context therapeutics

Advancing Medicines for Solid Tumors

Corporate Presentation

May 2024

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Lead Program: CTIM-76, a Claudin 6 (CLDN6) x CD3 Bispecific Antibody

Lead Asset

CTIM-76 is a potentially best-in-class CLDN6 T cell engaging (TCE) bispecific antibody

- CLDN6 is enriched in a wide range of cancers, but absent or expressed at low levels in normal adult tissue
- CTIM-76 is highly selective for CLDN6, exhibits excellent preclinical efficacy and tolerability
- IND cleared, targeting first patient enrolled in mid-2024

Phase 1 Trial

Phase 1 trial to focus on CLDN6-positive gynecologic and testicular cancers

- Clinical proof of concept achieved with BNT211 CART, highlighting the potential for TCE in reproductive cancers[1,2]
- Reproductive cancer focus creates clinical efficiencies for CTIM-76 program
- Potential to expand clinical footprint once competitors establish proof of concept in other tumor types (e.g., NSCLC)

TCE Gaining Momentum

Recent TCE clinical data demonstrates promising efficacy and safety in solid tumors

- Clinical activity across a broad range of targets, including DLL3, PSMA, and STEAP1
- Clinical activity across multiple tumor types, including SCLC, mCRPC, and neuroendocrine
- Low rates Grade ≥ 3 cytokine release syndrome (CRS)

Well Capitalized

Supported by high-quality investor syndicate with expected cash runway into 2028

- Recently announced private placement funds estimated duration of Phase 1 dose escalation/expansion trial with runway post data readout

1 Reproductive cancers include endometrial, ovarian, and testicular ; **2** Mackensen, ESMO 2023
SCLC = small cell lung cancer ; **NSCLC** = non- small cell lung cancer; **mCRPC** = metastatic castrate resistant prostate cancer

TCE Bispecific Data Targeting DLL3, PSMA, and STEAP1

Recent data supports promising efficacy with low rate of ≥ Grade 3 cytokine release syndrome (CRS)

	AMGEN	HARPOON Therapeutics	Janux		AMGEN
Asset	**Tarlatamab (AMG757)**	**HPN328**	**JANX007**		**Xaluritamig (AMG509)**
Bispecific Format	HLE BiTE (truncated Fc)	TriTAC (albumin)	TRACTr (albumin)		XmAb 2 x 1
Target x Effector	DLL3 x CD3	DLL3 x CD3	PSMA x CD3		STEAP1 x CD3
Indication	Small Cell Lung Cancer (SCLC)	SCLC	Metastatic Castration-resistant Prostate Cancer (mCRPC)		mCRPC
Normal tissue expression	Absent or limited	Absent or limited	Brain, endocrine, GI, pancreas, prostate, skin, marrow		Brain, respiratory, prostate
CD3 Detuning	No	No	Masked		Moderate (~7x; 27 vs 4 nM)
Stage	Phase 2	Phase 1b	Phase 1a		Phase 1
Selected Cohorts	10 mg	1st step dose ≥ 6 mg	1st dose ≥ 0.1 mg	1st step dose ≥ 0.2 mg	Target dose ≥ 0.75 mg
Patients (n)	100	19	18	6	44
Efficacy	**ORR: 40% mPFS: 4.9 months**	**ORR: 32%**	**PSA50: 56% PSA90: 6%**	**PSA50: 83% PSA90: 17%**	**PSA50: 59% PSA90: 36%**
≥ G3 CRS	**1%**	**3%**	**0%**	**0%**	**2%**
≥ G3 TRAEs	n.d.	25%	28%	17%	55%
Reference	Ahn 2023	ESMO 2023	12 Feb 2024 data cutoff	12 Feb 2024 data cutoff	Kelly 2023

Information provided in the table above is for illustrative purposes only and is not a head-to-head comparison. Differences exist between study or trial designs and subject characteristics, and caution should be exercised when comparing data across studies.

CLDN6 Therapies Have the Potential to Reach a Large Patient Population

>50,000 patients per year in the US only in Relapse/Refractory (R/R) Setting

Initial indications of interest based on:

- CLDN6 prevalence
- Patient population size
- Observed clinical responses
- Potential accelerated pathway

Selected Cancer indications	Incidence	R/R Incidence	CLDN6 Positive	Patient Population Based on R/R Incidence
Endometrial	65,900	14,000	51%[1]	**7,140**
Ovarian	19,900	12,800	44%[1]	**5,632**
Testicular	9,910	400	94%[1]	**376**
Non-Small Cell Lung	201,229	110,653	26%[1]	28,769
Breast	290,600	43,800	2-41%[2,8,9]	9,417
Gastric	26,380	11,090	13-55%[6,7]	3,771
Sarcoma	17,100	12,390	20%[11]	2,478
Glioma	19,000	10,000	21%[6]	2,100
Bladder	81,180	17,100	2-8%[2,10]	855
Small Cell Lung	35,511	19,527	2%[2]	391
Malignant Rhabdoid	50	500	29-44%[2,3-5]	183

1 Context internal data; **2** Reinhard, Science, 2020; **3** Wang, Diagn Pathol., 2013; **4** Micke, Intl J Cancer, 2014; **5** Soini, Pol J Path, 2022; **6** Antonelli, Brain Pathol., 2011; **7** Sullivan, Am J Surg Pathol., 2012; **8** Jia, Intl J Clin Exp Pathol., 2019; **9** Yafang, J Breast Cancer, 2011; **10** Ushiku, Histopath., 2012; **11** Mackensen, Nature Medicine, 2023. Incidences based on public estimates; Relapsed/refractory (R/R) or last-line patient population approximated by annual mortality; CLDN6 target prevalence is based on IHC or RNAseq from published reports. Patient population derived from midpoint of CLDN6 positive population multiplied by R/R incident population.

CLDN6 Clinical Proof of Concept in Ovarian and Testicular Cancers

- BNT211 CART exhibited encouraging clinical activity with low CRS rate
- CART activity increases the probability of clinical activity with a T cell engaging bispecific
- TORL-1-23 requires high CLDN6 expression for internalization; clinical activity currently limited to CLDN6-high ovarian
- TORL-1-23 requires G-CSF co-administration at doses ≥ 2.4 mg/kg

	BNT211 (CLDN6 CART)	TORL-1-23 (CLDN6 ADC)
Cutoff Date	September 10, 2023[1]	September 29, 2023[2]
Patients (n)	44 (38 evaluable) Ovarian = 17 Testicular = 16 Other =11	42 (36 evaluable) 17 pts at 3 mg/kg Ovarian = 30 Testicular = 5 Endometrial = 7
Median Prior Treatments, n (range)	4 (2-9)	4 (1-9)
ORR, n (%)	Overall: 44% (17/38) Dose Level 2: 59% (13/22) **Ovarian DL2: 77% (7/9)** **Testicular DL2: 38% (3/8)** Other DL2: 60% (3/5)	Overall: 31% (11/36) Ovarian: 33% (9/27) **Ovarian, ≥ 2.4mg/kg: 50% (6/12)** Other: 22% (2/9)
SAE	Grade 4: CRS (1pt @ DL3) Grade 5: sepsis (1 pt)	Grade 4: blood counts at higher doses Grade 5: pneumonia (1 pt)
Treatment-Related AEs	Blood counts, LFT, Bilirubin	Alopecia, Anemia, Neuropathy, Pneumonia

1 Mackensen, ESMO 2023; **2** Konecny, ESMO 2023

Claudin 6 (CLDN6)

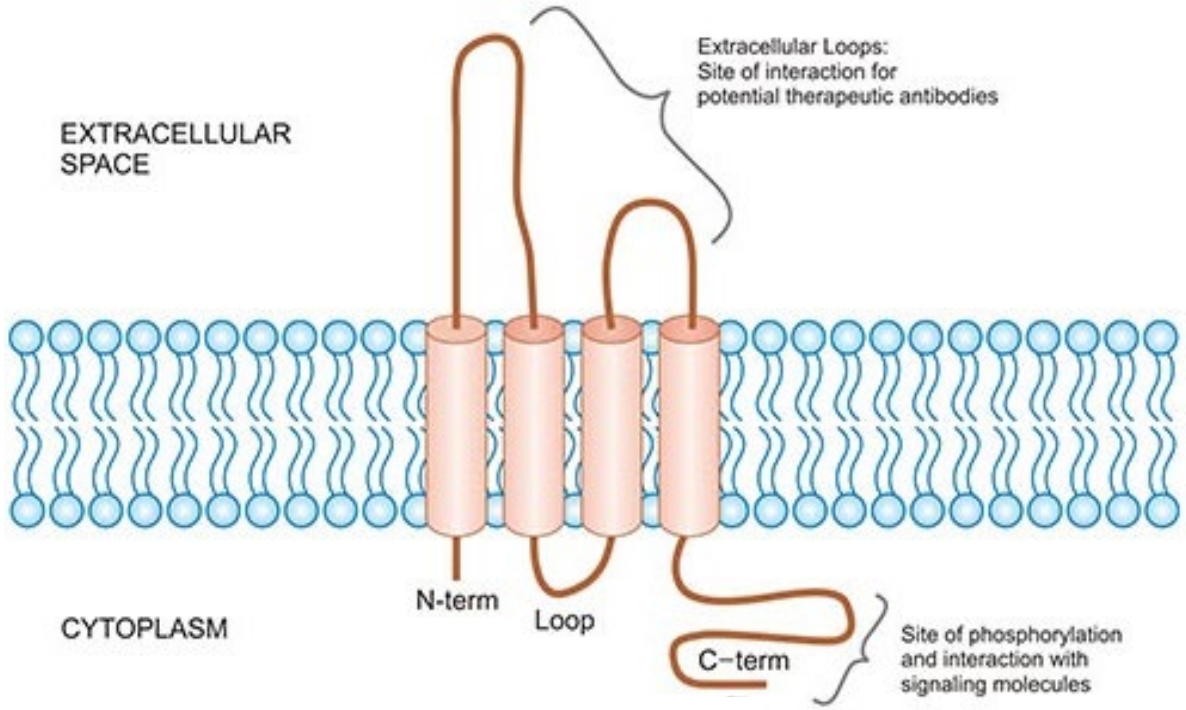
Target biology and therapeutic rationale

CLDN6 is an Oncofetal Protein

Oncofetal proteins are considered favorable candidates for immunotherapy

Oncofetal Characteristics of CLDN6

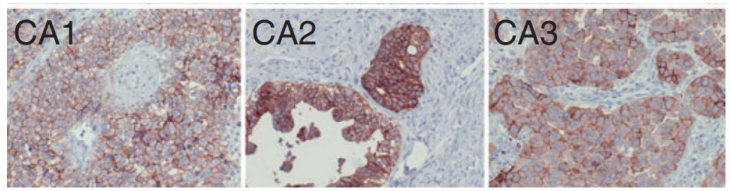
- Normally present at higher levels during embryonic development
- Turned off or have low levels of expression in adult tissues
- Increased expression across many solid tumors



Huan, Mol Med Reports, 2021

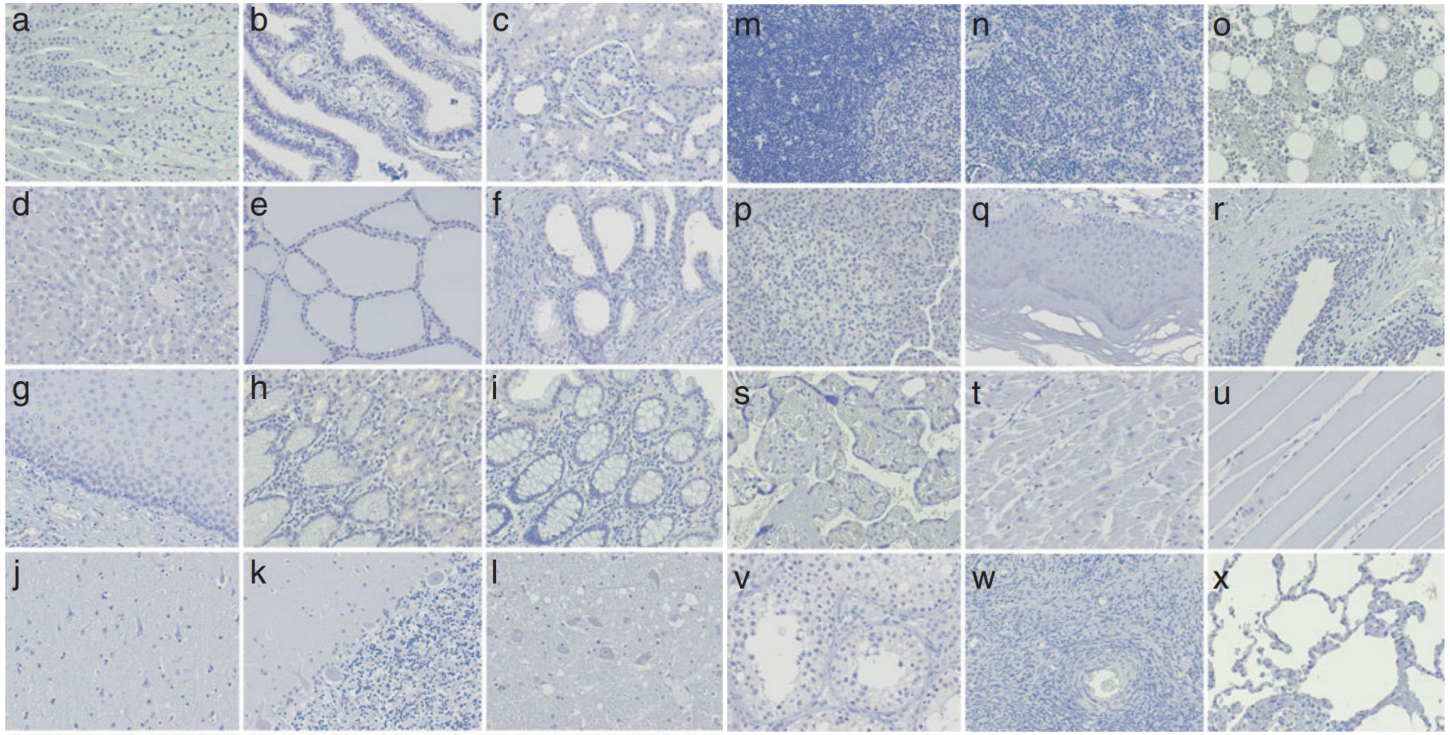
CLDN6 is Selectively Expressed on Cancer Cells

Cancer Tissue



(CA1) testicular cancer, (CA2) ovarian cancer, and (CA3) lung cancer

Normal Tissue

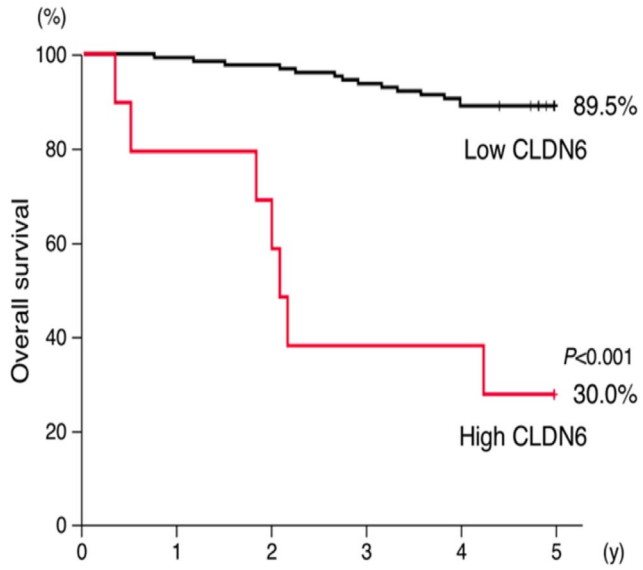


(a) adrenal gland, (b) fallopian tube, (c) kidney, (d) liver, (e) thyroid, (f) prostate, (g) esophagus, (h) stomach, (i) colon, (j) cerebrum, (k) cerebellum, (l) spinal cord, (m) thymus, (n) spleen, (o) bone marrow, (p) pancreas, (q) skin, (r) bladder, (s) placenta, (t) heart muscle, (u) striated muscle, (v) testis, (w) ovary, (x) lung

Reinhard, Science, 2020

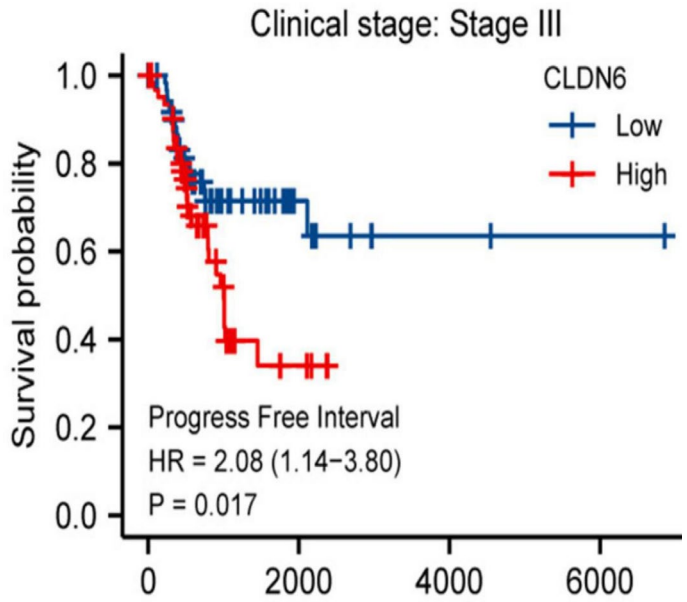
High CLDN6 Associated with a Worsened Prognosis in Cancer Patients

Endometrial Cancer[1]



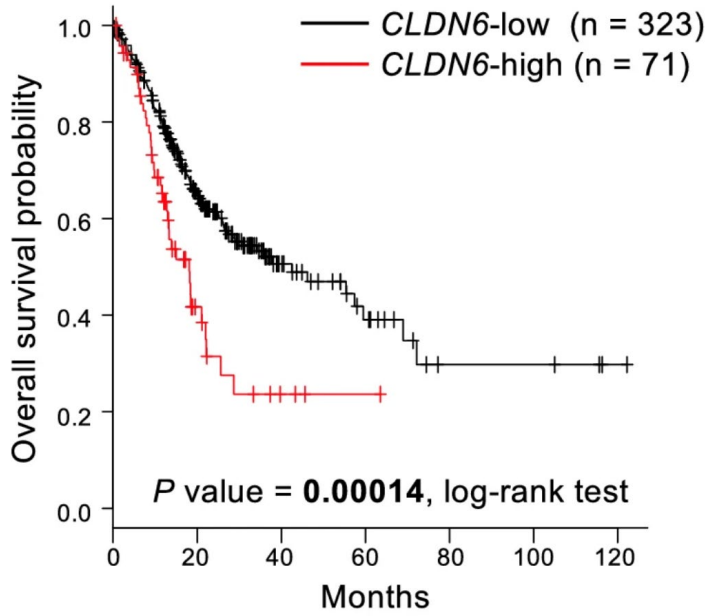
Overexpression of CLDN6 is associated with worse overall survival in endometrial cancer patients

Bladder Cancer[2]



Overexpression of CLDN6 is associated with worse overall survival and higher disease stage (more aggressive) in bladder cancer patients

Stomach Cancer[3]



Overexpression of CLDN6 is associated with worse overall survival in stomach cancer patients

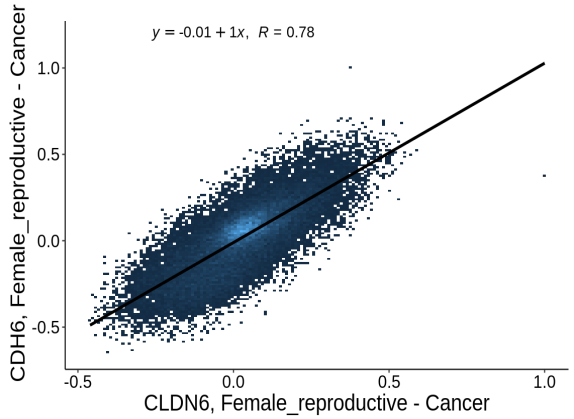
1 Kojima, Cancers, 2020; **2** Zhang, Front. Cell Dev. Biol., 2021; **3** Kohmoto, Gastric Cancer, 2020

CLDN6 Has Limited Overlap with Competing Targets for Female Reproductive Cancers

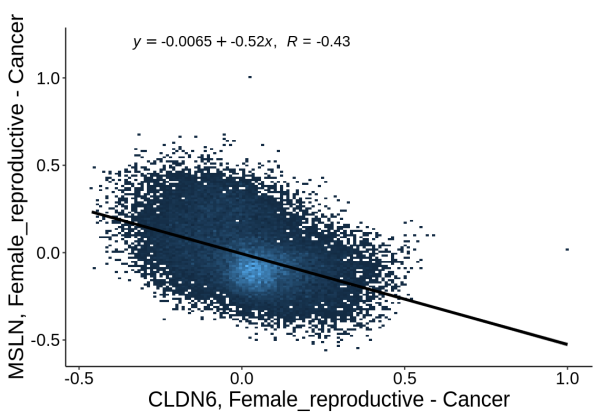
Female Reproductive Cancer

Correlation between CLDN6 and other targets via RNAseq biopsy data

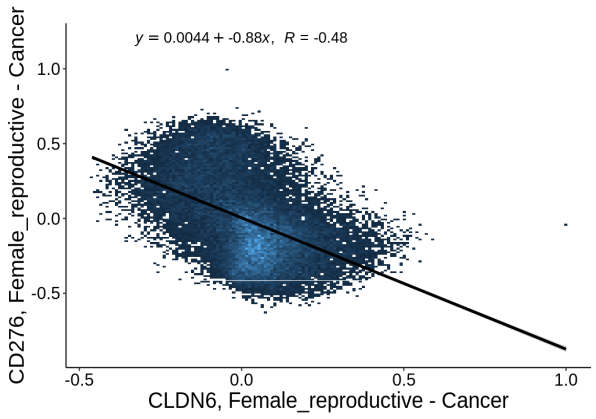
CLDN6 vs. CDH6



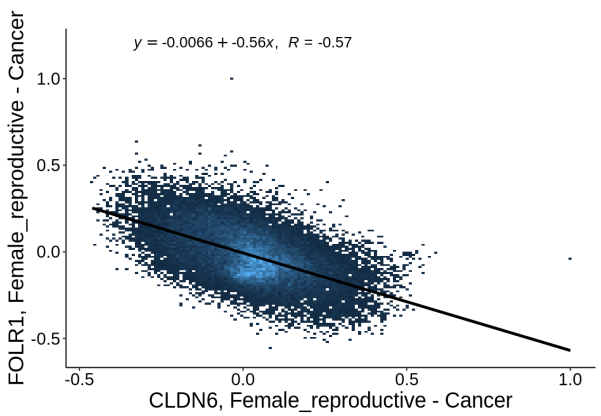
CLDN6 vs. Mesothelin



CLDN6 vs. B7H3



CLDN6 vs. FRα

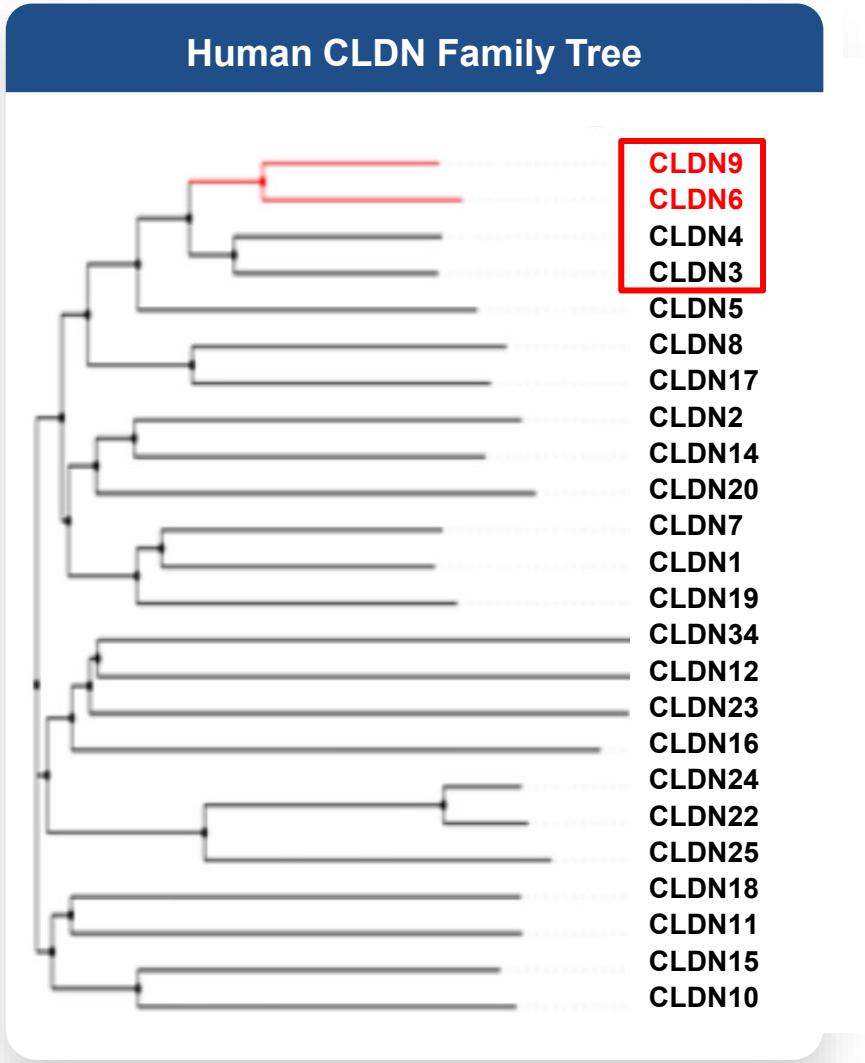


Bishop, AnalyzeR [Data Set] Accessed March 1, 2024

CTIM-76

Claudin 6 x CD3 Development Candidate

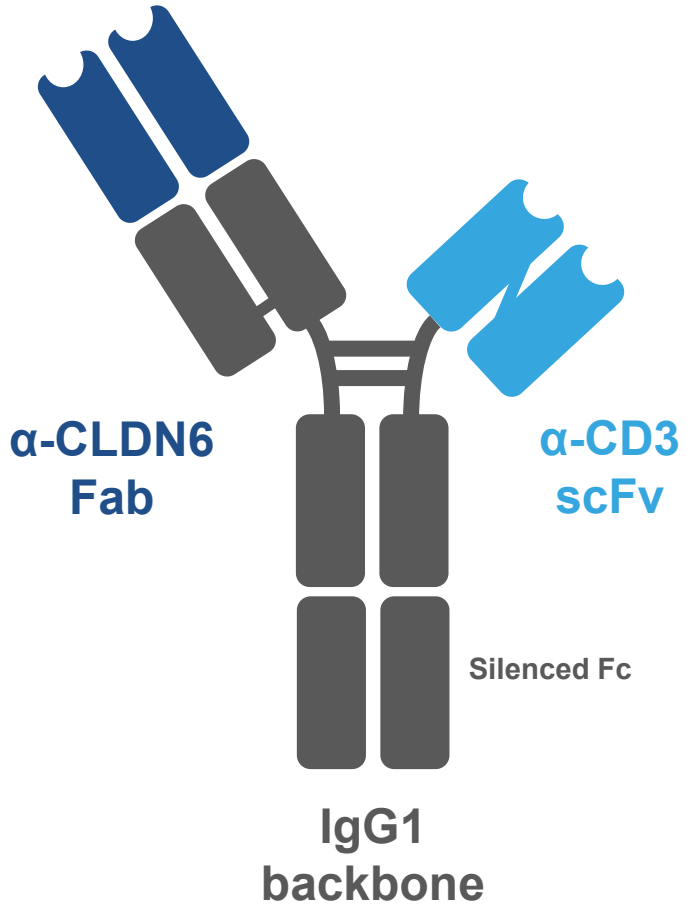
Developing a Highly Selective CLDN6 Antibody is Challenging



- CLDN6 antigen is **conformationally dependent**, which limits access to antibody-antigen binding
- Antigen binding region is **highly conserved** with CLDN3, CLDN4, and CLDN9, making CLDN6-selective binding a challenge[1]
- CLDN6 **selectivity is required** to avoid off-target liabilities identified in murine knockout and knockdown studies with CLDN3 (intestine)[2], CLDN4 (liver, pancreas)[3], and CLDN9 (liver, ear)[4]

1 Screnci, Cancer Res, 2022; **2** Tanaka, J Hepatol, 2018; **3** Cordat, Physiology, 2019; Li, FEBS Open Bio, 2020; **4** Nakano, PLoS Genet, 2009

CTIM-76: Claudin 6 x CD3 T cell Engaging (TCE) Bispecific Antibody



Established bispecific format

- Highly selective CLDN6 binding fragment antibody-binding (Fab) arm
- Immunostimulatory CD3 binding single-chain fragment variable (scFv) domain is functionally monovalent to avoid aberrant T-cell activation
- The fragment crystallizable region (Fc region) is the tail region of an antibody that interacts with cell surface receptors called Fc receptors. A mutation has been inserted into the Fc domain to silence the Fc domain function and avoid T-cell activation by Fc-gamma receptor positive cells

Potentially wide therapeutic window

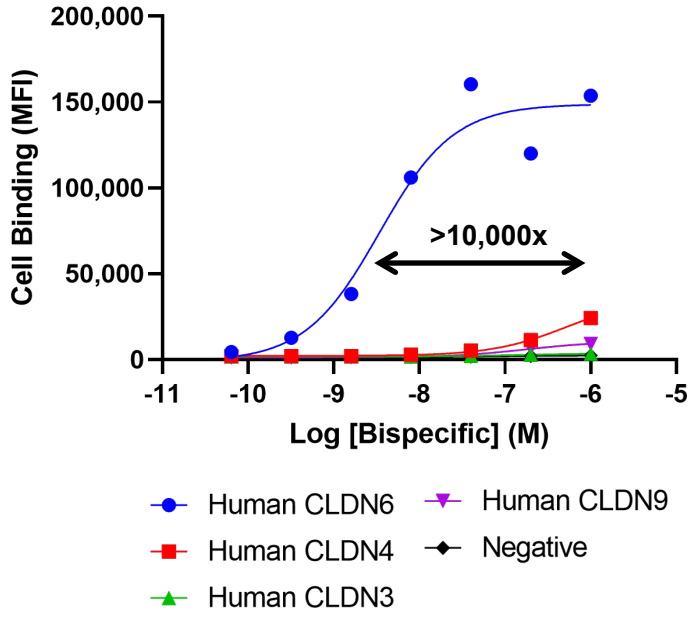
- T-cell dependent cellular cytotoxicity with no or minimal activation of circulating cytokines
- Humanized CLDN6 and CD3 binding domains

Ease of manufacturing

- IgG backbone is highly stable and enables high yield

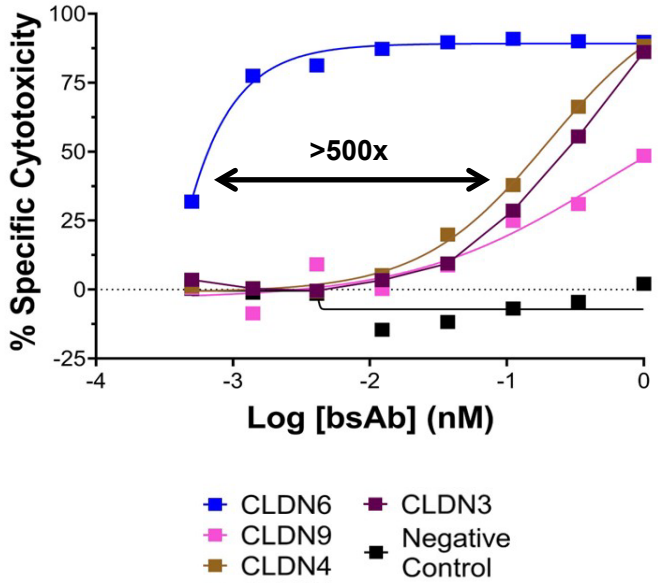
CTIM-76: T cell engaging (TCE) CLDN6 x CD3 Bispecific Antibody

Selectivity



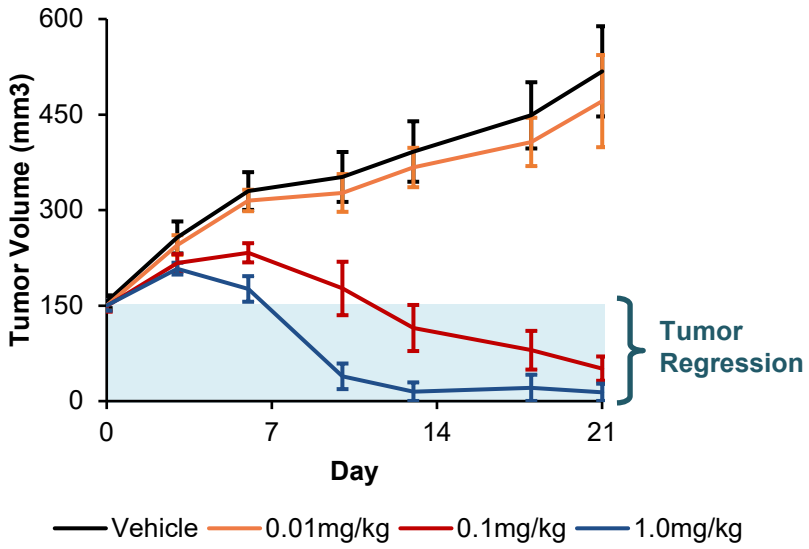
- CTIM-76 CLDN6 EC50 of 3.41 nM (binding)
- CTIM-76 preferentially binds to CLDN6 over CLDN3/4/9
- CLDN3/4/6/9 were transiently transfected in HEK-293F cells (4:1 Target:GFP)

Potency



- Potency assay provides a better assessment for a TCE bispecific than binding assays for off-target liabilities associated with CLDN3, CLDN4, or CLDN9
- CTIM-76 CLDN6 EC50 of 0.0004 nM (cytotoxicity)
- CTIM-76 preferentially targets CLDN6, with minimal binding and cytotoxicity against CLDN9-expressing cells

In Vivo Efficacy



- CTIM-76 effectively engaged systemically administered human PBMC cells to promote significant tumor regression and complete responses in OVCAR3 (~96,000 CLDN6 copies per cell) ovarian xenograft models in mice
- CTIM-76 was well tolerated in OVCAR3 xenograft study
- NSG-b2m knockout mice (n=14/arm) engrafted with human PBMCs and bearing advanced subcutaneous OVCAR3 tumor xenografts were treated twice per week

CTIM-76 Phase 1a/b Study

An open-label, multi-center, dose escalation / expansion, safety, and PK study

Part 1 – Dose Escalation (40 patients)

Dose Escalation:
Single patient with step dosing

↓

≥ Grade 2 AE

↓

Dose Escalation:
3 + 3 with step dosing
(3-6 patients per cohort)

↓

MTD or RP2D

Part 2 – Dose Expansion (30 patients)

↓

Cancer type to be selected based upon Dose Escalation data;
Two doses to be evaluated

- **Target population**
  - Platinum resistant ovarian cancer
  - Endometrial and testicular cancer relapsed to standard of care
- **Biomarker stratification**
  - CLDN6+ positive (10% ≥ 1+) ovarian and endometrial
  - Due to high CLDN6 prevalence, testicular cancer does not require prospective screening
- **Trial objectives**
  - Assess safety and tolerability at increasing dose levels
  - Pharmacokinetic and pharmacodynamic data
  - Evaluate preliminary anti-tumor activity
- **Dosing and Administration**
  - Weekly IV infusion starting at 22.5 µg, corresponding to MABEL dose
  - Premedication (steroid + NSAID) and step dosing to manage cytokine release syndrome (CRS)

MABEL = minimum anticipated biological effect level; **MTD** = maximum tolerated dose; **RP2D** = recommended Phase 2 dose

Competitive Landscape

CLDN6 Competitive Landscape

Strategy	Assets in Development	Assets in the Clinic	Characteristics
Bispecific	7	3	• Weak internalization makes CLDN6 ideal for bispecific targeting • Selective expression in cancer cells potentially mitigates CRS risk • Potential to address low-to-high CLDN6 expression due to potency advantage over ADC
ADC	4	2	• Internalization requires CLDN6-high expression • CLDN6-high requirement potentially limits commercial opportunity • Selection for CLDN6-high cells may drive early resistance, leading to weak treatment durability
Cell Therapy	3	3	• BNT211 CART established clinical proof of concept in CLDN6-high ovarian and testicular cancers • Low rate of ≥ G3 CRS • Currently expanding to other solid tumors
Mab	0	0	• CLDN6 has limited signaling activity in cancer cells • ASP1650 (Astellas) exhibited weak activity in Phase 2 testicular cancer trial and was discontinued

Analysis based on current understanding of publicly available information compiled as of March 1, 2024 and internal benchmarking studies

CLDN6 Competitive Landscape

Selective, Potent, Scalable

	Scalable Manufacturing Process	Complex Manufacturing Process	Potential / Disclosed Safety Liabilities
Selectivity for CLDN6 vs CLDN3,4,9	**TORL-1-23** CLDN6 + MMAE *FPI Q4 21* **CTIM-76**[1] bsAb CLDN6xCD3 *FPI mid-2024*	**BNT211** CAR-T + CARVac *FPI Q3 20*	**AMG-794**[3] BiTE CLDN6xCD3 *FPI Q1 23*
Limited Information on Asset	**XmAb541** 2+1 bsAb CLDN6xCD3 *IND Q4 23* **Undisclosed** bsAb CLDN6xCD3 *IND Q4 23*	**Undisclosed** CAR-NK *IND 2H 23* **CLDN6-CAR-NK** CAR-NK + IL7 *FPI Q2 22*	
Limited Selectivity	**SAIL66** bsAb CLDN6xCD3 *FPI Q1 23* **NBL-028** bsAb CLDN6 x CD137 *FPI Q2 24*		**DS-9606a** CLDN6/CLDN9 + 2nd gen toxin *FPI Q2 22* **GB-7008-01** CLDN6/CLDN9 + MMAE *Status Unknown* **BNT142** mRNA BsAb CLDN6xCD3 *FPI Q1 22*
Deprioritized	**TJ-C64B**[2] 2+2 bsAb CLDN6x4IBB		**SC004**[4] CLDN6/CLDN9 + PBD *Ph 1 DLT*

Analysis based on current understanding of publicly available information compiled as of May 1, 2024 and internal benchmarking studies; **1** Anticipated first patient enrolled **2** TJ-C64B deprioritization per Q2 2023 earnings guidance; **3** Pham et al, AMG 794, a Claudin 6-targeted half-life extended (HLE) bispecific T cell engager (BITE®), AACR 2022; **4** Hamilton, First-in-human study of SC-004, AACR 2020; **FPI** = First Patient In Phase 1 trial; **DLT** = Dose Limiting Toxicity

CLDN6 x CD3 T Cell Engaging Bispecifics

	CTIM-76	XmAb541	AMG794	SAIL66	NBL-028	Beigene
Company	Context	Xencor	Amgen	Chugai	NovaRock	Beigene
Stage	IND Open	IND Open	Ph 1 (active, not recruiting)[1]	Ph 1	Ph 1	IND filed Dec 2023
Bispecific Format	1 + 1	2 + 1	HLE Bite	Dual Specific Fab	1 + 1	n.d.
CLDN6 Selectivity	**High**	**Moderate / High[2]**	**High[3]**	**Moderate[4]**	**Moderate[5]**	n.d.
Preclinical Tolerability	**Well tolerated**	**Well tolerated**	**Poor tolerability**	**Poor tolerability**	n.d.	n.d.
Avidity Enhanced	No	Yes	No	No	No	n.d.
Target:CD3 Affinity	1	7	10	~1,000	n.a. (targets CD137)	n.d.
Half-life	1 week	2 weeks	< 1 week	3 weeks	2 weeks	n.d.

1 Clinical trials.gov accessed on April 22, 2024 **2** Faber, AACR 2021; Patent US11739144 **3** Rucker, SITC 2023; Pham, AACR 2022; Patent WO2022096700 **4** Kamikawa, SITC 2023; Patent WO2021006328 **5** Tong, AACR 2022 **N.D.**= not disclosed. Information provided in the table above is for illustrative purposes only and is not a head-to-head comparison. Differences exist between study or trial designs and subject characteristics, and caution should be exercised when comparing data across studies.

Corporate

Experienced Leadership Team

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Focus on Execution

Experienced team

Our management team is supported by a Board with strong public company operating and governance experience

Investment Highlights (Nasdaq: CNTX)

Large Unmet Need

Solid Tumors

High-Value Target

Claudin 6

Milestones

IND cleared April 2024

On track for first patient enrolled mid-2024

Strong Team

Oncology experience

Cash Runway

Expected cash runway into 2028

context therapeutics

Advancing Medicines for Solid Tumors

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