

Advancing Medicines for Solid Tumors

context

Corporate Presentation

March 2024

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2 Context Therapeutics Inc. - March 2024

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 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 CTIM-76 exhibits excellent preclinical efficacy and tolerability IND on track for end of March 2024
Future Development Plan	 Phase 1 trial to focus on CLDN6-positive gynecologic and testicular cancers Prevalence screen identifies CLDN6 expression in ~50% of ovarian and endometrial, and ~95% of testicular cancers Clinical proof of concept achieved with BNT211 CART, highlighting the potential for TCE in reproductive cancer^{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 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)

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

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

TCE Bispecific Data Targeting DLL3, PSMA, and STEAP1

Recent data supports promising efficacy with low rate of ≥ G3 cytokine release syndrome (CRS)

	AMGEN	HARPOON Therapeutics	🖞 Janux		AMGEN
Asset	Tarlatamab (AMG757)	HPN328	JAN	JANX007	
Target	DLL3 x CD3	DLL3 x CD3	PSMA x CD3		STEAP1 x CD3
Indication	Small Cell Lung Cancer (SCLC)	SCLC	Metastatic Castrate-resistant Prostate Cancer (mCRPC)		mCRPC
Bispecific Format	HLE BITE	TriTAC	TRACTr		XmAb 2 x 1
Stage	Phase 2	Phase 1b	Phase 1a		Phase 1
Selected Cohorts	10 mg	1 st step dose ≥ 6 mg	1 st dose ≥ 0.1 mg	1 st 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.

Claudin 6 (CLDN6)

Target biology and therapeutic rationale

Context

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 known to occur in some tumor cells, including non-small cell lung cancer (NSCLC), ovarian, and testicular



CLDN6 Has the Potential to Reach a Large Patient Population

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

	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
J N	Ovarian	19,900	12,800	44% ¹	5,632
U	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

Initial indications of interest based on:

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

Context internal data;
 Reinhard, Science, 2020;
 Wang, Diagn Pathol., 2013;
 Micke, Intl J Cancer, 2014;
 Soini, Pol J Path, 2022;
 Antonelli, Brain Pathol., 2011;
 Sullivan, Am J Surg Pathol., 2012;
 Intl J Clin Exp Pathol., 2019;
 Yafang, J Breast Cancer, 2011;
 Ushiku, Histopath., 2012;
 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 is Selectively Expressed on Cancer Cells

Cancer Tissue



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





(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

High CLDN6 Associated with a Worsened Prognosis in Cancer Patients



CLDN6 Has Limited Overlap with Competing Targets for Female Reproductive Cancers

Female Reproductive Cancer

Correlation between CLDN6 and other targets via RNAseq biopsy data



CTIM-76

Claudin 6 x CD3 Development Candidate

Context

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 CLDN6selective binding a challenge¹
- 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

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



- CLDN3/4/6/9 were transiently transfected in HEK-293F • cells (4:1 Target:GFP)
- associated with CLDN3, CLDN4, or CLDN9
- CTIM-76 CLDN6 EC50 of 0.0004 nM (cytotoxicity) ٠
- CTIM-76 preferentially targets CLDN6, with minimal • binding and cytotoxicity against CLDN9-expressing cells
- and complete responses in OVCAR3 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

Competitive Landscape

Context

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

CLDN6 Competitive Landscape¹

	Selective, Potent, Scalable			
	Scalable Manufacturing Process	Complex Manufacturing Process	Potential / Disclosed Safety Liabilities	
Selectivity for CLDN6 vs CLDN3,4,9	TORL-1-23 CTIM-76 ¹ CLDN6 + MMAE bsAb CLDN6xCD3 FPI Q4 21 IND March 24	BIONTECH BNT211 CAR-T + CARVac FPI Q3 20	AMG-794 ³ BITE CLDN6xCD3 FPI Q1 23	
Limited Information on Asset	ContentImage: ContentXmAb541Undisclosed2+1 bsAbbsAbCLDN6xCD3CLDN6xCD3IND Q4 23IND Q4 23	Vindisclosed CAR-NK IND 2H 23CLDN6-CAR-NK CAR-NK + IL7 FPI Q2 22		
Limited Selectivity	CHUGAI SAIL66 bsAb CLDN6xCD3 FPI Q1 23 NovaRock NBL-028 bsAb CLDN6 x CD137 FPI Q2 24		EDS-9606a CLDN6/CLDN9 + 2 nd gen toxin FPI Q2 22	
Deprioritized	TJ-C64B ² 2+2 bsAb CLDN6x4IBB		Stemcentrx SC004 ⁴ CLDN6/CLDN9 + PBD Ph 1 DLT	

Analysis based on current understanding of publicly available information compiled as of March 1, 2024 and internal benchmarking studies; 1 IND expected to be filed by end of March 2024 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 Q1 2024 ¹	IND Dec 2023	Ph 1	Ph 1	Ph 1	IND 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 IND expected to be filed by end of March 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

Context

Experienced Leadership Team



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)





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