

# **Alphamab Oncology Presentation**

September 2020

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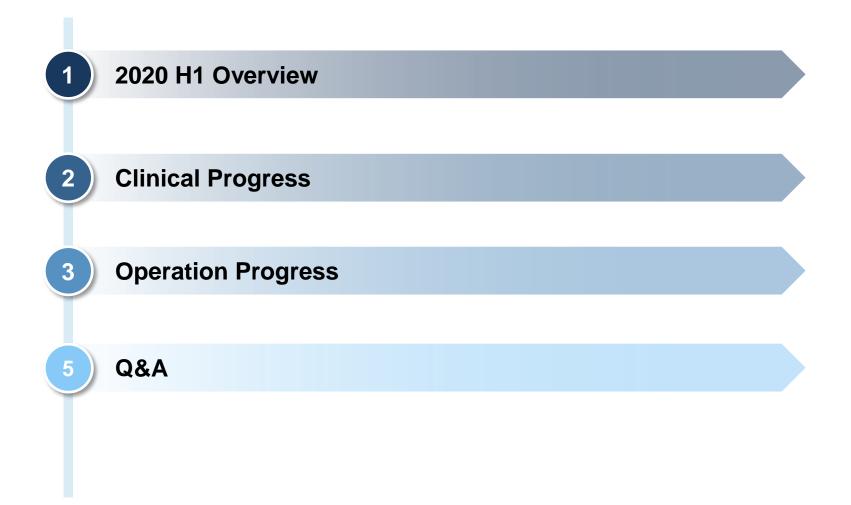
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Agenda



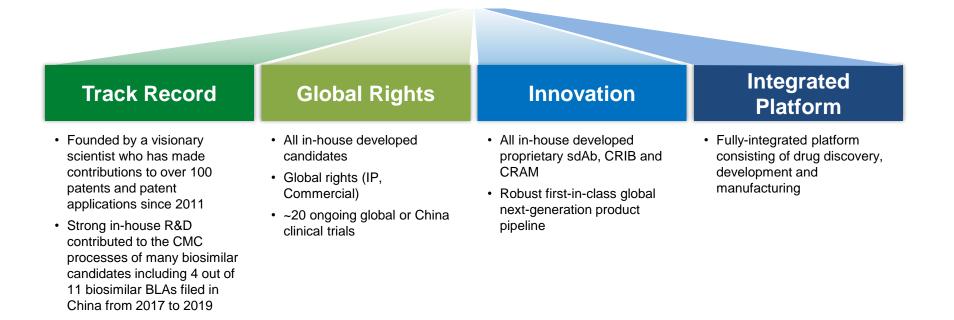


2020 H1 Overview

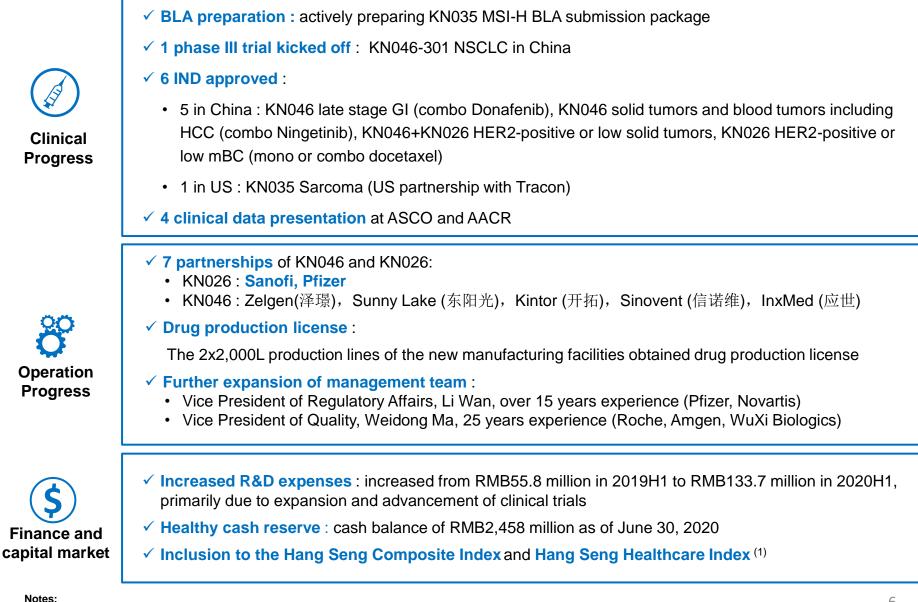
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We are a leading clinical-stage biopharmaceutical company in China with a fully-integrated proprietary biologics platform in bispecifics and protein engineering, delivering world-class innovative therapeutic biologics to cancer patients globally.



# Major progresses in 2020 H1



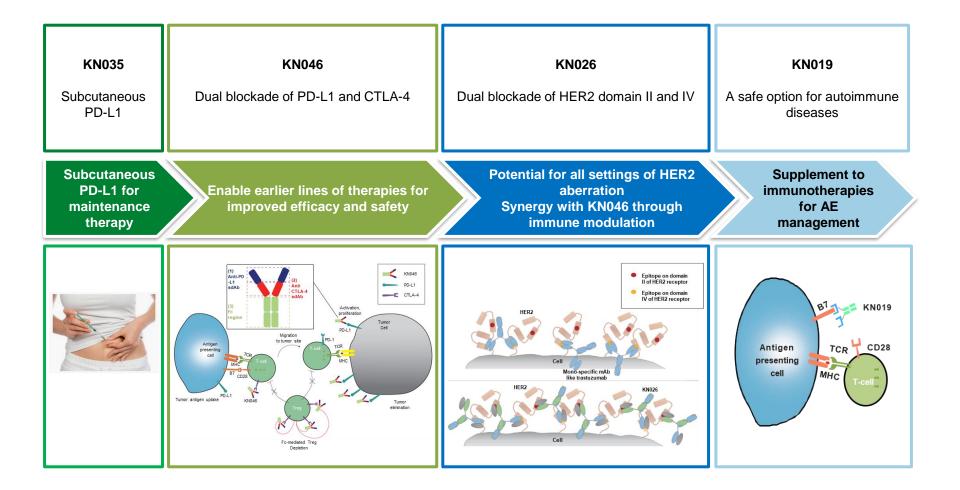
1. Effective on September 7, 2020



# **Clinical Progress**

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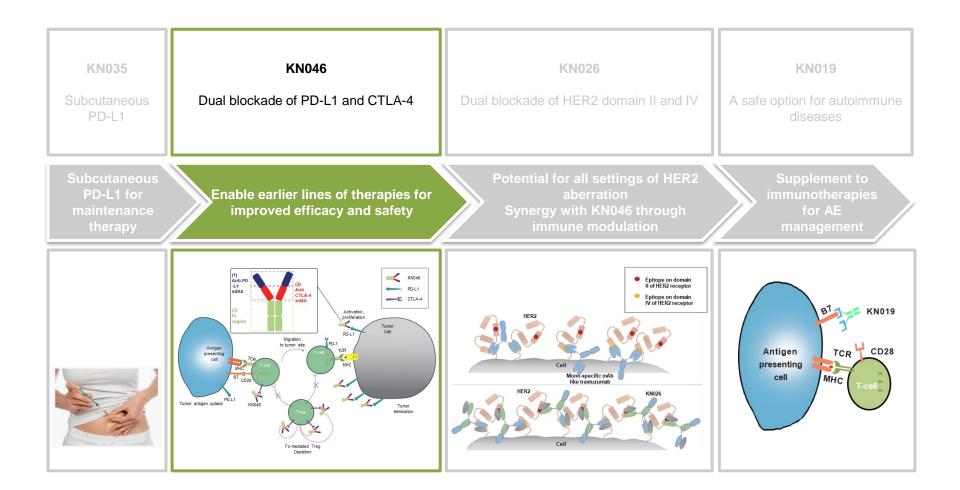
### **Strategy : Develop Next Gen Antibody to Enable Innovative Cancer Therapy**



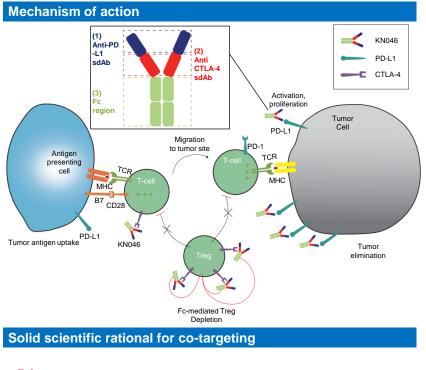
# **Pipeline overview**

Drug		Commercial				Statu	us		Expected
Candidate	Target(s)	Rights	Key Indications	NCT Number	Pre-Clinical	Phase I	Phase II	Phase III	First BLA Submission
			NSCLC, 1L (KN046+CT)	NCT04474119	China		Phase III		$\Delta$
	PD-L1/ CTLA4	Global	Thymic carcinoma	NCT04469725	China, U.S.	Phase II			
	CTLA4		TNBC, 1L (KN046+nab- paclitaxel)	NCT03872791	China		Phase II		H1 2022
KN046			ESCC, 1L (KN046+CT)	NCT03925870	China	Pha	se II		111 2022
			NSCLC, >=2L (KN046 or KN046+CT)	NCT03838848	China, U.S.	Phase II			
			NSCLC, stage III (KN046+RT)	NCT04054531	China	Phase II			
			HER2-positive/low mGC/GEJ, late line	NCT03925974	China		Phase II		
KN026	HER2/ HER2	Global	HER2-positive, 1L (KN026+ docetaxel) /HER2 low mBC	NCT04165993	China	PI	hase II		4Q 2022
			HER2-positive mBC, mGC/GEJ, late line	NCT03847168	U.S.	Phase I			
KN046+	PD-L1/		HER2-low mBC	NCT04165993	China	Phase II			
KN026 combo	CTLA4 + HER2/	Global		NCT04521179	China	Phase II			H2 2022
combo	HER2			10104321173	China	Phase II			
KN019	B7	Global	RA	NCT04038970	China		Phase II		Planning stage
			MSI-H or dMMR solid tumors	NCT03667170	China		Phase II completed	7	
KN035	PD-L1	Co- development	BTC (KN035+Gemcitabine	NCT03478488	China			Phase III	By the End of 2020
			Sarcoma and others	NCT04480502	Rest of the World				
KN052									
KN053	Undisclosed								
KN055	bispecifics	Global	Not available						Not available
KN058						-			
Antibody for COVID-19	Undisclosed	Co- development	COVID-19 treatment						Not available

### KN046 update



### KN046 – PD-L1/CTLA-4 BsAb



Science

RESEARCH ARTICLES

Cite as: D. Sugiura et al., Science 10.1126/science.aav7062 (2019).

# Restriction of PD-1 function by *cis*-PD-L1/CD80 interactions is required for optimal T cell responses

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

#### CANCER

# Dendritic cells dictate responses to PD-L1 blockade cancer immunotherapy

### **Highlights**

### 1) Targeted drug delivery

- Engineered to enable the anti-PD-L1 sdAb to dominate drug distribution
- Targeted drug delivery to tumor and limit exposure to nontumor tissues

### 2) Different CTLA-4 binding epitope

- Our anti-CTLA-4 sdAb blocks the CTLA-4/B7 ligands interaction with steric hindrance instead of direct competition as lpilimumab
- Lead to a potentially improved safety profile

### 3) Preservation of Fc-mediated effector functions

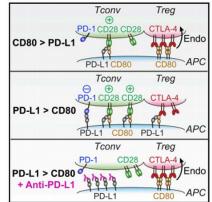
- Preserves the full Fc functions for Treg depletion

Article

### Immunity

### PD-L1:CD80 *Cis*-Heterodimer Triggers the Costimulatory Receptor CD28 While Repressing the Inhibitory PD-1 and CTLA-4 Pathways

#### Graphical Abstract



#### Authors

Yunlong Zhao, Calvin K. Lee, Chia-Hao Lin, ..., Li-Fan Lu, Jack D. Bui, Enfu Hui

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### In Brief

Combined immunotherapy targeting the checkpoint receptors CTLA-4 and PD-1, or CTLA-4 and the PD-1 ligand (PD-L1) results in superior anti-tumor responses. Zhao et al. show that PD-L1 heterodimerizes with CD80, a shared ligand for CTLA-4 and CD28, to selectively weaken CD80:CTLA-4 interaction but not CD80:CD28 interaction. Thus, PD-L1 can repress the CTLA-4 axis; this has implications to the synergy observed in combination immunotherapies.

### KN046's ongoing clinical trials

Drug		Commercial	<i></i>			Stat	us		Expected
Candidate	Target(s)	Rights	Key Indications	NCT Number	Pre-Clinical	Phase I	Phase II	Phase III	First BLA Submission
			NSCLC, 1L ( <i>KN046</i> +C7)	NCT04474119	China		Phase	In	↓ (1)
			Thymic carcinoma <sup>(3)</sup>	NCT04469725	China, U.S.	Phase II	T T	∧ (1) ≪	
	PD-L1/(2)	TNBC, 1L (KN046+nab-paclitaxel)	NCT03872791	China		Phase II			
KN046	CTLA4	Global <sup>(2)</sup>	Global <sup>(2)</sup> ESCC, 1L <i>(KN04</i> 6+CT)	NCT03925870	China	Pha	se II		H1 2022
		NSCLC, >=2L <sup>(4)</sup> (KN046 or KN046+CT)	NCT03838848	China, U.S.	Phase	II			
			NSCLC, stage III (KN046+RT)	NCT04054531	China	Phase I			

#### Notes:

- 1. Future BLA submission. Some indications may not require a non-pivotal phase II clinical trial prior to beginning the pivotal phase II/III clinical trials in China. Based on our experience, the need for comparison studies for our drug candidates is determined on a case-by-case basis and based on communications with the regulators including NMPA or US FDA.
- 2. No licensing partner as of the Latest Practicable Date.
- 3. US FDA just awarded ODD (Orphan Drug Designation) status
- 4. This trial comprises of using KN046 or KN046 in combination with other therapy to treat various cohorts of NSCLC patients including patients who have relapsed from first line platinum-based chemotherapy, patients who have failed prior PD-(L)1 treatment and patients whose tumor bear EGFR mutation.

# Clinical data : 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 ≥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

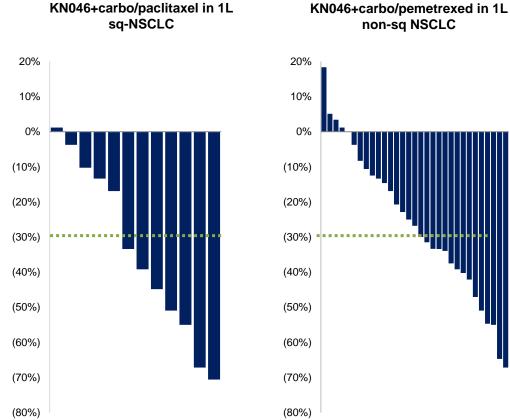


Objective responses rate was 12.0%



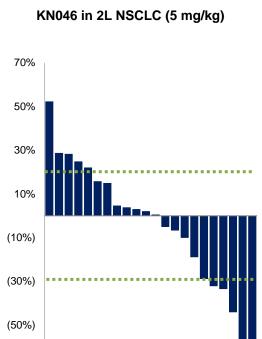
### Clinical data : promising 1L and 2L NSCLC led to the launch of Pivotal Phase 3 Trial KN046-301

non-sq NSCLC



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

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



(70%)

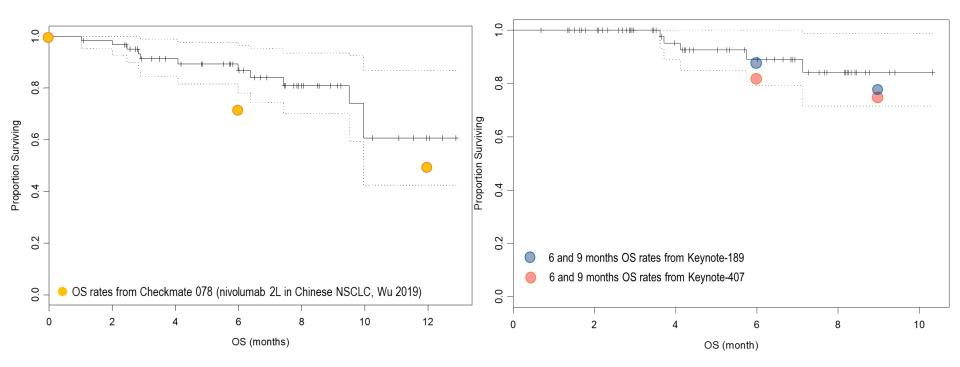
(90%)

Notes: As of May-2020. Trial ongoing 1.

# **OS comparison in NSCLC**



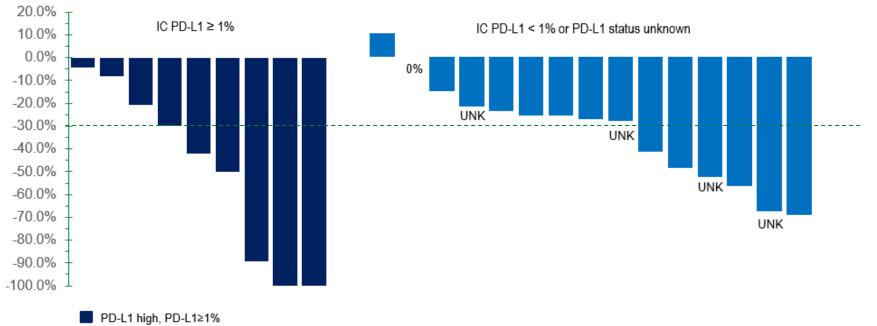
OS data comparison in 1L NSCLC



### Clinical data : KN046-203 TNBC

KN046 in combination with nab-paclitaxel in TNBC, 1L

• Deeper response is observed in IC PD-L1 ≥1% subgroup



PD-L1 low, PD-L1<1% or unknown

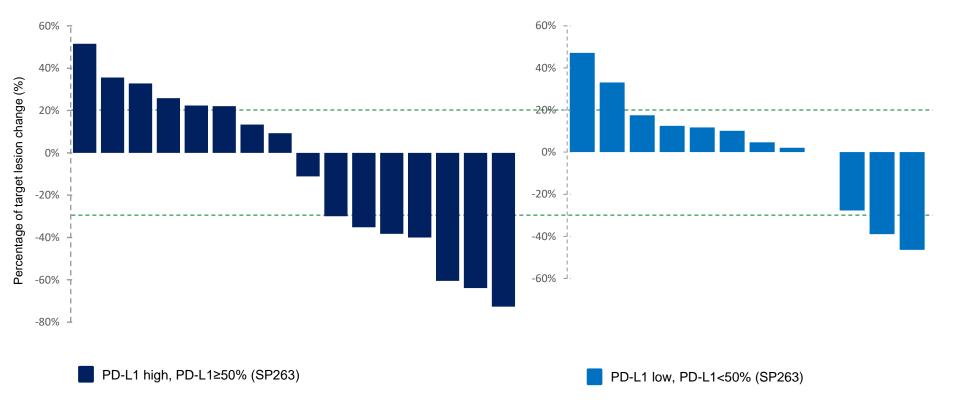
#### Notes:

- 1. As of 17-Aug-2020. Trial ongoing
- 2. UNK: PD-L1 status unknown

### Clinical data : KN046-CHN-001 NPC

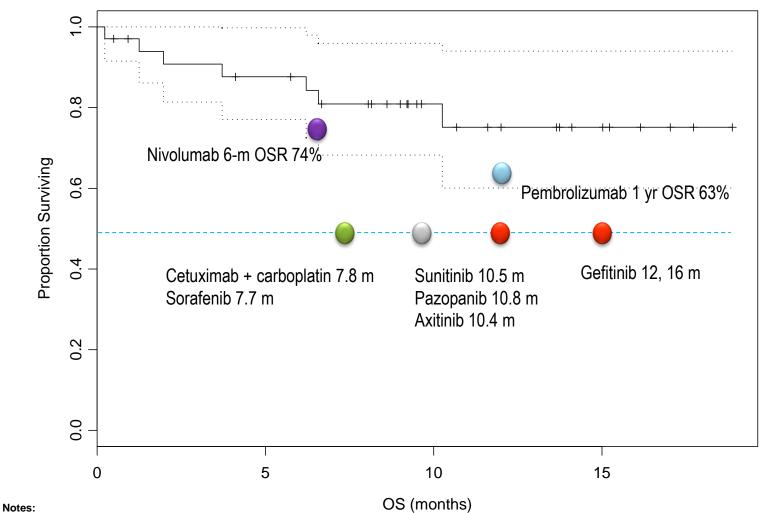
NPC unselected population: anti-PD-1 naïve, late line

- Encouraging efficacy observed particularly in PD-L1 high group
- 7/16 ORR (confirmed and unconfirmed) in PD-L1 high group



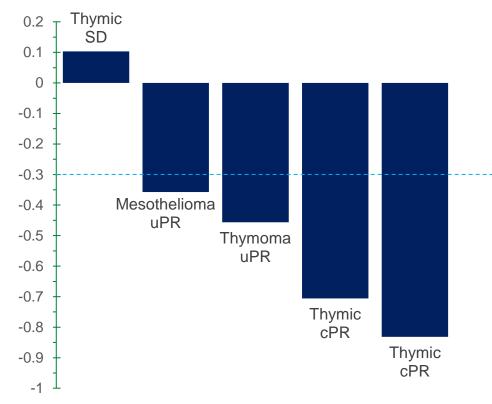
# **OS comparison in NPC**

NPC unselected population: anti-PD-1 naïve, late line



1. As of 20-Aug-2020 (data retrieved from EDC)

## Efficacy data in thymic epithelial tumor (TET)



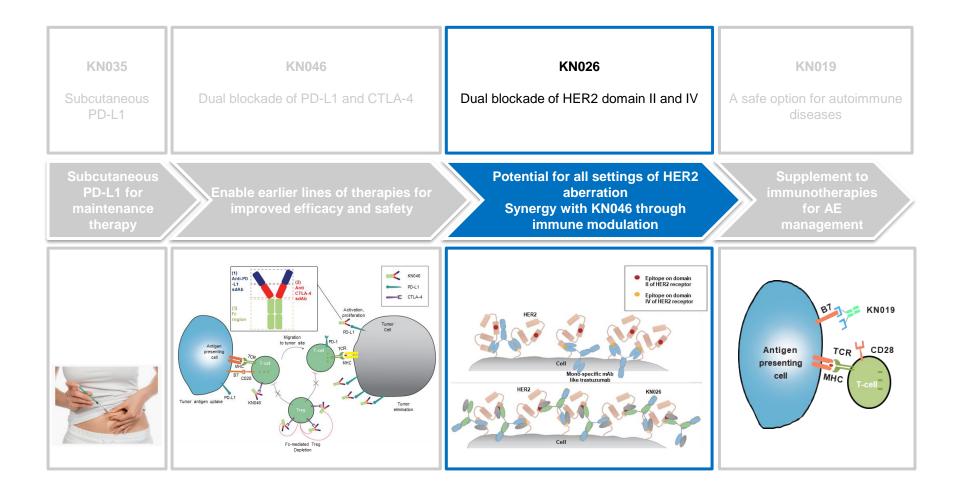
- ODD (Orphan Drug Designation) awarded by US FDA
- Phase II registration trial in China and US initiated

Left to right (prior anti-cancer treatment)

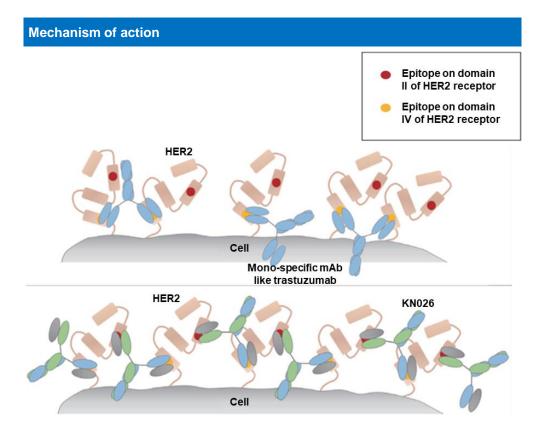
- 004-016: carboplatin/etoposide
- 003-016: palliative
- 005-005: cisplatin, adriamycin, cyclophosphamide
- 004-008: carboplatin/etoposide
- 005-011: carboplatin/paclitaxel

### Notes: 1. As of 06-Jul-2020. Data retrieved from EDC

### KN026 update



### KN026 – HER2/HER2 BsAb



### Highlights

- 1) Dual blockade of parallel HER2-related signaling pathways
  - Binds two distinct epitopes of HER2 receptors which have been clinically validated by the Herceptin and Perjeta combination therapy
  - Can induce synergistic inhibitory activities and potentially reduce drug resistance and relapse

### 2) Enhanced multiple HER2 receptor binding

- Crosslinking multiple HER2 receptors on the cell surface and promote HER2 internalization
- Binds Her2 more efficiently, particularly in low/intermediate expession

### 3) Fc-based BsAb with full effector functions

- Recruit immune cells to destroy HER2overexpressing target cells
- Increased presence of KN026 on tumor cells leads to increased tumor killing by effector functions

# **KN026 ongoing clinical trials**

	Drug	-	Commercial			Status				Expected
	Candidate	Target(s)	Rights	Key Indications	NCT Number	Pre-Clinical	Phase I	Phase II	Phase III	First BLA Submission
				HER2-positive/low mGC/GEJ, late line	NCT03925974	China		Phase II		
	KN026	HER2/ HER2		HER2-positive, 1L (KN026+ docetaxel) /HER2 low mBC	NCT04165993	China		Phase II		4Q 2022
				HER2-positive mBC, mGC/GEJ, late line	NCT03847168	U.S.	Phase I			
Ì	_				NCT04165993	Ohima				
	KN046+ KN026 combo HER2/ HER2		HER2-low mBC <sup>(2)</sup> NCT04		China	Phase II				
		+ Global <sup>(1)</sup> HER2/			NCT04521179	China	Phase II			H2 2022

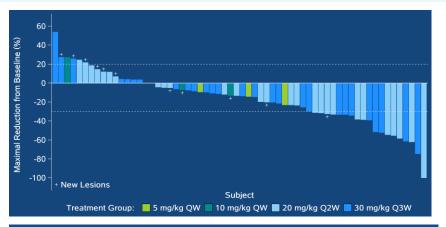
#### Notes:

1. No licensing partner as of the Latest Practicable Date.

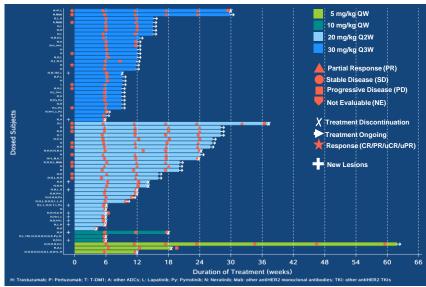
2. Patients with HER2 low expressing, HR negative MBC are enrolled in KN026-201 HER2-low cohort

### Clinical data : KN026-CHN-001

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



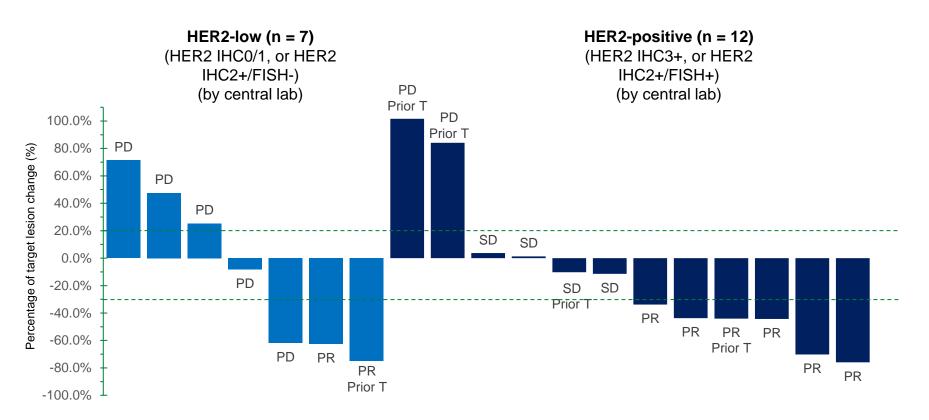
As of Jan.22, 2020	5 mg/kg QW (n=3)	10 mg/kg QW (n=3)	20 mg/kg Q2W (n=28)	30 mg/kg Q3W (n=28)	Total (n=62)	Pooling 20 mg/kg Q2W & 30 mg/kg Q3W (n=56)
CR	0	0	0	0	0	0
PR	0	0	10 (35.7%)	8 (28.6%)	18 (29.0%)	18 (32.14%)
SD	2 (66.7%)	1 (33.3%)	8 (28.6%)	17 (60.7%)	28 (45.2%)	25 (44.64%)
PD	1 (33.3%)	2 (66.7%)	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)

### Clinical data : KN026-202

KN026 monotherapy activity in HER2-low and HER2-positive GC/GEJ



HER2-low (n = 7) (HER2 IHC0/1, or IHC2+/FISH-) (by central lab)

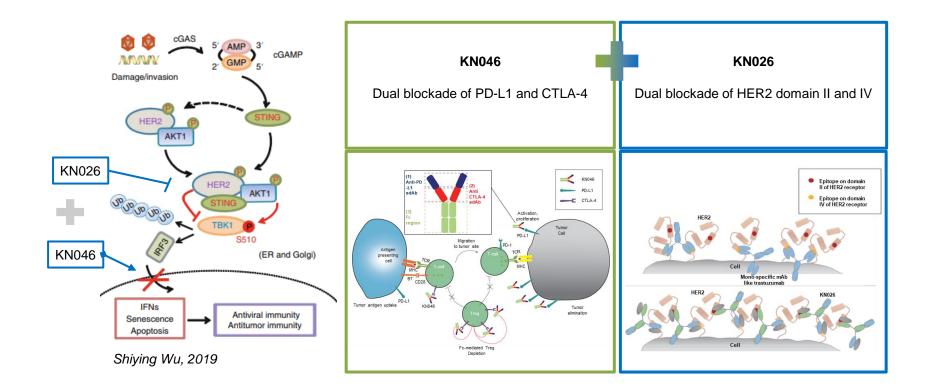
HER2-positive (n = 12)(HER2 IHC3+, or IHC2+/FISH+) (by central lab)

#### Notes:

- 1. As of 21-Aug-2020. Trial ongoing
- 2. HER2-positive according to ASCO/CAP 2018

3. Prior T : received Herceptin treatment previously

## KN026 + KN046 : Synergistic MOA

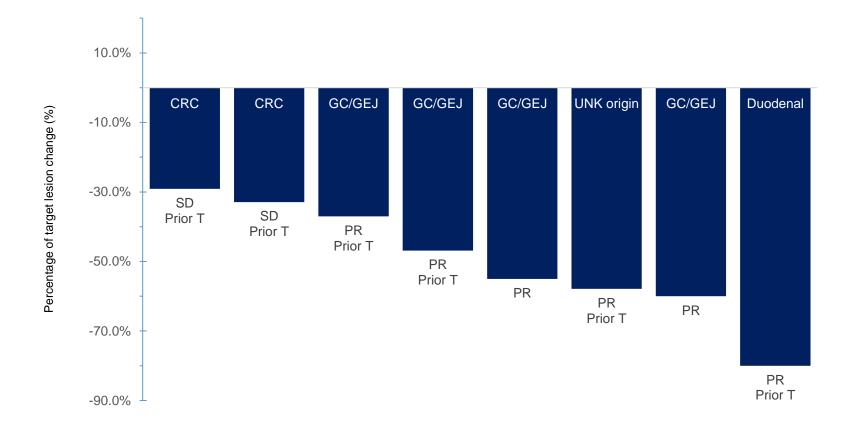


### Rational of the synergistic effect from KN026 plus KN046

- 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 IST in Her2 expression/mut late line solid tumor

### Clinical data : KN046-IST-02

KN026 and KN046 combination in HER2-positive solid tumors



#### Notes:

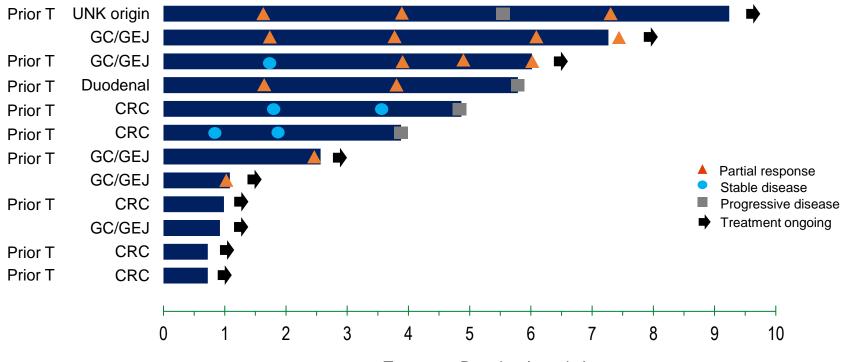
1. As of 17-Aug-2020. Trial ongoing

2. Prior T : received Herceptin treatment previously

3. Only late line patients' data are included, data of one first line patient with large tumor burden is excluded

### Clinical data : KN046-IST-02

KN026 and KN046 combination in HER2-positive solid tumors



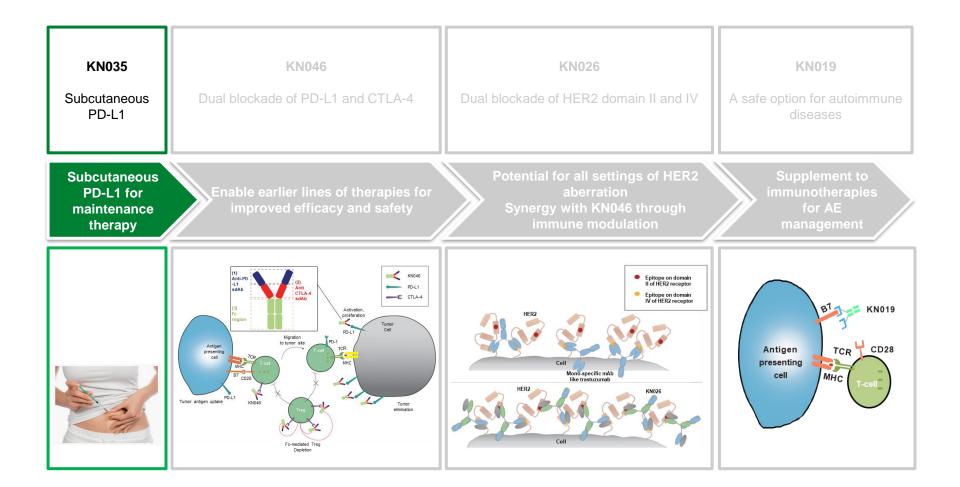
Treatment Duration (months)

#### Notes:

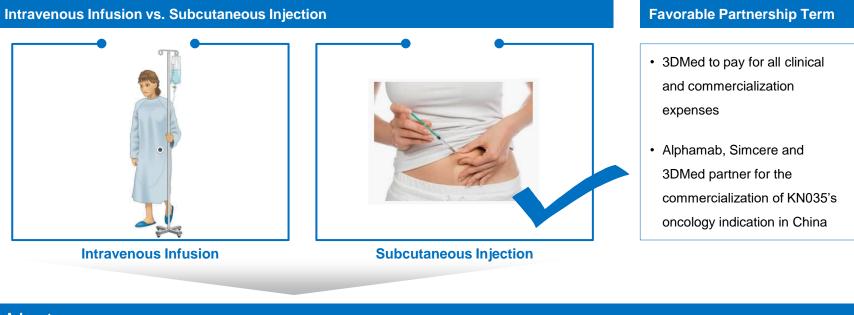
- 1. As of 17-Aug-2020. Trial ongoing
- 2. Prior T : received Herceptin treatment previously

3. Only first line patients' data are included, one second line patient's data has been excluded

### KN035 update



# KN035 – Potential First-global SC PD-L1 for Near-term Commercialization



### Advantages



Better/quicker administration



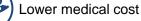
Preferred for patients with limited vein access



Prolonged half-life to support a less frequent dosing schedule



Precedent for strong competitiveness: 4 years after launch, SC Herceptin represents ~50% of Herceptin sales in European market

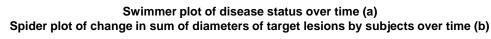


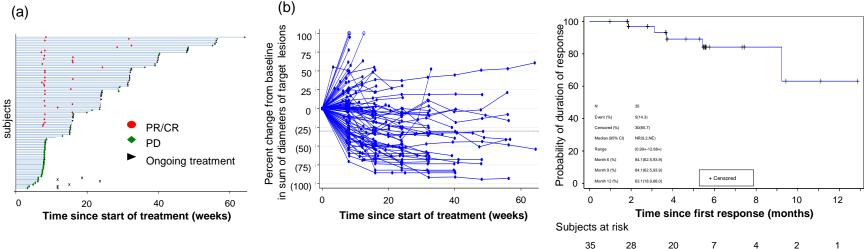
### Efficacy Results in Subjects Who Had Completed ≥ 2 On-Study Tumor Assessments

		PEPi <sup>(1)</sup>			
Drug Candidate	CRC (n=39)	GC (n=11)	Total (n=50)	CRC failed F and O or I (n=24)	Other tumors (n=20)
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



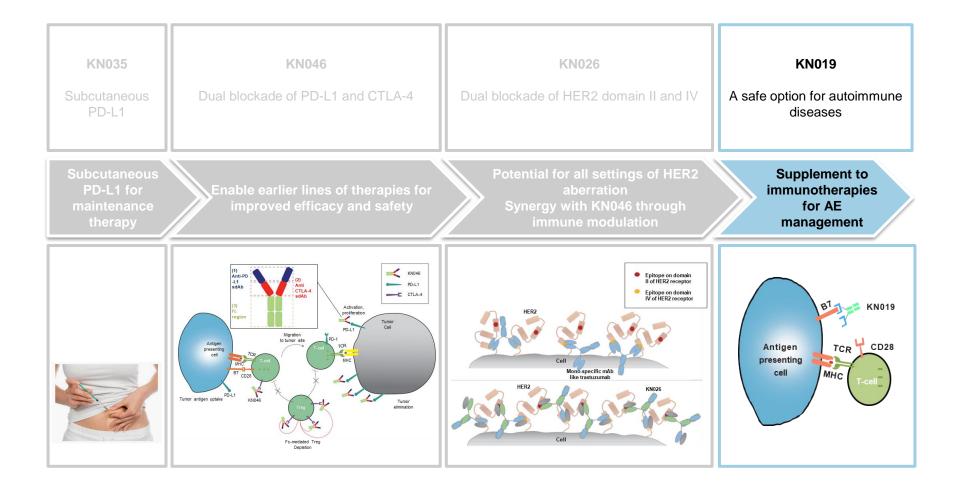


Safety profile was similar to other PD-(L)1 antibodies but without infusion reactions. No colitis or pneumonitis
case was reported in the study.

#### 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

### KN019 update

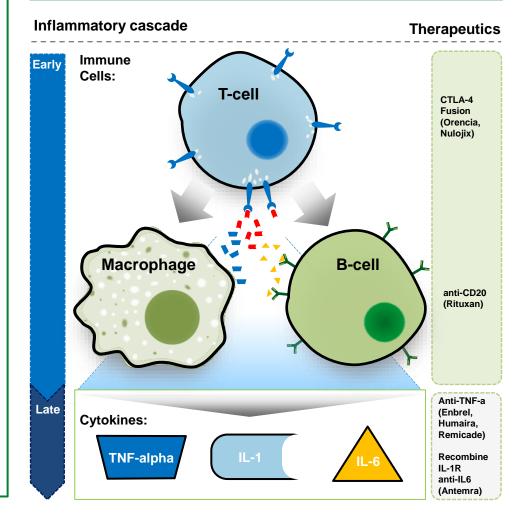


### **CTLA-4-Fusion Proteins : Immunosuppressant Drugs**

### 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)					
Indication	Planned Trial Stage	Type of Therapy	2017 2018 2019 202	20 2021	
N/A	Phase I <sup>(1)</sup>	Mono, intravenous formulation	4Q 2017 1Q 2019		
RA (targeting non- responders to TNF-α inhibitors)	Phase II <sup>(2)</sup>	Mono, intravenous formulation	4Q 2019	3Q 2021	
N/A	Bioavailability study <sup>(3)</sup>	Mono, intravenous and subcutaneous formulation		2Q 2021	

#### Notes:

- 1. A double-blinded, placebo-controlled dose-escalation trial in healthy subjects
- 2. A multi-center, open-label, single arm clinical trial

3. Abbreviations: mono = monotherapy

4. A bioavailability study in healthy subjects to switch the administration of KN019 from intravenous formulation to subcutaneous formulation

# **Preliminary Plan for Medical Conferences**

Year	Month	Conference	Title
2020	November	sitc	KN046-IST-02 KN046+KN026 in HER2- positive solid tumors
2021	January	<b>ASCO</b> <sup>•</sup> Gastrointestinal Cancers Symposium	KN046-IST-01 ESCC (CRT)
2021	lenuen	2020 World Conference	KN046-201 2L NSCLC
	January	on Lung Cancer Singapore	KN046-AUS-001 Thymic cancer
2021	April	American Association for Cancer Research	KN046-203 TNBC
			KN046-202 1L NSCLC
2021	June	ASCO	KN026-202 GC
			KN026-203 KN046+KN026 in HER2-positive solid tumors
2021	September	ESMO	KN046-204 ESCC

Note:

1. Essay must be accepted for submission

2. The results of clinical trials can not be predicted

3. 2020 WCLC conference is postponed to 2021, January

4. The preliminary plan for medical conferences is potentially subject to change



# 03

**Operation Progress** 

# **Business Development : comprehensive combo strategy**

### ..to unlock KN046's full potential

Target	Combo Drug	Partner
VEGFR-1, -2, -3; c-CRAF, BRAF, mBRAF; FLT3; KIT; PDGFRβ; RET, RET/PTC	Donafenib Tosylate	<b>Zelgen</b> 泽璟制药
MET; VEGFR-2; AXL; MER; FLT-3	Ningetinib Toluenesulfonate CT053	Sunshine Lake 广东东阳光
ALK-1 (Activin Receptor-Like Kinase-1)	GT90001	Kintor Pharmaceutical 开拓药业
Wnt pathway Porcupine protein	XNW7201	Sinovent 信诺维
Focal adhesion kinase inhibitor	IN10018	InxMed 应世生物

## **Business Development : strong potential MNC interest in KN026**

HER2-positive, HER2-int/low and HER2-mutation, KN026-based combination					
Target	Combo Drug	Partner			
CDK4/6	Ibrance® (palbociclib)	Pfizer			
Microtubule inhibitor	Taxotere® <sup>(1)</sup> (Docetaxel)	SANOFI			

#### Notes:

1. Sanofi has an exclusive option agreement for the strategic collaboration to advance clinical studies investigating KN026

### Further expansion of management team



- Vice President, Regulatory Affairs Li Wan, Ph.D., RAC
- Over fifteen years of industry experience in global regulatory affairs and project management
- Served various positions in a number of pharmaceutical companies including Pfizer and Novartis in the US, Luye Pharma
- Led many global IND/CTA/NDA submissions and obtained approvals for small molecules and biologics products, with expert knowledge of the FDA, EMA, NMPA, PMDA, and ICH regulations
- Doctoral degree in Pharmaceutical Science from Rutgers University, MS/BS degrees in Biology from Nanjing University

Vice President, Quality



- Weidong Ma
- 25 years of extensive experience in Quality Management
- Served various positions in a number of pharmaceutical companies including WuXi Biologics, Amgen China and Roche Shanghai
- Led team to pass several audits from FDA, EMA and NMPA
- B.S in Chemistry from Shanghai Normal University





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## **Further progress in manufacturing**

Jiangsu Alphamab's New Manufacturing Facilities' Phase I production lines Have Received "Drug Production License"

Alphamab Oncology announced the Phase I (2x2,000L) production lines of its new manufacturing facilities has obtained "Drug Production License" by Jiangsu Provincial Drug Administration.

The new manufacturing facility has a designed total capacity over 30,000L







Q&A