<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Phase 1 (5 First-in-Human)</th>
<th>Phase 1/2</th>
<th>Phase 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>mRNA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>BNT111</strong></td>
<td><strong>BNT112</strong></td>
<td><strong>BNT111</strong></td>
</tr>
<tr>
<td></td>
<td>Advanced melanoma</td>
<td>Prostate cancer</td>
<td>aPD1-R/R melanoma, + Pembrolizumab</td>
</tr>
<tr>
<td></td>
<td><strong>BNT116</strong></td>
<td><strong>BNT113</strong></td>
<td><strong>BNT113</strong></td>
</tr>
<tr>
<td></td>
<td>2L NSCLC</td>
<td>HPV16+ head and neck cancer</td>
<td>1L rec./met. HPV16+ PDL1+ head and neck cancer, + Pembrolizumab</td>
</tr>
<tr>
<td></td>
<td>Autogene cevumeran (BNT122)(^2)</td>
<td><strong>BNT141</strong> (CLDN18.2)</td>
<td>Autogene cevumeran (BNT122)(^2)</td>
</tr>
<tr>
<td></td>
<td>Multiple solid tumors</td>
<td>Multiple solid tumors</td>
<td>1L Adv. melanoma, + Pembrolizumab</td>
</tr>
<tr>
<td></td>
<td><strong>BNT131</strong> (SAR441000)(^3)</td>
<td><strong>BNT142</strong> (CLDN6)</td>
<td>Autogene cevumeran (BNT122)(^2)</td>
</tr>
<tr>
<td></td>
<td>Solid tumors (IL-12sc, IL15-sushi, GM-CSF, IFNα)</td>
<td>Multiple solid tumors</td>
<td>Adjuvant colorectal cancer</td>
</tr>
<tr>
<td></td>
<td><strong>BNT152 + BNT153</strong></td>
<td><strong>BNT151</strong> (IL-2 variant)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Multiple solid tumors (IL-7, IL-2)</td>
<td>Multiple solid tumors</td>
<td></td>
</tr>
<tr>
<td>Cell therapy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>BNT221</strong></td>
<td><strong>BNT211</strong> (CLDN6)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Refractory metastatic melanoma</td>
<td>Multiple solid tumors</td>
<td></td>
</tr>
<tr>
<td>Protein-based Therapeutics</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td><strong>BNT321</strong></td>
<td><strong>BNT311</strong> (GEN1046)(^4)</td>
<td><strong>BNT316</strong> (ONC-392)(^5)</td>
</tr>
<tr>
<td></td>
<td>Pancreatic cancer (sLea)</td>
<td>(PD-L1x4-1BB) Multi solid tumors</td>
<td>(PD-L1x4-1BB) Multi solid tumors</td>
</tr>
<tr>
<td></td>
<td><strong>BNT322</strong> (GEN1056)(^6)</td>
<td><strong>BNT312</strong> (GEN1042)(^7)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Multiple solid tumors (undisclosed)</td>
<td>(CD40x4-1BB) Multi solid tumors</td>
<td></td>
</tr>
<tr>
<td>SMIM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>BNT313</strong> (GEN1053)(^8)</td>
<td><strong>BNT323</strong> (DB-1303)(^9)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(CD27) Multi solid tumors</td>
<td>HER2 Multi solid tumors</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>BNT314</strong> (TLR7)</td>
<td><strong>BNT411</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Multi solid tumors</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. Investigator-initiated / Investigator-initiated and sponsored trial; 2. Partnered with Genentech, member of Roche Group; 3. Partnered with Sanofi; 4. Partnered with Genmab; 5. Partnered with OncoC4; 6. Partnered with DualityBio; 7. NSCLC = Non-small cell lung cancer; HPV = Human papillomavirus; CLDN = Claudin; IL = Interleukin; L = First line; TLR = Toll-like receptor; R/R = Relapsed/Refractory; Plat. - R = Platinum-resistant; ADC = Antibody-drug conjugate; SMIM = small molecule immunomodulator.
BNT316 (ONC-392)
Safety and clinical activity of target-preserving anti-CTLA-4 antibody ONC-392 as Monotherapy in NSCLC patients who progressed on PD(L)1-targeted immunotherapy
Monotherapy: Dose Finding
(Li T. et al. Poster #949, Presented at SITC 2021)

Objective: To estimate MTD or RP2D for Monotherapy
Patients with advanced or metastatic solid tumors with measurable or non-measurable disease as determined by RECIST version 1.1, who have progressed despite standard of care therapy, or for whom no standard therapies exist

- 6 patients dosed at 10 mg/kg dose level
- 2 patients dosed at 3 mg/kg dose level
- 2 pts dose escalated to 3 mg/kg dose level

ONC-392 dosed as mono-therapy and in combination with pembrolizumab were well tolerated
- TRAE were manageable, no DLTs, MTD not reached
- Monotherapy RP2D: 10 mg/kg, Combination RP2D: 6 mg/kg

Preliminary data demonstrated lower irAE rate than observed for comparable IO or IO-IO combinations

Safety profile of ONC-392 allows for higher dosing and longer duration of treatment in monotherapy and in combination with pembrolizumab

Safety data and study conclusions

Combination: Dose Escalation
(Hu-Lieskov et al. Poster #594. Presented at SITC 2022)

- Pembrolizumab: 200 mg, Q3W
- ONC-392: 3 mg/kg, Q3W

If ≤ 1/6 with DLT
- Pembrolizumab: 200 mg, Q3W
- ONC-392: 1 mg/kg, Q3W

If ≥ 2/6 with DLT
- Pembrolizumab: 200 mg, Q3W
- ONC-392: 6 mg/kg, Q3W

Dose expansion tested in multiple cancer types including:
- IO naive NSCLC
- IO R/R NSCLC
- IO naive Melanoma
- IO R/R Melanoma

Q3W = Every three weeks; MTD = Maximum tolerated dose; RP2D = Recommended phase 2 dose; DLT = Dose-limiting toxicity; TRAE = Treatment related adverse event; NSCLC = Non-small cell lung cancer; irAE = immune-related adverse event; IO = immuno-oncologic; R/R = relapsed/refractory
## Demographics and Safety Data Summary

<table>
<thead>
<tr>
<th>Categories</th>
<th>Data (Date Cutoff date: 03/10/2023)</th>
<th>System Organ Class</th>
<th>All Grades (≥2 cases)</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients enrolled</td>
<td>35</td>
<td>Preferred Term</td>
<td>N (%)</td>
<td>N (%)</td>
<td>N (%)</td>
</tr>
<tr>
<td>Median age (range) [Q1, Q3]</td>
<td>66 (43 - 89) [60, 75]</td>
<td>Gastrointestinal disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>15F (43%), 20M (57%)</td>
<td>Diarrhea</td>
<td>5 (14%)</td>
<td>1 (3%)</td>
<td>0</td>
</tr>
<tr>
<td>Race (white/Black)</td>
<td>33/2</td>
<td>Colitis</td>
<td>4 (11%)</td>
<td>3 (9%)</td>
<td>0</td>
</tr>
<tr>
<td>Ethnicity (Hispanic or Latino)</td>
<td>2</td>
<td>Nausea</td>
<td>2 (6%)</td>
<td>1 (3%)</td>
<td>0</td>
</tr>
<tr>
<td>Cohorts</td>
<td>2</td>
<td>Vomiting</td>
<td>3 (9%)</td>
<td>1 (3%)</td>
<td>0</td>
</tr>
<tr>
<td>Part A: NSCLC, PD-1 R/R, 10 mg/kg, q3w</td>
<td>2</td>
<td>General disorders an administration site conditions</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Arm I: NSCLC, PD-1 R/R, 10 mg/kg x 2, then 6 mg/kg, q3w</td>
<td>33</td>
<td>Fatigue</td>
<td>4 (11%)</td>
<td>1 (3%)</td>
<td>0</td>
</tr>
<tr>
<td>Non-squamous cell carcinoma</td>
<td>20 (57%)</td>
<td>Chills</td>
<td>4 (11%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>15 (43%)</td>
<td>Pyrexia</td>
<td>3 (9%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>ECOG score</td>
<td></td>
<td>Skin and subcutaneous tissue disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ECOG = 0</td>
<td>9 (26%)</td>
<td>Rash maculo-popular</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>ECOG = 1</td>
<td>26 (74%)</td>
<td>Pruritus</td>
<td>2 (6%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Have Metastatic Lesions</td>
<td>35 (100%)</td>
<td>Rash</td>
<td>2 (6%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>ONC-392 related AE (TRAE): All grades</td>
<td>26 (74%)</td>
<td>Injury, poisoning and procedural complications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TRAE: Grade 3–4</td>
<td>15 (43%)</td>
<td>Infusion related reaction</td>
<td>7 (20%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>irAEs: all grades</td>
<td>19 (54%)</td>
<td>Investigations</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>irAE: Grade 3-4</td>
<td>12 (34%)</td>
<td>AST/ALT increased</td>
<td>6 (17%)</td>
<td>1 (3%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>TRAE: Grade 3 and 4</td>
<td></td>
<td>Musculoskeletal and connective tissue disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TRAE leading to dose interruption</td>
<td>9 (26%)</td>
<td>Muscular weakness</td>
<td>3 (9%)</td>
<td>3 (9%)</td>
<td>0</td>
</tr>
<tr>
<td>TRAE leading to dose reduction</td>
<td>1 (3%)</td>
<td>Other significant Grade 3 TRAEs: Immune pancreatitis (1), Intestinal perforation (1), Adrenal insufficiency (1), Tubulointerstitial nephritis (1).</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TRAE leading to study drug discontinuation</td>
<td>7 (20%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Safety Summary

(03/10/2023 Datacut)

ONC-392/BNT316 was tolerated at a dose regimen of 10 mg/kg x 2 then 6 mg/kg, q3w.

- Longest dosing up to 19 cycles and continuing.

Grade 3–4 TRAEs were observed in 13 pts (39%) with a follow up period from 7 to 18 months. 10 pts (30%) had Gr 3–4 irAEs. No ONC-392/BNT316 related Gr. 5 AE was observed. Significant irAEs include:

- 2 Immune-mediated colitis
- 1 Intestinal perforation
- 1 Gr. 4 ALT/AST increased and immune hepatitis
- 1 Adrenal insufficiency
- 1 Tubulointerstitial nephritis
Clinical Activity

Response rate among the evaluable patients is 29.6% (22.2% confirmed and 7.4% unconfirmed)
- 1 CR and 1 SD in 2 patients with ONC-392/BNT316, 10mg/kg q3w for 4 doses.
- 7 PR and 10 SD among 25 evaluable patients in the expansion cohort with ONC-392 dose regimen of 10 mg/kg x 2, then 6 mg/kg q3w.
- Responders include those that failed multiple IO agents targeting PD-(L)1, CTLA-4, and TIGIT.
- All but 1 responders have been on treatment of PD-(L)1 targeting agents for >12 weeks, which is provisionally defined as PD-(L)1-resistant NSCLC.

Survival follow up is ongoing

Conclusions

- ONC-392/BNT316 was generally safe and tolerated at 10 mg/kg x2, followed by 6 mg/kg q3W. Treatment-related AEs are manageable.
- Severe irAE rate in dose expansion cohorts (30%) is considered lower than what was reported for drugs of the similar class.
- Early readout of the expansion cohort shows strong clinical activity in patients with IO-resistant NSCLC.
- These results support initiation of a pivotal study using ONC-392/BNT316 monotherapy for PD-(L)1-resistant NSCLC (Poster TPS#9146, NCT05671510).
First Phase 3 Study planned: BNT316 (ONC-392) in IO R/R NSCLC

PRESERVE-003 (NCT05671510) – Randomized, open-label, active controlled, multi-center Phase 3 trial

Inclusion criteria
- ≥ 18 years stage IV, metastatic NSCLC
- Prior PD-(L)1 +/- platinum-based chemotherapy
- Prior IO allowed
- ECOG Performance Status: 0 or 1
- Have RECIST 1.1 measurable lesions

Stage I (dose-confirmation stage):
Assess efficacy and safety of two BNT316 (ONC-392) dosing regimens in comparison to docetaxel

- BNT316 (ONC-392)
  6mg/kg with 2 loading doses of 10mg/kg, Q3W (N=40)

- BNT316 (ONC-392)
  3mg/kg, Q3W (N=40)

- Docetaxel 75 mg/kg, Q3W (N=40)

Stage II:
Assess safety and efficacy of BNT316 (ONC-392) at the selected dosing regimen versus docetaxel

- Docetaxel 75 mg/kg, Q3W (N=240)
- BNT316 (ONC-392)
  3mg/kg, Q3W (N=40)

Historic efficacy of docetaxel monotherapy (Garon et al. Lancet. 2014):
- ORR ~10%; mPFS = 3 months; mOS = 9 months

Key endpoints
- Primary: OS
- Secondary: ORR, PFS, Safety

Trial in Progress
PRESERVE-003 study, Abstract # TPS9146, Poster
Time: June 4, 8:00 AM-11:00 AM GMT, Poster #130b

1. Partnered with OncoC4.
PD-1 = Programmed cell death protein 1; IO = Immuno-oncology; NSCLC = Non-small cell lung cancer; RR = Relapsed/Refractory; Q3W = Every three weeks; OS = Overall survival; ORR = Objective response rate; PFS = Progression free survival; ECOG = Eastern Cooperative Oncology Group.
BNT323 (DB-1303)

FIH Phase 1/2 to Evaluate Safety and Tolerability of BNT323 (DB-1303) in Patients with Advanced HER2+ Solid Tumors

Phase 1/2a study design (NCT05150691), multicenter, non-randomized, open-label, multiple-dose, FIH study
Hamilton E. et al. TiP #9504. Presented at AACR 2023

Part 1: Dose Escalation (n=88 patients)
(HER2 IHC 3+, IHC 2+, IHC 1+ or ISH +, or HER2 amplification by NGS, or HER2 mutation by NGS)

Part 2a: Dose expansion (n=165 patients)

Indications
- HER2+ gastric, esophageal or gastroesophageal junction adenocarcinoma, CRC
- HR+/HER2-low breast cancer
- HER2+ breast cancer
- HER2 overexpression and HER2-low endometrial cancer
- HER2-mutated NSCLC

FPI: Jan 2022
Objective: To assess safety, tolerability, pharmacokinetic, preliminary anti-tumor activity at the selected MTD/RP2D

Inclusion criteria
- Pretreated advanced or metastatic solid tumors
- Histologically confirmed HER2-positive or HER2-expressing cancers
- Previous systemic therapies
- ECOG 0-1
- Adequate organ function

Disease progression, withdrawal of consent, unacceptable toxicity

IHC = immunohistochemistry; FIH = First in human; Q3W = every three weeks; DLT = dose limiting toxicity; HER2 = human epidermal growth factor 2; HR = hormone receptor; CRC = colorectal cancer; NSCLC = non-small cell lung cancer; MTD = maximum tolerated dose; RP2D = recommended phase 2 dose; ECOG = Eastern Cooperative Oncology Group; FPI = First patient in; LPO = Last patient out; ISH = in-situ hybridization; NGS = next-generation sequencing.
Baseline and characteristics

<table>
<thead>
<tr>
<th>Age, median range</th>
<th>Total (n = 85)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, n (%)</td>
<td>78 (91.8%)</td>
</tr>
<tr>
<td>Region, n (%)</td>
<td></td>
</tr>
<tr>
<td>US/AUS</td>
<td>30 (35.3%)</td>
</tr>
<tr>
<td>CHN</td>
<td>55 (64.7%)</td>
</tr>
<tr>
<td>ECOG PS, n (%)</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>20 (23.5%)</td>
</tr>
<tr>
<td>≥1</td>
<td>61 (71.8%)</td>
</tr>
<tr>
<td>Number of prior systemic regimes in the metastatic disease, median (range)</td>
<td>7.0 (1-27)</td>
</tr>
</tbody>
</table>

Cancer types, n (%)
- Esophageal cancer: 2 (2.4%)
- Colorectal cancer: 3 (3.5%)
- HER2 2 low breast cancer: 21 (24.7%)
- Endometrial carcinoma: 6 (7.1%)
- Ovarian cancer: 3 (3.6%)
- HER2 positive breast cancer: 42 (49.4%)
- Vaginal: 1 (1.2%)
- Gastroesophageal junction adenocarcinoma: 1 (1.2%)
- Gastric cancer: 1 (1.2%)
- Non-small cell lung cancer: 1 (1.2%)
- Bilateral metastasis, n (%)
  - Brain: 18 (21.2%)
  - Lungs: 43 (50.6%)
  - Liver: 34 (40.0%)
- HER2 IHC results, n (%)
  - 1+: 8 (9.4%)
  - 2+: 28 (34.1%)
  - ISH Positive: 10 (11.8%)
  - ISH Negative or NE: 18 (21.2%)
  - 3+: 40 (47.1%)
  - Prior anti-HER2 ADC therapy, n (%): 28 (32.9%)
  - Prior anti-HER2 antibody therapy, n (%): 47 (55.3%)
  - Prior anti-HER2 TKI therapy, n (%): 35 (41.2%)
  - SOD in target lesion, median (n, range): 55.0 (81.0-206.0)

Summary of overall safety

<table>
<thead>
<tr>
<th>2.2 mg/kg (n = 1)</th>
<th>4.4 mg/kg (n = 5)</th>
<th>6.0 mg/kg (n = 15)</th>
<th>7.0 mg/kg (n = 29)</th>
<th>8.0 mg/kg (n = 32)</th>
<th>10.0 mg/kg (n = 3)</th>
<th>Total (n = 85)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any TEAEs</td>
<td>1 (100.0%)</td>
<td>5 (100.0%)</td>
<td>14 (93.3%)</td>
<td>26 (89.7%)</td>
<td>26 (81.2%)</td>
<td>74 (87.1%)</td>
</tr>
<tr>
<td>Associated with treatment withdrawal</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 (3.4%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Associated with treatment dose reduction</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2 (6.9%)</td>
<td>1 (3.1%)</td>
<td>0</td>
</tr>
<tr>
<td>Associated with treatment dose interruption</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4 (26.7%)</td>
<td>8 (27.6%)</td>
<td>5 (15.6%)</td>
</tr>
<tr>
<td>Grade ≥3</td>
<td>0</td>
<td>3 (60.0%)</td>
<td>3 (20.0%)</td>
<td>9 (31.0%)</td>
<td>2 (6.2%)</td>
<td>1 (33.3%)</td>
</tr>
<tr>
<td>Serious AEs</td>
<td>0</td>
<td>3 (60.0%)</td>
<td>4 (26.7%)</td>
<td>4 (13.8%)</td>
<td>2 (6.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Treatment-related TEAEs</td>
<td>1 (100.0%)</td>
<td>3 (60.0%)</td>
<td>12 (80.0%)</td>
<td>26 (89.7%)</td>
<td>25 (78.1%)</td>
<td>2 (66.7%)</td>
</tr>
<tr>
<td>Grade ≥3</td>
<td>0</td>
<td>1 (20.0%)</td>
<td>2 (13.3%)</td>
<td>6 (20.7%)</td>
<td>1 (3.1%)</td>
<td>1 (33.3%)</td>
</tr>
<tr>
<td>Serious AEs</td>
<td>0</td>
<td>0</td>
<td>2 (13.3%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

DB-1303 was well tolerated and all AEs were manageable so far

- No DLT was observed in 6 dose levels during dose escalation
- No TEAEs associated with death occurred
  - Interstitial lung disease occurred in 2 patients (2.4%, grade 1), without any ≥grade 2
  - Few patients experienced neutropenia (10 [11.8%]; grade ≥3 in 1 [1.2%] patients,) and alopecia (3 [3.5%], grade 1)

The median duration of treatment was 63.0 (range, 21-211) days, and the median duration of follow-up was 77.0 (range, 7-350) days
DB-1303/BNT323: Clinical activity

Best overall response for all patients with post-baseline scans

Summary

At the data cutoff (January 13, 2023), 85 patients received DB-1303/BNT316 at 6 dose levels (2.2, 4.4, 6.0, 7.0, 8.0, and 10.0 mg/kg). Here we report the results from dose-escalation:

- A total of 68 patients (80.0%) remained on treatment

The unconfirmed ORR was 44.2% (23/52) and DCR was 88.5% (46/52) per RECIST v1.1 in heavily pretreated patients with 7 prior systemic regimens including HER2 ADCs. Among patients with post-baseline tumor scan (n = 52) data showed:

- Encouraging activity of DB-1303 was observed in HER2 expressing breast cancer (BC)
  - **HER2 positive BC**: ORR, 50% (13/26); DCR, 96.2% (25/26); with brain metastases: ORR, 55.6% (5/9); DCR, 100.0% (9/9)
  - **HER2 low BC**: ORR, 38.5% (5/13), DCR, 84.6% (11/13)

- Antitumor activity of DB-1303 was also observed in non-BC tumor types: ORR, CRC (66.7% [2/3]), EsC (50.0% [1/2]), OC (50.0% [1/2]), and EC (33.3% [1/3])

Preliminary antitumor activities were observed in the heavily pretreated HER2 expression patients.
BNT211

CLDN6 CAR-T cell therapy of relapsed/refractory solid tumors ± a CLDN6-encoding mRNA vaccine: Dose escalation data from the BNT211-01 phase 1 trial using an automated product.
BNT211: first-in-class approach for CLDN6+ solid tumors

**CLDN6 CAR T**

- αCLDN6
- scvf
- CD8
- hinge
- 4-1BB
- CD3ζ

✓ Highly sensitive and specific 2nd-generation CAR against CLDN6
✓ CLDN6 is absent from healthy adult tissue, but expressed in a variety of cancers

**±**

**CLDN6 CARVac**

✓ Clinically proven RNA-lipoplex vaccine for body-wide delivery of antigens to dendritic cells
✓ Amplification and persistence of CAR-T cells by repeat administration

Full-length CLDN6 RNA Liposomes
BNT211-01: Phase I/II, FIH, open-label, multicenter, dose escalation trial

**Primary endpoints:**
- Safety and tolerability, DLTs

**Secondary endpoints:**
- Immunogenicity, ORR, DCR, DoR

**Dosing:**
- Escalating doses of CLDN6 CAR-T cells ± CLDN6 CARVac (50 µg then 100 µg, if tolerated)
- Lymphodepletion prior to CAR-T cell infusion on Day 1 (DLTs assessed for 28 days)
- CLDN6 CARVac fixed dose (from Day 4) Q3W × 5, then Q6W. CAR-T cell redosing is permitted

**Assessments:** Efficacy assessments Q6W (RECIST v1.1)

**Key inclusion criteria**
- ≥50% tumor cells with 2+/3+ CLDN6 positivity
- Measurable disease or elevated tumor marker ECOG PS 0–1

**Phase I dose escalation (manual product): Completed ✓**

- Monotherapy
  - DL2 n=6
  - 1×10⁶ CAR T
  - DL1 n=3
  - 1×10⁷ CAR T

- Combination*
  - DL2 n=9 + fixed CARVac
  - DL1 n=4 + fixed CARVac

* Crossover is possible from monotherapy to combination

**Phase I dose escalation with an (automated product): Ongoing**

- Monotherapy
  - DL2 n=6
  - 1×10⁸ CAR T
  - DL1 n=3
  - 1×10⁷ CAR T

- Combination
  - DL3 n=0
  - 2-5×10⁸ CAR T
  - DL2 n=4
  - 1×10⁸ CAR T
  - DL1 n=3
  - 1×10⁷ CAR T

**Aim of current analysis**
Determine the safety and preliminary efficacy of the automated BNT211 product

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R/R advanced CLDN6+ solid tumors

- Measurable disease or elevated tumor marker ECOG PS 0–1
### BNT211-01: Safety

<table>
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<tr>
<th>Patients, n</th>
<th>Cohort</th>
<th>DLT0, Part 1 (N=2) [1]</th>
<th>DLT1, Part 1 (N=4)</th>
<th>DLT2, Part 1 (N=6)</th>
<th>DLT1, Part 2 (N=3)</th>
<th>DLT2, Part 2 (N=4)</th>
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</table>

Data cutoff: 10 MAR 2023. [1] Both patients crossed over to combination treatment; [2] CTCAE Gr. 3 events were mostly associated with lymphodepletion or elevations of transaminases and bilirubin; [3] 1 patient treated at DL0 experienced sepsis (CTCAE Gr. 3) and subsequently developed Klebsiella infection (CTCAE Gr. 3) and a second sepsis event (Gr. 3); [4] CRS events were all Gr. 1/2, except for 1 transient Gr. 3 event related to CLDN6 CAR-T(A) treatment; [5] Deaths were all due to disease progression.

CLDN6 CAR-T (A) cells ± CLDN6 CARVac were well tolerated at evaluated dose levels (no DLTs reported), with a clinical safety profile in line with that of manually produced CLDN6 CAR-T cells.
Change in target sum (best response) after CLDN6 CAR-T(A) ± CLDN6 CARVac administration

- DL2: ORR 11% (1/9); DCR 33% (3/9)
- DL2: ORR 75% (6/8); DCR 88% (7/8)

ORR = 41%
DCR = 65%

Data cutoff: 10 MAR 2023. Waterfall plot showing best percent change from baseline in sum of target lesion diameters for patients treated with CLDN6 CAR-T(A) ± CLDN6 RNA-LPX. One patient died prior to first assessment (BOR = PD) and one patient had non-measurable disease per RECIST (BOR = SD). Additionally, no response data was available for one patient at the data cutoff (N = 12). Dotted lines show standard response evaluation criteria in solid tumors (RECIST) borders for response assessment (CR = -100%, PR = 30 to -100%, SD = -30 to 20%, and PD = 20% or higher).
BNT211-01: Long-term survivors – Testicular germ cell tumor patients

Three of 13 treated germ cell tumor patients (from the manual product cohort) show ongoing clinical benefit
Safety: CLDN6 CAR-T (A) cells ± CLDN6 CARVac has a moderate safety profile in line with that of manually produced CLDN6 CAR-T cells.

Efficacy: Encouraging signs of activity, with dose-dependent expansion of CAR-T cells translating into ORR of 41% with 7 responses in 17 evaluable patients (ORR 75% at DL2).

Outlook: Follow-up on treated patients and further recruitment to DL2 and DL3 is ongoing. After determination of RP2D for CLDN6 CAR-T (A) cells, a pivotal trial in GCT will be initiated (PRIME designation).