Preliminary Safety, Efficacy and Pharmacokinetics (PK) Results of KN026, a HER2-targeted Bispecific Antibody in Patients (pts) with HER2-positive Metastatic Breast Cancer

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Unmet Need in Cancers with HER2 Aberration

HER2 overexpression and amplification observed in a range of cancers

- HER2 overexpression and amplification occurs in multiple tumor types and often associated with poorer prognosis and a shorter survival

Current HER2-targeted therapies effective, but the pressing unmet medical need exists

- Inevitably patients developed resistance to HER2-targeted therapies. Developing novel therapies to achieve continuous HER2 pathway inhibition will benefit patients

KN026: Bispecific HER2-Targeted Antibody

- Fully humanized, IgG1-like antibody, binds to two distinct HER2 epitopes, the same domains as trastuzumab (ECD4) and pertuzumab (ECD2).
- IgG1 Fc fragment of KN026 binding FcγRIIIa mediates potent ADCC

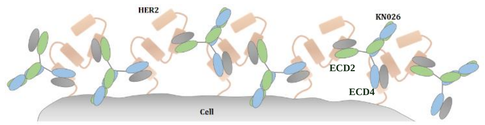

Figure 1. Mechanism of action of KN026

KN026 Phase I Study

- First-in-human (FIH) study of KN026 in Chinese pts with HER2 positive breast cancer (failed at least one prior line of HER2-targeted therapy including trastuzumab)
- 3+3 Dose Escalation & Schedule Exploration

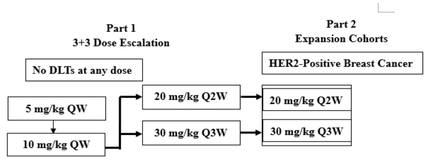

Figure 2. KN026 Phase I Study design

Pharmacokinetics:

- Liner PK across dose range from 5 mg/kg to 30 mg/kg
- 20 mg/kg Q2W and 30 mg/kg Q3W steady state through levels exceed predicted target efficacious concentration from preclinical translational research and declared as recommended phase 2 doses (RP2Ds) for KN026

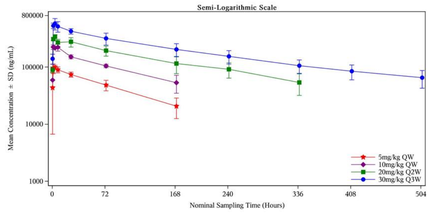

Figure 3. Mean Plasma Concentration of KN026-Time Plots (Single Dose)

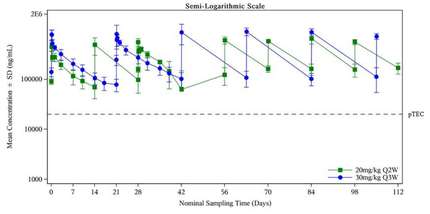

Figure 4. Mean Plasma Concentration of KN026-Time Plots (Multiple Dose)

pTEC: predicted target efficacious concentration based on preclinical translational research

Safety:

Well tolerated at all doses and schedules

- No dose limiting toxicities (DLTs)
- Treatment-related AEs majority Grade 1 or 2
- 4 patients (20 mg/kg Q2W expansion cohort) reported 4 Grade 3 TEAEs

Reversible Grade 3 hypertension, transaminases increased, infusion related reaction, ventricular arrhythmia

- No LVEF decreases ≥ 15% during treatment
- No treatment-related serious adverse events leading to death

	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

Table 1.KN026 related TEAEs (as of 22-Jan-2020) (frequency ≥10%)

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

- **Preclinical results indicate KN026 has better anti-tumor activity than either Trastuzumab or Pertuzumab used alone**
- **Of 62 evaluable pts, the objective response rate was 29.0% and disease control rate was 74.2%. At RP2D levels, the objective response was 32.1% and disease control rate was 76.8%**
- **No DLTs were observed in all 4 dose levels**
- **Majority of AEs were Grade 1 or 2**

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Clinical trial information: NCT03619681

Table 2. Patient demographics, disease characteristics and treatment duration (as of 22-Jan-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)
Gender, n (%)					
Male	0	0	0	0	0
Female	3 (100%)	3 (100%)	28 (100%)	29 (100%)	63 (100%)
Age (years)					
Median（Min, Max）	56 (45, 57)	57 (43, 57)	50.5 (31, 68)	54.0 (33, 69)	54.0 (31, 69)
ECOG, n (%)					
0	0	0	6 (21.4%)	11 (37.9%)	17 (27.0%)
1	3 (100%)	3 (100%)	22 (78.6%)	18 (62.1%)	46 (73.0%)
Duration of Treatment (weeks)					
Median (Min, Max)	18.57 (12.0, 61.9)	6.00 (6.0, 18.0)	16.00 (4.1, 37.3)	11.71 (5.9, 30.0)	12.00 (4.1, 61.9)
Discontinuation treatment, n (%)					
Progressive Disease	2 (66.7%)	3 (100%)	13 (46.4%)	3 (10.3%)	21 (33.3%)
Adverse Events	0	0	1 (3.6%)	0	1 (1.6%)

Table 3. Summary of efficacy results (as of 22-Jan-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%)

Note: CR: complete response, including confirmed and unconfirmed. PR: partial response, including confirmed and unconfirmed. CBR: clinical benefit response. SD: stable disease; PD: progressive disease; NE: not evaluable; ORR = CR+PR; DCR=CR+PR+SD≥37 days

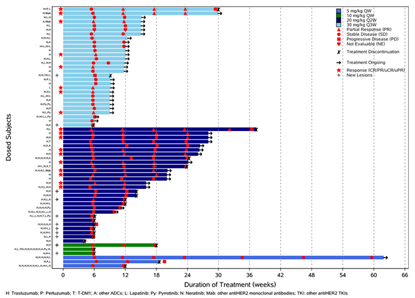

Figure 5. Swimming lane plot by dose level (safety analysis set, as of 22-Jan-2020)

Median prior lines of therapies are 3 (range: 1~15), and median prior lines of HER2 target therapies are 2 (range: 1~12)

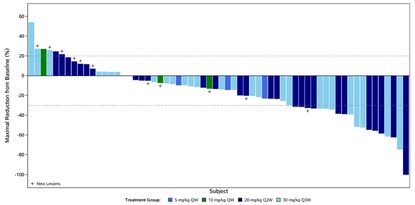

Figure 6. Waterfall plot by dose level (evaluable analysis set, as of 22-Jan-2020)