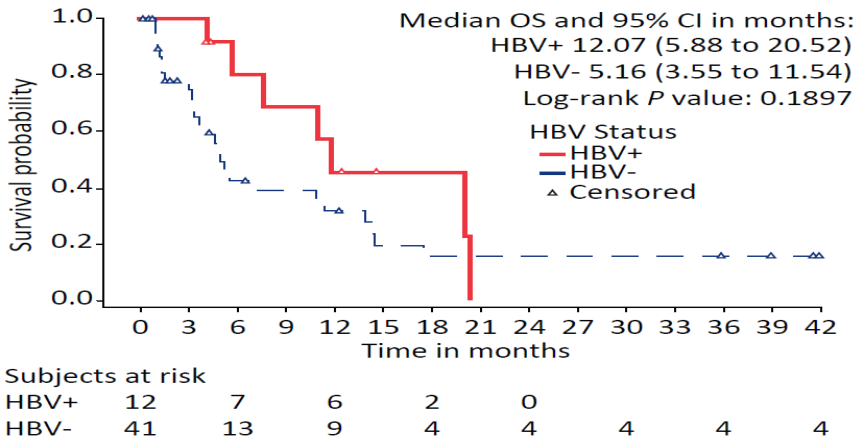
Huge Unmet Medical Need

- Hepatocellular Carcinoma (HCC) is the **second most common cause of death** from cancer in the world
- Chronic Hepatitis B Virus (HBV) infection now accounts for **80% of all newly diagnosed HCC in Asia**
- Hepatitis B virus (X protein) **up-regulates PI3K/mTOR signaling** which **increases cell proliferation and VEGF production**



Promising Clinical Data in the Previous Phase II CC-223-ST-001 Study

- Evaluated **53 subjects with HCC**, who has received at least one dose of ATG-008
  - **Median Overall Survival (mOS) in the HBV+ subgroup was 52.4 weeks**, while the mOS in the HBV- subgroup was 22.1 weeks



Source: Zhu et al, 2016; Andrew X et al, 2014; Internal data on file

ATG-008 "TORCH" Clinical Trial Design

ANTENGENE

An Open-label Phase II Trial of Dual TORC1/TORC2 Inhibitor ATG-008 (Onatasertib) in HBV+ Advanced Hepatocellular Carcinoma (HCC) Subjects Who Have Received At Least One Prior Line of Systemic Therapy

Location: Mainland China, South Korea, Taiwan

Key Eligibility Criteria:

- Advanced HCC with at least 1 prior systemic therapy
- HBV+ by serum
- No prior mTOR inhibitor

Dose Escalation

ATG-008 (Onatasertib) *(28-day cycle)* — **N = 6**

Onatasertib: 15 mg PO once daily

Until disease progression or unacceptable toxicity

ATG-008 (Onatasertib) *(28-day cycle)* — **N = 24**

Onatasertib: 30 mg PO once daily

Until disease progression or unacceptable toxicity

ATG-008 (Onatasertib) *(28-day cycle)* — **N = 20**

Onatasertib: 45 mg PO once daily

Until disease progression or unacceptable toxicity

ATG-008 (Onatasertib) *(28-day cycle)* — **N = 20**

Onatasertib: 20 mg PO twice daily

Until disease progression or unacceptable toxicity

Dose Expansion — N = ~110

ATG-008 (Onatasertib) *(28-day cycle)*

Onatasertib: 45 mg PO once daily

or

Onatasertib: 20 mg PO twice daily

Until disease progression or unacceptable toxicity

Primary endpoint: C_{max}, AUC, Safety, ORR; Dose Expansion: ORR

Secondary endpoints: OS, TTP, PFS, DCR, DOR, TTR, survival rate (6, 9, 12 months)

ATG-008-HCC-001
Sponsor: Antengene

AUC: area under the curve; DCR: disease control rate; DOR: duration of response; HBV: hepatitis B virus; HCC: hepatocellular carcinoma; ORR: overall response rate; OS: overall survival; PFS: progression free survival; TTP: time to progression; TTR: time to response

“TORCH” Safety Analysis – Treatment Emergent Adverse Events (TEAE) Overall Summary

ANTENGENE

No Potential New Safety Signal that Warrants a Further Investigation

Grade 3-4 TEAEs with high rate (≥5%,) include:

- Rash (21.9%)
- Hyperglycemia (19.2%)
- Diarrhea (11%)
- Fatigue (9.6%)
- Pruritus (6.8%)

Details of 45mg cohort :

- Rash (22.2%)
- Hyperglycemia (16.7%)
- Diarrhea (16.7%)
- Stomatitis (16.7%)
- Decreased Appetite (11.1%)

Data Cut-off Date: 11th July, 2022	15 mg QD (N=7) n (%)	30 mg QD (N=28) n (%)	20 mg BID (N=20) n (%)	45 mg QD (N=18) n (%)	Total (N=73) n (%)
Subjects with at least one TEAE	7 (100)	28 (100)	20 (100)	18 (100)	73 (100)
Serious TEAE	4 (57.1)	7 (25.0)	6 (30.0)	8 (44.4)	25 (34.2)
Grade 3 or 4 TEAE	7 (100)	25 (89.3)	15 (75.0)	16 (88.9)	63 (86.3)
TEAE Leading to Dose Modification	7 (100)	14 (50.0)	14 (70.0)	16 (88.9)	51 (69.9)
TEAE Leading to Dose Reduction	0	8 (28.6)	5 (25.0)	5 (27.8)	18 (24.7)
TEAE Leading to Dose Interruption	7 (100)	8 (28.6)	12 (60.0)	14 (77.8)	41 (56.2)
TEAE Leading to Treatment Discontinuation	1 (14.3)	7 (25.0)	5 (25.0)	4 (22.2)	17 (23.3)
TEAE Leading to Death	0	1 (3.6)	0	0	1 (1.4)

"TORCH" Efficacy Analysis – ORR, DCR, DOR, PFS & OS Overall Summary

ANTENGENE

- ATG-008 (Onatasertib) **45 mg QD** demonstrated **single agent activity in advanced HBV+ Hepatocellular Carcinoma (HCC)**
  - **ORR** is **16.7%** (3/18)
  - **mDOR** is **4.3 months**
  - **DCR** is **55.6%**
  - **Longer mPFS (5.3 months)** than the whole population (3.0 months)
  - OS was not evaluable in the 45 mg QD cohort; **OS of the whole ITT population is 13.4 months**
- **15 out of 18 patients** exposed to **prior PD-1/PD-L1 treatment**
  - **2 checkpoint inhibitor-treated patients** achieved **PR**

Data Cut-off Date: 11th July, 2022	15 mg QD (N=7) n (%)	30 mg QD (N=28) n (%)	20 mg BID (N=20) n (%)	45 mg QD (N=18) n (%)
Partial Response (PR)	0	0	0	**3 (16.67)**
Stable Disease (SD)	3 (42.86)	16 (57.14)	11 (55)	7 (38.89)
Progressive Disease (PD)	4 (57.14)	11 (39.29)	5 (25)	6 (33.33)
Non Evaluable (NE)	0	1 (3.57)	4 (20)	2 (11.11)
Overall Response Rate (ORR)	0 (0)	0 (0)	0 (0)	**3 (16.67)**
ORR 95% CI	(0, 41.0)	(0, 12.3)	(0, 16.8)	(3.6, 41.4)
Disease Control Rate (DCR)	3 (42.86)	16 (57.14)	11 (55)	**10 (55.56)**
DCR 95% CI	(9.9, 81.6)	(37.2, 75.5)	(31.5, 76.9)	(30.8, 78.5)

Key Takeaways of ATG-008 (Onatasertib) Clinical Programs

ANTENGENE

- **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

ANTENGENE

XPO1 INHIBITOR

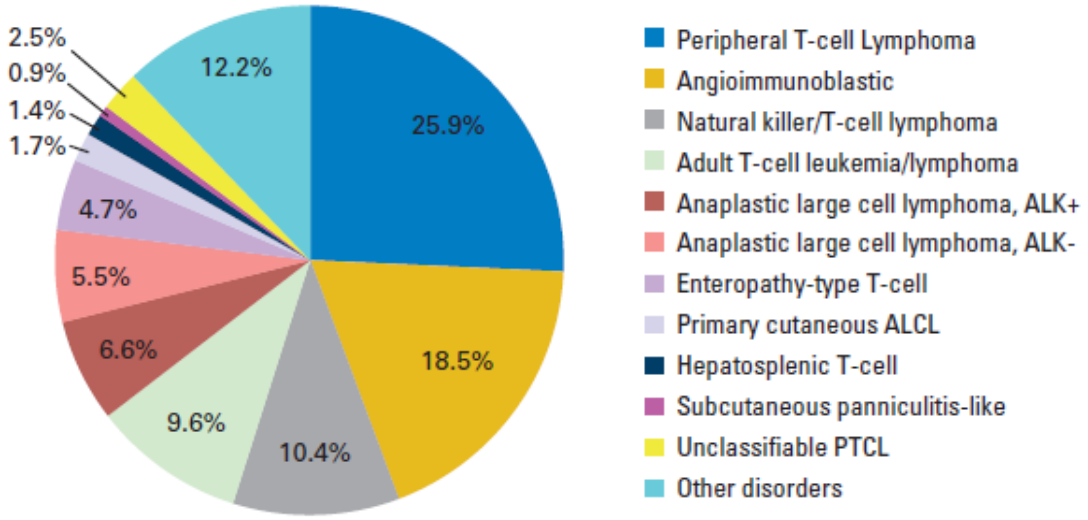
T-cell and NK-cell Lymphoma – An Endemic Disease in Asia that is Under-served with Current Treatments

ANTENGENE

Geographic Variation Lymphoma Highly Prevalent in Asia

Table 1. Major Lymphoma Subtypes by Geographic Region

Subtype	% North America	% Europe	% Asia
PTCL-NOS	34.4	34.3	22.4
Angioimmunoblastic	16.0	28.7	17.9
ALCL, ALK positive	16.0	6.4	3.2
ALCL, ALK negative	7.8	9.4	2.6
NKTCL	5.1	4.3	22.4
ATLL	2.0	1.0	25.0
Enteropathy-type	5.8	9.1	1.9
Hepatosplenic	3.0	2.3	0.2
Primary cutaneous ALCL	5.4	0.8	0.7
Subcutaneous panniculitis-like	1.3	0.5	1.3
Unclassifiable T-cell	2.3	3.3	2.4



Current Treatment Paradigm

- No standard of care treatment for **relapsed/refractory disease**
- **Poor outcomes after first relapse**, with **limited improvement** in the past decade

Disease	ORR	2nd PFS (months)	Overall Survival (OS) After 1st Relapse/Progression (months)
R/R PTCL	25-30%	3.7	6.5
R/R ENKTL	30-35%	4.1	6.4

Source: Vose J, et al. 2008; Liu W, et al. 2020; S. H. Lim et al. 2017; Mak V, et al. 2013

ATG-010 “TOUCH” Clinical Trial Design and Status Updates

ANTENGENE

A Phase I/II, Open-label, Multi-center Study to Evaluate the Safety and Efficacy of ATG-010 (Selinexor) Combined With Chemotherapy or Tislelizumab in R/R Mature T and NK Cell Lymphoma *(Common Subtype of NHL in Asia)*

Location: Mainland China

Key Eligibility Criteria:

- R/R Peripheral T-cell Lymphoma or T/NK-cell Lymphoma
- At least 1 prior standard treatment

V5 sIND approval, August 2022
Arm C FPI, December 2022

Arm A — Terminated

Selinexor + ICE

Arm B — N = 46

Selinexor + GemOx

Arm C — N = 51

Selinexor + Tislelizumab

Dose Escalation (N = 12)
Dose Expansion (N = 39)

Until disease progression or unacceptable toxicity

→ **Maintenance Therapy with Selinexor**

Primary endpoint: Safety, MTD/RP2D (Arm C), ORR
Secondary endpoints: DOR, TTR, DOR, PFS, OS, PK (Arm C)

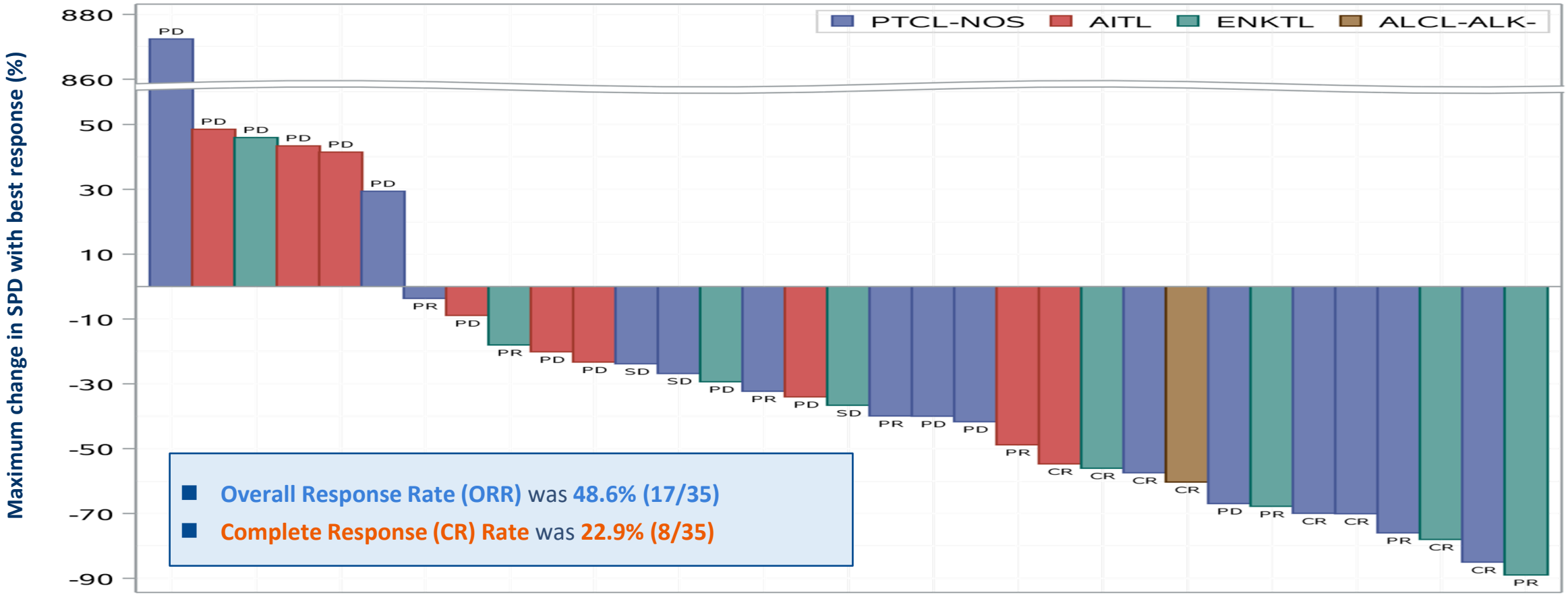
ATG-010-T/NK-001
Sponsor: Antengene

ORR: overall response rate; DOR: duration of response; OS: overall survival; PFS: progression free survival; ICE: ifosfamide, carboplatin, etoposide; GEMOX: gemcitabine, oxaliplatin

"TOUCH": Efficacy of Arm B – 2022 ASH Abstract #2916

Impressive Early Efficacy Signal

ANTENGENE

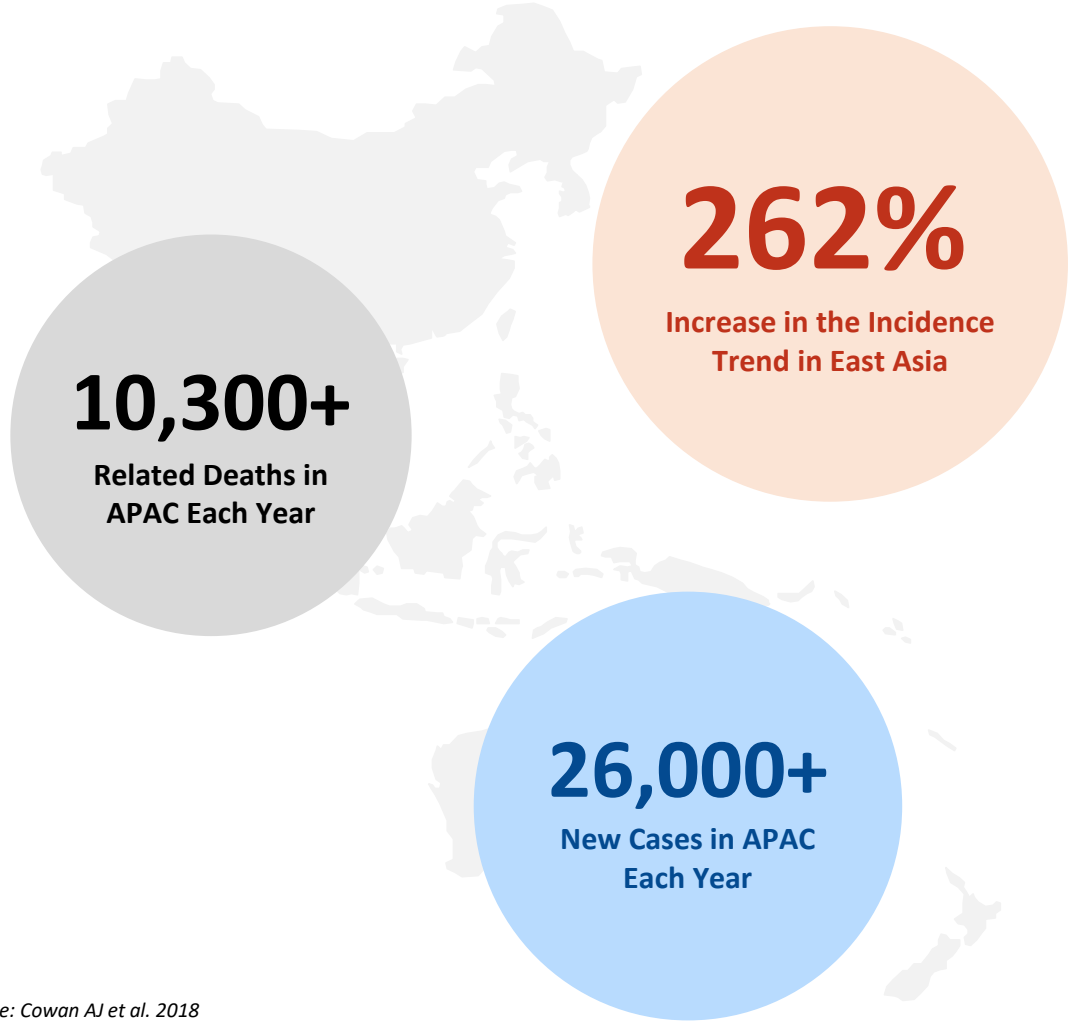


	PTCL-NOS (n=15)	ENKTL (n=10)	AITL (n=9)	ALCL(n=1)	All Patients (N=35)
Median PFS (95% CI), months	4.4 (1.51, 9.59)	4.7 (1.22, NE)	1.5 (0.59, NE)	3.2 (NE, NE)	2.9 (1.51, 4.67)
Median OS (95% CI), months	NE (5.55, NE)	14.1 (8.28, NE)	NE (2.2, NE)	NE (NE, NE)	NE (11.47, NE)

Opportunity Continues to Exist in Multiple Myeloma

ANTENGENE

Multiple Myeloma is the Second Most Common Hematological Malignancy



10,300+
Related Deaths in APAC Each Year

262%
Increase in the Incidence Trend in East Asia

26,000+
New Cases in APAC Each Year

Current Treatment Paradigm

- Multiple Myeloma Remains Incurable
- Patients with Multiple Myeloma Will Eventually Experience Relapse or Become Refractory to Existing Treatments
- Fewer Treatment Options are Available in APAC as Compared to the U.S.
- There is a High Unmet Medical Need for Treatments with Novel Mechanisms of Action in R/R Multiple Myeloma

Source: Cowan AJ et al. 2018

ATG-010 "BENCH" Clinical Trial Design and Status Updates

ANTENGENE

A Pivotal Phase III Confirmatory Study (China Bridging Study for BOSTON) Evaluating the Safety and Efficacy of ATG-010 (Selinexor), Bortezomib, and Dexamethasone (SVd) Versus Bortezomib and Dexamethasone (Vd) in Patients with Relapsed or Refractory Multiple Myeloma (R/R MM)

Location: Mainland China

Key Eligibility Criteria: **N = 150**

- R/R Multiple Myeloma with 1-3 prior therapies

First Patient In (FPI): July, 2021
Positive 1st DSMB review in August 2022

Randomization 2:1

ATG-010 (Selinexor) + Bortezomib + Dexamethasone (SVd)
(35-day cycle)

Selinexor: 100 mg PO on days 1, 8, 15, 22, 29
Bortezomib: 1.3mg/m^2 SC on days 1, 8, 15, 22
Dexamethasone: 20 mg PO on days 1, 2, 8, 9, 15, 16, 22, 23, 29, 30

Until PD

***Crossover at PD**

Bortezomib + Dexamethasone (Vd)

Cycle 1-8 (21-day cycle)
Bortezomib: *1.3mg/m^2 SC on days 1, 4, 8, 11*
Dexamethasone: *20 mg PO on days 1, 2, 4, 5, 8, 9, 11, 12*

Cycle 9+ (35-day cycle)
Bortezomib: *1.3mg/m^2 SC on days 1, 8, 15, 22*
Dexamethasone: *20 mg PO on days 1, 2, 8, 9, 15, 16, 22, 23, 29, 30*

*Until PD**

Primary endpoint: PFS
Secondary endpoints: ORR, OS, DOR, Grade ≥2 Peripheral Neuropathy

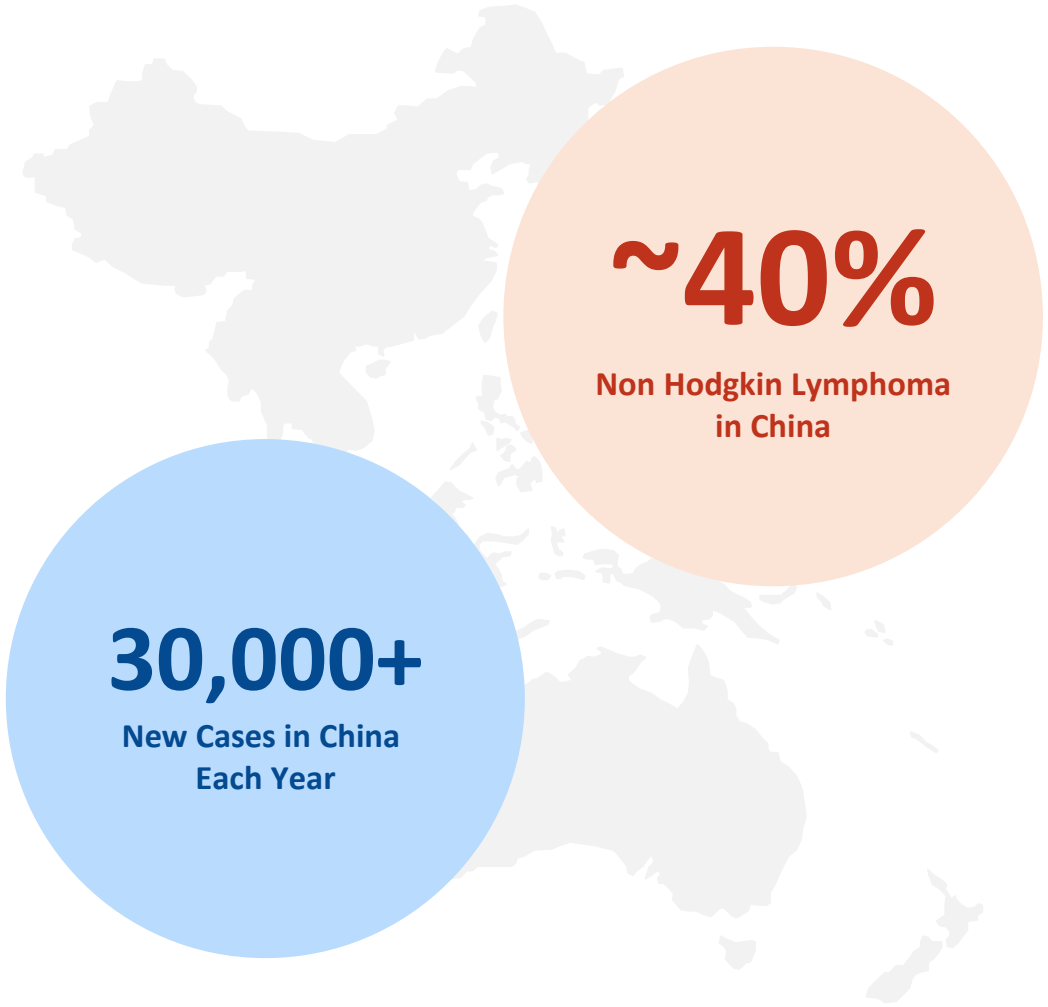
ATG-010-MM-002
Sponsor: Antengene

rrMM: relapsed or refractory multiple myeloma; ORR: overall response rate; DOR: duration of response; OS: overall survival; PD: progressive disease; PFS: progression free survival; PN: peripheral neuropathy

High Unmet Needs Provide An Opportunity in Diffuse Large B-cell Lymphoma

ANTENGENE

Diffuse Large B-cell Lymphoma is the Most Common and Aggressive Subtype of Non Hodgkin Lymphoma in Adults



~40%

Non Hodgkin Lymphoma in China

30,000+

New Cases in China Each Year

Current Treatment Paradigm

- R-CHOP is only curative in ~50-60% of front line patients
- Patients in specific subgroups such as double/triple hit lymphoma and double expressor lymphoma face poor outcomes and limited treatment options
- **No standard of care for R/R diffuse large B-cell lymphoma** in China
- **Very few novel treatments approved in China (e.g., Axicabtagene Ciloleucel, Relmacabtagene Autoleucel)**

Source: Publications & primary research

ATG-010 “SEARCH” Clinical Trial Design and Status Updates

ANTENGENE

A Pivotal Phase II Confirmatory Study (China Bridging Study for SADAL) Evaluating the Safety and Efficacy of ATG-010 (Selinexor) in Patients with Relapsed or Refractory Diffuse Large B-cell Lymphoma (R/R DLBCL)

Location: Mainland China

Key Eligibility Criteria: **N = 60**

- Previously treated de novo or transformed DLBCL
- 2-5 prior therapies

Currently in pre-sNDA process based on efficacy and safety evaluation
sNDA in 1H 2023

ATG-010 (Selinexor)

Selinexor: 60 mg PO twice weekly

Until disease progression or unacceptable toxicity

≥PR

ATG-010 (Selinexor)

Selinexor: 60 mg PO once weekly

Until disease progression or unacceptable toxicity

Primary endpoint: ORR
Secondary endpoints: DOR, OS, PFS

ATG-010-DLBCL-001
Sponsor: Antengene

ORR: overall response rate; DOR: duration of response; OS: overall survival; PFS: progression free survival; BIW: twice a week; QW: once a week, R/R: relapsed or refractory

ATG-010 “XPORT-DLBCL-030” Clinical Trial Design

ANTENGENE

A Global Pivotal Phase II/III Confirmatory Study of Rituximab-Gemcitabine-Dexamethasone-Platinum (R-GDP) With or Without ATG-010 (Selinexor) in Patients with Relapsed or Refractory Diffuse Large B-cell Lymphoma (R/R DLBCL)

Location:
Mainland China (Antengene), Rest of the World (Karyopharm)

Phase II

N = 120 (CN = 12 enrolled)

Key Eligibility Criteria:

- De novo or transformed DLBCL
- 1-2 prior therapies

Randomization 1:1:1

Combination		Maintenance
Selinexor 40 mg once weekly + R-GDP	≥PR	Selinexor 60 mg once weekly
Selinexor 60 mg once weekly + R-GDP	≥PR	Selinexor 60 mg once weekly
R-GDP		

Primary endpoint: ORR
Secondary endpoints: PFS, OS, DOR, safety

Phase III

N = 381 (CN = 60)

Key Eligibility Criteria:

- De novo or transformed DLBCL
- 1-2 prior therapies

Randomization 1:1:1

Combination		Maintenance
Selinexor (selected dose) + R-GDP	≥PR	Selinexor 60 mg once weekly
Selinexor (selected dose) + R-GDP	≥PR	Placebo once weekly
Placebo + R-GDP	≥PR	Placebo once weekly

Primary endpoint: PFS
Secondary endpoints: ORR, OS, DOR, safety

XPORT-DLBCL-030

Co-sponsor: Karyopharm Therapeutics | ANTENGENE

CN: China, ORR: overall response rate; DOR: duration of response; OS: overall survival; PFS: progression free survival; QW: once weekly; R-GDP: rituximab, gemcitabine, dexamethasone, platinum; R/R: relapsed or refractory

ATG-010 "MATCH" Clinical Trial Design and Status Updates

ANTENGENE

Rationale

- Unmet medical need in R/R DLBCL, especially in double-hit/triple-hit, double expresser, or transformed DLBCL
- Preclinical data showed synergistic effects of ATG-010 (Selinexor) + ATG-008 (Onatasertib), both of which are molecules from Antengene's pipeline

An Open-label Phase Ib Study of ATG-010 (Selinexor) Plus ATG-008 (Onatasertib) in Patients with Relapsed or Refractory Diffuse Large B-cell Lymphoma (R/R DLBCL)

Location: Mainland China

Key Eligibility Criteria: **N = 88**

- R/R Diffuse Large B-cell Lymphoma
- 2-5 prior regimens (1-5 prior therapies for DH/TH, DE or transformed DLBCL)

Recruitment: On-going
Currently in dose escalation phase

Dose Escalation

ATG-010 + ATG-008 *(28-day cycle)*

Selinexor: 60 mg PO once weekly
Onatasertib: 15 mg PO once daily

Until disease progression or unacceptable toxicity

"BOIN design" dose escalation

MTD, RP2D

Dose Expansion

ATG-010 + ATG-008 *(28-day cycle)*

Selinexor: MTD/RP2D PO
Onatasertib: MTD/RP2D PO daily

Until disease progression or unacceptable toxicity

"Simon Two-stage" dose expansion

Primary endpoint: MTD, RP2D, Safety
Secondary endpoints: ORR, PFS, DOR, TTP, OS, PK

ATG-008&010-DLBCL-001
Sponsor: Antengene

DE: dual expressor; DH: double hit; DLBCL: diffuse large B-cell lymphoma; DOR: duration of response; MTD: maximum tolerated dose; ORR: overall response rate; OS: overall survival: PFS: progression free survival; PK: pharmacokinetics; RP2D: recommended phase 2 dose; RR: relapsed/refractory; TH: triple hit; TTP: time to progression

ATG-010 "SWATCH" Clinical Trial Design and Status Updates

ANTENGENE

Rationale

- Limited therapies for elderly or ASCT-ineligible patients with R/R DLBCL and indolent B-NHL
- Selinexor with accelerated approval by FDA, and R2 showed preliminary efficacy in R/R DLBCL and indolent B-NHL

An Open Label Phase I/II Study of ATG-010 (Selinexor) Plus R2 (Rituximab + Lenalidomide) in Patients with B-cell Non-Hodgkin Lymphoma

Location: Mainland China

Key Eligibility Criteria: **N = 84**

- R/R Diffuse Large B-cell Lymphoma, R/R indolent Non-Hodgkin Lymphoma (dose expansion)
- At least 1 prior regimen
- Not eligible for HDC/ASCT

Recruitment: On-going
Currently is on dose escalation phase

Dose Escalation

ATG-010 (Selinexor) + Rituximab + Lenalidomide
(28-day cycle)

Starting Dose level
Selinexor: 40 mg PO on Day 1, 8, 15
Rituximab: 375 mg/m^2 IV on Day 1, Cycle 1-6
Lenalidomide: 25 mg PO from Day 1-10

Until disease progression or unacceptable toxicity

MTD, RP2D

Dose Expansion

ATG-010 (Selinexor) + Rituximab + Lenalidomide
(28-day cycle)

2 cohorts:
1) R/R DLBCL
2) R/R iNHL

Until disease progression or unacceptable toxicity

Primary endpoint: MTD, RP2D, Safety
Secondary endpoints: ORR, PFS, DOR, TTP, OS

ATG-010-B-NHL-002
Sponsor: Antengene

DE: dual expressor; DH: double hit; DLBCL: diffuse large B-cell lymphoma; DOR: duration of response; MTD: maximum tolerated dose; ORR: overall response rate; OS: overall survival: PFS: progression free survival; PK: pharmacokinetics; RP2D: recommended phase 2 dose; RR: relapsed/refractory; TH: triple hit; TTP: time to progression

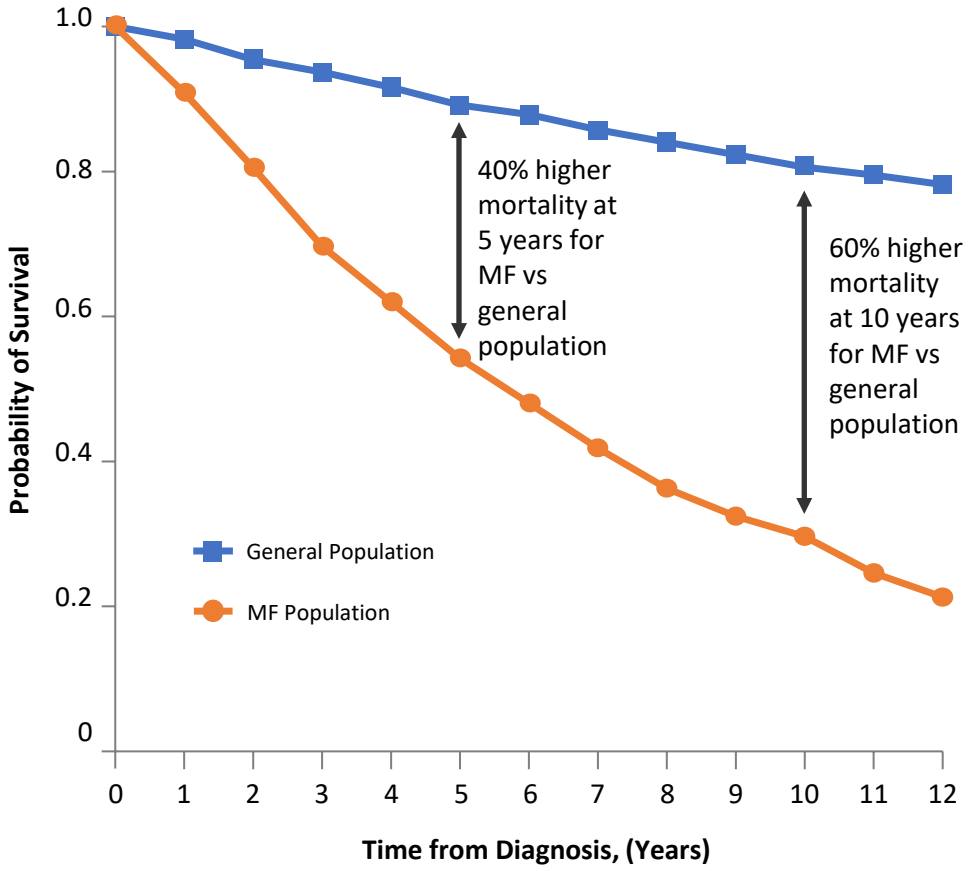
Patients with Myelofibrosis Have a Considerably Higher Risk of Death

ANTENGENE

There is an Unmet Medical Need in Myelofibrosis

- Myelofibrosis (MF) is a **myeloproliferative neoplasm that develops de novo** (primary myelofibrosis [PMF]) **or progress from antecedent polycythemia vera** (post-PV-MF) **or essential thrombocythemia** (post-ET-MF)
- **JAK2 is present** in almost all persons with post-PV-MF and about 50% of persons with post-ET-MF and PMF[1-3]
- MF is **relatively rare but incidence estimates vary widely**
  - Crude incidence: 0.22–0.99 per 100,000 per year[4]
- Allogeneic Hematopoietic Stem Cell Transplant (Allo-HSCT) is regarded as the only curative therapy for myelofibrosis. **JAK inhibitors and other medicines could only relieve the symptoms**
- Clinical features include **progressive anemia and/or splenomegaly and constitutional symptoms**
  - In 8–23% of patients, **MF transforms to Acute Myeloid Leukemia (AML)** within the first 10 years of diagnosis[6–7]

Survival Rates in Patients with Myelofibrosis[5]



Source: 1. Mesa RA,et al. Leuk Res. 2011; 2. Tefferi A.Am J Hematol. 2014; 3. Kralovics R,et al. N Engl J Med. 2005; 4.Titmarsh GJ et al. Am J Hematol 2014;5. Cervantes F et al. Blood 2009; 6. Mesa RA et al. Blood 2005; 7. Okamura T et al. Int J Hematol

ATG-010 “XPORT-MF-035” Clinical Trial Design, Status Updates and Plans for the “XPORT-MF-034” Study

ANTENGENE

A Global Pivotal Phase II Study of to Evaluate the Efficacy of ATG-010 (Selinexor) Versus Treatment of Physician’s Choice in Participants with Previously Treated Myelofibrosis

Location:
Mainland China (Antengene),
Rest of the World (Karyopharm)

N = 112 (CN = 18)

Key Eligibility Criteria:

- Primary Myelofibrosis (MF) or post-essential thrombocythemia (post-ET) or post-polycythemia vera (post-PV) MF
- Previous treatment with JAK inhibitors for at least 6 months
- Relapsed, refractory or intolerant to JAK inhibitors

First Patient In (FPI) China: August, 2022

Randomization
1:1

ATG-010 (Selinexor)

Selinexor:
80 mg PO once weekly for 2 cycles
60 mg PO once weekly in following cycles

Physician’s Choice

May include ruxolitinib retreatment, fedratinib, chemotherapy, anagrelide, corticosteroid, hematopoietic growth factor, androgen, IFN, and may include supportive care only

Primary endpoint: Rate of SVR35 by IRC
Secondary endpoints: Rate of total symptom score reduction of 50% (TSS50) in the myelofibrosis symptom assessment form (MFSAF); rate of spleen volume reduction of ≥25% (SVR25); OS and ORR; anemia response, duration of SVR35, TSS50, and SVR25, AEs, AUC and Cmax

XPORT-MF-035

Co-sponsor: Karyopharm Therapeutics | ANTENGENE

*MF: myelofibrosis; QW: once a week; SVR35: spleen volume reduction of ≥35%; SVR25: spleen volume reduction of ≥25%; CN=China; *ASCO 2022,Abs 7060*

"XPORT-MF-034" Clinical Trial Showed Encouraging Preliminary Data Across Key Efficacy Across Key Efficacy Endpoints with Updated Results To Be Presented at ASH 2022

ANTENGENE

A Global Phase I Multicenter Open-label Study to Evaluate the Safety and Efficacy of Selinexor Plus Ruxolitinib in Treatment Naïve Myelofibrosis Patients

Karyopharm Therapeutics

Location: United States (Karyopharm)

Key Eligibility Criteria:

- Patients with treatment-naïve myelofibrosis

Dose Escalation

Selinexor + Ruxolitinib — N = 3

Dose Level 1:
Selinexor: 40 mg once weekly
Ruxolitinib: 15/20 mg twice daily

Selinexor + Ruxolitinib — N = 3

Dose Level 2:
Selinexor: 60 mg once weekly
Ruxolitinib: 15/20 mg twice daily

Dose Expansion — N = 18

Selinexor + Ruxolitinib

Selinexor: 40/60 mg once weekly
Ruxolitinib: 15/20 mg twice daily

Primary endpoint: MTD, RP2D, AEs
Secondary endpoints: SVR35, TSS50, OS, anemia response, AEs, ORR, PK analysis

Spleen Responses at 12 & 24 Weeks

- **79%** of evaluable patients (11/14) achieved SVR35 at week 12
- **86%** of evaluable patients (6/7) achieved SVR35 at week 24

Rapid Reduction in Total Symptom Scores (TSS)

- **69%** of evaluable patients (9/13) achieved TSS50 at week 12

Positive Impacts on Hemoglobin Levels

- **65%** of patients (11/17) maintained stable hemoglobin (+ 2g/dL) or improved hemoglobin level (>2g/dL, increase) at last follow up

Safety and Tolerability

- Most common TEAE[6] (n=19): Nausea (58%), anemia (42%), vomiting (42%), majority Grade 1-2
- Most common Grade ≥3 TEAEs: thrombocytopenia (26%) and anemia (21%)

AE: adverse event; MTD, maximum tolerated dose; ORR: overall response rate; OS: overall survival; PK: pharmacokinetics; RP2D: recommended phase 2 dose; SVR35: spleen volume reduction of at least 35%; TSS50: total symptom score reduction ≥ 50%.

Source: Karyopharm Investor Presentation dated November 3rd, 2022

Highlights of ATG-010 (Selinexor) Clinical Programs

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Multiple Myeloma

- Phase III "BENCH" bridging study evaluating ATG-010 (selinexor) in combination with bortezomib and dexamethasone is well on track

Lymphomas

- **T and NK-cell Lymphoma**
  - Selinexor plus GemOx regimen demonstrated favorable efficacy and a manageable safety profile in Phase I/II "TOUCH" study
  - Cohort of selinexor plus anti-PD-1 antibody tislelizumab in Phase I/II "TOUCH" study will commence in December 2022
- **Diffuse Large B-cell Lymphoma (DLBCL)**
  - Selinexor monotherapy for R/R DLBCL is in pre-sNDA submission process in Mainland China
  - Selinexor in combination with R-GDP in 2L+ DLBCL is potentially proceeding to Phase III pivotal stage
- **B-cell Non-Hodgkin's Lymphoma (B-NHL)**
  - Innovative combinations with selinexor to explore the potential of SINE in R/R B-NHL has been initiated

Myelofibrosis

- Starting potential pivotal programs with selinexor in myelofibrosis

EARLY CLINICAL DEVELOPMENT

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

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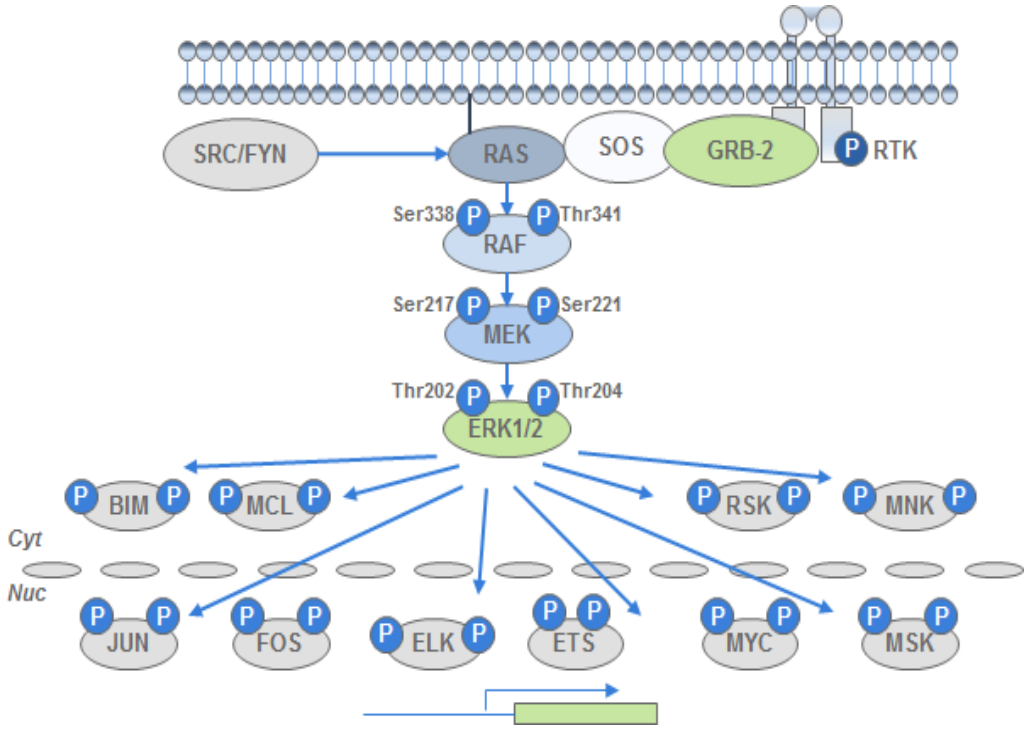
Summary of ATG-017 (Tizaterkib)

- 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 **6th 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

Source: F Liu et al. Acta Pharmaceutica Sinica B2018; 8(4); 552-652. Targeting ERK, an Achilles' Heel of the MAPK pathway, in cancer therapy
Note: RAS= renin-angiotensin system, SOS=son of sevenless; GRB-2=growth factor receptor bound protein 2; RTK=receptor tyrosine kinase; RAF=renin-angiotensin system; MEK=MAPK/ERK kinase; MRK=mantle cell lymphoma; RSK=ribosomal S6 kinase; MNK=MAPK-interacting kinase; MSK=mitogen-activated and stress-activated protein kinase.

ATG-017 (Tizaterkib) Has Best-In-Class Potential

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- Comparable in vivo efficacy; dual IoC and PoA activity with high residency time at the target
- Demonstrates regression at 50 mg/kg QD or 15 mg/kg BID
- Effective at a relatively lower dose level

Dimensions of Comparison		ATG-017 Tizaterkib	ERAS-007	BVD523 Ulixertinib	LY3214996 Temuterkib	ASTX029
Company		Antengene	Erasca	BioMed Valley	Eli Lilly	Astex
Molecular Mechanism of Action		**IoC + PoA**	IoC	IoC	IoC + PoA (tbc)	IoC + PoA
Binding Kinetics/ Potency Indicators	**ERK1/2 Enzyme Assay IC_{50} (nM)**	**- / 0.7**	2/2	- / <0.3	5 / 5	2.7-3 / -
	A375 Cell pRSK/pERK IC_{50} (μM)	**0.006 / 0.002**	0.007/ NA	0.16 / 3	0.32 / NA	~0.003/ ~0.1
	Cell Proliferation Calu 6/A375 GI_{50} (μM)	**0.2 / 0.06**	0.007/ 0.007	0.5 / 0.19	1.1 / NA	0.06/ <0.01
	SPR/$T_{1/2}$ (Non-phosphorylated/ Phosphorylated ERK)	193 / 265 mins	225 mins	2.8 / 26 mins	2.44 / 10.2 mins	NA
In Vivo Efficacy	**Calu6 Regression Dose (mg/kg)**	**50 QD**	NA	50 QD	NA	75 QD
	A375 Regression Dose (mg/kg)	**15 BID**	30 BID	NA	NA	75 QD

IoC = Inhibitor of catalysis; PoA = Prevention of Activation (as defined by A375 cell mode of action assay)

Source: publications & primary research

ATG-017 (Tizaterkib) Has Broad Combinational Potential With Various IO Agents and Target Therapies

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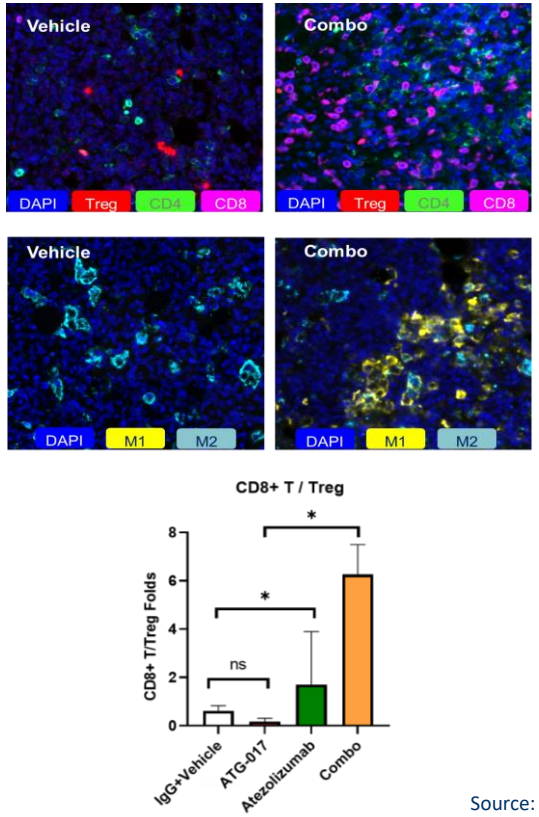
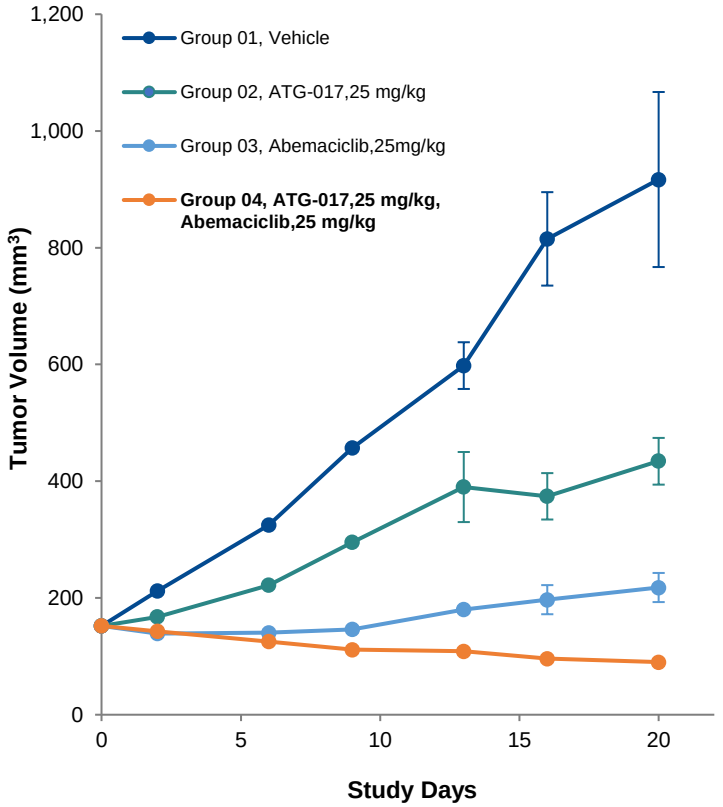
- ATG-017 showed in vivo synergism with inhibitors of MEK, EGFR, CDK4/6 and KRAS G12C
- ATG-017 modulates the tumor microenvironment and demonstrated synergism with immune checkpoint inhibitor
- Clinical trials evaluating ATG-017 in combination with other agents are being developed

In Vivo Synergy with Anti-PD-L1 in EL4 Syngeneic T cell Lymphoma CDX

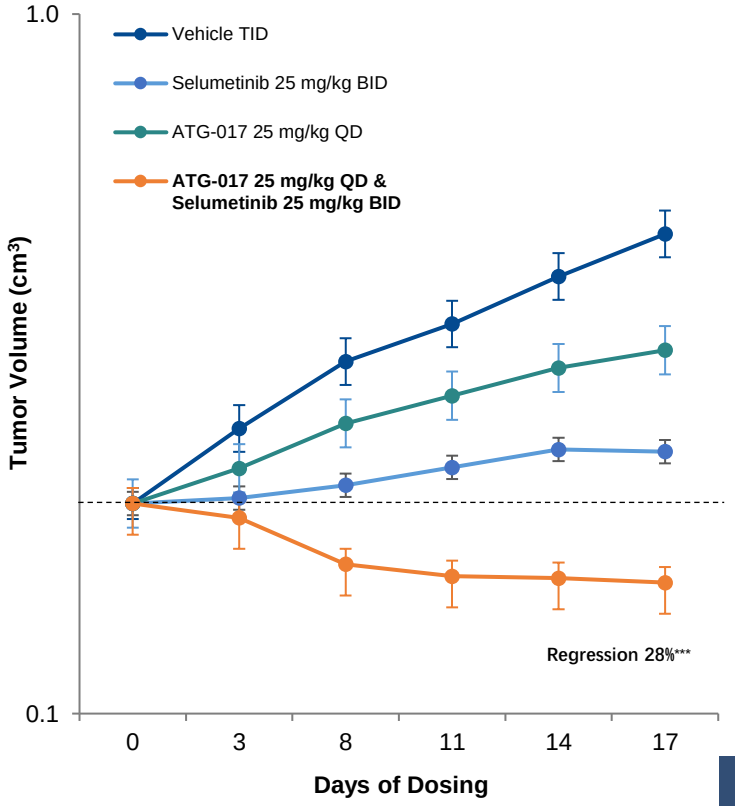


Source: SITC 2021

In Vivo Synergy with CDK4/6 Inhibitor in NCI-H358 NSCLC CDX



In Vivo Synergy with MEK Inhibitor in A549 ($KRAS^{G12S}$) NSCLC CDX



ATG-017 "ERASER" Clinical Trial Design and Status Updates

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Phase I, Open-Label, Multi-Center Dose Finding Study to Investigate the Safety, Pharmacokinetics, and Preliminary Efficacy of ATG-017 Monotherapy or Combination Therapy with Nivolumab in Patients with Advanced Solid Tumors and Hematological Malignancies

Location:

- Dose Escalation: Australia
- Dose Expansion: Australia, United States, Mainland China

Key Eligibility Criteria:

- Solid tumor or hematological malignancies (AML, MDS, B-NHL, MM)
- RAS-MAPK mutation positive
- Without prior ERK1/2 inhibitor exposure (module A+B) and PD-[L]1 inhibitor refractoriness (module B)

	Dose Escalation of ATG-017		Dose Expansion at RP2D
Module A **Monotherapy** (ST/Hema)	**ATG-017:** oral BID, **continuous dosing** (21 day/cycle)	**Status:** Currently in Cohort 6 in Australia at 30 mg BID for both dosing schedules	**Dosing at RP2D to further explore safety and efficacy signals in multiple subtypes of solid tumors and hematological malignancies**
	ATG-017: oral BID, **intermittent dosing** (7 day/7 day off, 28 day/cycle)		
Module B **Combination Therapy** (ST only)	**ATG-017:** oral BID, **continuous dosing** (28 day/cycle) **Nivolumab** dosed at fixed 480 mg, IV, CxD1		**Expansion Cohort 1** ■ PD-[L]1 inhibitor-naïve or PD-[L]1 inhibitor-exposed with SD for ≥12 week; at least 50% of this cohort will include potential PD-[L]1 inhibitor-responsive indications **Expansion Cohort 2** ■ PD-[L]1 inhibitor-refractory; regardless if RAS MAPK Mutation
	ATG-017: oral BID, **intermittent dosing** (7 day/7 day off, 28 day/cycle) **Nivolumab** dosed at fixed 480 mg, IV, CxD1		

Treatment until PD or Unacceptable Toxicity

Primary endpoint: Safety
Secondary endpoints: PK profile, ORR, DOR, PFS, OS
Exploratory endpoints: PDx biomarkers (cytokines, pERK, phospho-p90RSK, and PD-L1, immune cell populations), FDG-PET

NCT04305249
ATG-017-001
Sponsor: Antengene

AML: acute myeloid leukaemia; B-NHL: B cell non Hodgkin lymphoma; BIDL twice per day; d: day(s); DOR: duration of response; IV: intravenous; MDS: myelodysplastic syndrome; MM: multiple myeloma; ORR: overall response rate; PD: progressive disease; PDx: pharmacodynamics; PFS: progression free survival; PK: pharmacokinetics; RP2D: recommended phase 2 dose; SD: stable disease; ST: solid tumor; Hema: hematological malignancies; w: week(s);

ATG-017: Clinical Project Progressing Smoothly to MTD Determination

Currently in the 6th cohort in solid tumors of the Phase I ERASER trial

- In the process of MTD determination with continuous dosing
- Starting to exploring the intermittent dosing schedule (7 day on/7day off, 28-day cycle)

Efficacy signal observed in ATG-017 monotherapy at current dose level of 30 mg BID

ATG-101: Novel PD-L1/4-1BB Bispecific Antibody with Best-in-Class Potential

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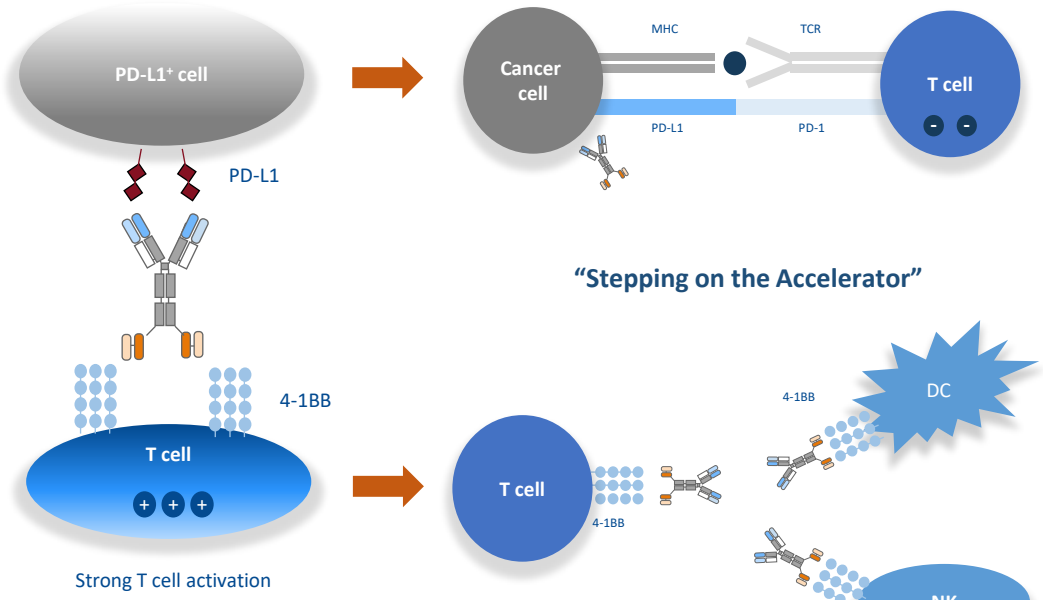
Summary of ATG-101

- Clinical stage bispecific antibody with **best-in-class potential**
- Received **orphan drug designation** from the US FDA for patients with pancreatic cancer

Complementary Mechanism of PD-L1/4-1BB



Excellent Safety Profile

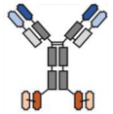
- High affinity of PD-L1 and conditional activation of 4-1BB results in 4-1BB agonist activity only when crosslinked by PD-L1-positive tumor cells, **reducing risk of 4-1BB related liver toxicity**
  - **No liver toxicity observed** in GLP toxicology study in cynomolgus monkeys with **dose up to 100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

ATG-101 is a Potentially Best-in-Class Bispecific Antibody of PD-L1/4-1BB

- Greater PD-L1 arm affinity and moderate 4-1BB arm affinity to balance the efficacy and safety risk
  - PD-L1/4-1BB arm affinity ratio of 65 to ensure the tumor enrichment of ATG-101
- 2+2 format enables potent 4-1BB activation with low risk of hook effect





	ATG-101	GEN1046	ES101/INBRX-105-1	MCLA145	ABL-503
Company	Antengene	Genmab/BioNTech	Inhibrx	Merus/Incyte	ABL
Format	**2+2**	1+1	2+2	1+1	2+2
PD-L1 Arm affinity	**1.77E-10**	1.6E-10	Not available	3E-10	3E-9
4-1BB Arm affinity	**1.14E-8**	1.5E-10	Higher than ATG-101	1.9E-9	1E-8
PD-L1/4-1BB Arm Affinity Ratio	**65**	1	Not available	3.6	3
Valent	**Tetravalent**	Bivalent	Tetravalent	Bivalent	Tetravalent
Hook Effect Risk	**Low**	High	Low	High	High
4-1BB Activation	Trimer-dependent	Trimer-dependent	Trimer-dependent	Trimer-dependent	Trimer-dependent

Source: publications & primary research

ATG-101 Induces Maximum Trimer Formation and >90% PD-L1 Receptor Occupancy at 2 mg/kg in Humans

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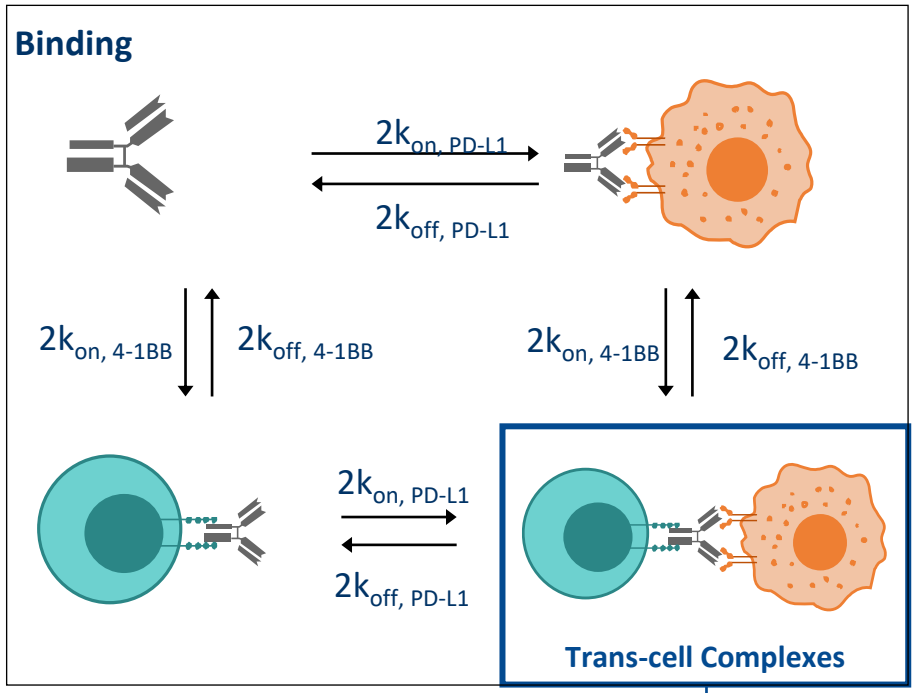
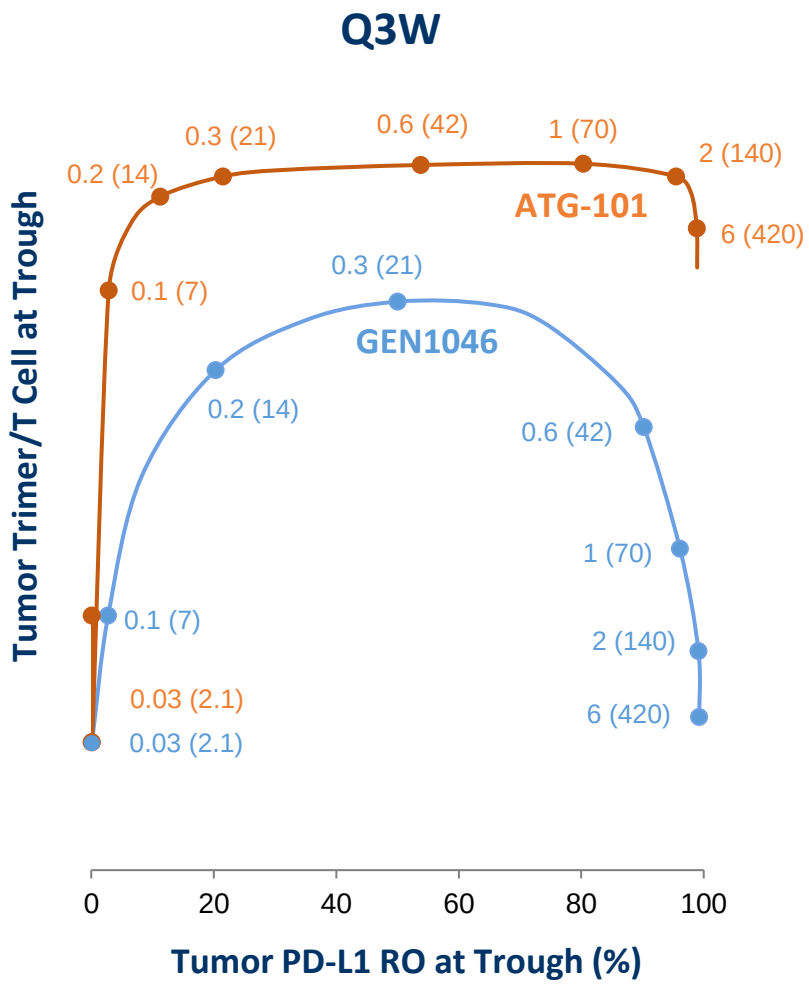
A Computational Semi-mechanistic Pharmacology Model Predicts that ATG-101 Induces Max Trimer Formation and >90% PD-L1 RO at 2mg/kg in Humans

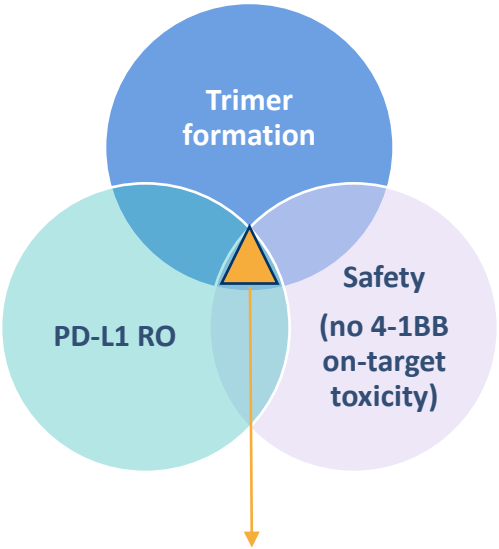
Model Structure and Strategy



Trans-cell complexes (i.e., trimers) are assumed to drive the **pharmacological activity of ATG-101**

Activation of Cytokine Release Cytotoxicity





Sweet Spot

The avidities of each arm of ATG-101 allows a dose level at which drug induces max trimer formation, >90% PD-L1 RO, with no 4-1BB on target toxicity

Source: SITC 2021

ATG-101 Induced Potent Anti-tumor Efficacy in Anti-PD-L1-Resistant Tumor Models

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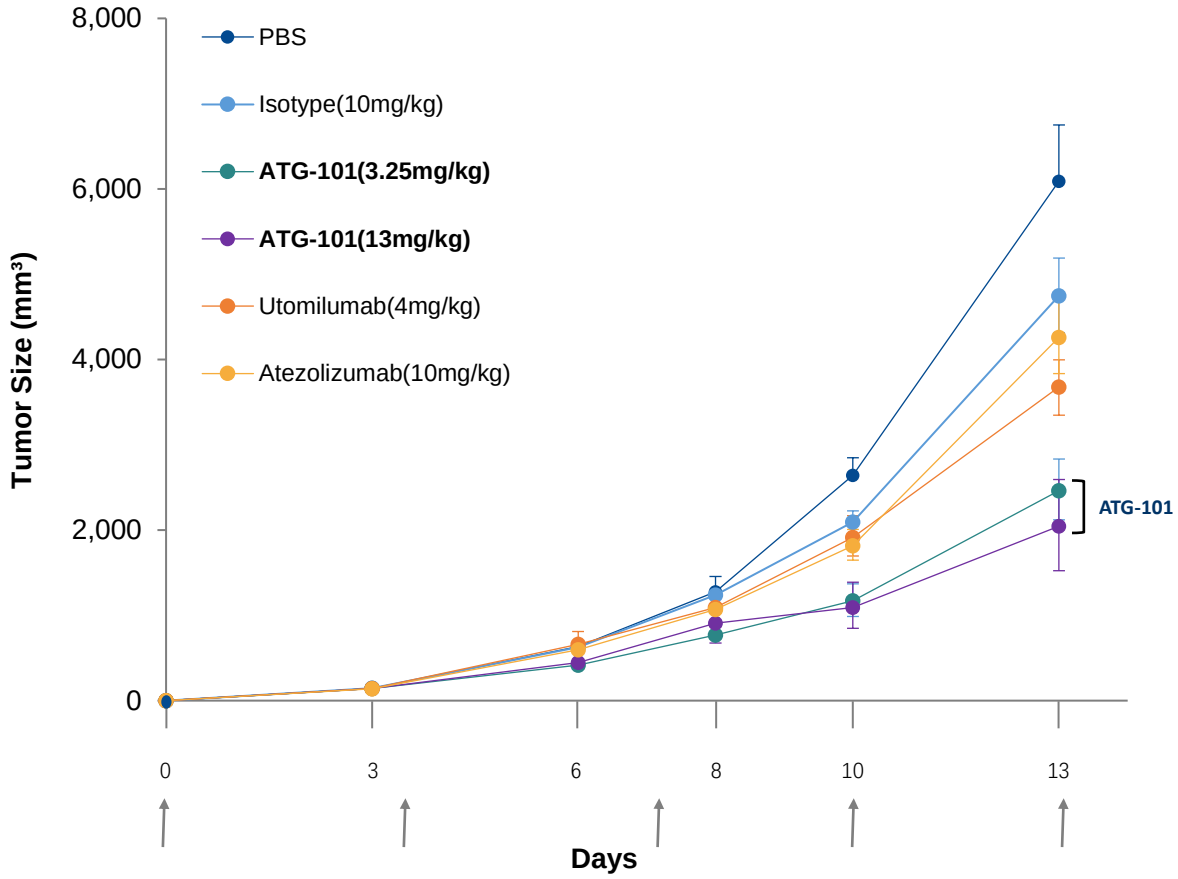
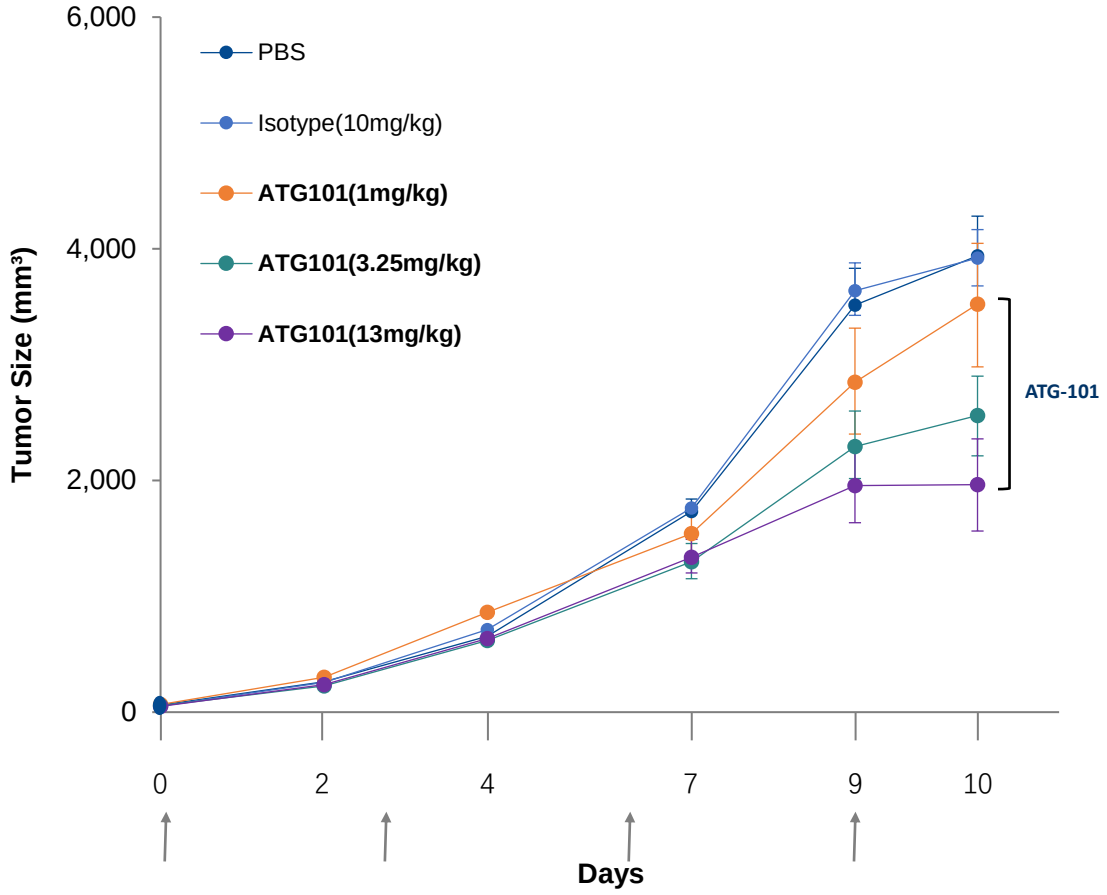
Anti-tumor Efficacy in Primary Anti-PD(L)1 Resistant Tumor Models

Anti-PD(L)1 Resistant B16F10 (Melanoma) Tumor Cells



Anti-PD(L)1 Resistant EL4 (Lymphoma) Tumor Cells



ATG-101 Has Been Granted an Orphan Drug Designation (ODD) by the U.S. FDA for the Treatment of Pancreatic Cancer

ANTENGENE

Pancreatic Cancer is a Highly Malignant Type of Gastrointestinal Cancer

495,000+
New Cases Globally Each Year

13th
Globally by Incidence

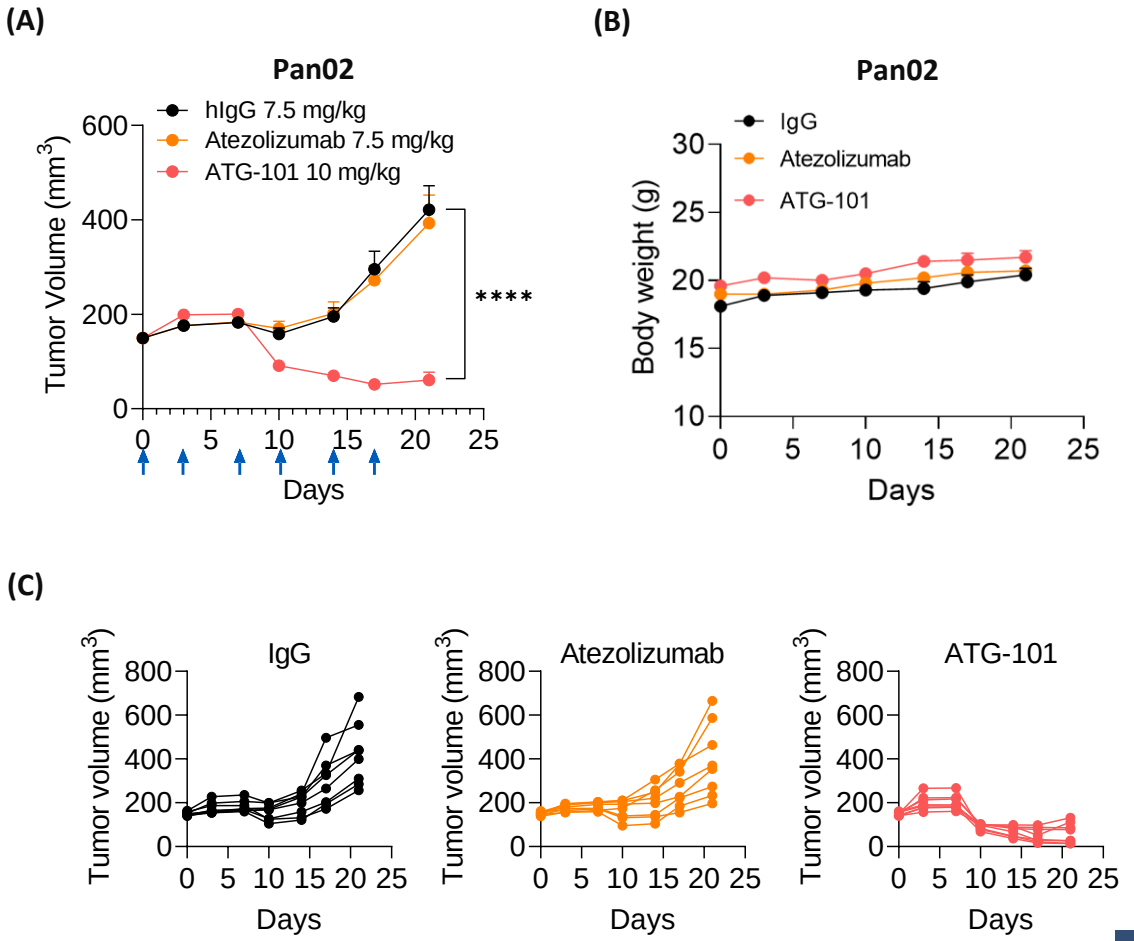
7th
Globally by Mortality Rates

466,000+
Related Deaths Globally Each Year

2nd
Most Common Cause of Cancer-related Deaths by 2030

Source: World Health Organization, World Cancer Research Fund International, SITC 2022.

ATG-101 Demonstrated Potent In Vivo Efficacy in Pan02, ICI-resistant Murine Syngeneic Pancreatic Cancer Model



ATG-101 Overall Clinical Development Plan

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	"PROBE"	"PROBE – CN"
Dose Escalation	**Australia/United States – MRCT** Regimen: **Q3W** ■ Enrolling patients in the 4th cohort (0.2 mg/kg) of dose escalation ■ IND clearance in the US October 2021; Granted orphan drug designation by the US FDA September 2022	**China** Regimen: **Q4W** ■ IND clearance March 2022; Enrolling patients in the 3rd cohort (0.2 mg/kg) of dose escalation
Dose Expansion	**Australia/United States/China – MRCT** Regimen: TBD based on escalation outcome (Q3W and/or Q4W) Competitive enrollment	

ATG-101 "PROBE" Clinical Trial Design and Status Updates

ANTENGENE

First-in-Human Phase 1 Trial of ATG-101 in Patients with Metastatic/Advanced Solid Tumors and B-NHL

Location: Australia, United States

Key Eligibility Criteria:

- **Dose Escalation:**
  - Adv. Solid tumors (regardless of PD-L1 expression, not HCC) OR R/R B-NHL
  - Exhausted available standard therapies
- **Dose Expansion (8 cohorts):**
  - Adv. Solid tumors of any histology (except HCC) and *CPI-exposed*:
    1. DP following prior response/SD for ≥6mths to anti-PD-1/PD-L1
    2. Best response of SD <6mths or DP after anti-PD-1/PD-L1
  - Adv. Solid tumors/haematological malignancies with specific histologies below who have failed prior therapies but are *CPI naïve*:
    3. TNBC
    4. GBM
    5. Gastric cancer, GEJ, oesophageal cancer
    6. HPV+ HNSCC,
    7. Cervical cancer
    8. B-NHL

Dose Escalation — N = ~40-50

COHORT 1 *(21-day cycle)* — N = 1
ATG-101: Q3W, 0.014 mg/kg IV on day 1

COHORT 2 *(21-day cycle)* — N = 1
ATG-101: Q3W, 0.03 mg/kg IV on day 1

COHORT 3 *(21-day cycle)* — N = 1
ATG-101: Q3W, 0.07 mg/kg IV on day 1

COHORT 4+ *(21-day cycle)*
Starting dose level
ATG-101: Q3W, 0.2 mg/kg IV on day 1

For duration of clinical benefit, as determined by investigator
"BOIN design" dose escalation

Status:
- Enrolling patients in the 4th cohort (0.2 mg/kg) of dose escalation;
- IND clearance in the US October 2021;
- Granted orphan drug designation by the US FDA September 2022

MTD, OBD

Dose Expansion — N = 12 - 40 *(per cohort)*

ATG-101 CPI-exposed *(21-day cycle)*

ATG-101: Q3W, MTD/OBD IV on day 1

2 cohorts, adv. Solid tumors of any histology:
1) DP following prior response/SD for ≥6mths to anti-PD-1/PD-L1
2) Best response of SD <6mths or DP after anti-PD-1/PD-L1

For duration of clinical benefit, as determined by investigator

ATG-101 CPI-naïve *(21-day cycle)*

ATG-101: Q3W, MTD/OBD IV on day 1

6 cohorts:
1) TNBC
2) GBM
3) Gastric cancer, GEJ, oesophageal cancer
4) HPV+ HNSCC
5) Cervical cancer
6) B-NHL

For duration of clinical benefit, as determined by investigator

Primary endpoint: MTD, OBD, safety
Secondary endpoints: ORR, BOR, DOR, PFS, PK/PD
Exploratory endpoints: incidence of ADA, immune microenvironment, biodistribution

ATG-101-001
Sponsor: Antengene

ADA: anti-drug antibody; Adv.: advanced; BOR: best overall response; BOIN: Bayesian optimal interval; B-NHL: B-cell non Hodgkin Lymphoma; CPI: checkpoint inhibitor; DOR: duration of response; DP: disease progression; GBM: glioblastoma multiforme; GEJ: gastroesophageal junction adenocarcinoma; HCC: hepatocellular carcinoma; HNSCC: head and neck squamous cell carcinoma; HPV: human papilloma virus; MTD: maximum tolerated dose; OBD: optimal biological dose; ORR: overall response rate; PFS: progression free survival; PD: pharmacodynamics; PK: pharmacokinetics; R/R: relapsed or refractory; SD: stable disease; TNBC: triple negative breast cancer; TPS: tumor proportion score

ATG-101 "PROBE-CN" Clinical Trial Design and Status Updates

ANTENGENE

First-in-Human Phase 1 Trial of ATG-101 in Patients with Advanced Solid Tumors and B-NHL

Location: China

Key Eligibility Criteria:

- **Dose Escalation:**
  - Adv. Solid tumors (regardless of PD-L1 expression, not HCC)
  - Exhausted available standard therapies
- **Dose Expansion:**
  - Adv. Solid tumors with primary resistant to CPI
  - Adv. Solid tumors with secondary resistant to CPI
  - Failed prior therapies, but are CPI naive (incl. TNBC, GBM, gastric cancer, GEJ, oesophageal cancer, HPV+ HNSCC, cervical cancer and ≥2L B-NHL)

Dose Escalation — N = ~40-50

COHORT 1 *(21-day cycle)* — N = 1

ATG-101: Q4W, 0.014 mg/kg IV on day 1

COHORT 2 *(21-day cycle)* — N = 1

ATG-101: Q4W, 0.07 mg/kg IV on day 1

COHORT 3+ *(21-day cycle)*

Starting dose level
ATG-101: Q4W, 0.2 mg/kg IV on day 1

For duration of clinical benefit, as determined by investigator

"BOIN design" dose escalation

MTD, OBD

Dose Expansion — N = 12 - 40 *(per cohort)*

ATG-101 *(28-day cycle)*

ATG-101: RP2D , Q4W, 8 cohorts ≥12 pts each:

- Adv. Solid tumors with primary resistant to CPI
- Adv. Solid tumors with secondary resistant to CPI
- Failed prior therapies, but are CPI naive
  1) TNBC
  2) GBM
  3) Gastric cancer, GEJ, oesophageal cancer
  4) HPV+ HNSCC
  5) Cervical cancer
  6) ≥2L B-NHL

For duration of clinical benefit, as determined by investigator

Status:

- IND clearance March 2022;
- Enrolling patients in the 3rd cohort (0.2 mg/kg) of dose escalation

Primary endpoint: MTD, OBD, safety
Secondary endpoints: ORR, BOR, DOR, PFS, PK/PD
Exploratory endpoints: Immune microenvironment, biodistribution

ATG-101-001-CN
Sponsor: Antengene

Adv.: advanced; BOR: best overall response; BOIN: Bayesian optimal interval; B-NHL: B-cell non Hodgkin Lymphoma; CPI: checkpoint inhibitor; DOR: duration of response; DP: disease progression; GBM: glioblastoma multiforme; GEJ: gastroesophageal junction adenocarcinoma; HCC: hepatocellular carcinoma; HNSCC: head and neck squamous cell carcinoma; HPV: human papilloma virus; MTD: maximum tolerated dose; OBD: optimal biological dose; ORR: overall response rate; PFS: progression free survival; PD: pharmacodynamics; PK: pharmacokinetics; R/R: relapsed or refractory; SD: stable disease; TNBC: triple negative breast cancer; TPS: tumor proportion score

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

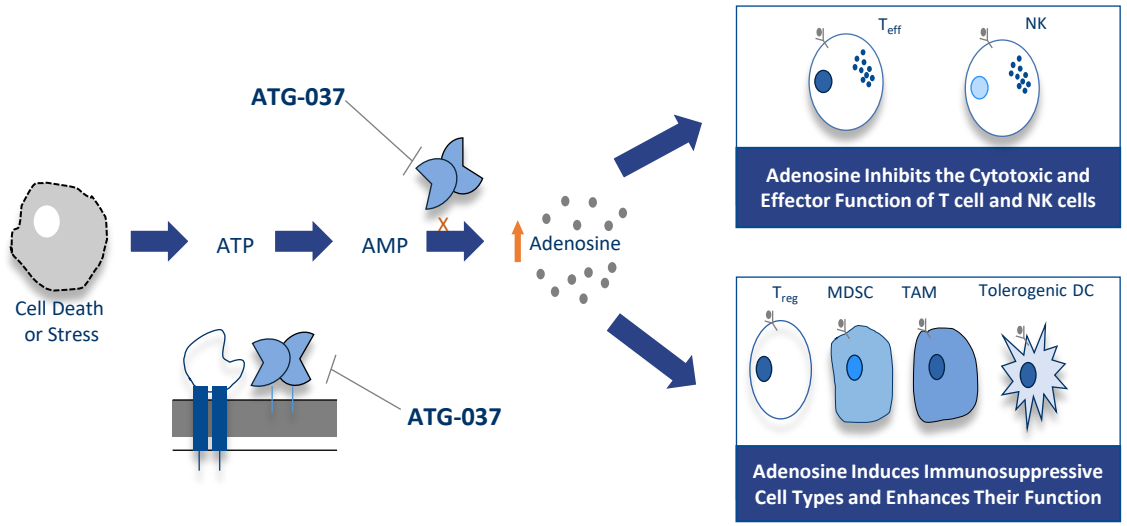
ANTENGENE

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**

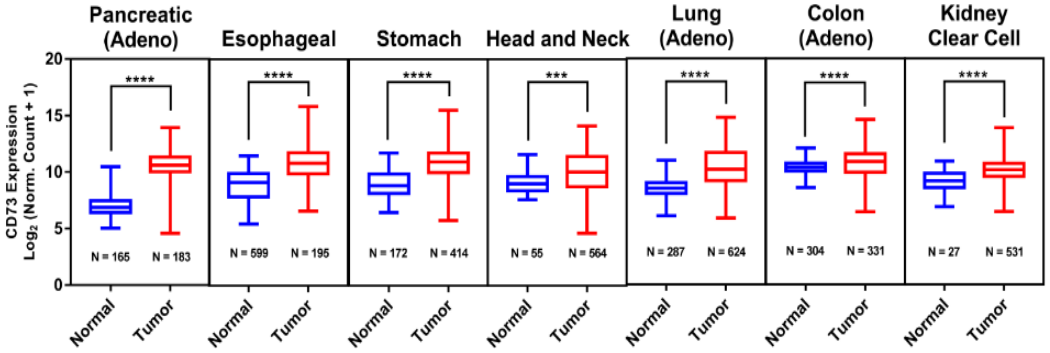


Excellent Safety Profile

- **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-037 is a Potentially Best in Class Small Molecule Inhibitor of CD73

ANTENGENE

- Orally bioavailable small molecule, with tissue penetrance not achievable with monoclonal antibodies
- Better cell surface CD73 enzyme inhibition than antibodies with no hook effect
- Showed the highest CD73 enzyme inhibition activity for small molecule inhibitors reported so far

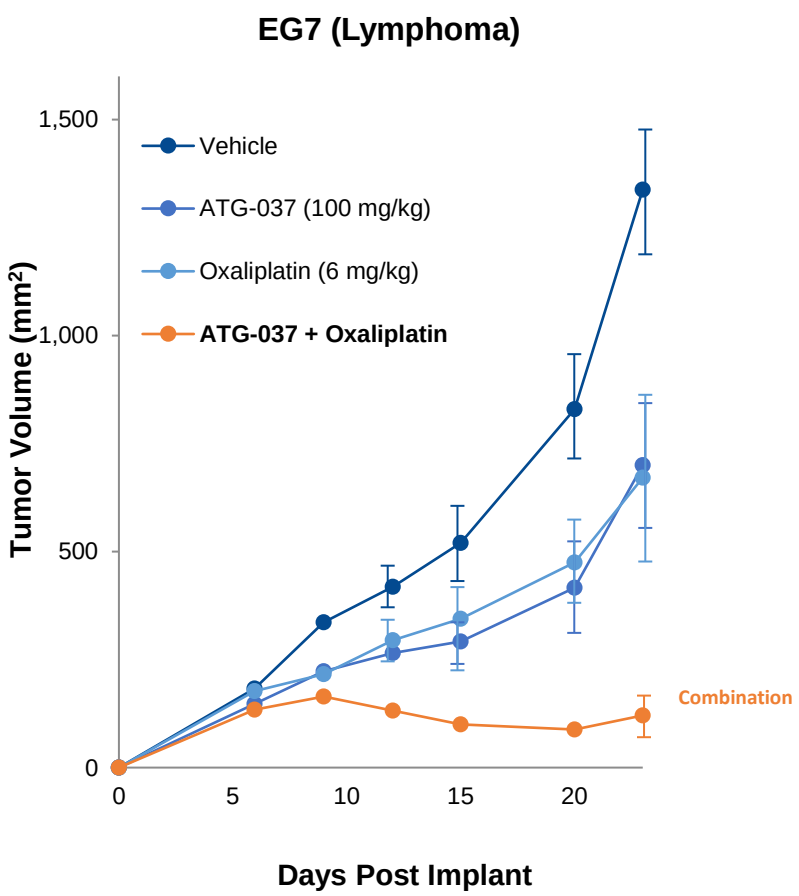
		ATG-037	Quemliclustat/AB680	ORIC-533	Oleclumab/MEDI9447	Ulileclimab/Hu101-28
Company		Antengene	Arcus	ORIC	AZ	IMAB
Global Status		Phase I	Phase I/II	Phase I	Phase II/III	Phase II
Modality		Small molecule	Small molecule	Small molecule	Antibody	Antibody
Binding kinetics / Potency indicators	**Cell surface CD73 inhibition (IC_{50}) in buffer**	**0.4 nM (Antengene test in A375 cells)**	5.3 nM (ORIC test in H1568 cells)	0.1 nM (ORIC test in H1568 cells)	3.5 nM (Antengene test in A375 cells)	20.9 nM (Antengene in house test in A375 cells)
	CD73 inhibition (% of control activity) in buffer	100%, no hook effect	>90%, no hook effect	100%, no hook effect	~50%, hook effect	100%, no hook effect
	Human plasma CD73 protein inhibition (IC_{50})	**0.38 nM**	19.9 nM (report)	No report		
	CD8+T cell rescue at high AMP (> 100 µM)	**Complete rescue at 1 mM AMP (proliferation, activation, cytokine)**	No rescue	Complete rescue at 1 mM AMP (proliferation, activation, cytokine)	No rescue (Antengene in house test)	No rescue (Antengene in house test)
Efficacy *in vivo*		Monotherapy in EG7 and CT26 (100 mpk, ~60% TGI), synergism with oxaliplatin, docetaxel, or PD-L1 antibody	Combination with aPD-1 in B16F10	150 mpk in EG7 model, 67% TGI of monotherapy	Combination with aPD-(L)1	Monotherapy of A375 in PBMC engrafted; combination with aPD-(L)1 in HCC827, PBMC engrafted

Source: publications & primary research

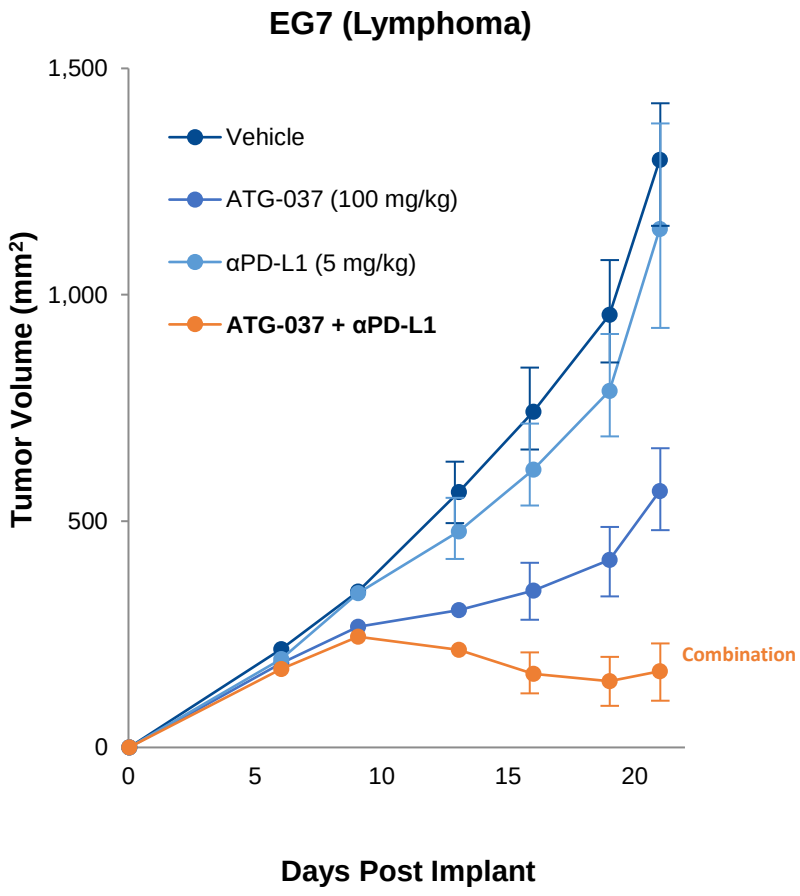
ATG-037 Demonstrates In Vivo Synergy with Chemotherapy, Checkpoint Inhibitors and ATG-010 (Selinexor)

ANTENGENE

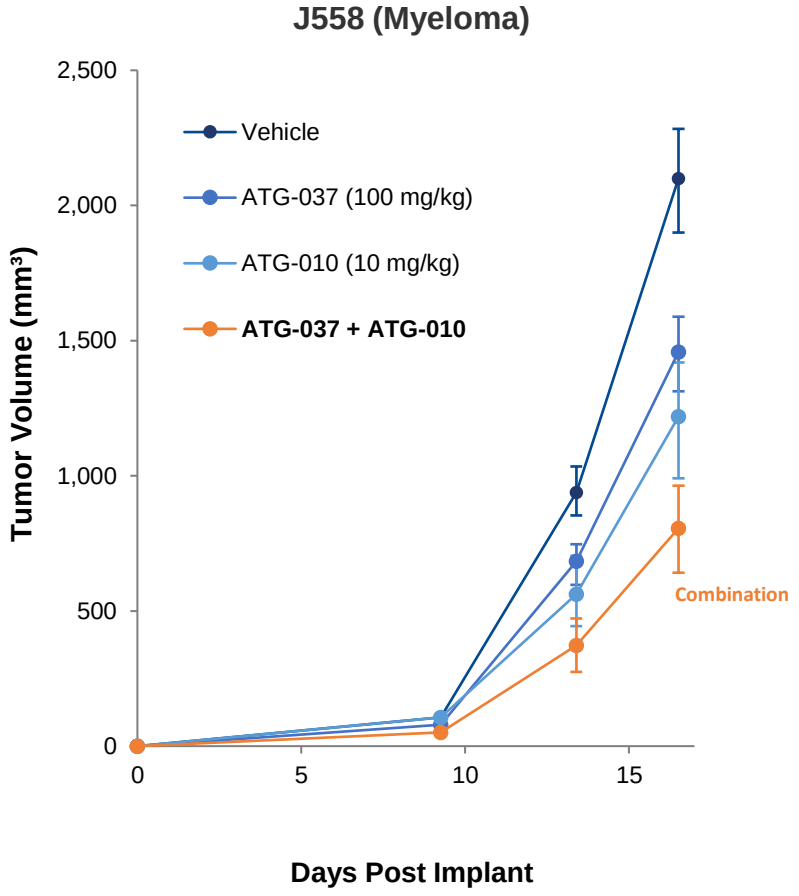
In Vivo Synergy with Chemotherapy in Mouse EG7 Lymphoma



In Vivo Synergy with Anti-PD-L1 in Mouse EG7 Lymphoma Model



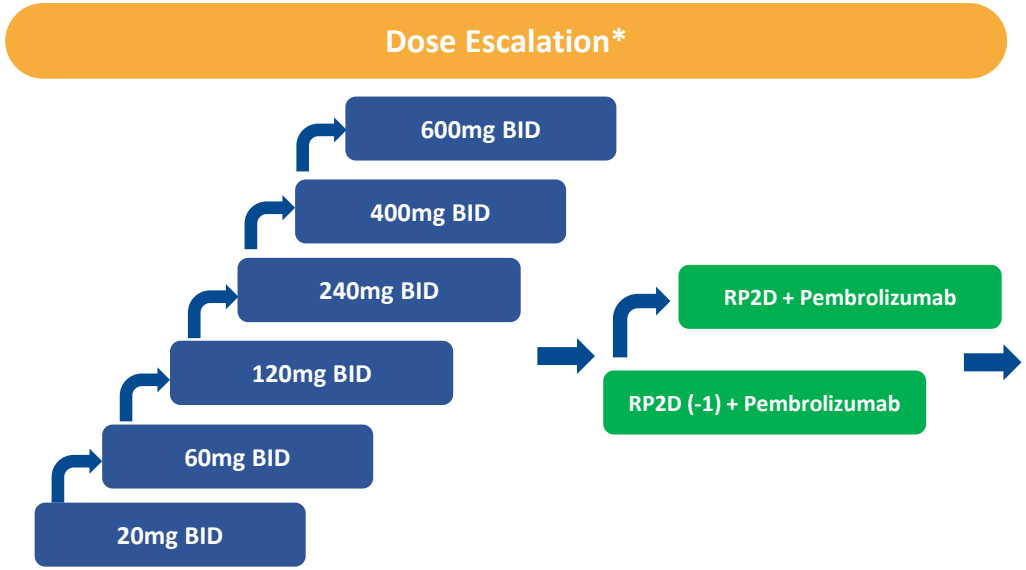
In Vivo Synergy with ATG-010 (Selinexor) in Mouse J558 Myeloma Model



ATG-037 “STAMINA” Clinical Trial Design and Status Updates

ANTENGENE

Phase I/Ib, Multi-center, Open-label, and Dose-finding Study to Assess the Safety, Pharmacokinetics, Pharmacodynamics, and Preliminary Efficacy of ATG-037 Monotherapy and Combination Therapy with Pembrolizumab in Patients with Locally Advanced or Metastatic Solid Tumors



*After 2 cycles of ATG-037 monotherapy, Australian subjects will receive ATG-037 combination therapy with pembrolizumab

Part I: Monotherapy* | **Part II: Upfront Combination**

Status:

- First patient dosed in June 2022 in Australia, currently in cohort 2;
- IND approval in China expected in Q4 2022

Target Population

- Patients with locally advanced or metastatic solid tumors
- Demonstrated disease progression after standard therapies or for which no standard of care (SoC) therapies exist
- Patients with acquired CPIs resistance

Primary Objectives:

- To assess the safety and tolerability of ATG-037 monotherapy and combination therapy with pembrolizumab
- To determine the Recommended Phase II Dose (RP2D) of ATG-037 monotherapy and combination therapy with pembrolizumab

Secondary Objectives:

- To evaluate the preliminary anti-tumor activity of ATG-037 alone or combination with pembrolizumab
- To characterize the PK/PDx profile of ATG-037

ATG-037-001
Sponsor: Antengene

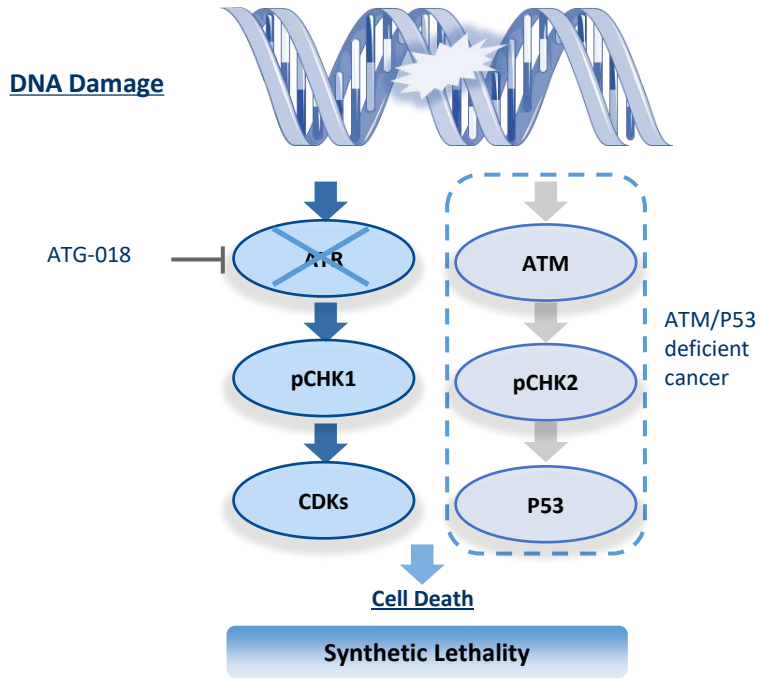
CPIs: checkpoint inhibitors; CRC: colorectal cancer; CRPC: castrate-resistant prostate cancer; NSCLC: non-small cell lung cancer; PDx: pharmacodynamics; PK: pharmacokinetics; SCCHN: squamous cell carcinoma of head and neck

ATG-018: DNA Damage Repair Inhibitor with Superior In Vivo Efficacy

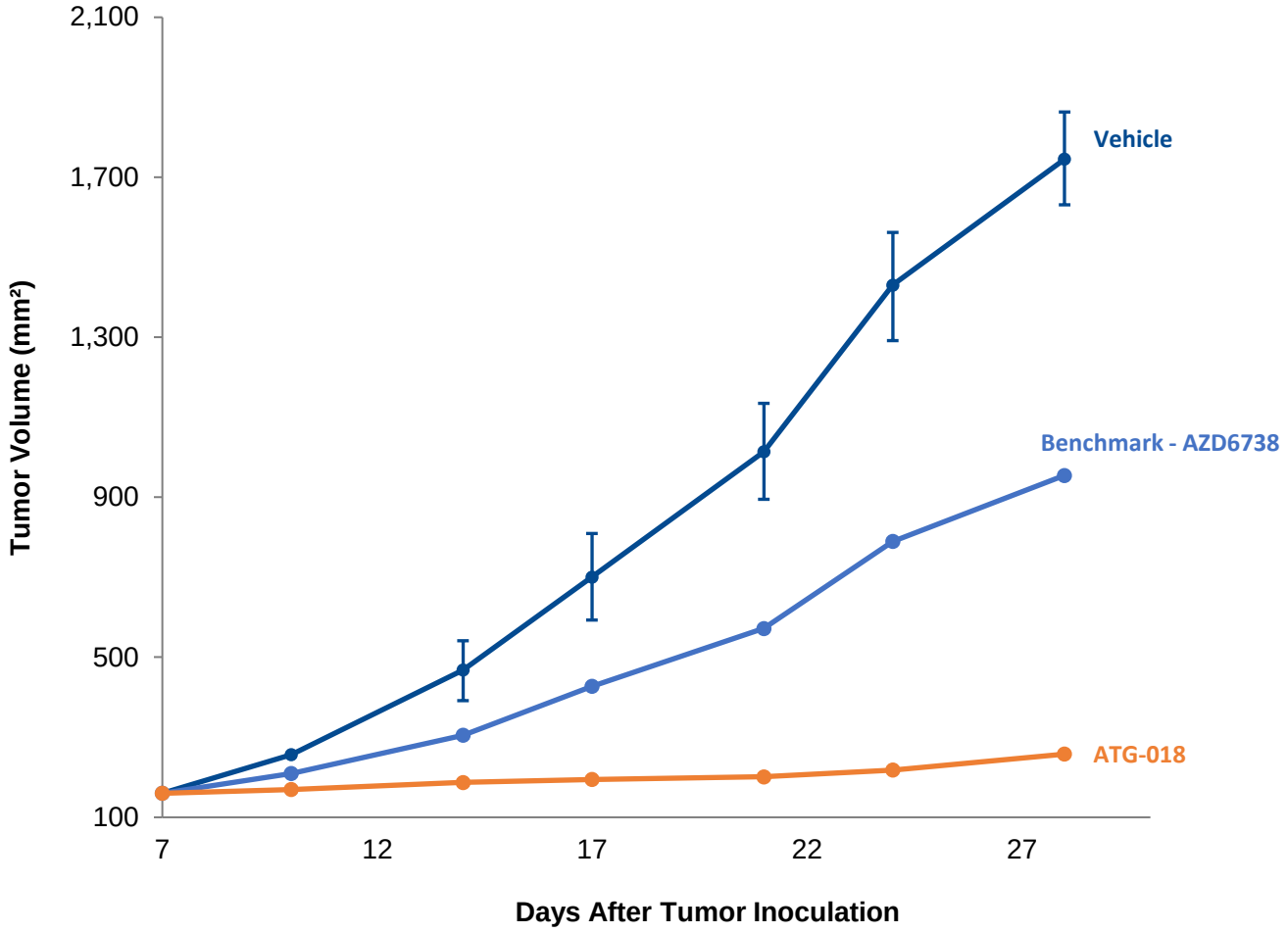
ANTENGENE

Summary of ATG-018

- ATG-018 Inhibits DNA damage repair, releasing tumor cells from cell cycle arrest and inducing tumor cell death by **synthetic lethality**
- Demonstrated **superior in vivo efficacy**, compared with clinical benchmark in pre-clinical CDX models
- **Biomarker strategies** have been developed for ATG-018



In Vivo Efficacy Comparison (LOVO CDX) [1]



Source: AACR 2022.

ATG-018 is a Potentially Best-in-class Small Molecule Inhibitor of ATR

ANTENGENE

- Better ATR downstream (CHK1) phosphorylation inhibition and cell anti-proliferation potency than AZD6738*
- Demonstrates better safety profiles (CYP and hERG Inhibition) than BAY189534**
- Demonstrates better in vivo efficacy in LoVo CDX model than reference compounds

Dimensions of Comparison		ATG-018	RP3500/Camonsertib	AZD6738/Ceralasertib	BAY1895344/Elimusertib
Company		Antengene	Repare	AstraZeneca	Bayer
Global Status		Phase I	Phase I/II	Phase III	Phase I/II
Binding kinetics / Potency indicators	ATR Enzyme Assay IC_{50} (nM)	16	1.00	2.9	18
	pCHK1 Cell IC_{50} (nM)	**2.2**	0.33	13.7	0.7
	CYP inhibition 1A2/2C9/2C19/2D6/3A4$^{(M)}$/3A4$^{(T)}$ IC_{50} (μM)	**>50/>50/>50/21.26/>50/>50**	-	> 50 ^{3}A4$^{(M)}$	3.14 (ref=10~15) 3A4$^{(M)}$
	Transporters OATP1B1/OATP1B3 IC50 (μM)	> 40/ >40	-	2.0/ -	>10 / -
	hERG IC50 (μM)	**> 50**	-	> 40	15 $^{(ref)}$
TGI (%, LoVo CDX 25mpk BID, 5 on 2 off)		**74.7**	~65 (15 mpk QD, continuous, >15% BW loss)	21.3	39.5

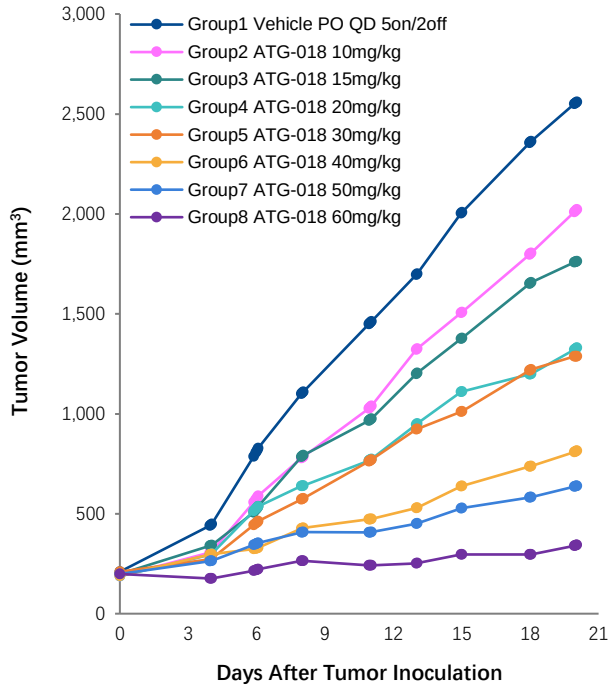
** AZD6738 is Ceralasertib currently being developed by AstraZeneca*
*** BAY189534 is Elimusertib currently being developed by Bayer*

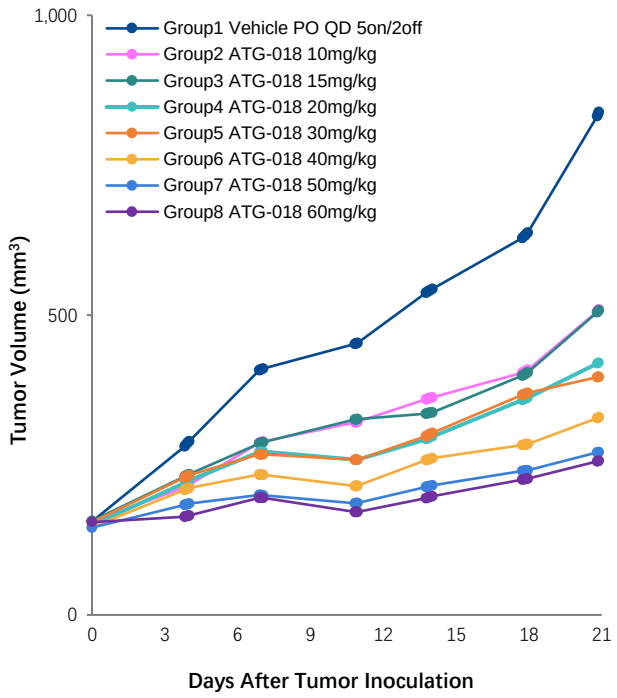
Source: Publications & primary research

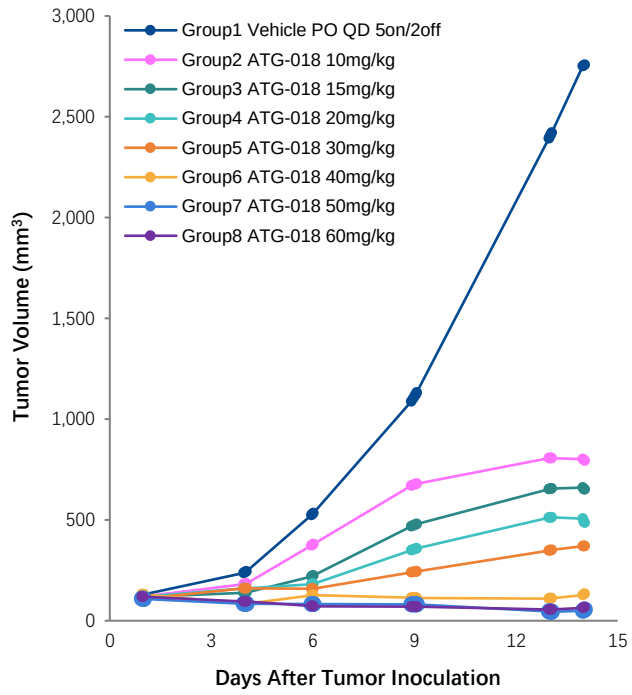
ATG-018 Shows Strong Anti-Tumor Efficacy in DNA Damage Response-Sensitive CDX Models

ANTENGENE

Model	LoVo	OE21	OCI-LY-19
Cancer	Colorectal Cancer	Esophageal Cancer	Lymphoma
DDR Mutation	MRE11, ARID1A	ARID1A	ARID1A
ATG-018: 10 mg/kg – TGI	20.93% (Day 20)	39.20% (Day 21)	73.52% (Day 14)
ATG-018: 50 mg/kg – TGI	74.59% (Day 20)	67.72% (Day 21)	100.83% (Day 14)

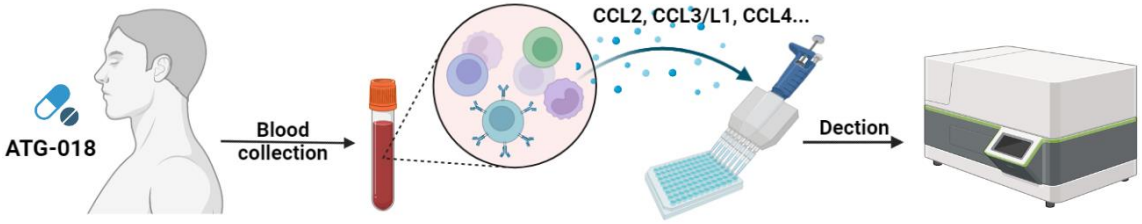


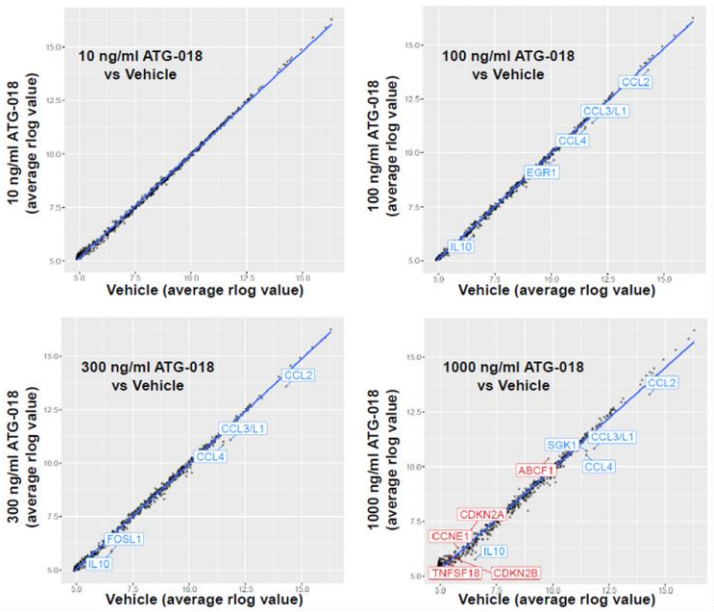


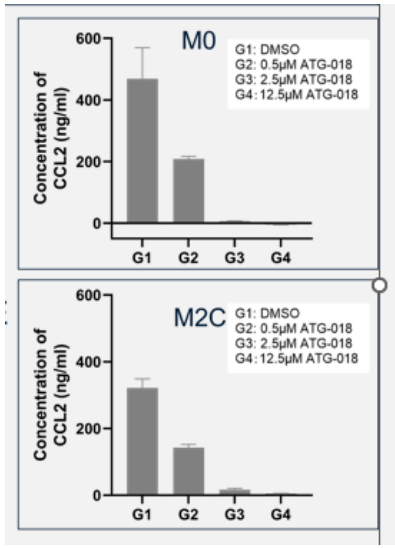


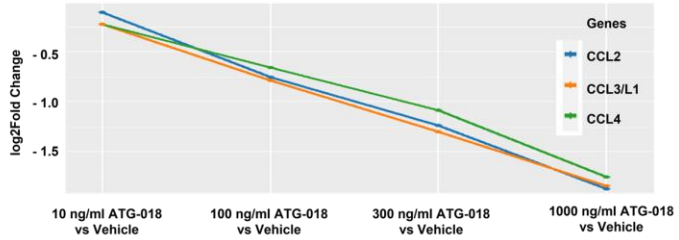
Source: AACR 2022.

Discovery of Blood Pharmacodynamic Biomarkers for ATR Inhibitors









Source: SITC 2022.

Blood Pharmacodynamic Biomarkers

- Pharmacodynamic (PD) biomarkers are crucial to help guide dose and scheduling and support mechanism of action studies
- Phosphorylation of Chk1 or γH2AX has been reported to be PD markers of ATR inhibitors. However, these markers are difficult to measure directly using blood samples
- By unbiased gene expression screening, we found the expression of some chemokines, especially CCL2, **CCL3/L1, and CCL4 are potential novel PD biomarkers of ATG-018**, which could be detected in unmanipulated blood samples, and may **guide dose and scheduling and support mechanism of action studies** of both ATG-018 and other ATR inhibitors in clinic

ATG-018 "ATRIUM" Clinical Trial Design and Status Updates

ANTENGENE

Phase I, Open-Label, Multi-Center Dose Finding Study to Investigate the Safety, Pharmacokinetics, and Preliminary Efficacy of ATG-018 (ATR inhibitor) Treatment in Patients with Advanced Solid Tumors and Hematological Malignancies

Anticipated Dose Escalation Schedule (For Solid Tumors Group)

Dose Level[1]	ATG-018 Dose at Each Treatment Administration Point	Planned Subject Numbers
1[2]	5 mg QD	1
2[2]	5 mg BID	1
Per BOIN Design (maximum number of subjects: 42)		
3[2]	10 mg BID	-
4[2]	20 mg BID	-
5[2]	30 mg BID	-
6[2]	45 mg BID	-
7[2]	60 mg BID	-
8[2]	75 mg BID	
9[2]	90 mg BID	

Status:

- Enrollment of the 3rd cohort on-going.
- China and US IND to be submitted upon completion of dose escalation in Australia

[1] *If tolerated at the highest doses, then further escalation may be allowed to higher dose levels.*
[2] *Subject(s) will receive intermittent dosing in a 3 days on/4 days off schedule in 21-day cycles until disease progression or unacceptable toxicity.*

Target Population

- Patients with mixed solid tumors or B-NHL

- **Primary Objectives:**
  - To evaluate the safety and tolerability of ATG-018
  - To establish MTD and/or RP2D of ATG-018 in subjects with advanced solid tumors and hematological malignancies
- **Secondary Objectives:**
  - To characterize the PK of ATG-018 following a single dose administration and at steady state after multiple dosing
  - To assess the preliminary anti-tumor activity of ATG-018 in subjects with advanced solid and hematological malignancies
- **Other Objectives:**
  - To explore the PDx of ATG-018 following a single dose administration and at steady state after multiple dosing
  - To explore the relationship between biomarkers and clinical results

ATG-018-001
Sponsor: Antengene


德琪医药
ANTENGENE
DRUG DISCOVERY

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

ANTENGENE

Summary of ATG-022

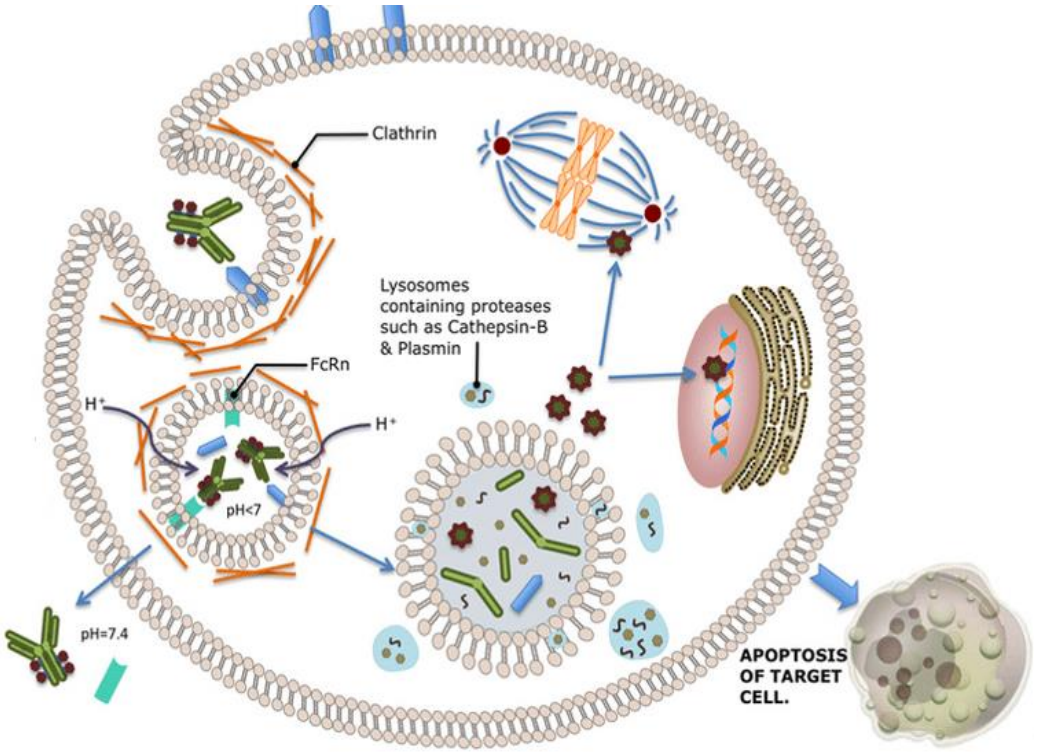
- Claudin 18.2 is a **tumor-associated antigen** overexpressed particularly in gastric, esophageal and pancreatic cancers, occasionally in other tumors including lung, ovarian, and head & neck malignancies
- Clinical ADC candidate with **vc-MMAE as linker payload (DAR4)**

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 CLDN18.2**, the primary target, on both fixed and live cells



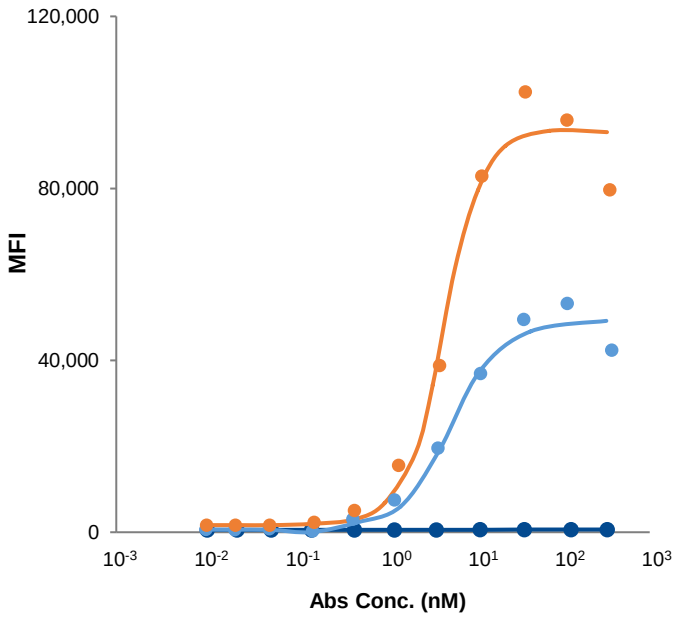
Christina Peters, Stuart Brown
Antibody–drug conjugates as novel anti-cancer chemotherapeutics

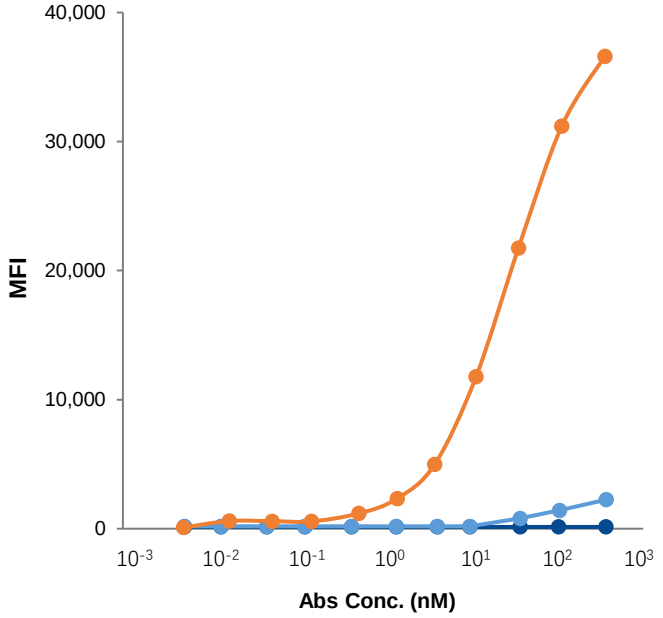
ATG-022 Binds to hCLDN18.2 with High Affinity, Allowing Reorganization of Tumor Cells with Low-CLDN18.2 Expression

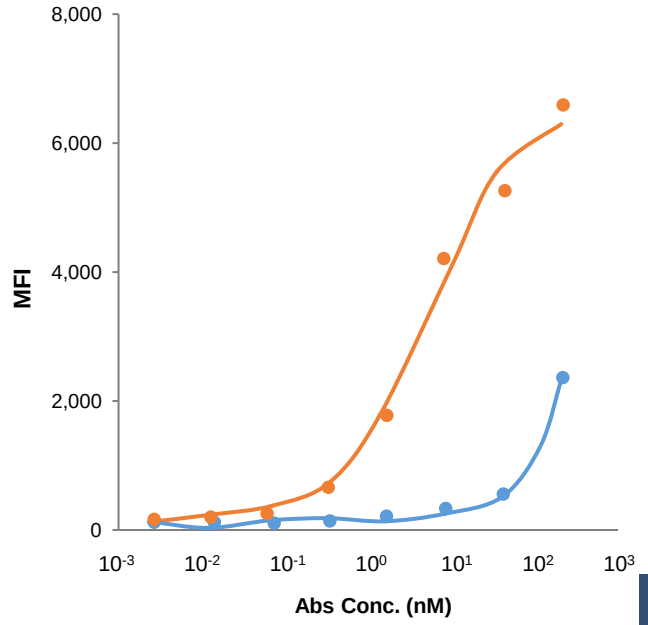
ANTENGENE

Cell-based Binding Affinity (EC_{50}) of ATG-022 mAb and Clinical Benchmark Antibodies

	I. CHOK1-hCLDN18.2 (High CLDN18.2 expression)	II. GAXC031 (Moderate CLDN18.2 expression)	III. SNU-620 (Low CLDN18.2 expression)
hIgG1 Ctrl	/	/	/
IMAB362	5.808nM	/	~7,537nM
ATG-022	4.645nM	32.25nM	5.317nM







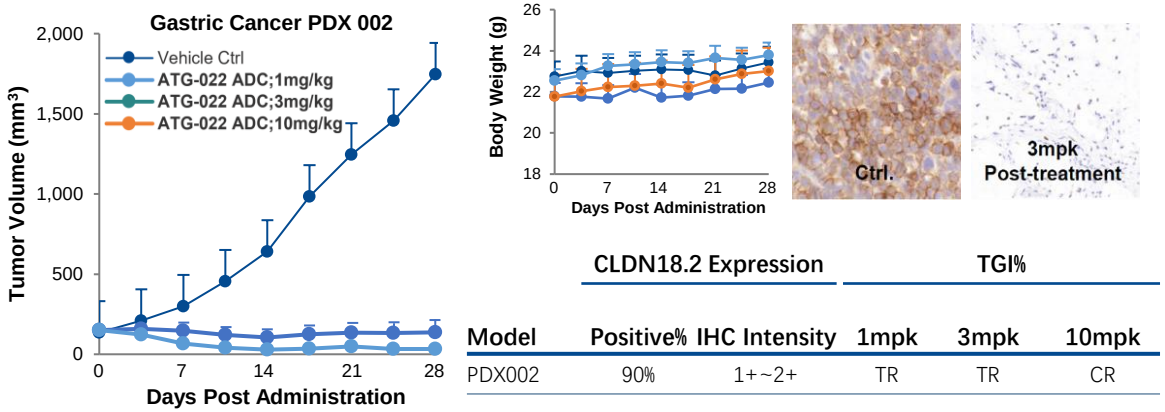
Source: AACR 2022.

ATG-022 Demonstrated Strong In Vivo Efficacy in Various CLDN 18.2 Level PDX Models

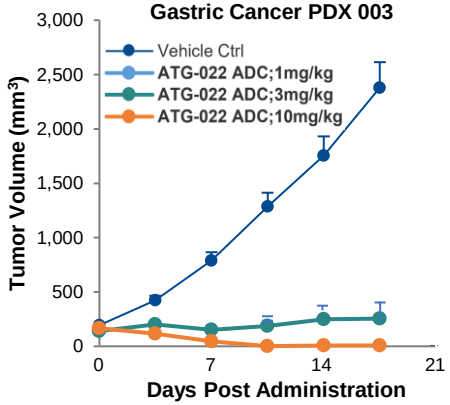
ANTENGENE

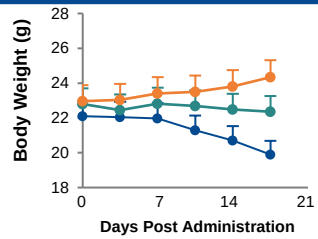
High Expression Level of Claudin 18.2

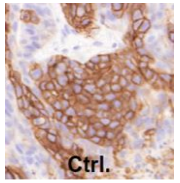
ATG-022 Induced Tumor Regression (TR) or Complete Remission (CR)

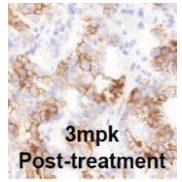


			CLDN18.2 Expression		TGI%	
Model	Positive%	IHC Intensity	1mpk	3mpk	10mpk
PDX002	90%	1+~2+	TR	TR	CR





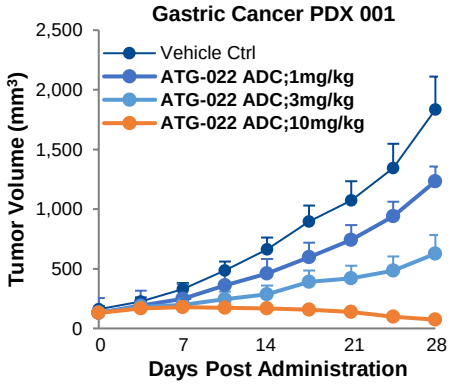


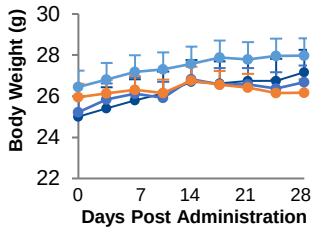


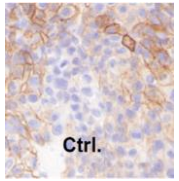
			CLDN18.2 Expression		TGI%	
Model	Positive%	IHC Intensity	3mpk	10mpk
PDX003	70%	2+~3+	94%	CR

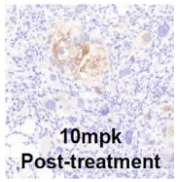
Moderate Expression Level of Claudin 18.2

ATG-022 Induced Tumor Regression (TR) or Complete Remission (CR)





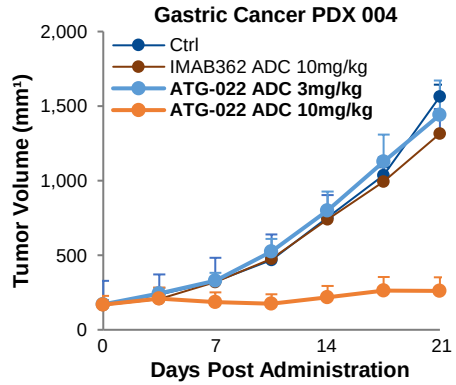


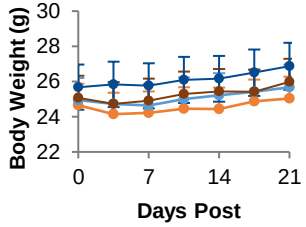


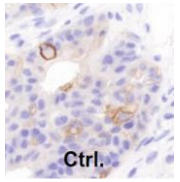
			CLDN18.2 Expression		TGI%	
Model	Positive%	IHC Intensity	1mpk	3mpk	10mpk
PDX001	60%	1+	35%	72%	TR

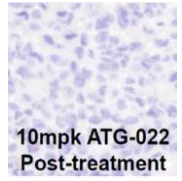
Extremely Low Expression Level of Claudin 18.2

ATG-022 Inhibited Tumor Growth









			CLDN18.2 Expression		TGI%	
Model	Positive%	IHC Intensity	BMK	3mpk	10mpk
PDX004	<5%	0~1+	NS	NS	93

Source: AACR 2022.

ATG-022 “CLINCH” Clinical Trial Design and Status Updates

ANTENGENE

Open, Multi-center Phase I Clinical Study of ATG-022 in Patients With Advanced/Metastatic Solid Tumors

Location: Australia, China, United States

Key Eligibility Criteria:

- **Dose Escalation:**
  - Adv./Meta solid tumors
  - No requirement for CLDN18.2 expression
  - At least 1 measurable lesion per RECIST v1.1
  - Prior standard therapies
- **Dose Expansion:**
  - Adv. Solid tumors with CLDN18.2 positive at any level
  - Have not exposed to a Claudin 18.2 targeting agent
  - Adequate organ function
  - ECOG 0 or 1

Dose Escalation — N = ~21

ATG-022 *(21-day cycle)*

Priority tumor types:
Gastric cancer, Esophageal cancer, gastroesophageal junction cancer, pancreatic cancer, ovarian cancer, and cholangiocarcinoma

Until disease progression or unacceptable toxicity

Status:
- EC submitted in October 2022 in Australia;
- IND submission in China is planned for December 2022

Primary endpoint:
MTD, RP2D, AE/SAE; DLT

Secondary/other endpoints:
PK, ORR, DOR, DCR, incidence of ADA, CLDN18.2 expression and clinical outcomes

MTD, OBD

Dose Expansion — N = 30-160 *(per cohort)*

ATG-022 *(21-day cycle)*

ATG-022: RP2D, IV, Q3W

3 cohorts (~10-12 pts each first):
1) Pancreatic cancer
2) Gastric cancer, including gastroesophageal junction cancer
3) Adv./Meta solid tumors

Until disease progression or unacceptable toxicity

ATG-022-ST-001
Sponsor: Antengene

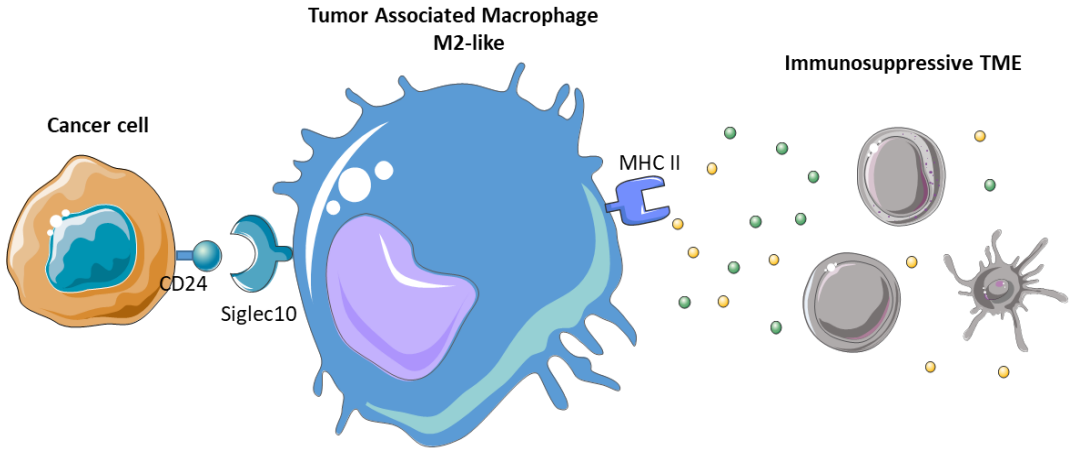
ADA: anti-drug antibody; Adv.: advanced; CLDN: Claudin; IV inf: intravenous infusion; MTD: maximum tolerated dose; ORR: overall response rate; PK pharmacokinetics; PO: oral; RP2D: recommended phase 2 dose;

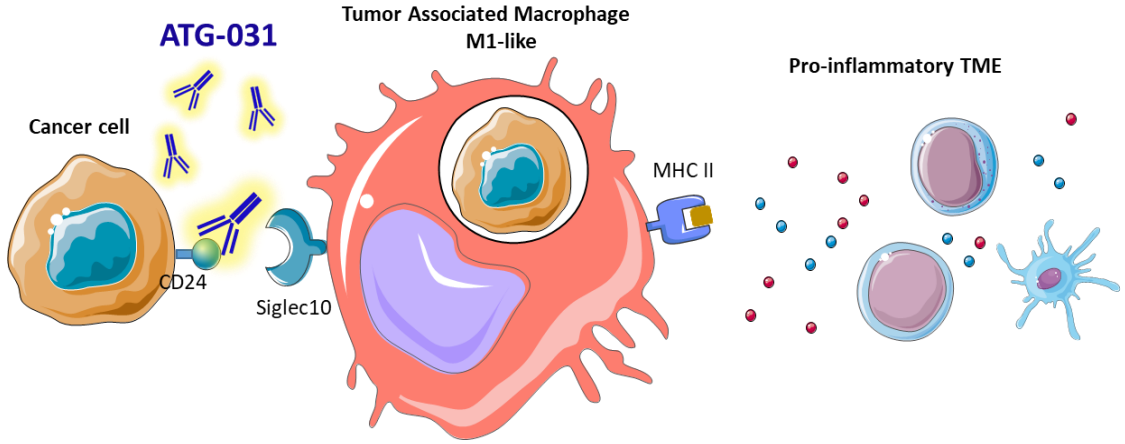
ATG-031: First-in-Class CD24 Antibody to Inhibit the “Don’t Eat Me” Signal

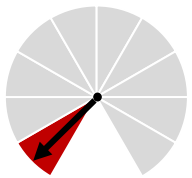
ANTENGENE

Summary of ATG-031

- CD24 is a “Don’t eat me” signal 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**

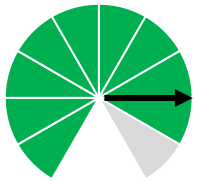






“Don’t Eat Me”

- Reduced phagocytosis
- M2-like Tumor Associated Macrophage
- Immunosuppressive Tumor Microenvironment
- Less tumor antigen presentation
- In-activated T and NK cells



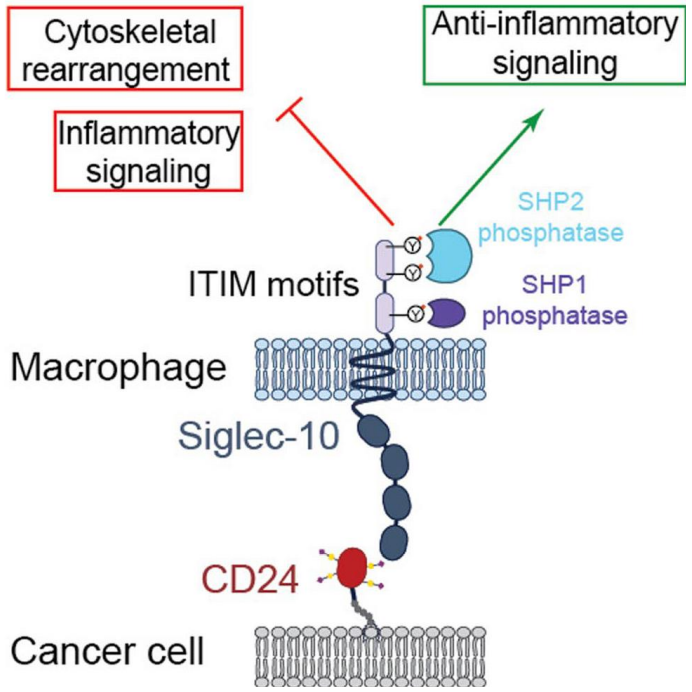
“Eat Me”

- Increased phagocytosis
- M1-like Tumor Associated Macrophage
- Pro-inflammatory Tumor Microenvironment
- Enhanced Tumor Antigen presentation
- Activated T and NK cells

Rationale for Targeting CD24 in Cancer

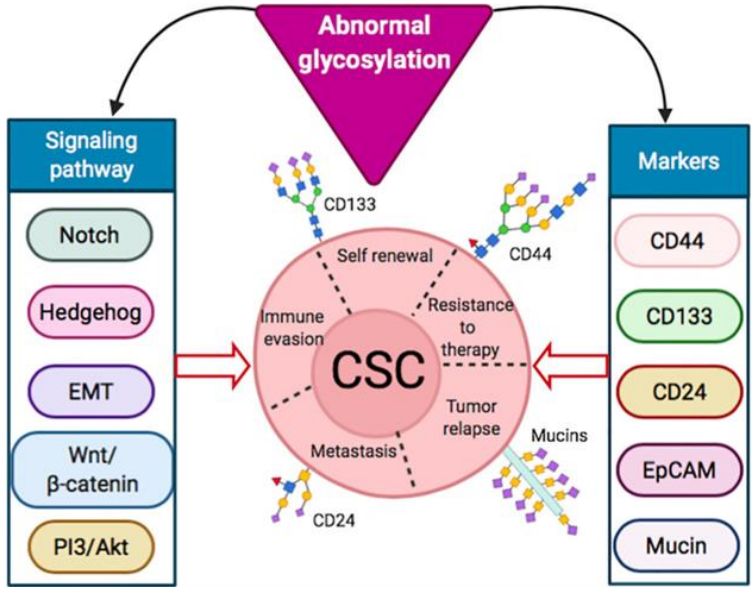
ANTENGENE

CD24 is a "Don't eat me" Protein on Cancer Cell and Triggers Anti-inflammatory Signaling in the TME



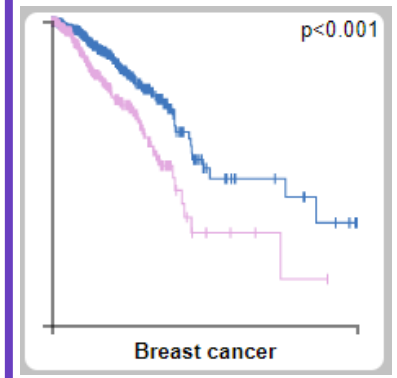
Nature. 2019; 572(7769): 392–396.

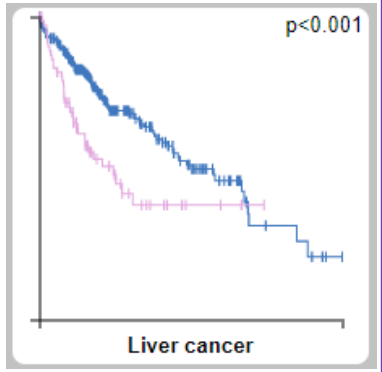
CD24 is a Marker of Cancer Stem Cells for Multiple Tumor Types, Such as Ovarian, Liver, Stomach and Pancreatic Cancer



Front Oncol. 2021; 11: 649338.

High Expression of CD24 is a Poor Prognostic Marker for Multiple Tumor Types

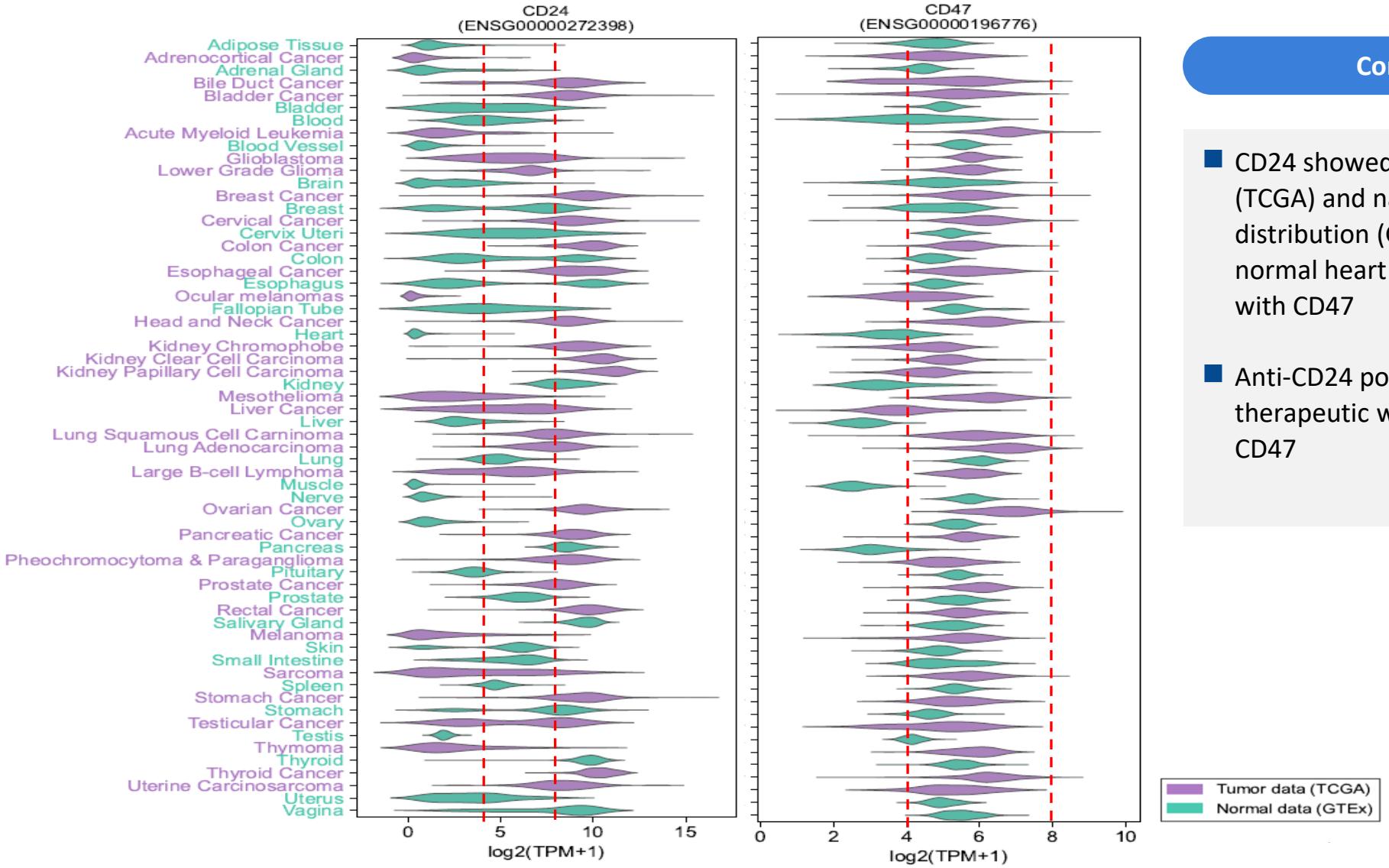




Human Protein Atlas

CD24 Has Higher Tumor Expression Compared to CD47

ANTENGENE



Comparison Analysis

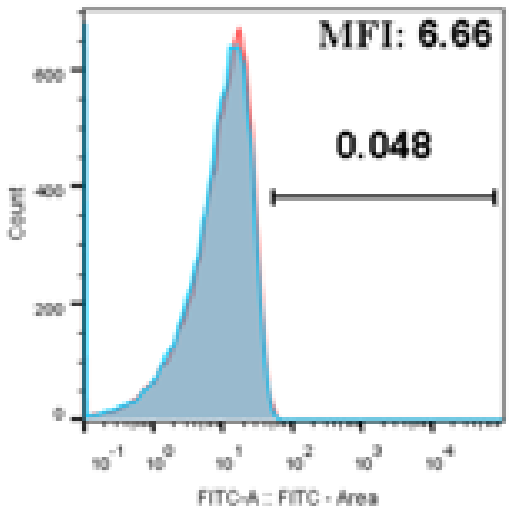
- CD24 showed much higher tumor expression (TCGA) and narrower normal tissue distribution (GTEx), with significantly lower normal heart and CNS expression, compared with CD47
- Anti-CD24 potentially has a larger therapeutic window compared with anti-CD47

CD24 is Not Expressed on Human Red Blood Cells, Unlike CD47

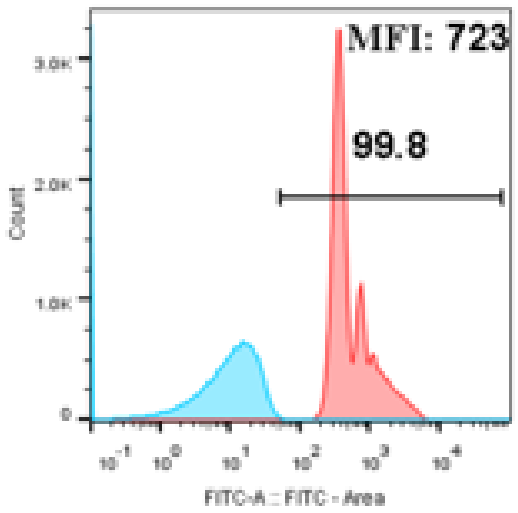
ANTENGENE

- Due to the normal tissue distribution of CD47 (eg. Expression on red blood cell), the clinical development of CD47 binding molecules that retain substantial FcR activating capacity (e.g. human IgG1) has been hampered by the on-target-off-tumor toxicity, such as erythrocyte depletion
- **Unlike CD47, CD24 is not expressed on human red blood cells**

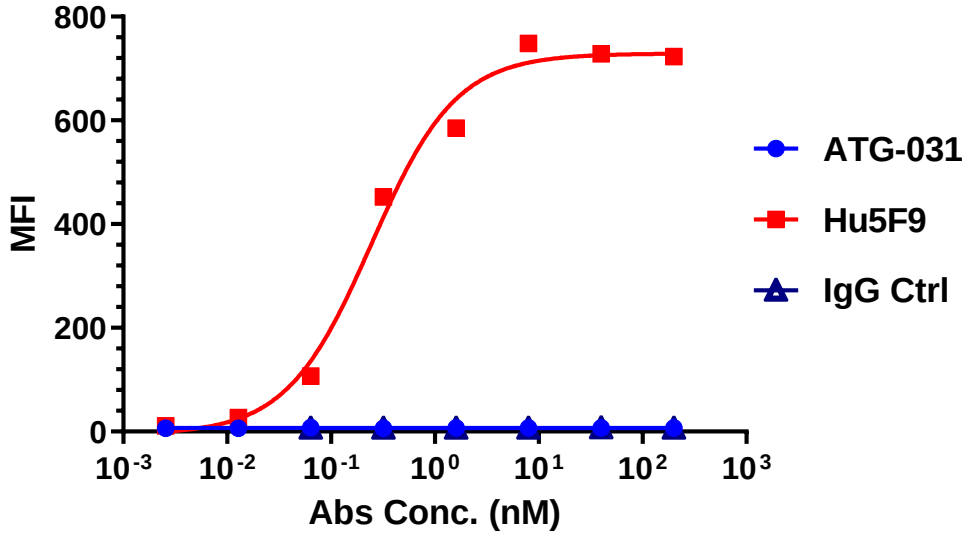
ATG-031



Anti-CD47



Human RBC



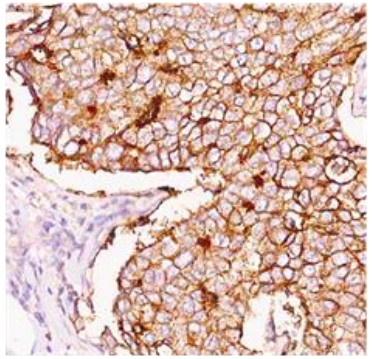
Human RBC Expressed CD47 but Not CD24

CD24 is Over-expressed in Multiple Tumor Types

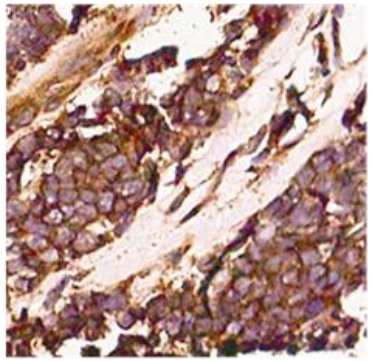
ANTENGENE

- A highly selective CDx antibody for IHC was developed in house
- IHC staining on tumor tissue microarray revealed that 50-80% of patients with lung, breast, bladder, ovarian, or liver cancer have CD24 expression on tumor cell surface
- CD24 over expression was also detected in other solid tumor types and hematological malignancies

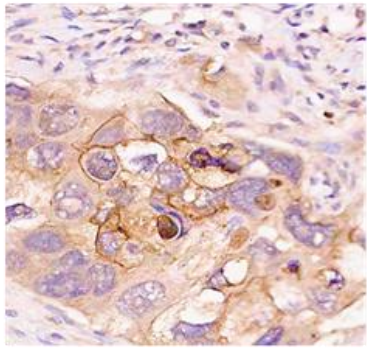
Breast Cancer



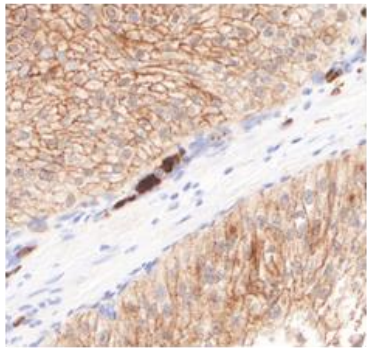
Small Cell Lung Cancer



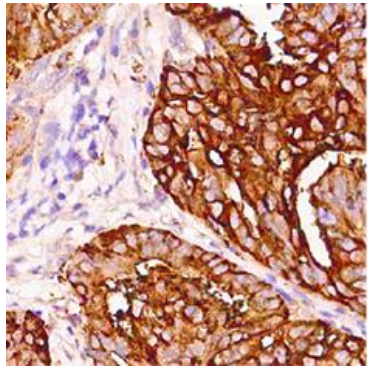
NSCLC-Sq



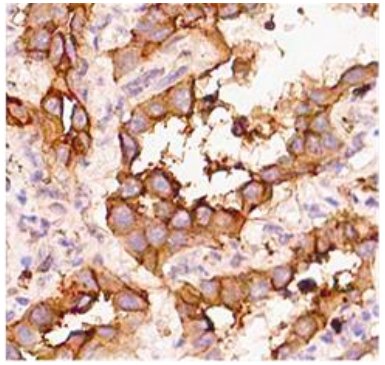
Bladder Cancer



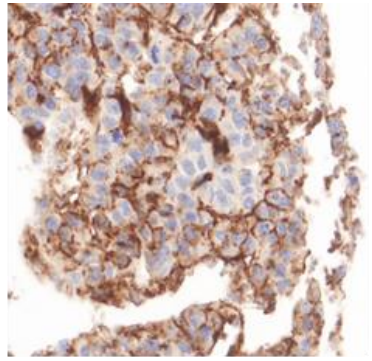
Ovarian Cancer



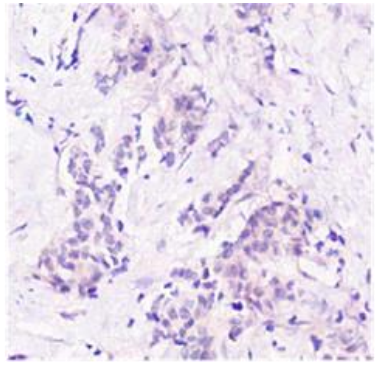
NSCLC-Adeno



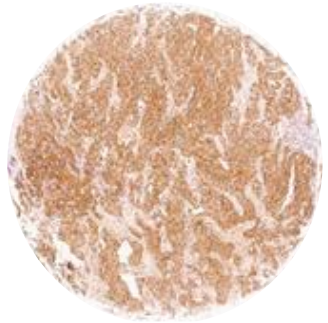
Liver Cancer



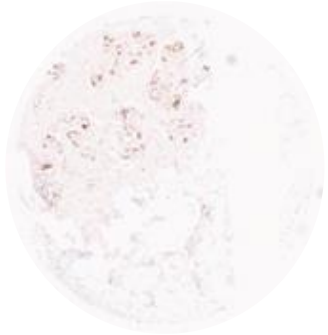
Negative Stained Tumor



CD24 Expression in Cancerous Tissue and Para-cancerous Normal Tissue



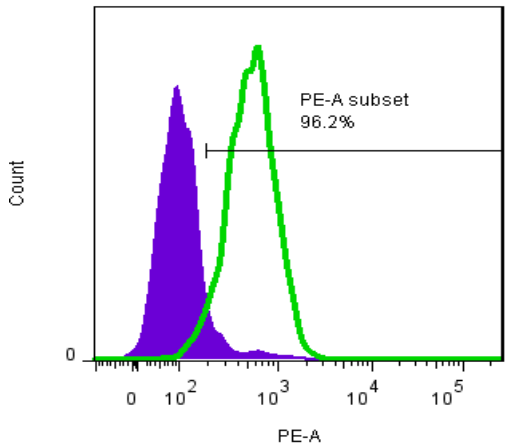
Breast Cancer Tissue



Para-cancerous Normal Tissue

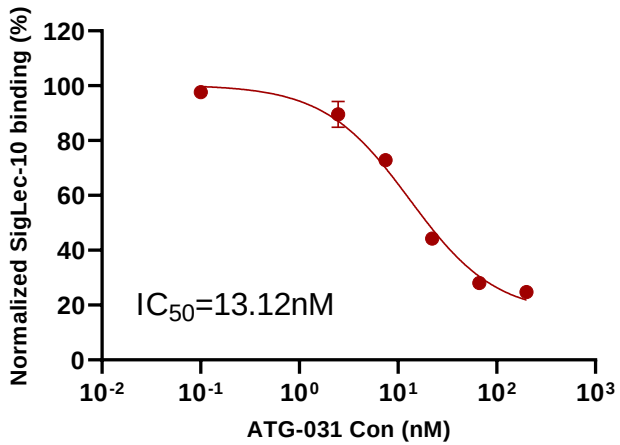
ATG-031 Blocks the Interaction of CD24 and Siglec-10 and Induces Potent Macrophage-dependent Phagocytosis

ATG-031 Blocks the Interaction of CD24 and Siglec-10 Protein



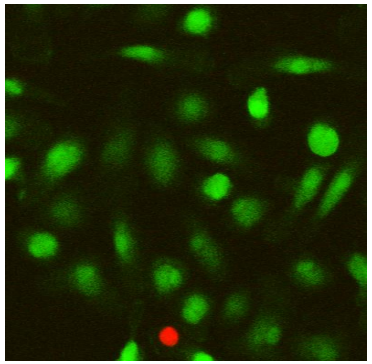
hSigLec-10 expression on M2 macrophage

ATG-031 Blocks Interaction of hCD24 and hSigLec-10

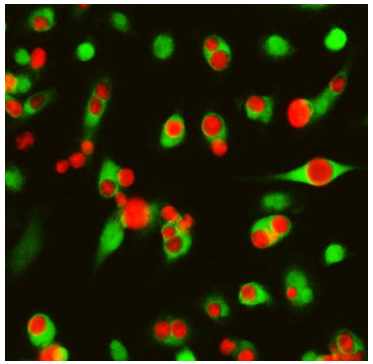


ATG-031 Enhances TAM-mediated Phagocytosis of Tumor Cell

+IgG Ctrl

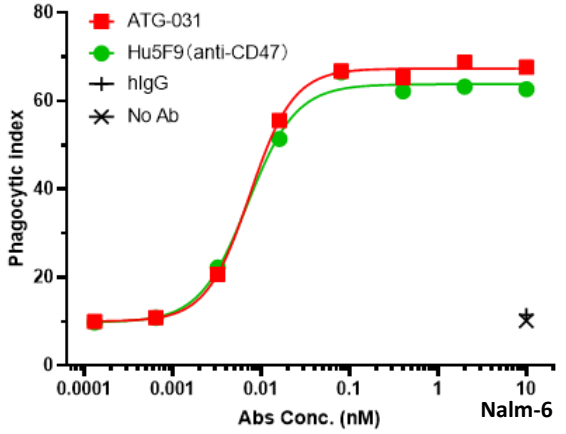


+ATG031

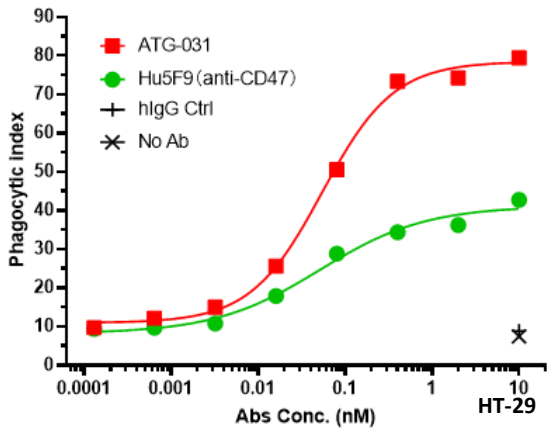


Macrophage
Nalm6

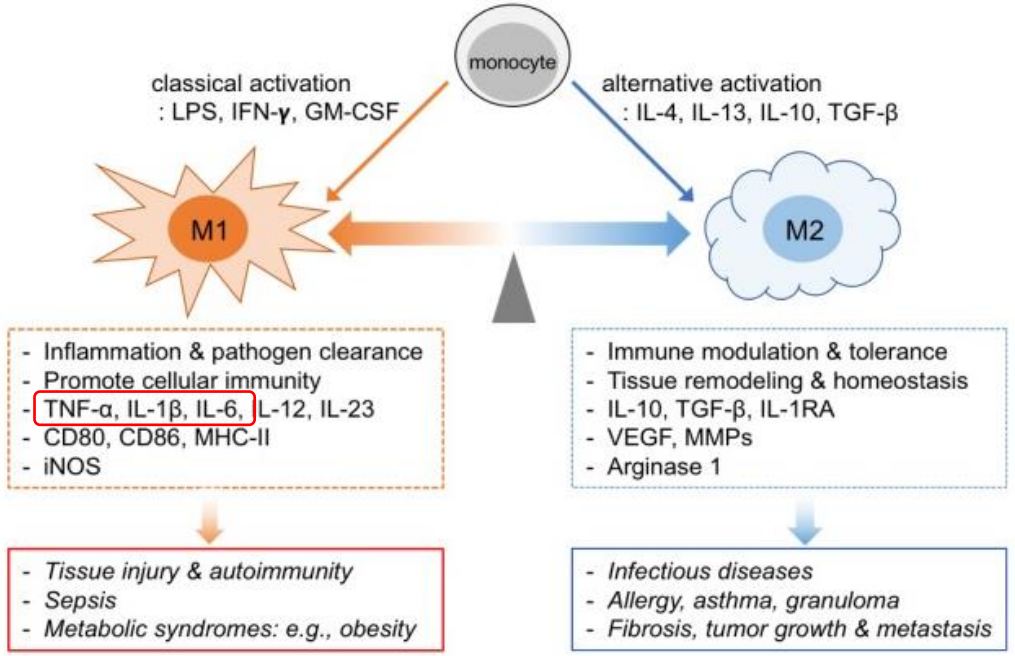
	ATG-031	Hu5F9
EC50	0.0074 nM	0.007 nM



	ATG-031	Hu5F9
EC50	0.054 nM	0.051 nM



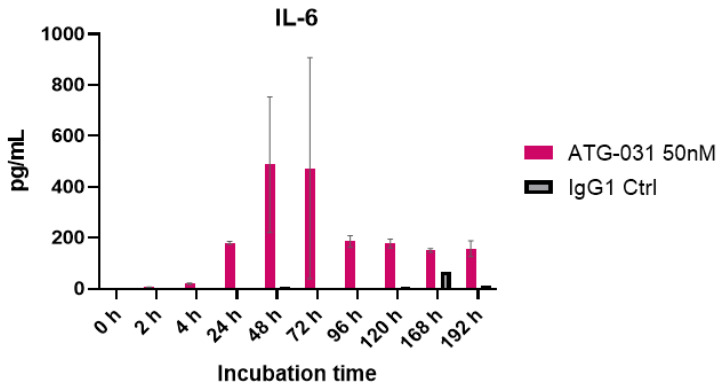
Phagocytosis Induced by ATG-031 Promotes Inflammatory Cytokine Release by M2 Macrophages

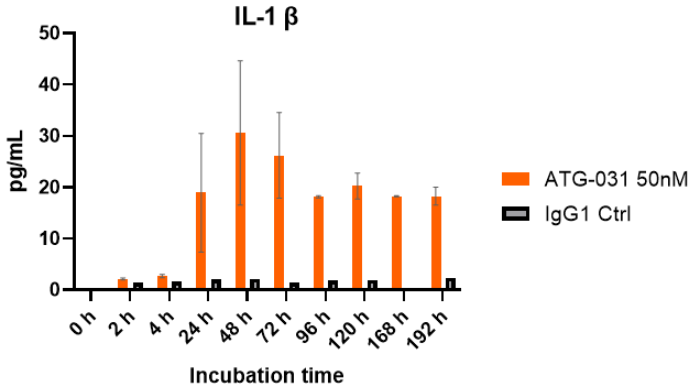


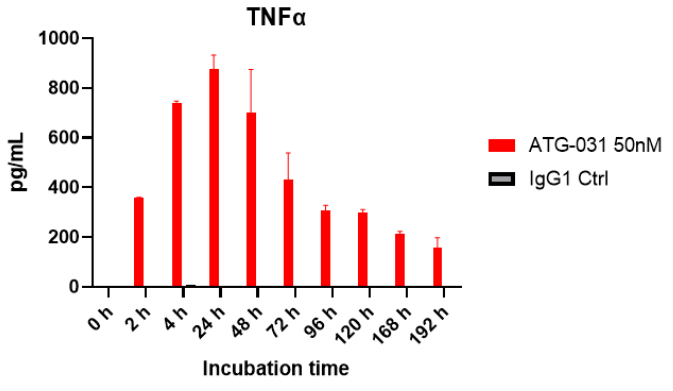
Source: BMB Rep. 2019 Jun;52(6):360372

Analysis

- Tumor cells were co-cultured with M2 macrophage with the presence of ATG-031 or IgG control
- Macrophages were then cultured for 192h and supernatant were collected at different time points. The concentration of macrophage-related cytokines in the supernatant were measured.
- Upon phagocytosis, M2 macrophages start to release M1-like cytokines suggesting a repolarization from **immunosuppressive M2 to immuno-active M1 phenotype**



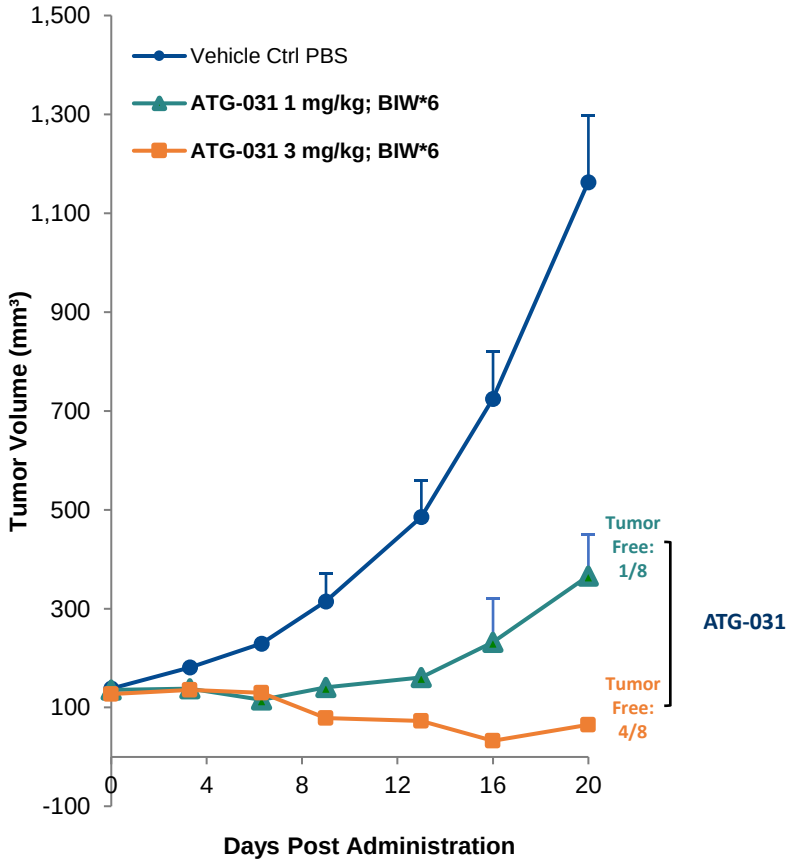




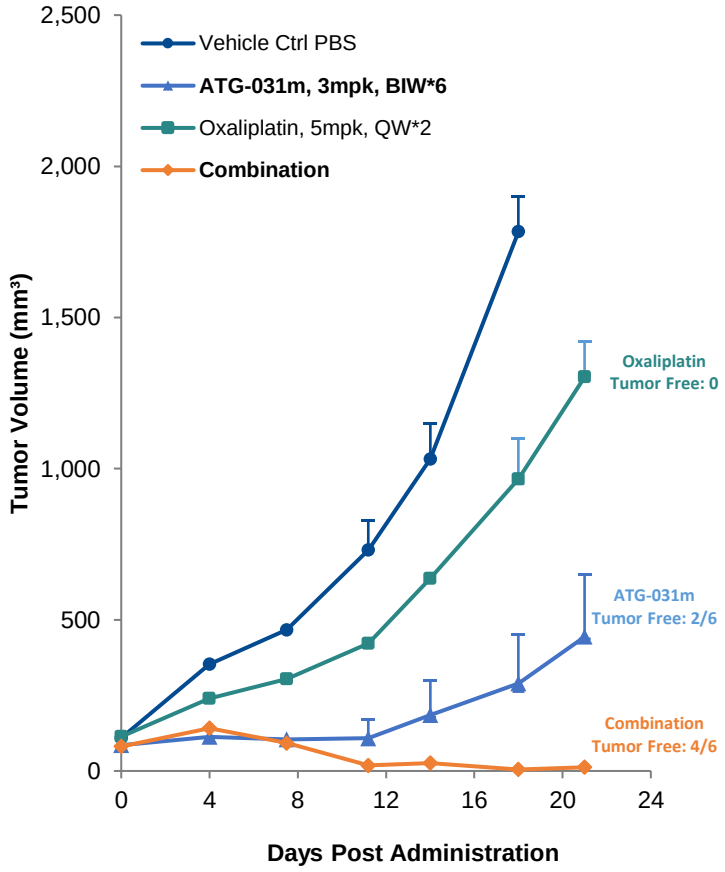
ATG-031 Demonstrates In Vivo Single Agent Efficacy As Well As Synergism with Chemotherapy or Checkpoint Inhibitor

ANTENGENE

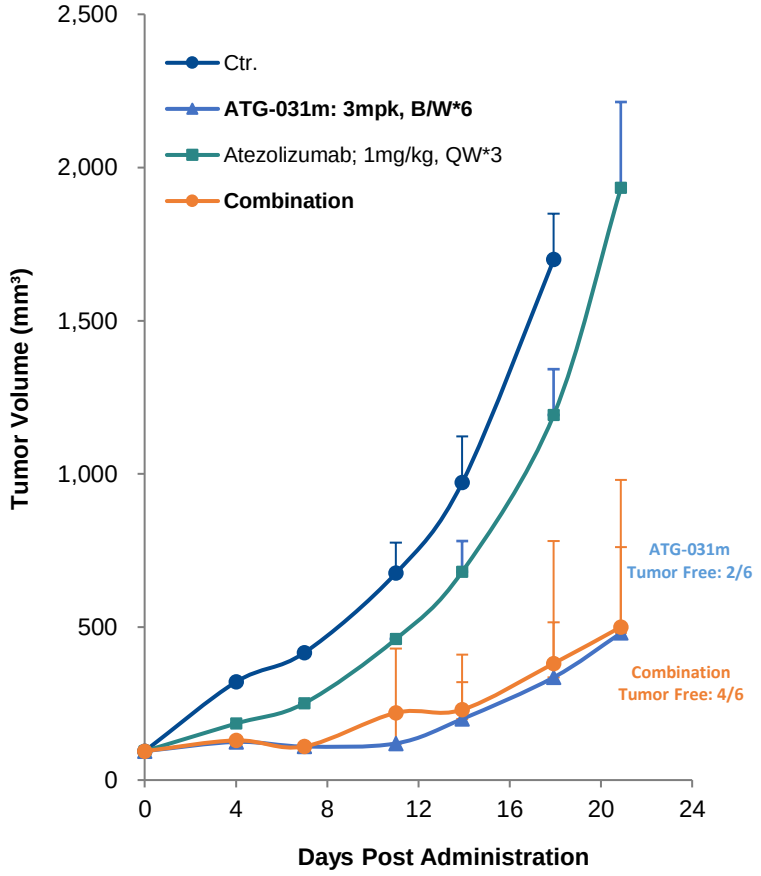
Single Agent Activity in MC38-hCD24 Mouse Tumor Model



In Vivo Synergy with Oxaliplatin in MC38-hCD24 Mouse Tumor Model



In Vivo Synergy with Anti-PD-L1 mAb in MC38-hCD24 Mouse Tumor Model



Key Takeaways of ATG-031

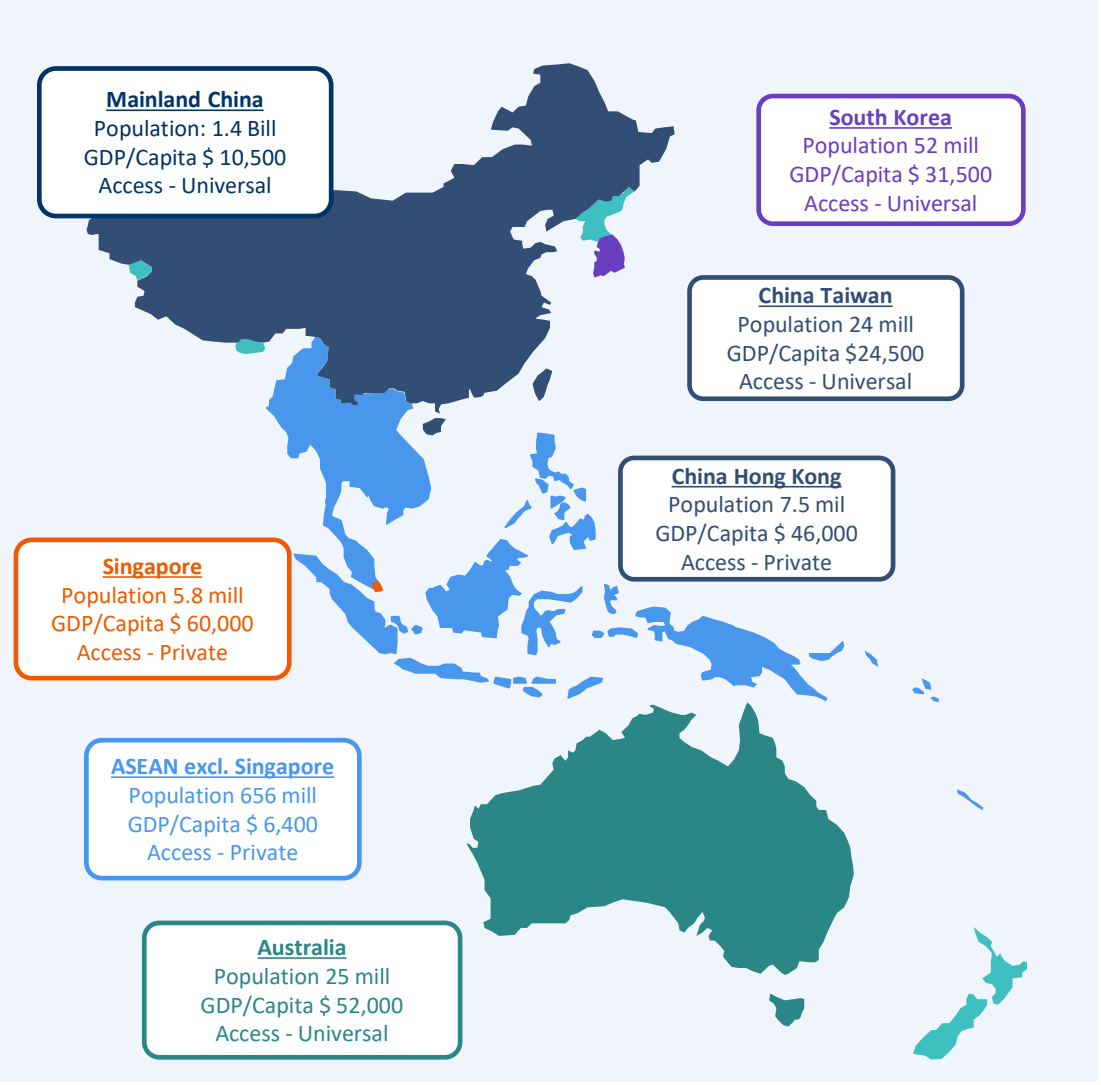
ANTENGENE

- **First-in-class humanized CD24 antibody**, which Inhibits the “Don’t eat me” signal by **blocking the CD24-Siglec10 pathway**
- **Enhances macrophage-mediated phagocytosis of cancer cells**, and polarized M2 macrophages towards **anti-tumor M1 phenotype**
- Demonstrated **potent single agent efficacy** as well as **synergy** with Oxaliplatin or ICI in Mouse Tumor Models
- A companion diagnostic antibody has been developed for patient selection, **indicating potential priority evaluation in breast, lung, ovarian, liver and bladder cancers, as well as B-cell malignancies**
- **Well tolerated** in non-human Primates
- IND is planned for **H1 2023**

德琪医药
ANTENGENE

XPOVIO® (SELINEXOR) / ATG-010
COMMERCIAL LAUNCH

Antengene Has been Focused on Executing on our Defined Strategy

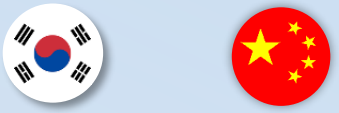


- Commercialization strategy focuses on selection of **6 core stage I markets**
- Initial focus is to **build Antengene presence** in the core markets
- Ensure **successful commercial launch of XPOVIO®**
- **Expand portfolio** in core markets and **expand Antengene presence** to other stage II ASEAN markets

Building XPOVIO® Launch Momentum with Regulatory Approvals Across Core Markets

ANTENGENE

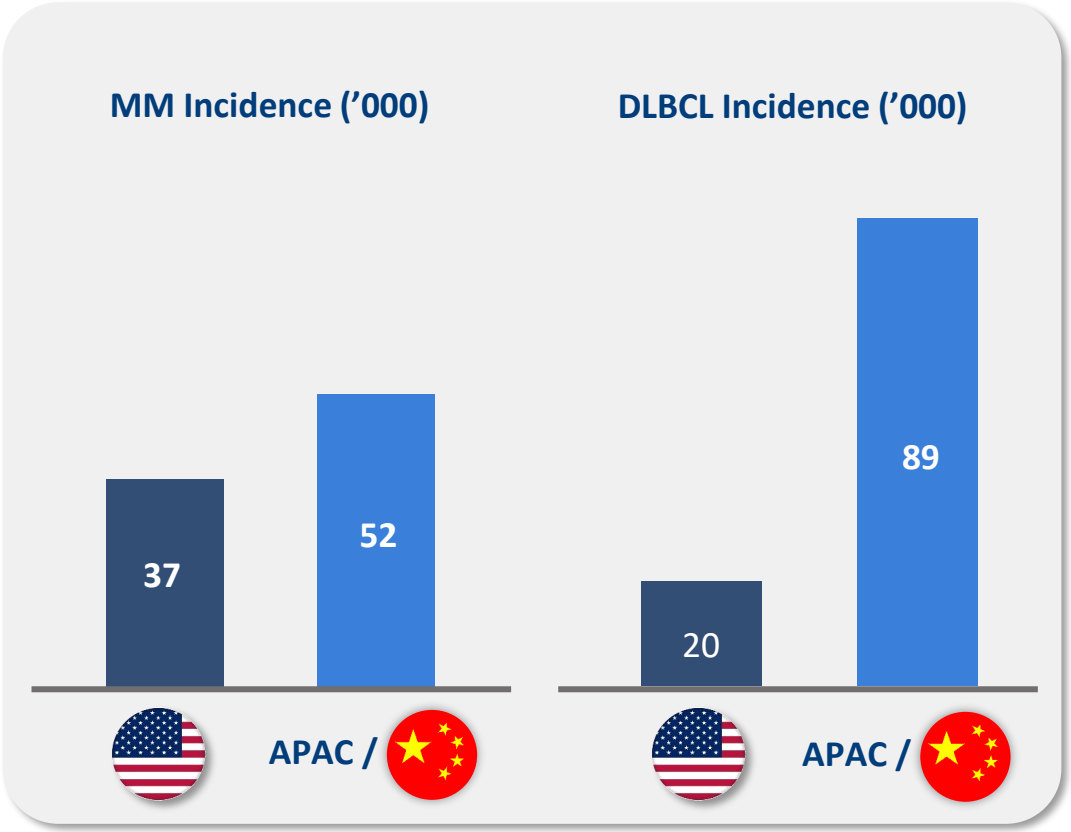
塞利尼索片 20mg
希维奥®
XPOVIO®
(selinexor)

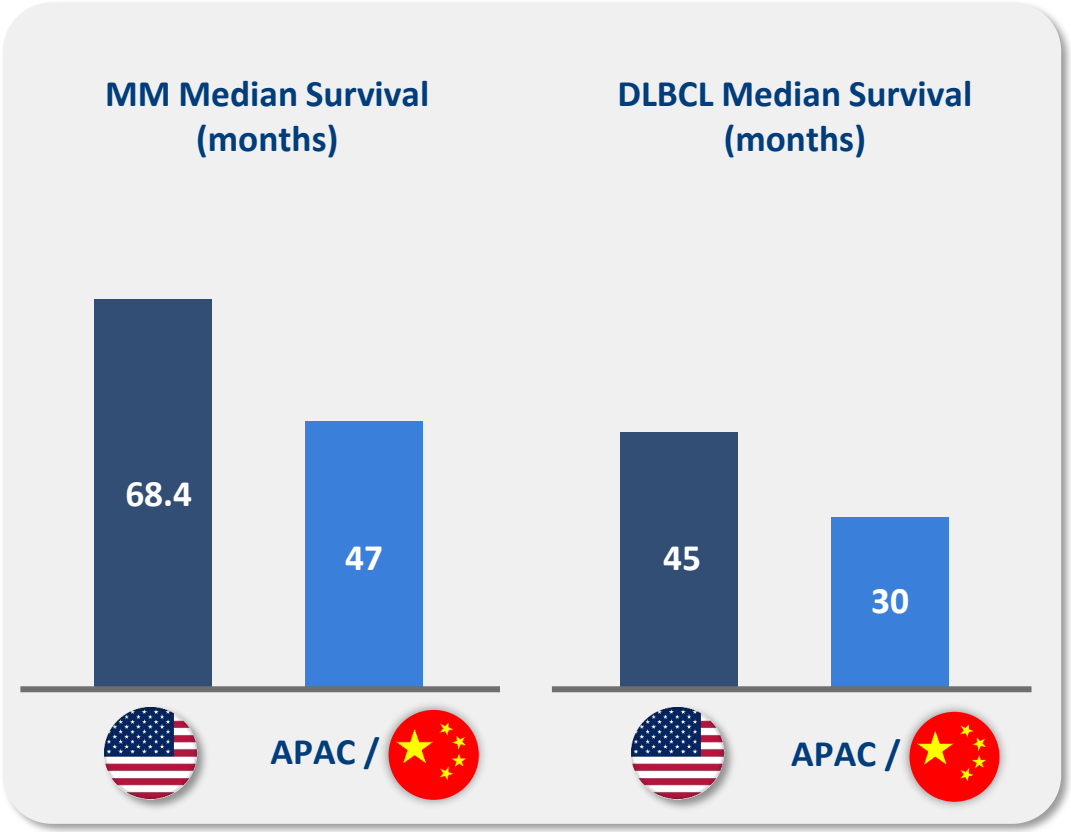
Years	2021	2022	2023	2024+
NDA Approvals		 Taiwan Markets	Hong Kong Markets	
Projected Reimbursement	N/A		N/A	 Taiwan Markets

Significant Opportunity for XPOVIO® with High Potential for Future Growth

ANTENGENE

- Tremendous **commercial opportunities in selected APAC markets*** relative to US in key disease areas such as **multiple myeloma (MM) and diffuse large B-cell lymphoma (DLBCL)**





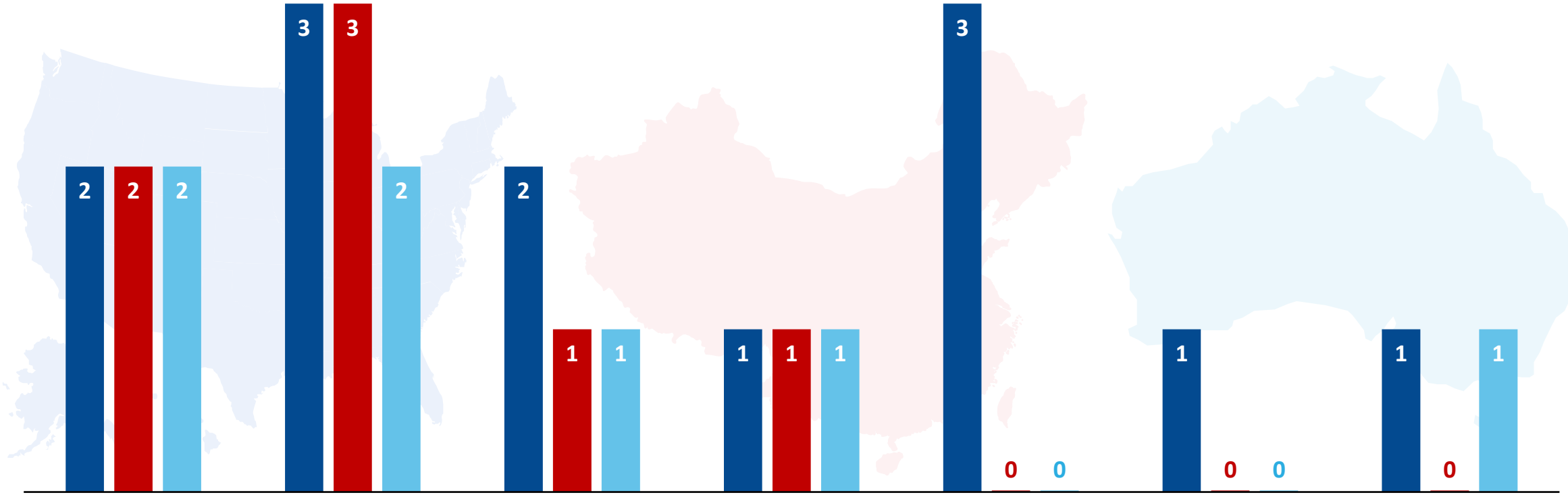
**APAC region includes Hong Kong, Macao, Taiwan, South East Asia, South Korea and Australia*

Source: Frost & Sullivan Analysis

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

ANTENGENE

United States – 13 drugs | **China – 7 drugs** | **Australia – 7 drugs**



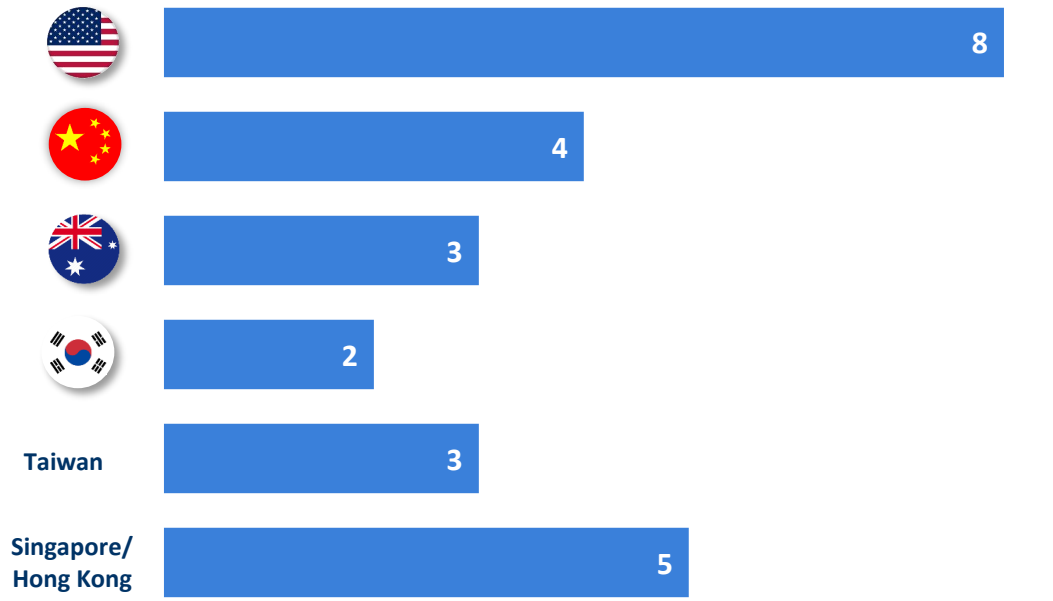
Source: Kantar Health Market Research Report, APAC July 2021, IQVIA Sales data

Limited Combination Regimens Available across APAC Providing a Compelling and Differentiated Launch Opportunity for XPOVIO® in R/R MM and R/R DLBCL

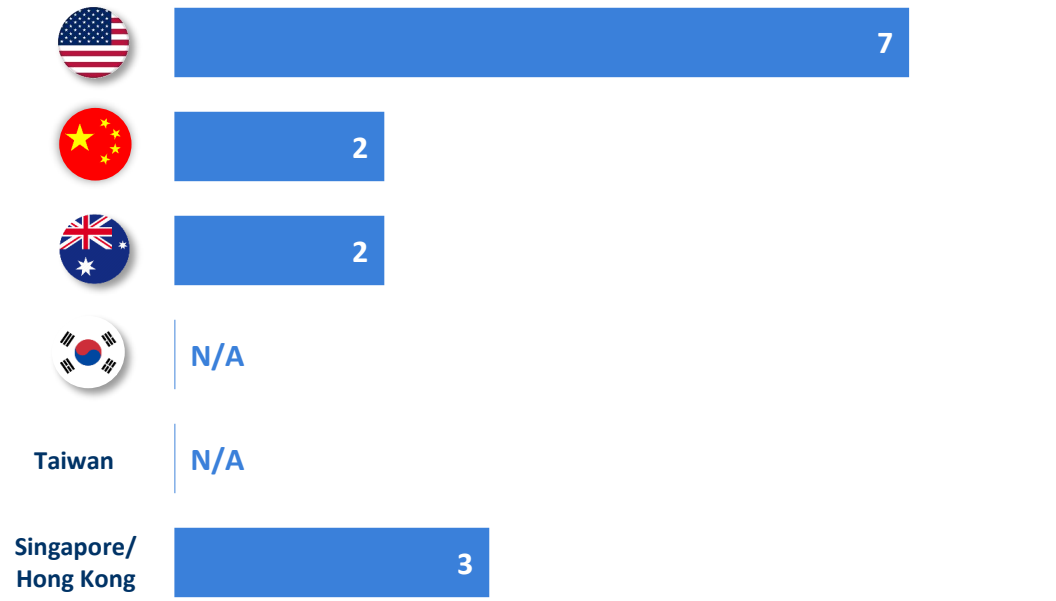
ANTENGENE

- With limited availability, hematologists are highly motivated to provide patients novel treatment options and MOAs
  - **Increasing desire to utilize triplet regimens in R/R MM and provide additional non-chemo based treatments for R/R DLBCL**

Number of Triplet Regimens Accessible in 2L and 3L MM



Number of Novel Therapies Accessible in R/R DLBCL

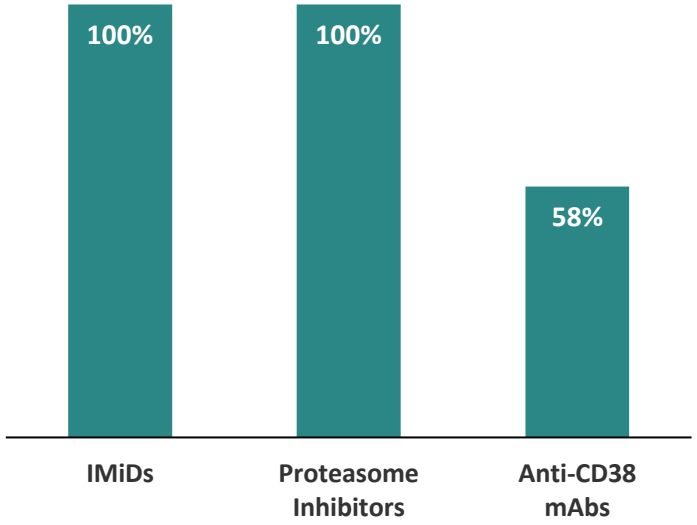


Source: Kantar Health Market Research Report, APAC July 2021, IQVIA Sales data

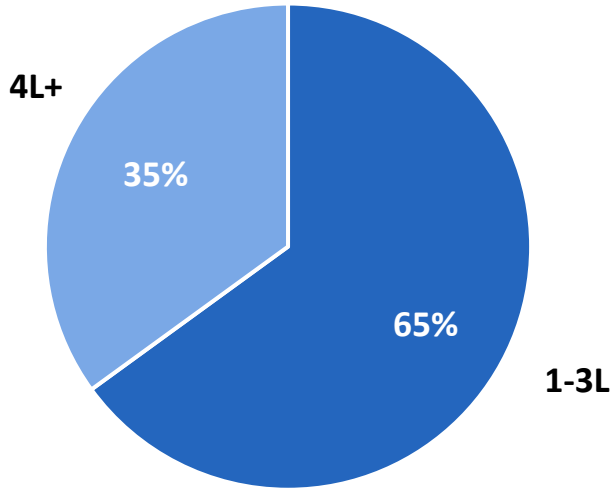
Initial Observations for XPOVIO® Launch in China Market – XPOVIO® Being Prescribed in Earlier Lines of Therapy in a Range of Combination Regimens

ANTENGENE

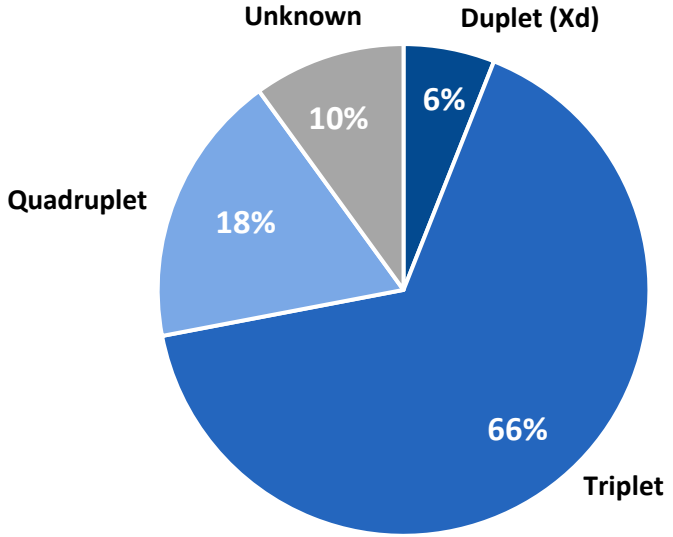
By 3L, Most Patients are Exposed to IMiDs, Proteasome Inhibitors, and anti-CD38 mAbs



Usage and Lines of Therapy Amongst XPOVIO® Patients



Treatment Regimen Among Prescribed Patients



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

Data cut off Sept 2022

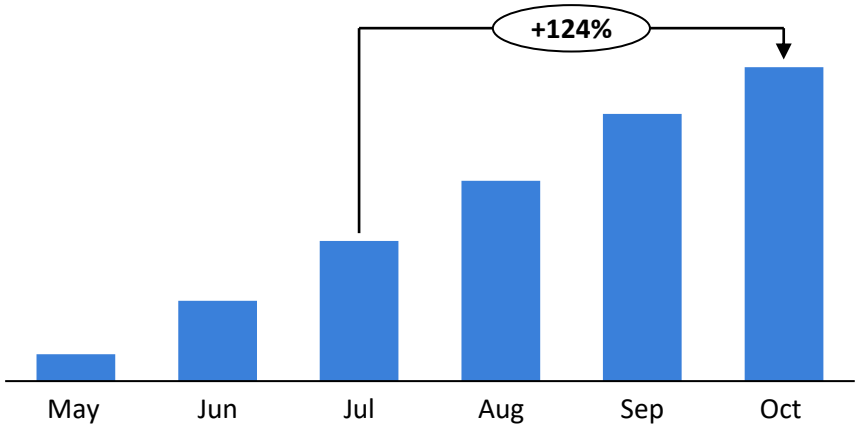
Asia Pacific Markets – Executing on XPOVIO® Launch Plans

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® 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 H2 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
  - Pre-reimbursement **Patient Familiarization Program activated**
- ASEAN markets expansion commencing with **NDA submissions in Thailand, Malaysia & Indonesia in 2022**

2023 Core Priorities

ANTENGENE

Continue to execute on launch strategy across key markets driving share uptake and duration

Build on positive XPOVIO® experience and KOL Advocacy

Secure reimbursement of Xd/XVd indications across APAC markets

- **Australia** XVd H2 2023
- **Singapore** CDL Q1 2023
- **Hong Kong** DTC/DAC H2 2023
- **Taiwan** XVd/DLBCL 2024

Continue to build commercial capabilities

- **Headcount gated to reimbursement milestones**

Portfolio and Geographic Expansion into ASEAN markets

CDL: Cancer Drug List, DTC: Hospital Drug & Therapeutics Committee DAC= Drug Advisory Committee

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Q&A SESSION

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CLOSING REMARKS:
BUILDING A LEADING BIOPHARMACEUTICAL COMPANY

Steady Stream of Catalysts Continue to Drive Value for Investors

ANTENGENE

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 30th June 2022

ANTENGENE

ANTENGENE CORPORATION LIMITED
(SEHK: 6996.HK)

NOVEMBER 2022

THANK YOU

TREATING PATIENTS BEYOND BORDERS