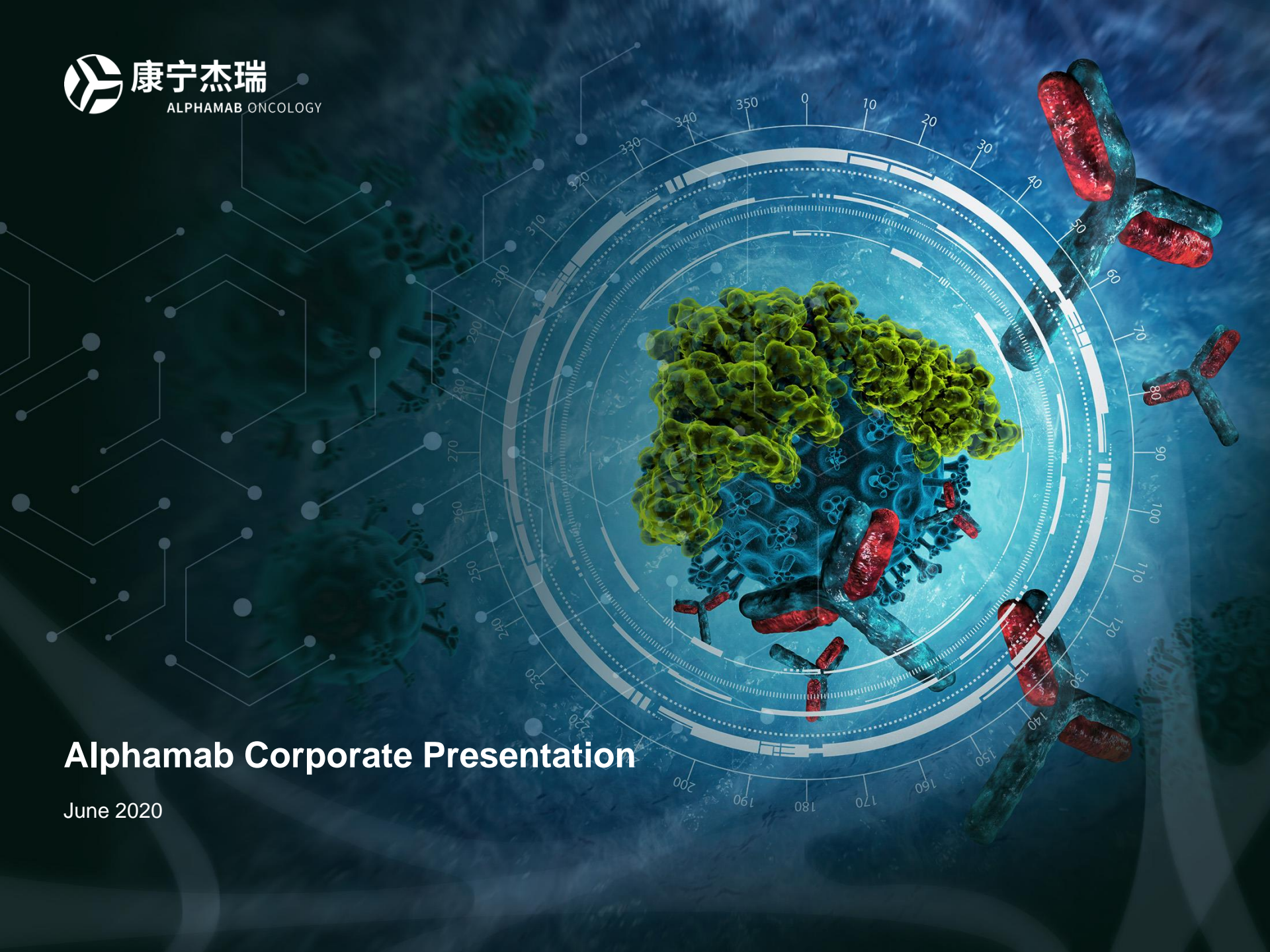


# Alphamab Corporate Presentation

June 2020



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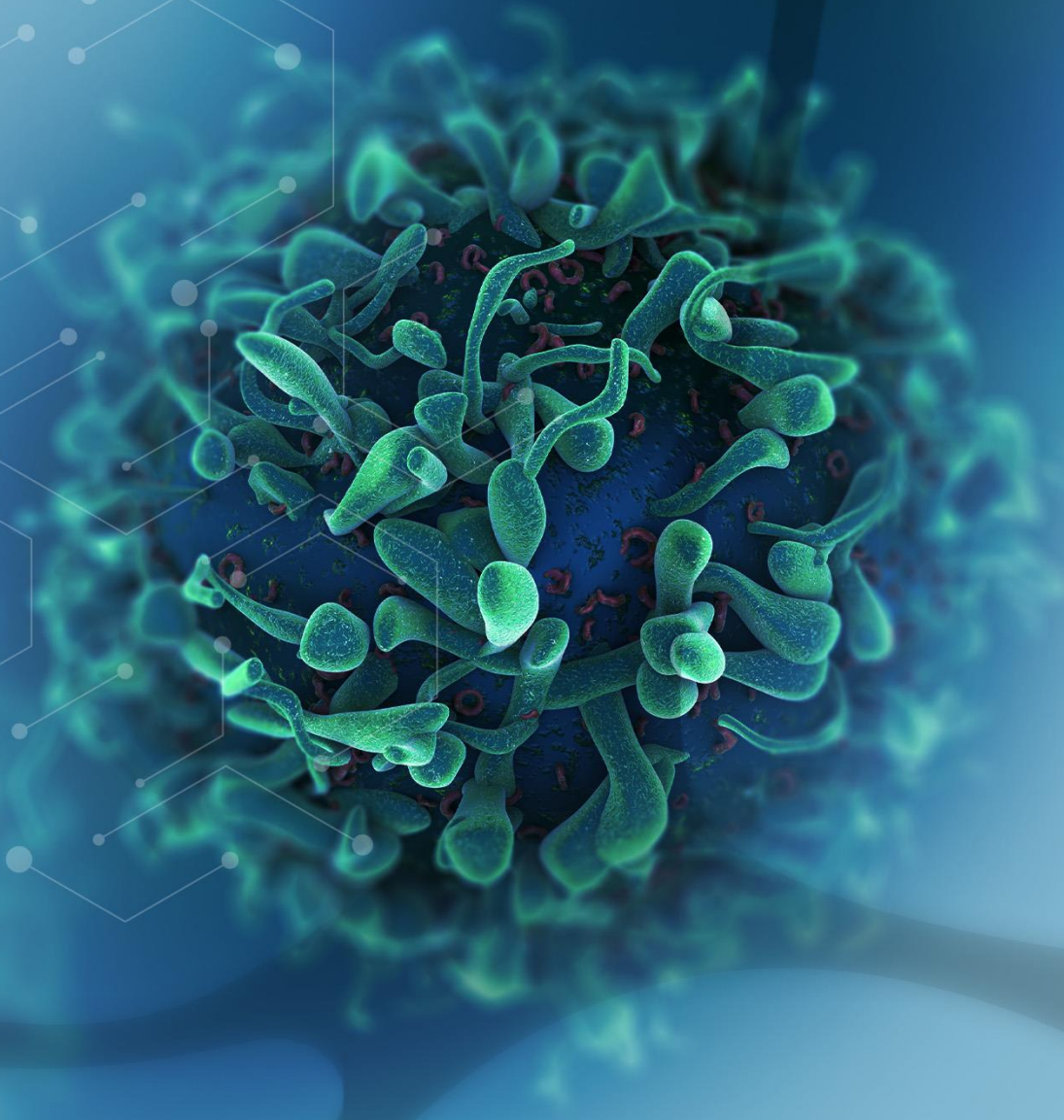
# Agenda



- 1 Clinical Strategy Overview
- 2 Clinical Data Updates
- 3 Q&A

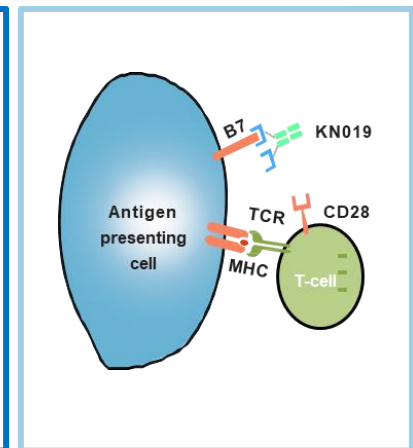
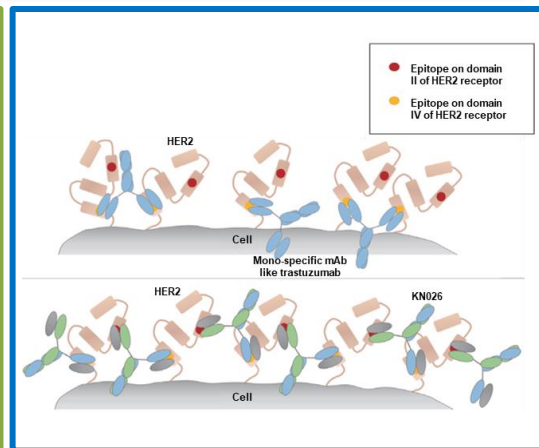
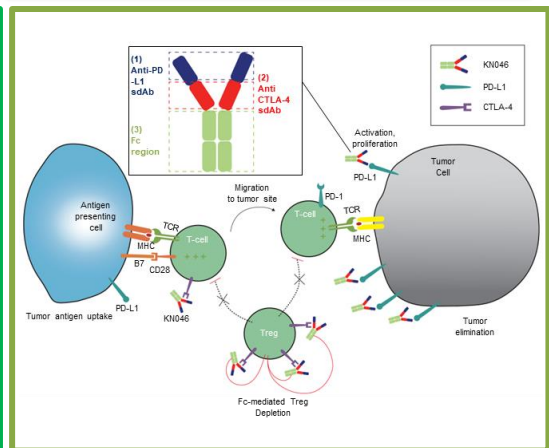
# 01

## Clinical Strategy Overview



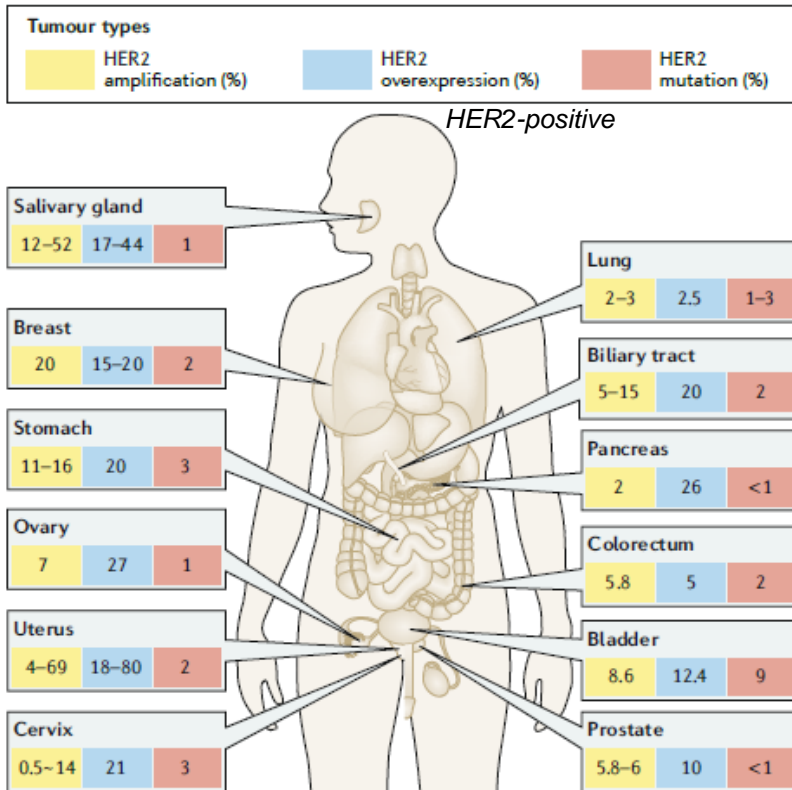
# Strategy : Develop Next Gen Antibody to Enable Innovative Cancer Therapy

<p><b>KN035</b></p> <p>Subcutaneous PD-L1</p>	<p><b>KN046</b></p> <p>Dual blockade of PD-L1 and CTLA-4</p>	<p><b>KN026</b></p> <p>Dual blockade of HER2 domain II and IV</p>	<p><b>KN019</b></p> <p>A safe option for autoimmune diseases</p>
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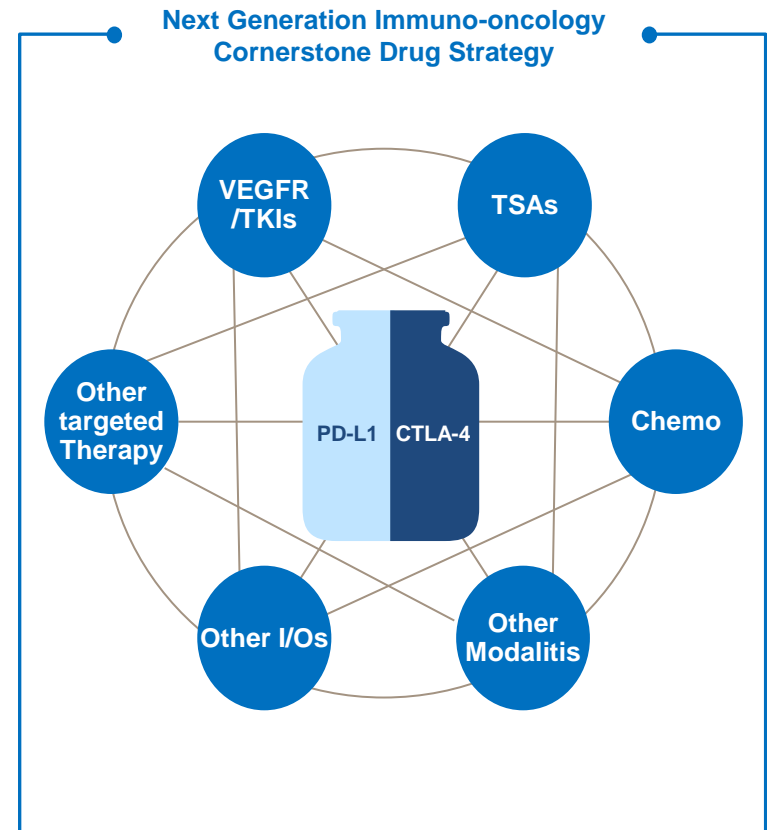


# Strategy : Develop Next Gen Antibody for Solid Tumors

HER2-positive, HER2-int/low and HER2-mutation  
KN026-based combination & KN026+KN046



HER2-negative solid tumors  
KN046 & KN046-based combination













Do-Youn Oh 2019

**Notes:**

1. Herceptin's label only covers Her-2 High, about 25% of breast cancer patients. While total Her-2 High, Midium and Low is about 80% of patients
2. Herceptin's label only covers Her-2 High, about 10-18% of gastric cancer patients. While total Her-2 High, Midium and Low is about 40% of patients

# Strategy : Develop Next Gen Antibody to Enable Innovative Cancer Therapy

## KN046 KN026

Program	Key indication	Preclinical	Phase I	Phase II	Phase III	BLA
KN046 (PD-L1/CTLA-4)	Thymic carcinoma	Registration trial (in preparation)			★	 
	NPC	Registration trial (in preparation)			★	
	NSCLC, 1L (KN046+CT)	Registration trial (in preparation)			★	
	NSCLC, PD1/PD-L1 ref/rel (KN046 or KN046+TKI)					 
	NSCLC, stage III (KN046+RT)					
	TNBC, 1L (KN046+nab-paclitaxel)					
	TNBC, neoadjuvant					
	MSI-H/dMMR CRC, neoadjuvant					 
	HCC, 1L (KN046+TKIs)					
	ESCC, 1L (KN046+CT, KN046+CRT)					
KN026 (HER2 bispecific)	HER2-positive MBC, 1L (KN026+docetaxel)	Registration trial (in preparation)			★	
	HER2/HR-positive MBC, late line (KN026+CDK4/6+fulvestrant)					
	HER2-low MBC & mGC/GEJ, late line (KN026)					
KN026+KN046	HER2-positive mGC/GEJ (KN026+KN046)					 
	HER2-positive solid tumors (KN026+KN046)					 

# Strategy : Develop Next Gen Antibody to Enable Innovative Cancer Therapy

KN035 KN019 and more

Program	Key indication	Preclinical	Phase I	Phase II	Phase III	BLA	
KN035 <i>(subcutaneous anti-PD-L1)</i>	MSI-H/dMMR solid tumors						BLA
	Biliary tract cancer						
	Renal cell carcinoma						
	Soft tissue sarcoma						
KN019 <i>(CTLA-4 Ig)</i>	Dose ranging in rheumatoid arthritis						
	Renal transplantation						
	Subcutaneous formulation						
KN052 <i>(undisclosed bispecifics)</i>	Solid tumors						
KN053 <i>(undisclosed bispecifics)</i>	Solid tumors						
KN055 <i>(undisclosed bispecifics)</i>	Solid tumors						
KN058 <i>(undisclosed bispecifics)</i>	Solid tumors						




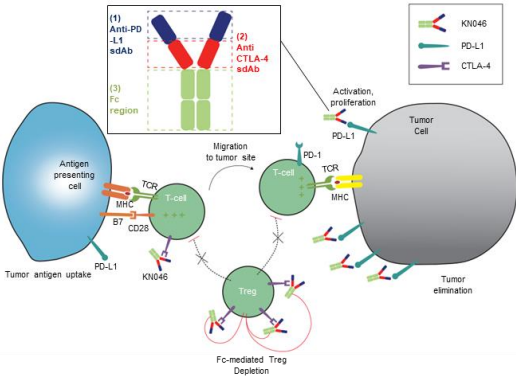
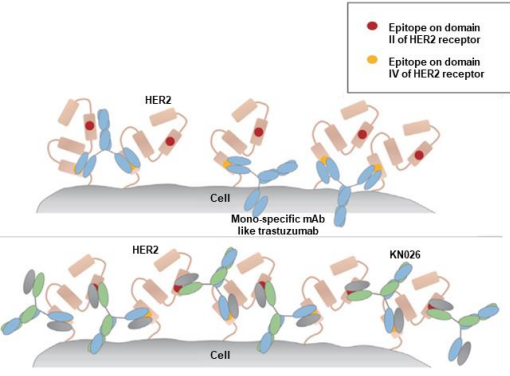
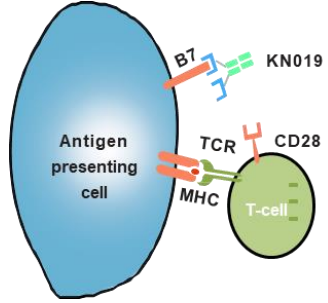
# 02

## Clinical Data Updates

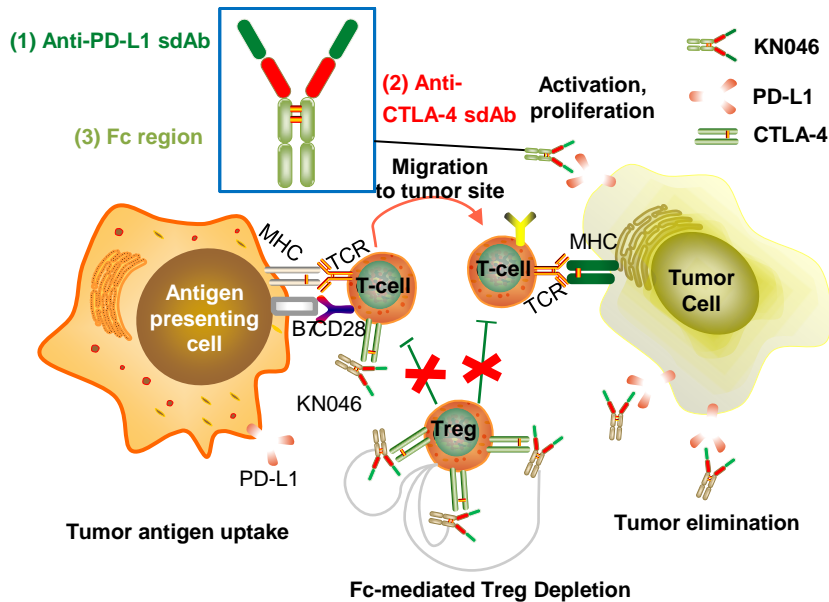


# Strategy : Develop Next Gen Antibody to Enable Innovative Cancer Therapy

## KN046 update

<p><b>KN035</b></p> <p>Subcutaneous PD-L1</p>	<p><b>KN046</b></p> <p>Dual blockade of PD-L1 and CTLA-4</p>	<p><b>KN026</b></p> <p>Dual blockade of HER2 domain II and IV</p>	<p><b>KN019</b></p> <p>A safe option for autoimmune diseases</p>
<p>Subcutaneous PD-L1 for maintenance therapy</p>	<p>Enable earlier lines of therapies for improved efficacy and safety</p>	<p>Potential for all settings of HER2 aberration Synergy with KN046 through immune modulation</p>	<p>Supplement to immunotherapies for AE management</p>
			

# KN046 : MOA and Clinical Study Design



## Mechanism of action of KN046

- Blocking CTLA-4 with B7 and PD-L1 with PD-1.
- Limited peripheral distribution reduces treatment-associated on-target off-tumor toxicity.
- IgG1 Fc domain, CTLA-4 blocking-mediated Treg cells deletion.

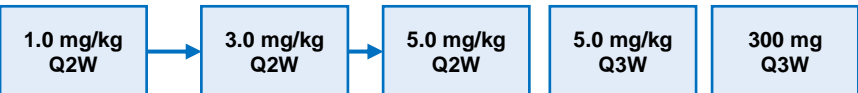
## Trial KN046-CHN-001

### Eligibility

- Men/Women  $\geq 18$  y/o
- ECOG 0 or 1
- Advanced/metastatic solid tumors
- Refractory/intolerant to standard of care
- Treatment by previous immune checkpoint inhibitors (ICIs) allowed

### Trial design

- Dose escalation (mTPI-2)
- Dose expansion

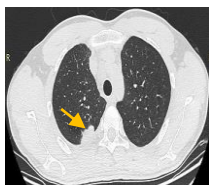
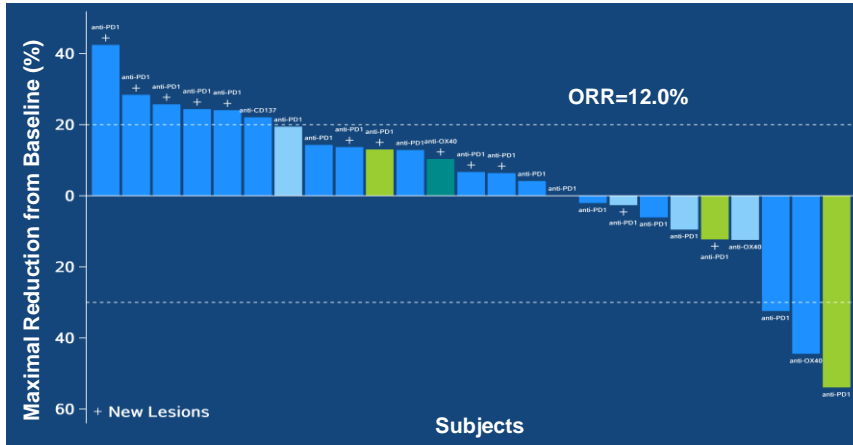


	n = 30	n = 44	n = 6	n = 6	Prior ICIs Total, n
Dose escalation, N	3	3	3	3	
<i>Prior ICIs, n</i>	0	1	2	1	4
Dose expansion, N	27	41	3	3	
<i>Prior ICIs, n</i>	3	19	2	1	25
					<b>29</b>

--- Represents patients previously treated by immune checkpoint inhibitors from each dose cohort and hereby reported in this presentation

# KN046-CHN-001 Efficacy Evaluation in ICI Refractory Patient

Waterfall Plot



Baseline



24 weeks

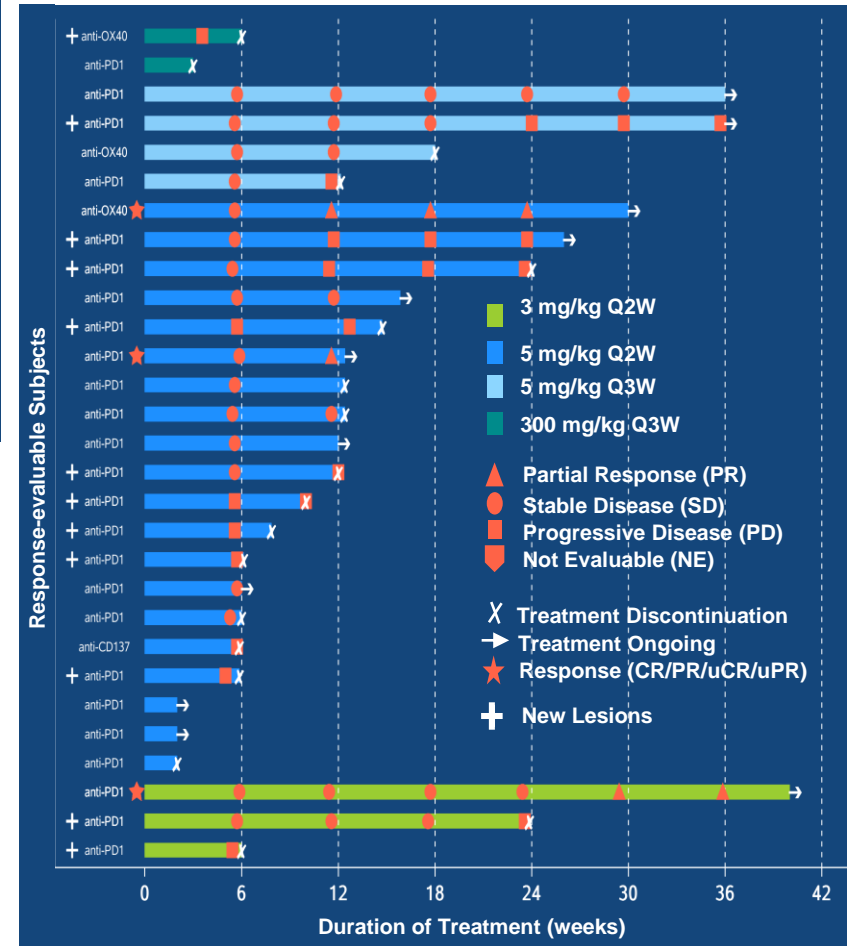


Baseline



18 weeks

Swimming Lane Plot



## Summary of KN046-CHN-001 in ICI Refractory Patient

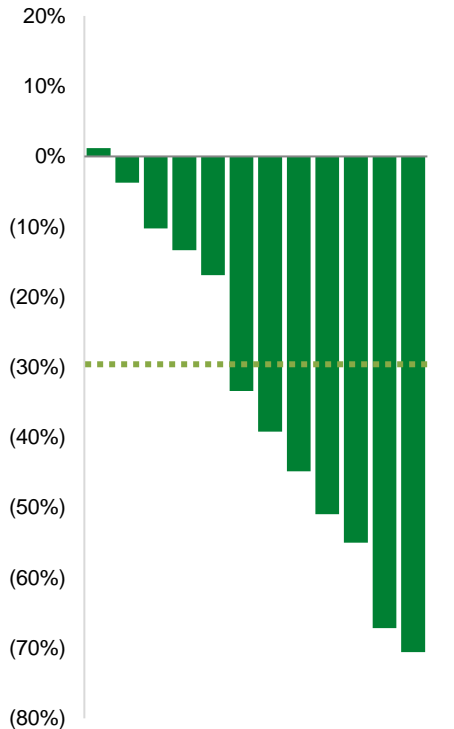
**KN046 showed a favorable safety profile and promising clinical benefit in advanced solid tumor patients who failed on prior ICIs therapy**

- ✓ Patients enrolled are those who failed on prior immune checkpoint inhibitors therapy
- ✓ Grade  $\geq 3$  related TRAEs were experienced in 2 out of 29 patients (6.9%)
- ✓ Median progression free survival was 2.69 months (95%CI 1.31, 5.52)
- ✓ Median overall survival was not reached
- ✓ Objective responses rate was 12.0%



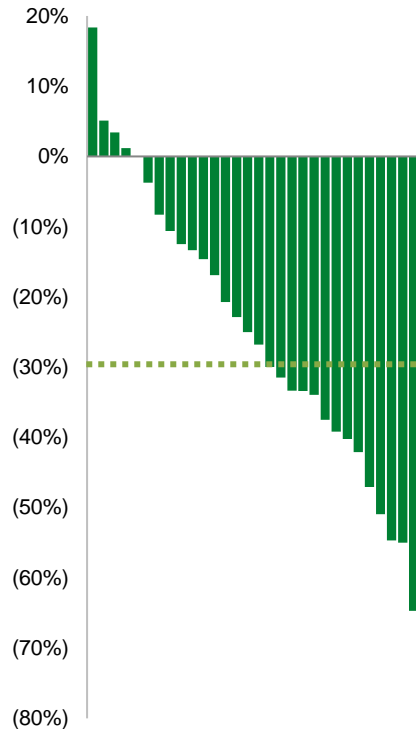
# Promising Efficacy Data in 1L and 2L NSCLC Led to the Initiation of Pivotal Phase 3 Trial KN046-301

**KN046+carbo/paclitaxel in 1L sq-NSCLC**



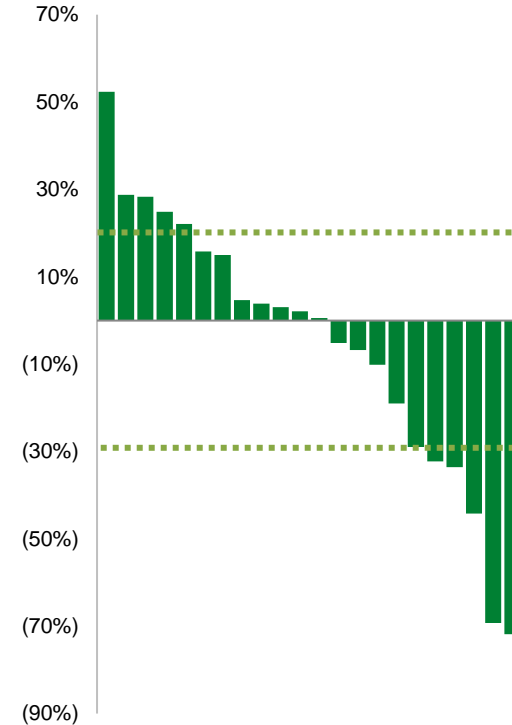
*\*: preliminary efficacy data. Only 5/12 subjects have more than 2 post baseline tumor assessments*

**KN046+carbo/pemetrexed in 1L non-sq NSCLC**



*\*: preliminary efficacy data. Only 15/31 subjects have more than 2 post baseline tumor assessments*

**KN046 in 2L NSCLC (5 mg/kg)**



## KN046 : Advancement in Registration Trials and Earlier Lines Development

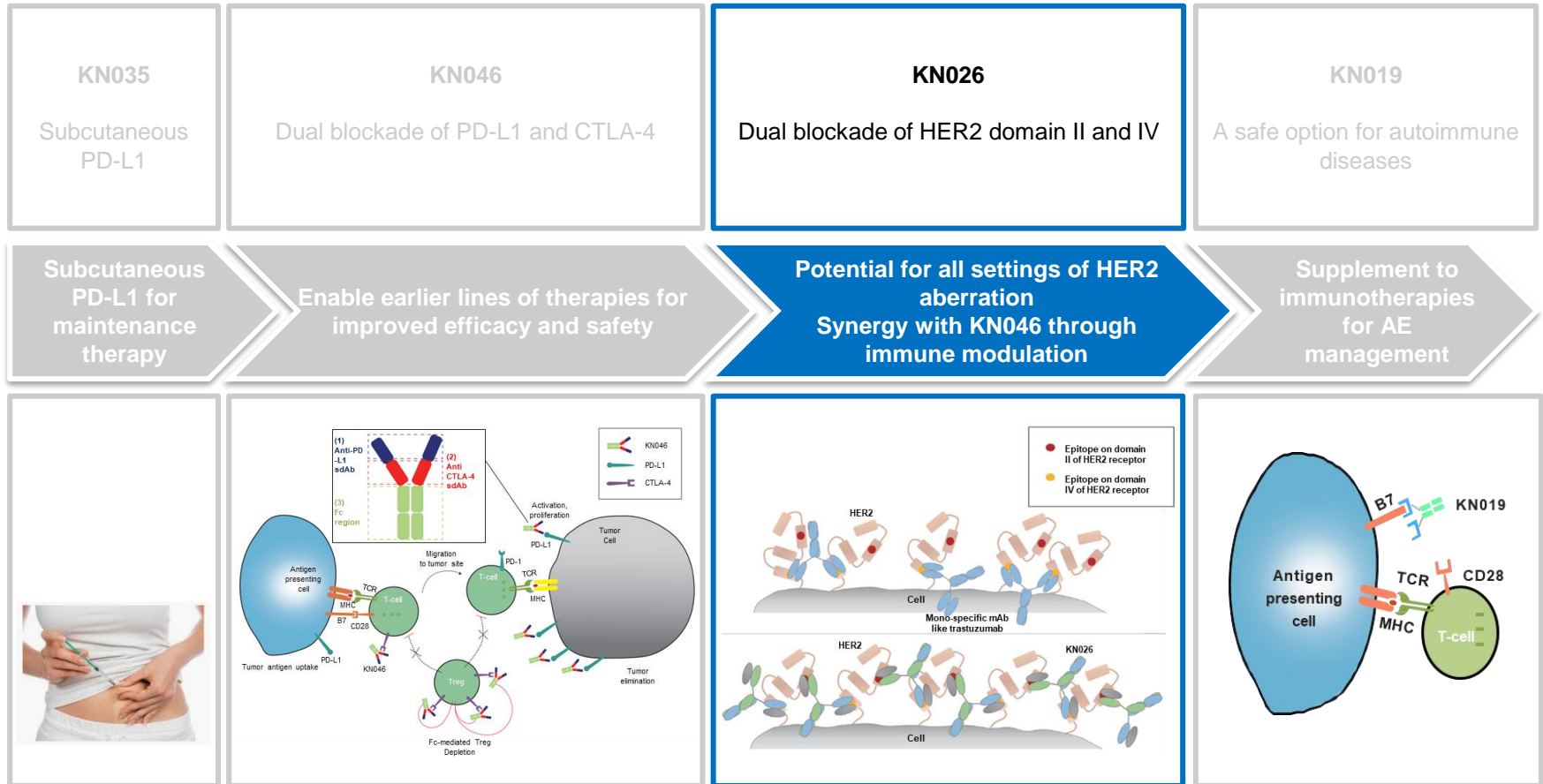
<b>1</b> Initial global registration in thymic carcinoma and NPC	2020	<b>Fast to market pivotal studies planned in thymic carcinoma and NPC</b> <ul style="list-style-type: none"><li>• FPI planned in Q3/Q4</li></ul>
<b>2</b> Quick advance to pivotal phase 3 trials in major indications	2020 – 2021	<b>First major pivotal study planned in NSCLC</b> <ul style="list-style-type: none"><li>• FPI planned in Q3-Q4</li></ul> <b>Follow on major pivotal studies planned in TNBC<sup>(1)</sup> and ESCC</b>
<b>3</b> Fast move to earlier lines of development	2020 – 2021	<b>NSCLC stage III</b> <ul style="list-style-type: none"><li>• KN046+definitive RT</li></ul> <b>TNBC neoadjuvant</b> <ul style="list-style-type: none"><li>• KN046+chemotherapy</li></ul>
<b>4</b> Develop next generation I-O combination	2021	<b>Chemo-free 1L trial in HER2-positive GC/GEJ</b> <ul style="list-style-type: none"><li>• KN026+KN046</li></ul>

### Notes:

1. preliminary result from phase II trial of KN046 in combination with Nab-Paclitaxel in 1L TNBC, I-O Naïve, has shown 5 out of 6 patients (PD-L1  $\geq$  1%) have PR or CR

# Strategy : Develop Next Gen Antibody to Enable Innovative Cancer Therapy

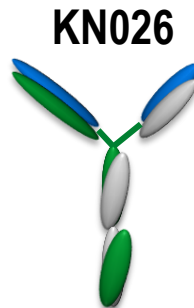
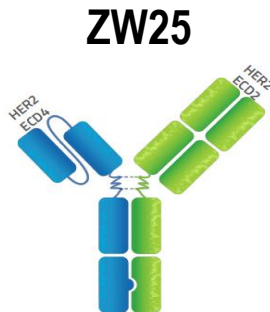
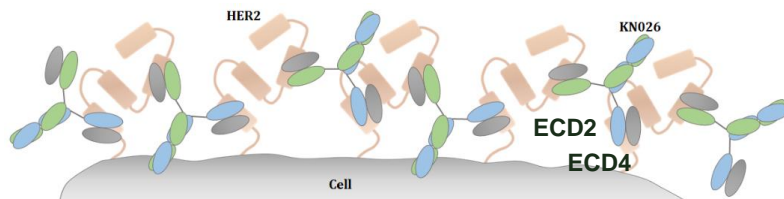
KN026 update





# KN026 : MOA and Clinical Study Design

- Unmet need in cancers with HER2 aberration exists
- KN026 simultaneously binds two HER2 epitopes
- Unique binding results in novel mechanisms of action



## KN026 Phase I Study design

### Part 1

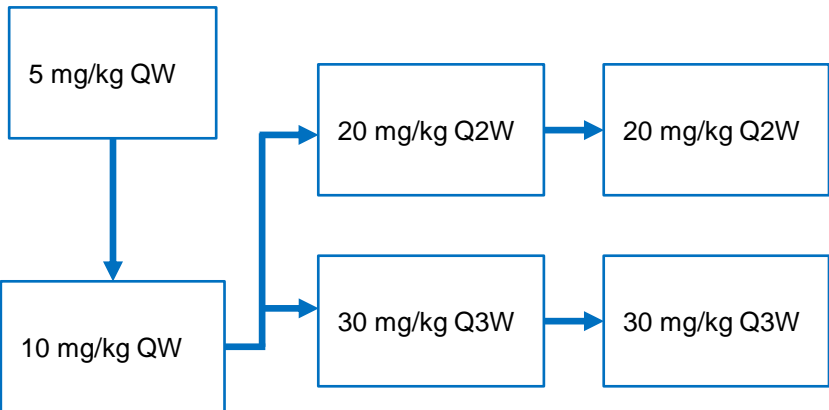
3+3 Dose Escalation

No DLTs at any dose

### Part 2

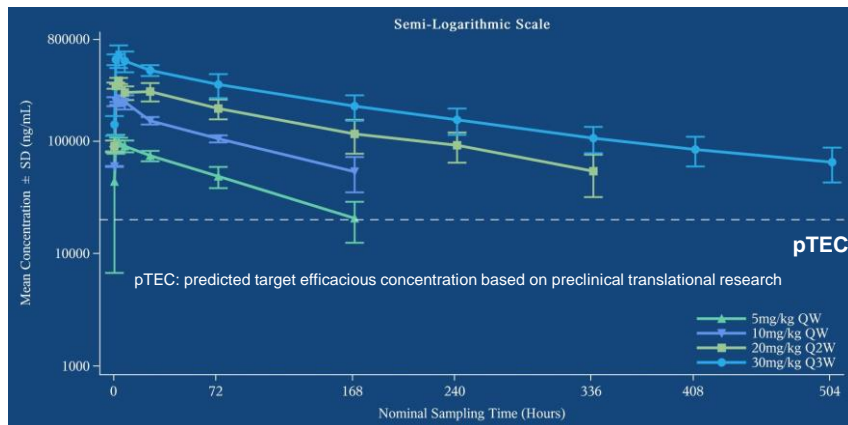
Expansion Cohorts

HER2-Positive Breast Cancer

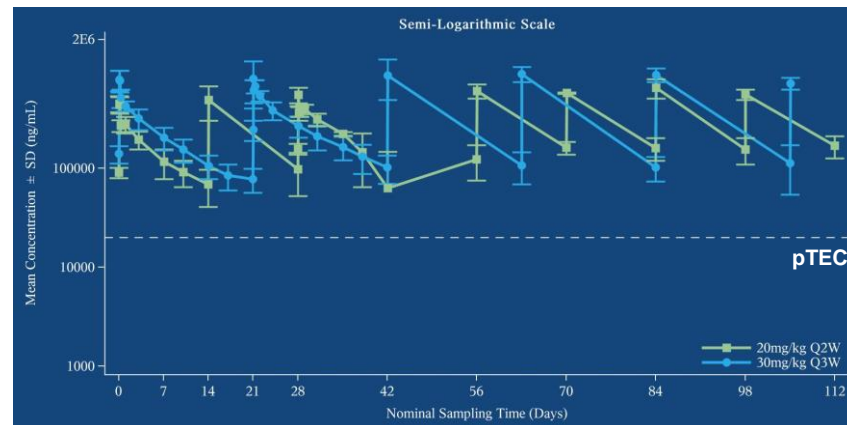


# KN026-CHN-001 Pharmacokinetics and Safety

## Single Dose



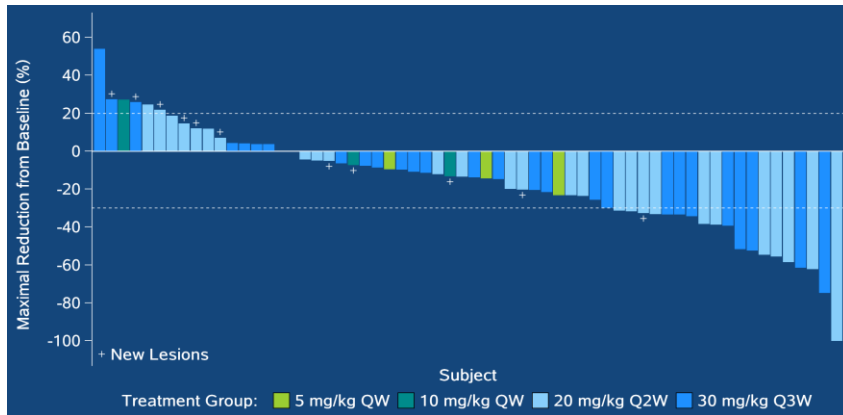
## Multiple Dose



As of Jan. 22, 2020	5 mg/kg QW (n=3)		10 mg/kg QW (n=3)		20 mg/kg Q2W (n=28)		30 mg/kg Q3W (n=29)		Total (n=63)	
Preferred Term	All Grade	≥Grade 3	All Grade	≥Grade 3	All Grade	≥Grade 3	All Grade	≥Grade 3	All Grade	≥Grade 3
Subjects with at least 1 KN026 related TEAE	3 (100%)	0	2 (66.7%)	0	25 (89.3%)	2 (7.1%)	19 (65.5%)	2 (6.9%)	49 (77.8%)	4 (6.3%)
Pyrexia	1 (33.3%)	0	1 (33.3%)	0	8 (28.6%)	0	5 (17.2%)	0	15 (23.8%)	0
Diarrhoea	1 (33.3%)	0	1 (33.3%)	0	6 (21.4%)	0	4 (13.8%)	0	12 (19.0%)	0
Aspartate aminotransferase increased	0	0	0	0	6 (21.4%)	0	4 (13.8%)	0	10 (15.9%)	0
Neutrophil count decreased	1 (33.3%)	0	0	0	4 (14.3%)	0	2 (6.9%)	0	7 (11.1%)	0
White blood cell count decreased	2 (66.7%)	0	0	0	3 (10.7%)	0	2 (6.9%)	0	7 (11.1%)	0

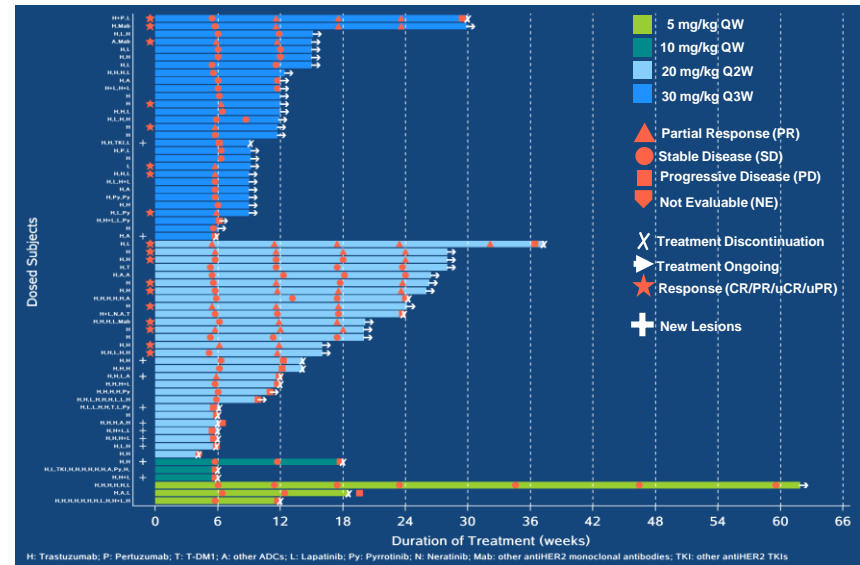
# KN026-CHN-001 Efficacy

KN026 is well tolerated and has demonstrated encouraging anti-tumor activity in HER2-positive breast cancer patients who have failed standard anti-HER2 therapies.



As of Jan. 22, 2020	5 mg/kg QW (n=3)	10 mg/kg QW (n=3)	20 mg/kg Q2W (n=28)	30 mg/kg Q3W (n=28)	Total (n=62)	Pooling 20 mg/kg Q2W & 30 mg/kg Q3W (n=56)
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CR	0	0	0	0	0	0
PR	0	0	10 (35.7%)	8 (28.6%)	18 (29.0%)	18 (32.14%)
SD	2 (66.7%)	1 (33.3%)	8 (28.6%)	17 (60.7%)	28 (45.2%)	25 (44.64%)
PD	1 (33.3%)	2 (66.7%)	9 (32.1%)	3 (10.7%)	15 (24.2%)	12 (21.43%)
NE	0	0	1 (3.6%)	0	1 (1.6%)	1 (1.79%)
ORR (%)	0	0	10 (35.7%)	8 (28.6%)	18 (29.0%)	18 (32.14%)
DCR (%)	2 (66.7%)	1 (33.3%)	18 (64.3%)	25 (89.3%)	46 (74.2%)	43 (76.79%)



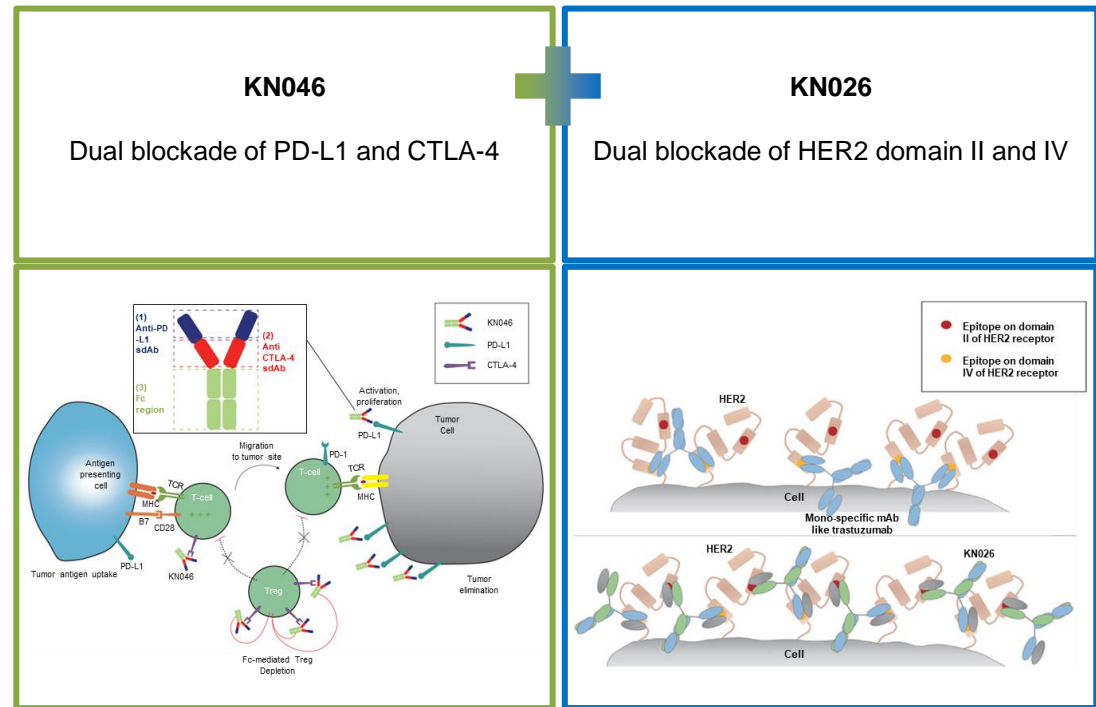
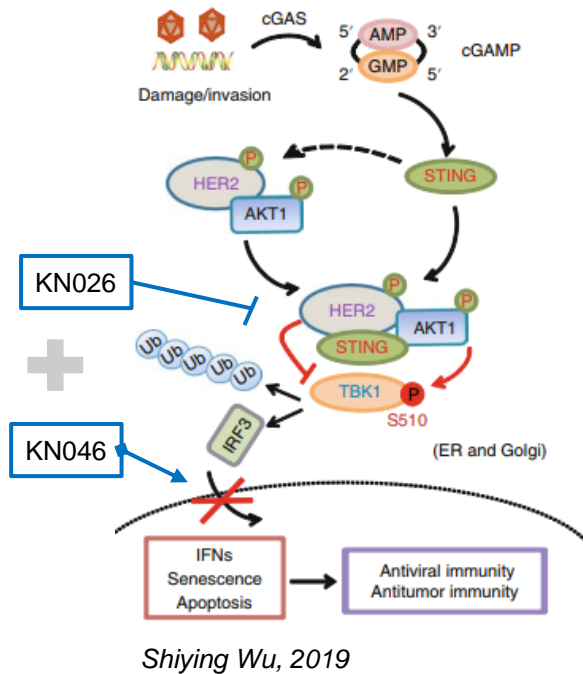
- HER2 positive breast cancer
- Median age: 54 (range: 31~69)
- Median exposure duration: 12 weeks (range: 4~62)
- Median prior lines of HER2 target therapies: 2 (range: 1~12)

## Efficacy Data in MBC : KN026 vs ZW25

	Trastuzumab+pertuzumab	ZW25	KN026
<b>Study population</b>	2L HER2-positive BC (fail T) 3L HER2-positive BC (fail T, P)	>2L HER2-positive BC	>2L HER2-positive BC
<b>Study</b>	BO17929 (Cohort A, B) BO17929 (Cohort C)	ZW25 Phase I	KN026-CHN-001
<b>Subject number</b>	66; 17	20	56 (RP2Ds)
<b>Schedule</b>	800 mg loading + 400 mg Q3W	20 mg/kg Q2W	20 mg/kg Q2W; 30 mg/kg Q3W
<b>ORR</b>	24.2% (2L); 17.6% (3L)	33% (all; 1/8 responder at 20 mg/kg Q2W)	32%
<b>DCR</b>	50%; 41.2%	50%	76.8%
<b>PFS (months)</b>	5.5 (2L); 2.5 (3L)	Approx. 3 months	5.5 months
<b>AE</b>	Diarrhea 64% Rash 26% Fatigue 33% Nausea 27% No change of LVEF	IRR 55% Diarrhea 52% Rash 21% LVEF not reported	Pyrexia 23.8% Diarrhea 19% No change of LVEF

Source: ZW25 2018 ASCO; KN026 2020 ASCO; Jose' Baselga 2009; Javier Corte's 2012

# KN026 + KN046 : Synergistic MOA

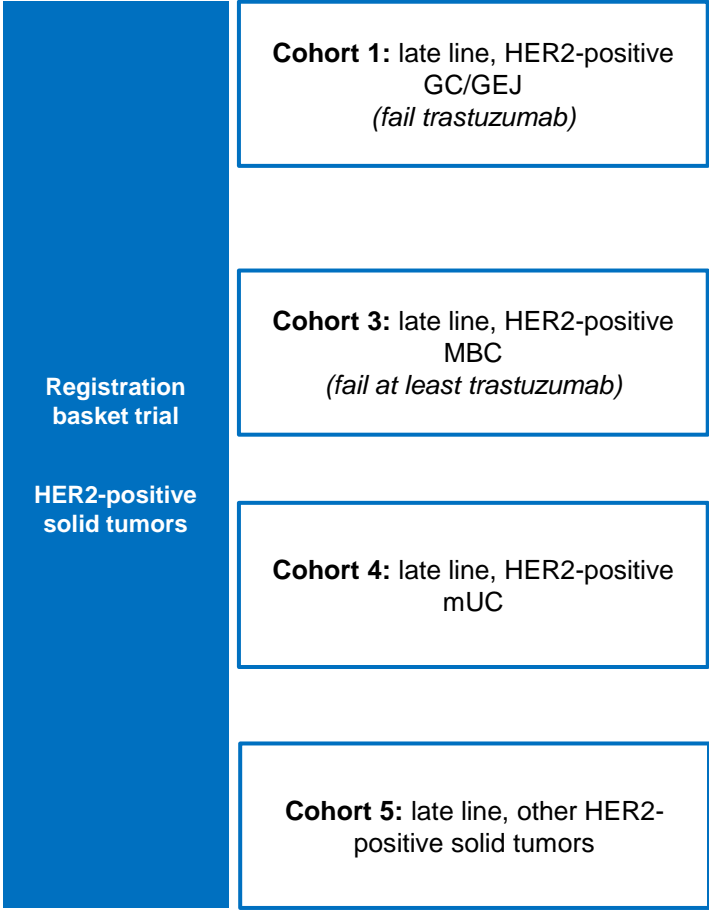


## Rational of the synergistic effect from KN026 plus KN046

- Activation of HER2 pathway interferes STING pathway, key component in innate immunity
- Blocking HER2 pathway lift the inhibition to the innate immunity
- Anti-tumor activity further enhanced by activation of adaptive immunity by KN046
- Supported by early efficacy from IIT in Her2 expression/mut late line solid tumor

# KN026 + KN046 : Highly Differentiated Strategy in Late Line HER2+ Solid Tumors

Frequency of HER2-positive (HER2 IHC3+)	Tumor type	HER2 therapy approved
> 10%	Bladder cancer	✗
	Gastroesophageal junction cancer	✓
	Breast cancer	✓
5%~10%	Cholangiocarcinoma (extrahepatic)	✗
	Gastric cancer	✓
	Cervical cancer	✗
2%~5%	Uterine cancer	✗
	Tumor of unknown of origin	✗
	Colorectal cancer	✗
<2%	Ovarian (epithelial) cancer	✗
	Head and neck carcinoma	✗
	Non-small cell lung cancer	✗
	Intestinal malignancies	✗
	Pancreatic adenocarcinoma	✗
	Cholangiocarcinoma (intrahepatic)	✗
	Prostate cancer	✗



Min Yan 2015 (Benchmark XT, Ventana, USA) (n = 37,992)

## KN026 : Broad Clinical Development Plan in HER2-positive and HER2-low Diseases

1	Initial registration opportunity in 1L MBC	2020	<b>First major pivotal study planned in first line MBC</b> <ul style="list-style-type: none"> <li>FPI planned in 4Q</li> </ul>
2	Highly differentiated strategy in HER2-positive solid tumors	2020	<b>Late line basket trial in HER2-positive solid tumors</b> <ul style="list-style-type: none"> <li>Pivotal trial planned late 2020</li> </ul>
3	Move into all lines of BC	2021	<b>2L trial in HER2-positive MBC with best-in-class profile</b> <ul style="list-style-type: none"> <li>KN026+CDK4/6i</li> <li>KN026+HER2-TKI+Ct</li> </ul> <b>Neoadjuvant trial in HER2-positive ABC/EBC</b> <ul style="list-style-type: none"> <li>KN026+KN046+Ct</li> </ul>
4	Extend to HER2-low diseases	2022	<b>1L trial in HER2-int/low/HR+MBC</b> <ul style="list-style-type: none"> <li>KN026+CDK4/6i+AI</li> </ul>
5	Highly differentiated strategy in HER2-positive GC/GEJ	2021	<b>Chemo-free 1L trial in HER2-positive GC/GEJ</b> <ul style="list-style-type: none"> <li>KN026+KN046</li> </ul>

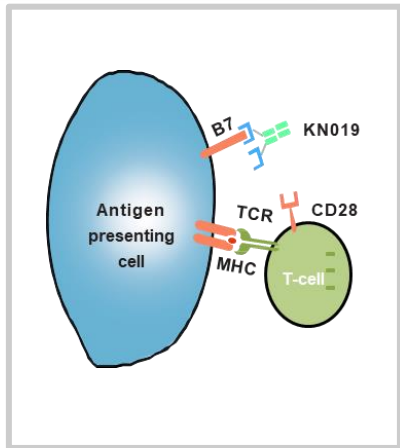
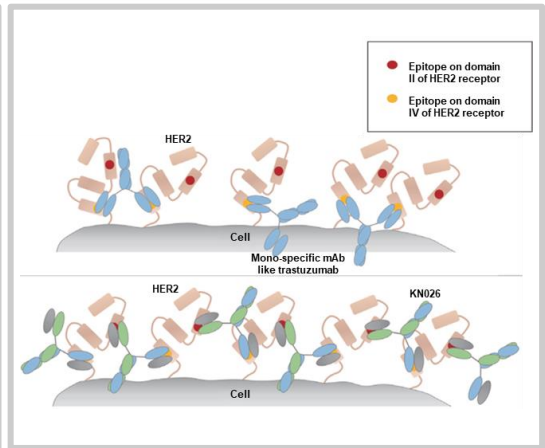
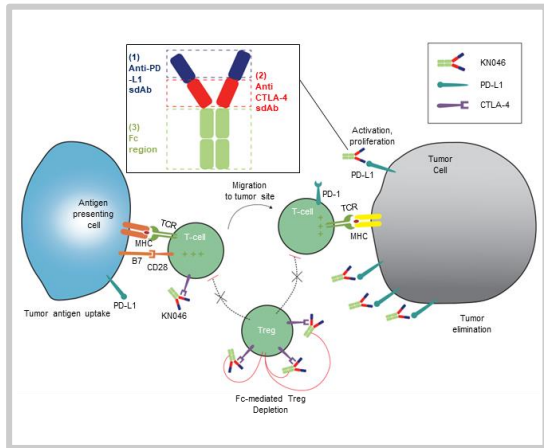
### Notes:

- KN026 mono trial in late-line GC has shown preliminary result of target lesion shrinkage for 4 out of 7 patients (Her-2 low)
- KN026 + KN046 trial in late-stage GI cancer has shown preliminary result of PR for 5 out of 6 patients (Her-2 high)

# Strategy : Develop Next Gen Antibody to Enable Innovative Cancer Therapy

KN035 update

<p><b>KN035</b></p> <p>Subcutaneous PD-L1</p>	<p><b>KN046</b></p> <p>Dual blockade of PD-L1 and CTLA-4</p>	<p><b>KN026</b></p> <p>Dual blockade of HER2 domain II and IV</p>	<p><b>KN019</b></p> <p>A safe option for autoimmune diseases</p>
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# KN035 Registration Trial in MSI-H / dMMR Solid Tumors

## Key Eligibility Criteria

- Age  $\geq$  18 years
- Locally advanced or metastatic solid tumors
- Centrally confirmed MSI-H for colorectal cancer (CRC) and gastric cancer (GC), and locally confirmed dMMR for other tumors
- $\geq$  1 prior line of therapy
- ECOG PS 0~1
- Measurable disease per RECIST 1.1



*Tumor assessments were every 8 weeks*

### Envafolimab

150 mg  
weekly

Until PD,  
unacceptable toxicity,  
or withdrawal

Survival follow-  
up

- **Primary endpoint:** objective response rate (ORR) per RECIST v1.1 by blinded independent radiology review (BIRC).
- **Secondary endpoints:** duration of response (DoR), disease control rate (DCR), progression free survival (PFS) and overall survival (OS).

# Efficacy Results in Subjects Who Had Completed $\geq 2$ On-Study Tumor Assessments

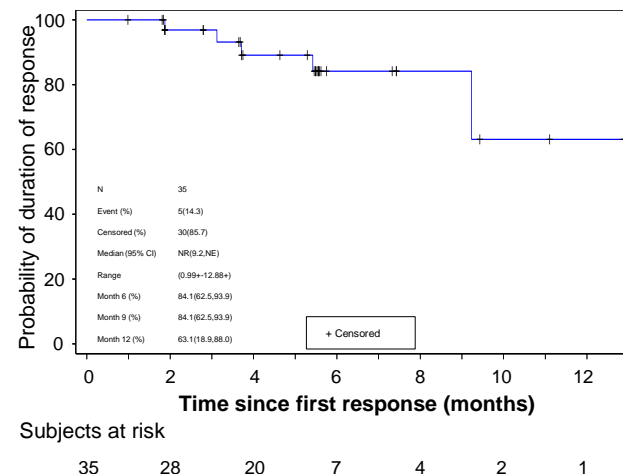
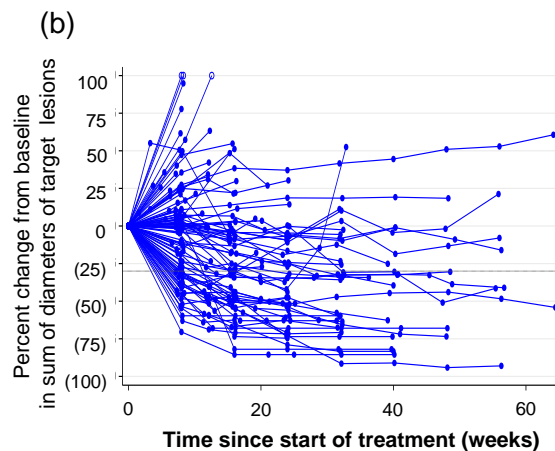
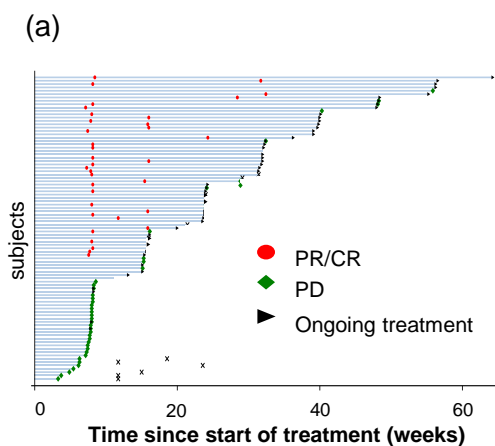
Drug Candidate	PEP <sup>(1)</sup>			CRC failed F and O or I (n=24)	Other tumors (n=20)
	CRC (n=39)	GC (n=11)	Total (n=50)		
Confirmed ORR (BIRC)	28.2%	36.4%	30.0%	54.2%	35.0%
DCR (BIRC)	59.0%	72.7%	62.0%	66.7%	65.0%
6-month DoR (BIRC)	63.0%	100.0%	71.9%	88.9%	100%
Median PFS (BIRC), months	4.9	11.1	6.6	11.1	5.6
Median OS, months	Not reached				
12-month OS rate	61.5%	68.2%	63.7%	90.5%	76.8%

## Tumor response over time in overall population

## DoR in subjects with a confirmed response per BIRC in overall population

Swimmer plot of disease status over time (a)

Spider plot of change in sum of diameters of target lesions by subjects over time (b)



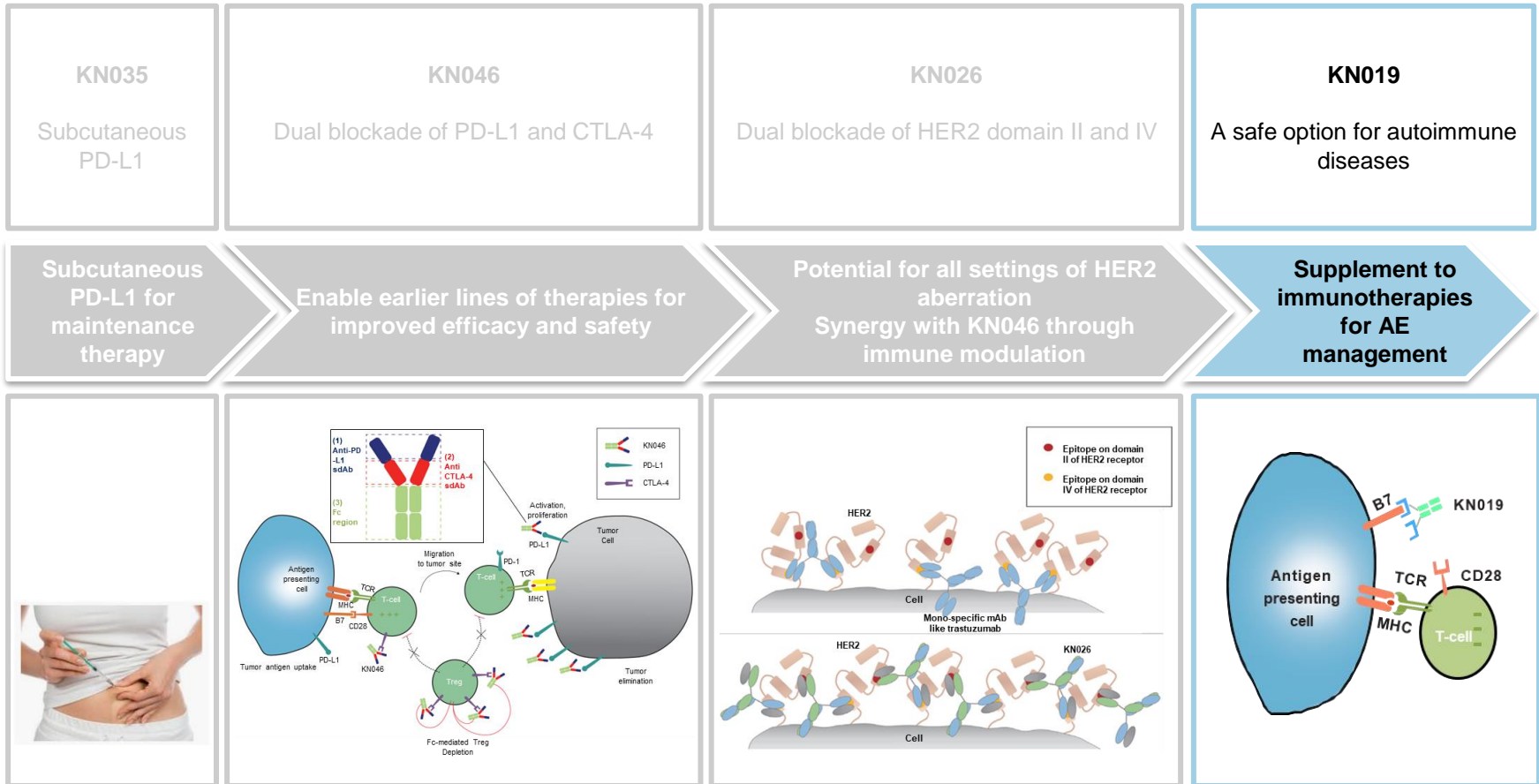
- Safety profile was similar to other PD-(L)1 antibodies but without infusion reactions. No colitis or pneumonitis case was reported in the study.

### Notes:

1. PEPi refers to the primary efficacy population for interim analysis, patients in the PEP who had at least two post-baseline tumor assessments

# Strategy : Develop Next Gen Antibody to Enable Innovative Cancer Therapy

KN019 update

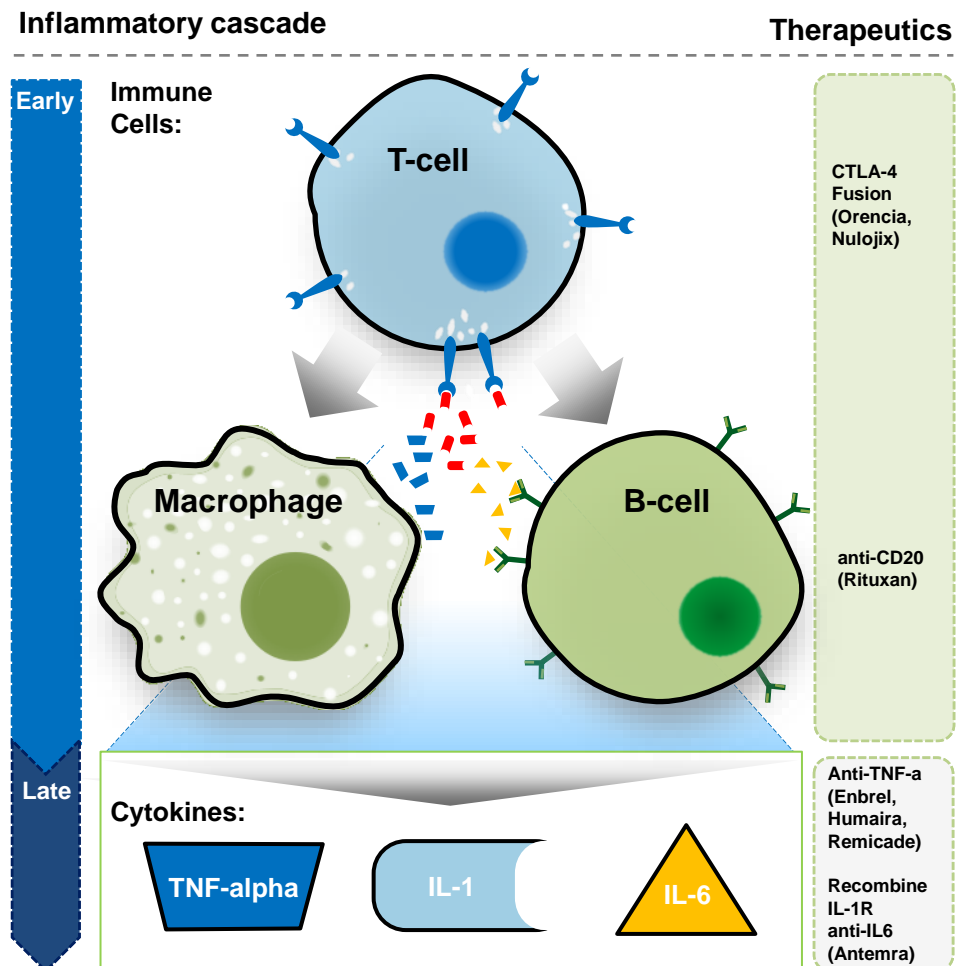


# CTLA-4-Fusion Proteins : Immunosuppressant Drugs

## Overview of CTLA-4-Fusion Proteins

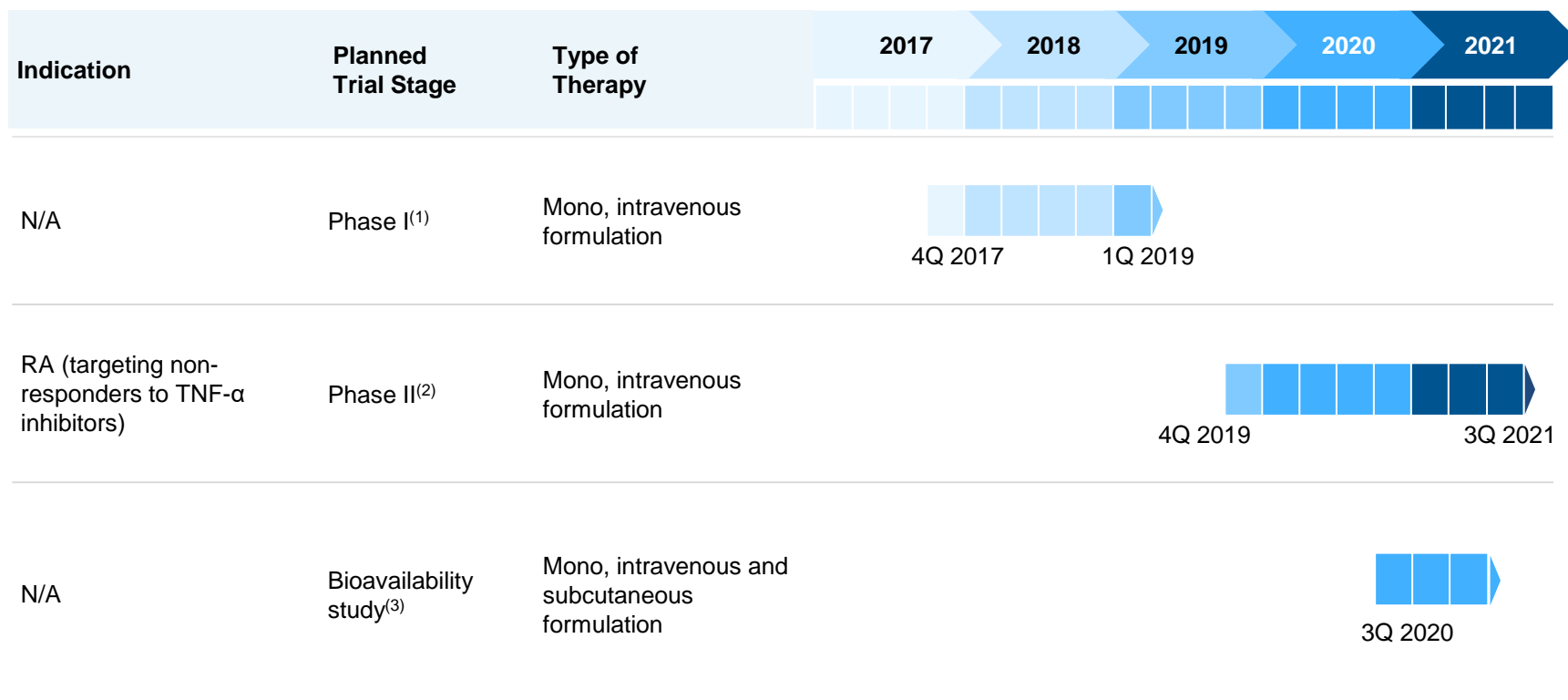
- Function in the early stage of T-cell activation and may achieve efficient global downregulation of unwanted immune responses
- Clinically-validated for treatment of RA, idiopathic arthritis, psoriatic arthritis and prophylaxis of organ rejection after kidney transplant outside China
- Potentials to become a **supportive therapy for o mitigate IO treatment–induced immune disorders** (*N Engl J Med* 2019; 380:2377-2379)
- Approx. **100,000 patients** suffering below immune disorders in China without effective treatment
  - IrAEs in patients treated with immune checkpoint inhibitor therapy
  - Severe cytokine release syndrome (CRS) due to massive cytokine release by certain cell therapies (CAR-T and TCR-T) and CD3 agonists
  - Graft-versus-host diseases during leukemia treatment

## Major Lymphocytes and Signals for Activation & Maintenance of Immune Response



# KN019 – Targeted Clinical Strategy

## Clinical Development Plan (China)



Abbreviations: mono = monotherapy

**Notes:**

1. A double-blinded, placebo-controlled dose-escalation trial in healthy subjects
2. A multi-center, open-label, single arm clinical trial
3. A bioavailability study in healthy subjects to switch the administration of KN019 from intravenous formulation to subcutaneous formulation

03

Q&A

