context therapeutics

Advancing Medicines for Solid Tumors

Corporate Presentation

March 2023

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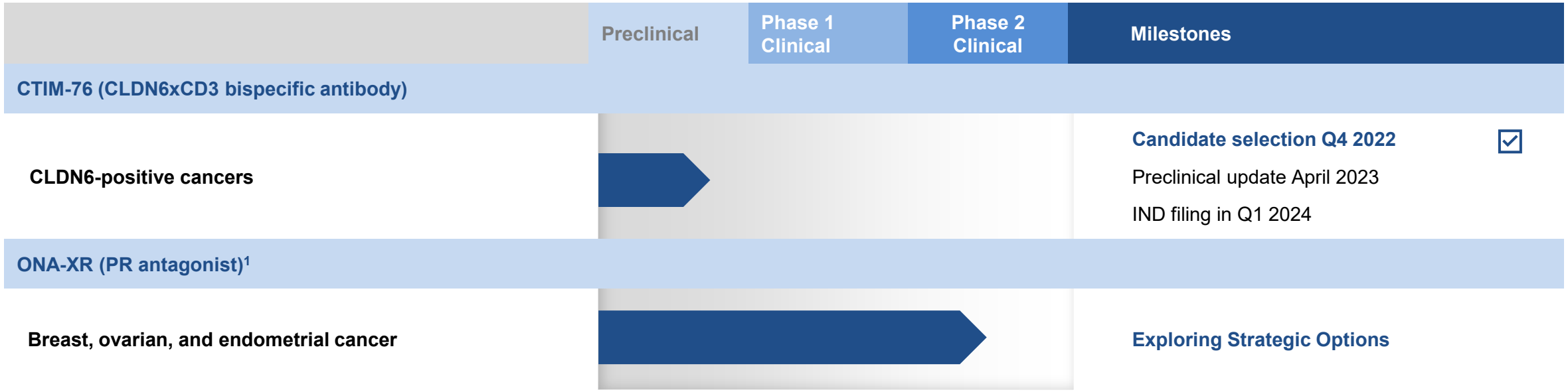
Context Therapeutics Overview

CTIM-76
CLDN6 x CD3 bispecific antibody

- CTIM-76 is Context's CLDN6 x CD3 bispecific antibody Development Candidate
- Claudin 6 (CLDN6) is uniquely expressed in a broad range of solid tumors, including ovarian, lung, and testicular
- CTIM-76 is selective for CLDN6 over other CLDN proteins, reducing the risk of potential off-target side effects

Cash Guidance

- Expected cash runway into late 2024



1 Tyligand Biosciences Ltd licensed rights to ONA-XR in China, HK, Macau

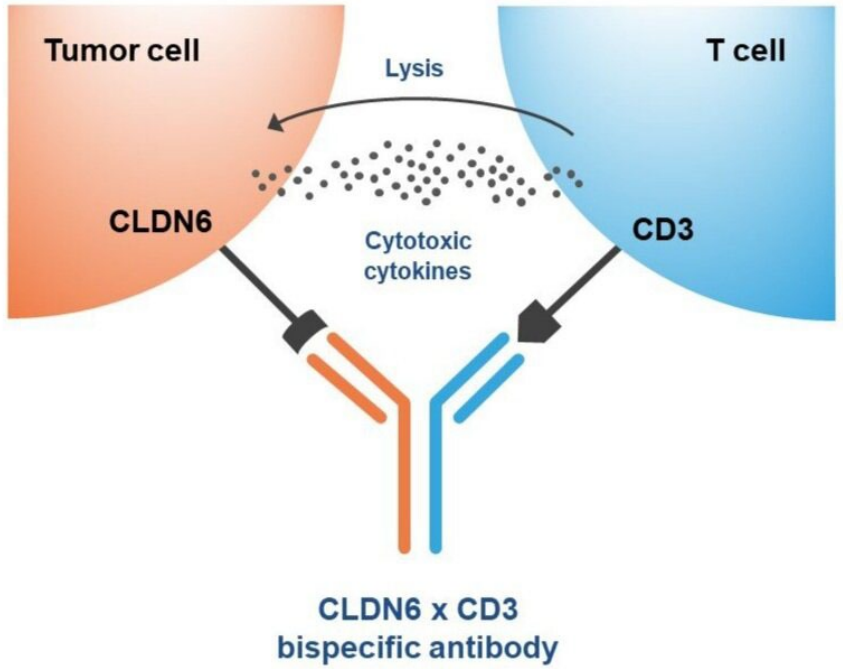
Emerging Role of Bispecific Antibodies in Treating Solid Tumors

Harnessing the Immune System to Attack Solid Tumors

- A challenge for targeting solid tumors is that many tumor-associated antigens are also expressed on normal tissues, raising concerns about “on-target off-tumor” toxicities
- Bispecific antibodies (BsAbs) are antibodies with two binding sites directed at two different targets, which can be exploited for targeting a tumor cell (e.g., CLDN6) and an immune cell (e.g., CD3)
- Compared with monoclonal antibodies, bispecific antibodies not only have stronger specificity, better targeting ability and lower off-target toxicity, but also can effectively prevent drug resistance, reduce treatment costs and improve patient access to drugs, achieving a superior therapeutic effect

Bispecific Antibody R&D is Expanding

- Over 50 CD3 bispecific T-cell engagers in clinical development
- Common solid cancer targets include Claudin 18.2, DLL, GPC3, HER2, PSMA
- 9 BsAbs are currently approved worldwide and business development activity for BsAbs was particularly robust in 2022



Select Early-stage Bispecific Antibody Transactions in 2022[1]

Licensee	Licensor	Target	Asset	Stage	Geography	Upfront ($M)	Milestones($M)
TeneoTwo	AstraZeneca	CD19 x CD3	TNB-486	Phase 1	Worldwide	$100	$1,165
Macrogenics	Gilead	CD123 x CD3	MGD024	IND	Worldwide	$60	$1,700
LAVA	Seagen	EGFR x γδ T cell	LAVA-1223	Preclinical	Worldwide	$50	$650
Harbour	AstraZeneca	Claudin 18.2 x CD3	HBM7022	Preclinical	Worldwide	$25	$350

1 Representative transactions based on publicly available information and represents a non-head-to-head summary comparison

Claudin 6 (CLDN6) is an Ideal Target for Bispecific Antibodies

Opportunity	• CLDN6 is a **tumor-specific protein** that is present at high surface density across many adult and pediatric cancers[1] • CLDN6 is expressed at **very low levels or absent** in normal adult tissue
Challenge	• CLDN6 antigen is **conformationally dependent,** which limits access to antibody-antigen binding and antibody development • The CLDN6 antigen binding region is **highly conserved** with CLDN3, CLDN4, and CLDN9, which increases the risk of off-target binding and potential side effects associated with CLDN3 (pancreas), CLDN4 (kidney, pancreas), and CLDN9 (ear, gut)
Target Validation	• BioNTech's BNT211 CAR-T cell therapy establishes **Proof of Concept**[2]: – BNT211 cell therapy evaluated in Phase 1 dose-escalation study in CLDN6-positive solid tumors – **50% response rate** (ORR) in second dosing cohort
CTIM-76	• **Selective for CLDN6:** limited off-target effects • **Potent:** effective CLDN6-positive tumor killing at low doses • **Wide therapeutic window:** decreased risk of dangerous immune response • **Manufacturability:** ability to treat many patients

1 Faber MS, et al. Bispecific claudin-6 x CD3 antibodies AACR Annual Meeting; 2021; Virtual. Abstract 1860
2 Haanen JB, et al. BNT211: A Phase I trial. ESMO Annual Meeting; 2022; Paris, France. LBA38

CLDN6 Has the Potential to Reach a Large Patient Population

~62,500 patients per year in the US only in Relapse/Refractory Setting

Initial indications of interest based on:

- CLDN6 prevalence
- Patient population size
- Observed clinical responses
- Eligibility for Orphan Designation

Selected Cancer indications	Incidence	R/R Incidence	CLDN6 Positive	Patient Population Based on R/R Incidence
Testicular	9,910	400	95%[1]	**380**
Ovarian	19,900	12,800	54-55%[1,2]	**6,982**
Non-Small Cell Lung	201,229	110,653	6-50%[3,4,5]	**35,221**
Gastric	26,380	11,090	13-55%[8,9]	3,771
Malignant Rhabdoid	50	500	29-44%[1,2,6,7]	183
Breast	290,600	43,800	2-41%[1,10,11]	9,417
Endometrial	65,900	12,500	20-31%[1,12,13]	3,188
Glioma	19,000	10,000	21%[8]	2,100
Bladder	81,180	17,100	2-8%[1,13]	855
Small Cell Lung	35,511	19,527	2%[1]	391

1 Reinhard, Science, 2020; 2 Wang, Diagn Pathol., 2013; 3 Gao, Oncol Lett., 2013; 4 Kohmoto, Gastric Cancer, 2020; 5 Lin, Diagn Pathol., 2013; 6 Micke, Intl J Cancer, 2014; 7 Soini, Pol J Path, 2022; 8 Antonelli, Brain Pathol., 2011; 9 Sullivan, Am J Surg Pathol., 2012; 10 Jia, Intl J Clin Exp Pathol., 2019; 11 Yafang, J Breast Cancer, 2011; 12 Kojima, Cancers, 2020; 13 Ushiku, Histopath., 2012

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.

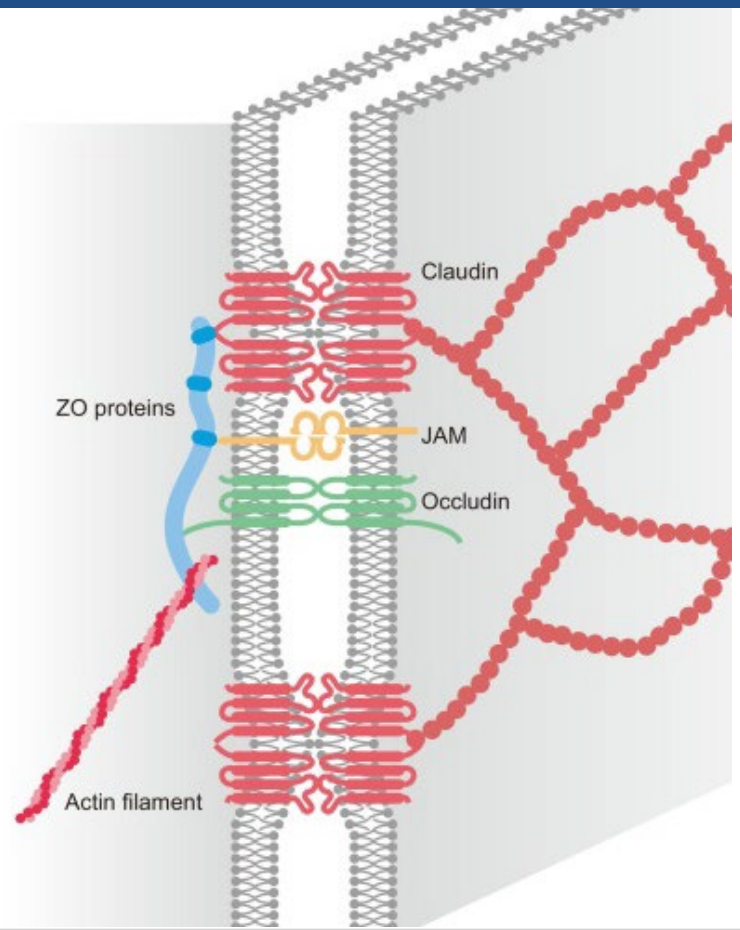
Claudin 6 (CLDN6)

Target biology and therapeutic rationale

Claudin (CLDN) Protein Family

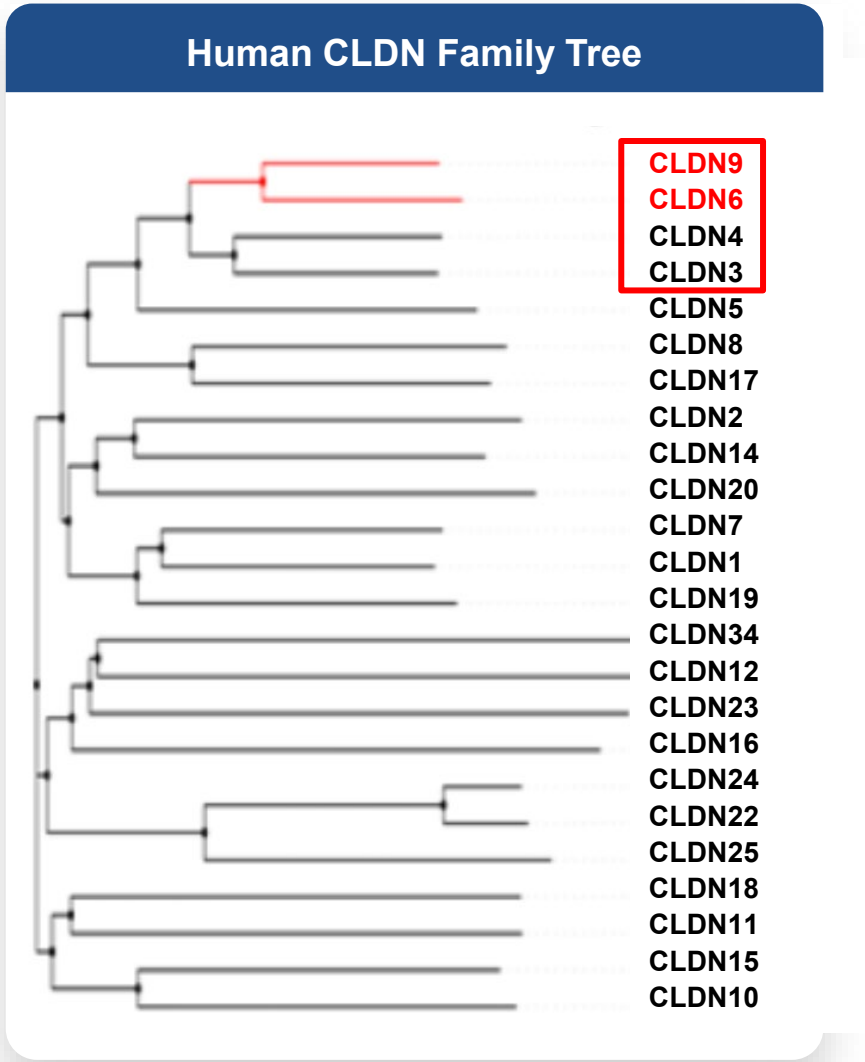
- Tight junctions (TJ) regulate cell barrier and permeability
- CLDN proteins constitute a structural core of TJ, along with junction adhesion molecule (JAM) and occludin
- 27 CLDN proteins have been characterized to date
- Dysregulation of CLDN protein expression and function occurs in multiple diseases, including cancer

Tight Junction Structure



Otani, Trends in Cell Biology, 2020

The Challenge: developing a highly selective CLDN6 antibody



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

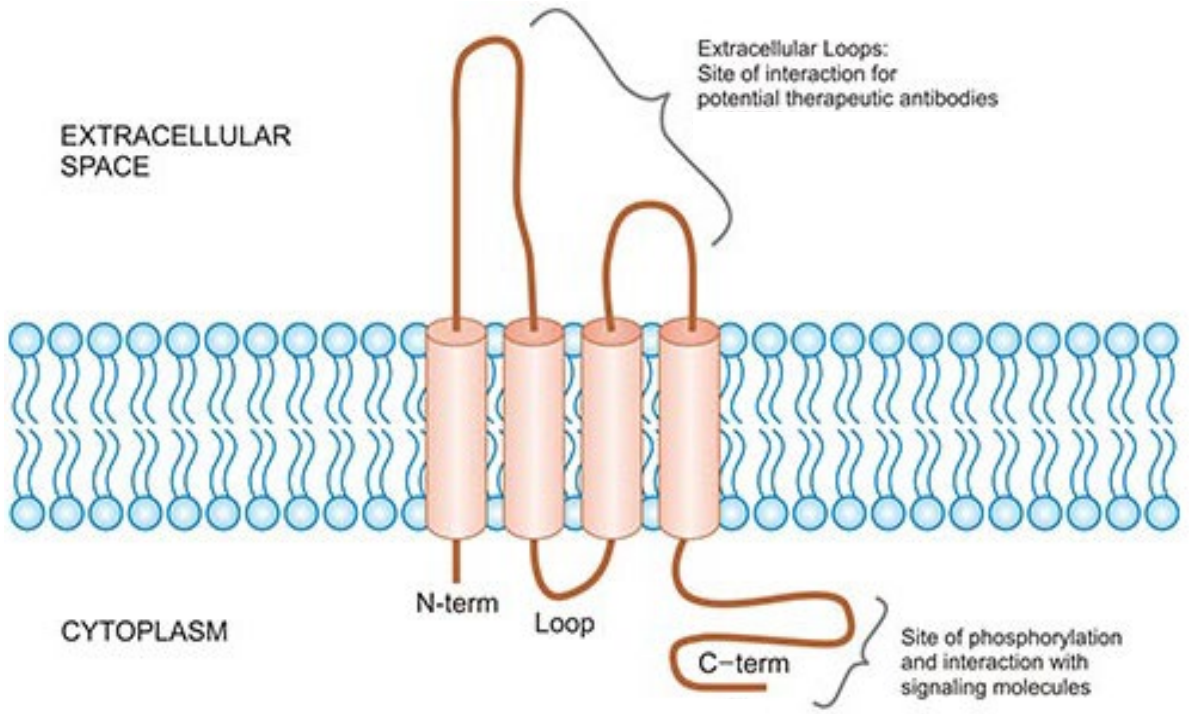
1 Screnci, Cancer Res, 2022
2 Tanaka, J Hepatol, 2018
3 Cordat, Physiology, 2019; Li, FEBS Open Bio, 2020
4 Nakano, PLoS Genet, 2009;

CLDN6 is an Oncofetal Protein

Oncofetal proteins are considered favorable candidates for immunotherapy

CLDN6 Biology

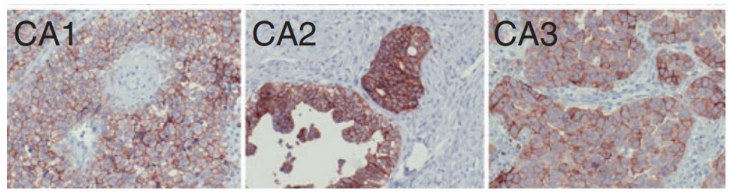
- Normally present at higher levels during embryonic development
- Turned off or have low levels of expression in adult tissues
- Increased expression of these antigens can occur in some tumor cells, and are referred to as “tumor-associated antigens” or TAA



Huan, Mol Med Reports, 2021

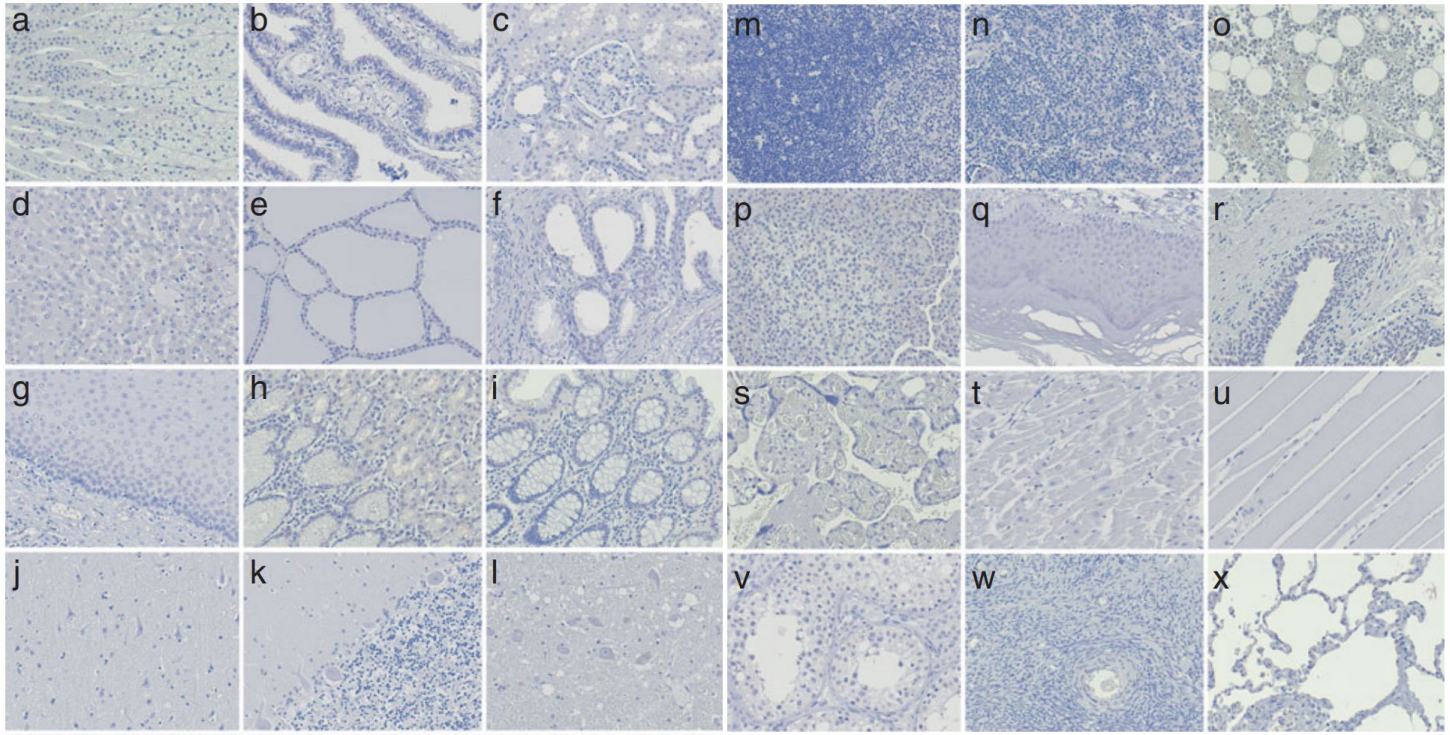
CLDN6 is Selectively Expressed on Cancer Cells

Cancer Tissue



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

Normal Tissue

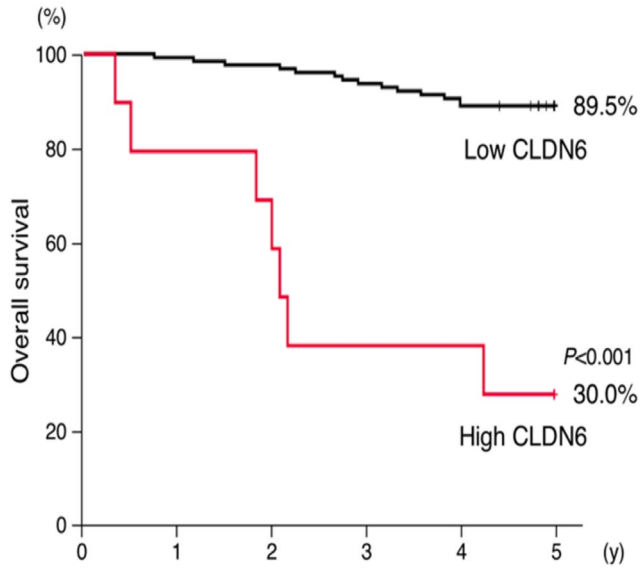


(a) adrenal gland, (b) fallopian tube, (c) kidney, (d) liver, (e) thyroid, (f) prostate, (g) esophagus, (h) stomach, (i) colon, (j) cerebrum, (k) cerebellum, (l) spinal cord. (m) thymus, (n) spleen, (o) bone marrow, (p) pancreas, (q) skin, (r) bladder, (s) placenta, (t) heart muscle, (u) striated muscle,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

Reinhard, Science, 2020

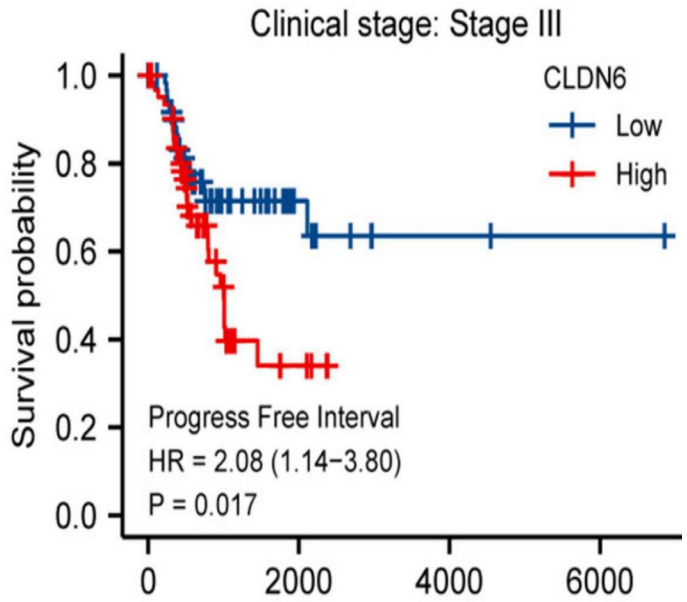
High CLDN6 Associated with a Worsened Prognosis in Cancer Patients

Endometrial Cancer[1]



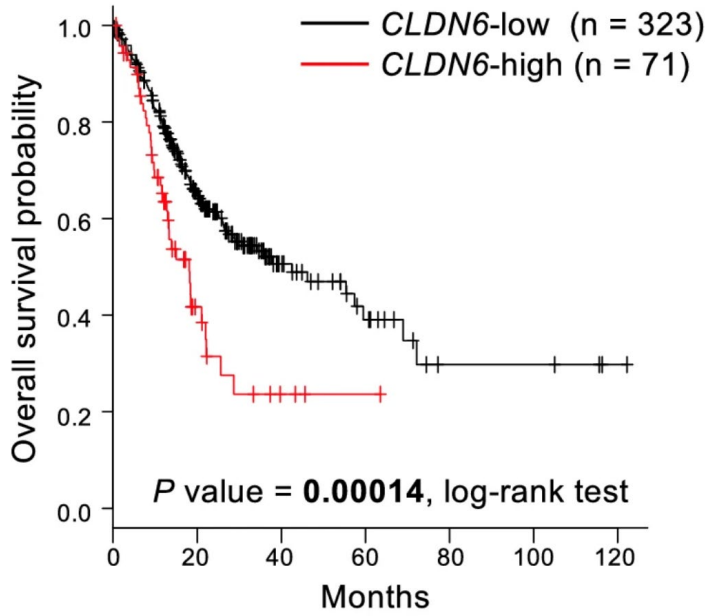
Overexpression of CLDN6 is associated with worse overall survival in endometrial cancer patients

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

CTIM-76

Claudin 6 x CD3 Development Candidate

Bispecific Antibody Considerations

Bispecific scaffold and CLDN6/CD3 arms evaluated to optimize selectivity, potency, and manufacturability

CLDN6 Targeting Arm

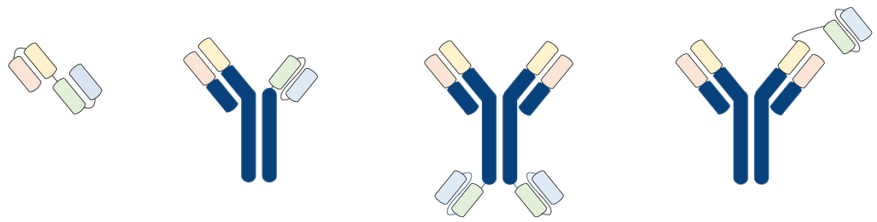
- High affinity anti-CLDN6 binding
- High specificity for CLDN6 vs other CLDN
  - Especially CLDN3, CLDN4, CLDN9

CD3 T-cell Engaging Arm

- Clinically validated
- Freedom to operate
- Explore a range of potencies

Bispecific Scaffolds

- Multiple formats evaluated

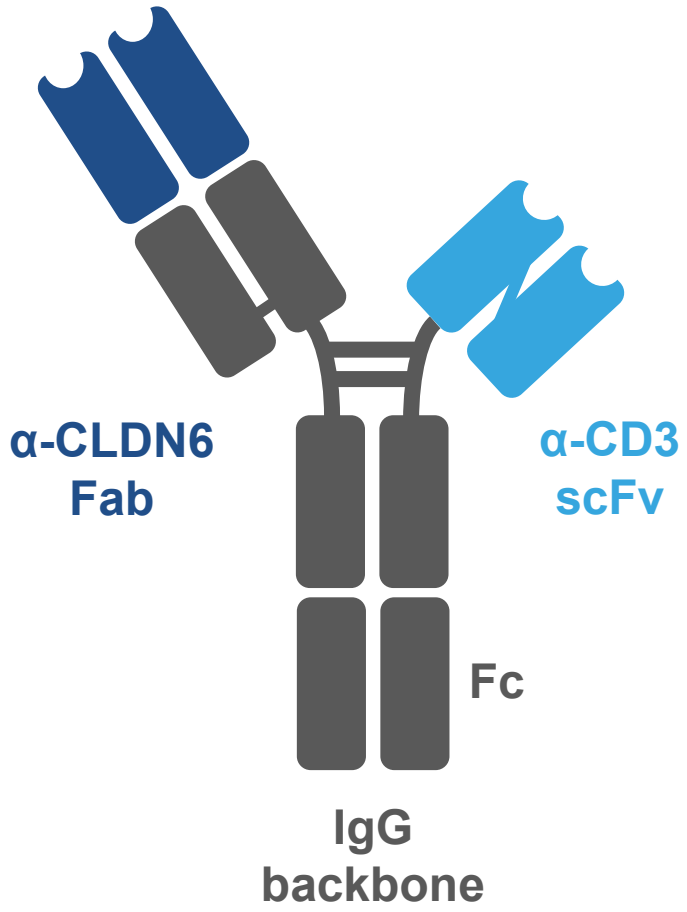


Other Factors

- Cross reactivity to NHP desirable for both arms
- Silencing variants to eliminate FcR binding
- FcRn binding for half-life extension

NHP = non-human primate
FcR = fragment crystallizable region (Fc region) is the tail region of an antibody that interacts with cell surface receptors called Fc receptors (FcRn) and some proteins of the complement system

CTIM-76: Claudin 6 x CD3 Bispecific Antibody



Wide therapeutic window

- Highly selective CLDN6 binding fragment antibody-binding (Fab) arm
- Immunostimulatory CD3 binding single-chain fragment variable (scFv) domain is designed to be functionally monovalent to avoid aberrant T-cell activation, potentially enhancing safety profile
- 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

Convenient dosing with low immunogenicity risk

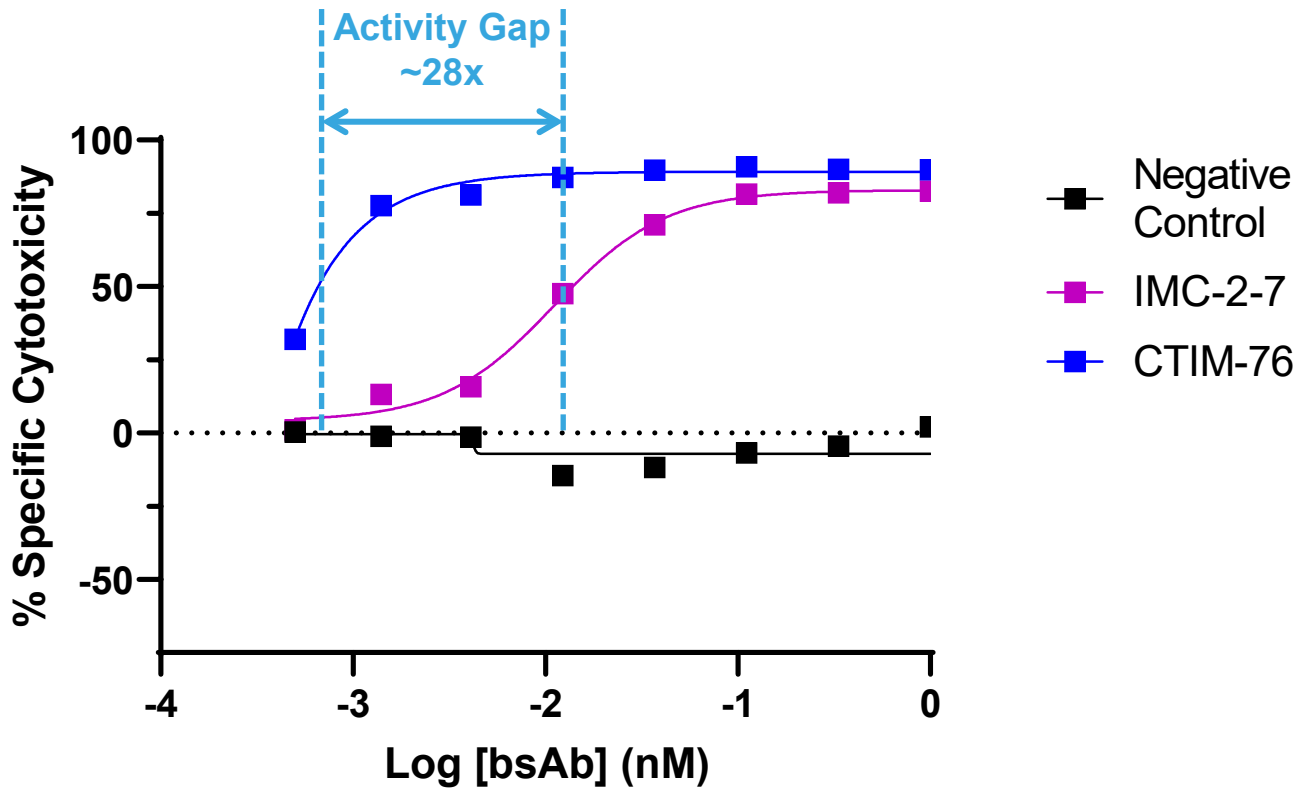
- T-cell dependent cellular cytotoxicity with no or minimal activation of circulating cytokines
- Humanized CLDN6 and CD3 binding domains

Ease of manufacturing

- IgG backbone is highly stable and enables high yield

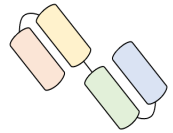
Role of Bispecific Format in Activity

CTIM-76 format demonstrates superior potency compared to a traditional BiTE molecule

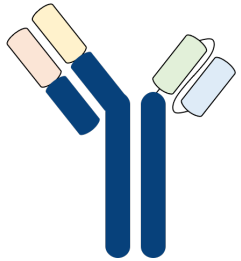


CTIM-76 vs BiTE

IMC-2-7
Tandem scFvs
(BiTE)



CTIM-76
scFv-Fab IgG

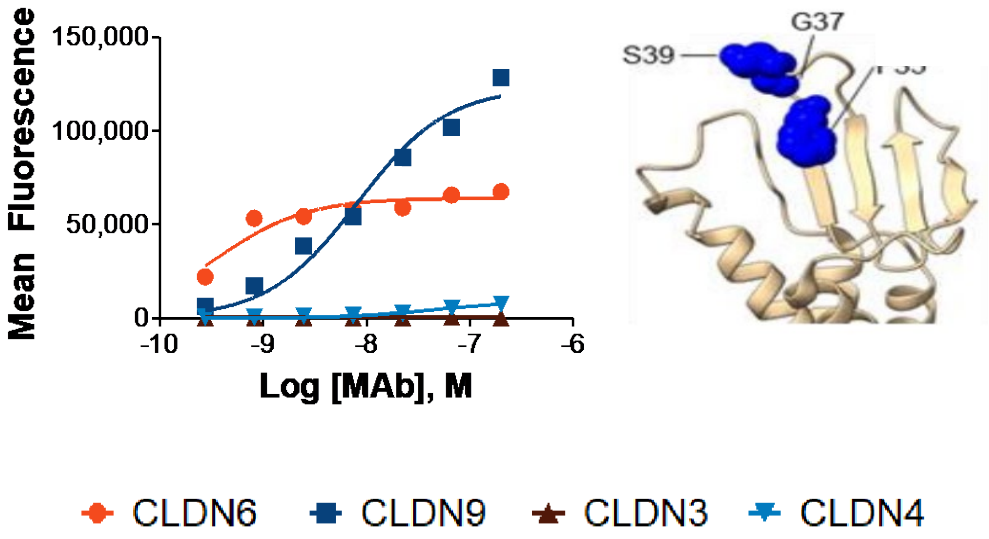


Study Design: K562 cells stably expressing CLDN6 and luciferase were co-cultured with human T-cells at an E:T ratio of 10:1 for 48 hours. Cytotoxicity was determined by luminescence imaging.

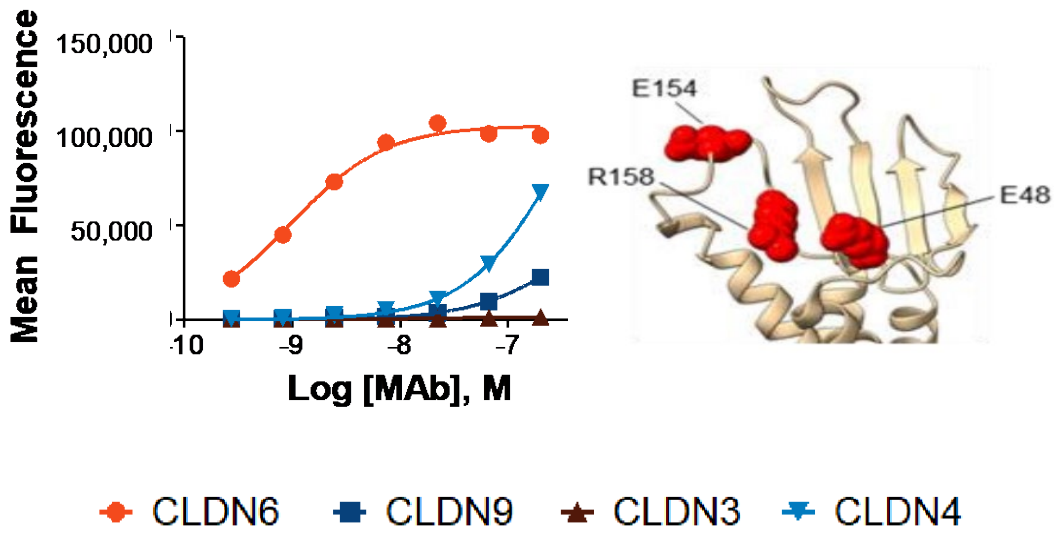
Identification of Selective CLDN6 MAbs

- IM301 (CLDN6 arm of CTIM-76) exhibits high CLDN6 selectivity[1]
- Epitope mapping of IM301 identifies unique binding location relative to benchmark IMAB027/ASP150 (Ganymed/Astellas)

IMAB027/ASP1650



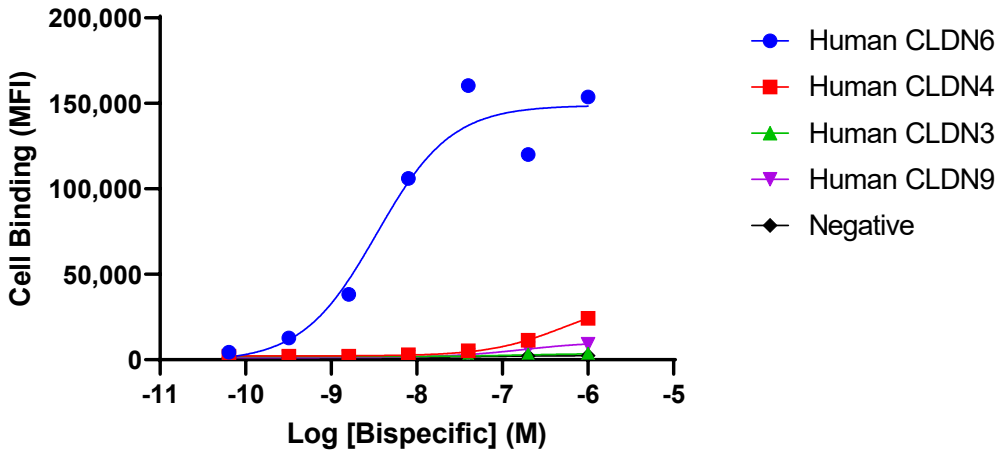
IM301



1 Screnci, iScience, 2022

CTIM-76 Exhibits Excellent Selectivity

CLDN6 Selectivity



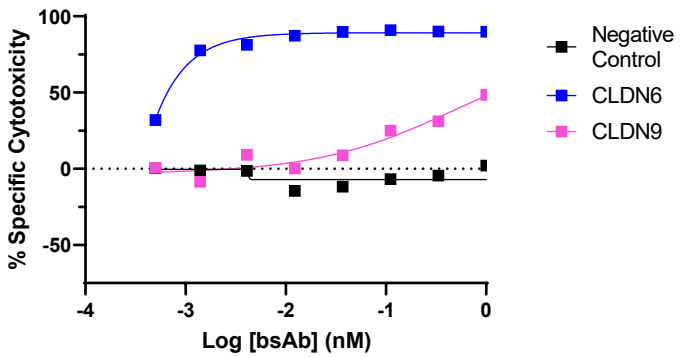
- CTIM-76 **CLDN6 EC50 of 3.41 nM**
- CTIM-76 **preferentially binds** to CLDN6 over CLDN3/4/9
- CLDN3/4/6/9 were transiently transfected in HEK-293F cells (4:1 Target:GFP)

CTIM-76 Preferentially Targets CLDN6 Over Other Claudin Family Proteins

- There is high sequence homology between CLDN6 and CLDN9 in the extracellular loops
- CTIM-76 preferentially targets CLDN6, with minimal activity against CLDN9-expressing cells
- No binding is observed to other CLDN family proteins (CLDN3 and CLDN4) that have <85% homology in the extracellular loops

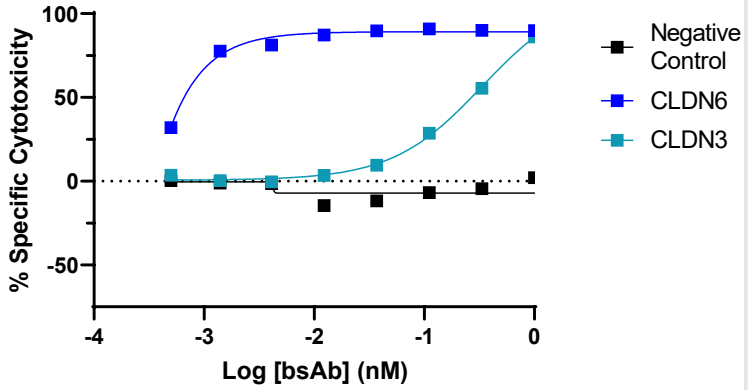
CLDN6:CLDN9

Activity Gap ~1192x



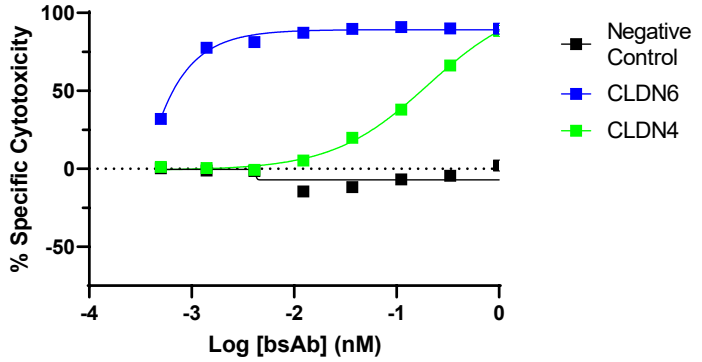
CLDN6:CLDN3

Activity Gap ~836x



CLDN6:CLDN4

Activity Gap ~504x

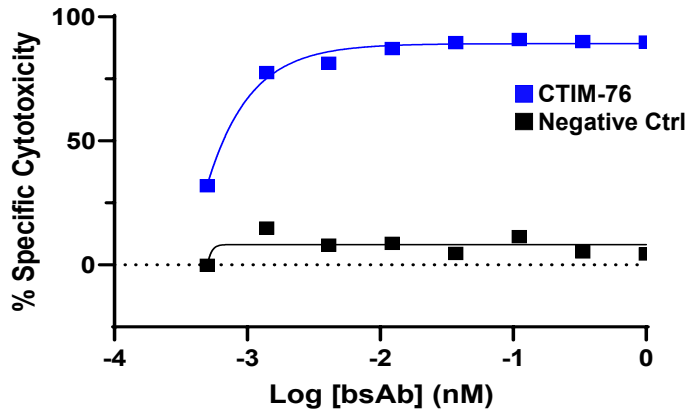


Study Design: K562 cells stably over-expressing CLDN3, CLDN4, CLDN6, or CLDN9 were co-cultured with human T-cells at an E:T ratio of 10:1 for 48 hours. Cytotoxicity was determined by luminescence imaging.

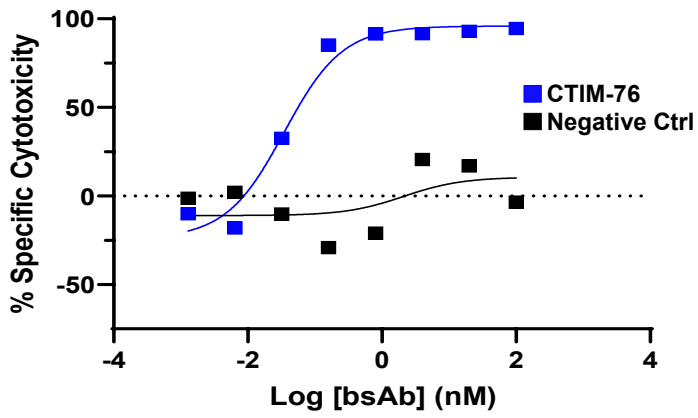
CTIM-76 Activity Requires CLDN6 Expression

T-cell mediated cell killing is dependent on CLDN6 expression

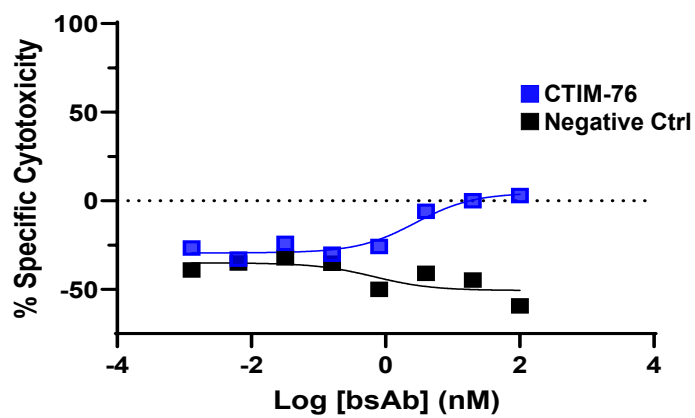
K562-CLDN6 Cell Line



OV90 Cell Line



HEK Cell Line



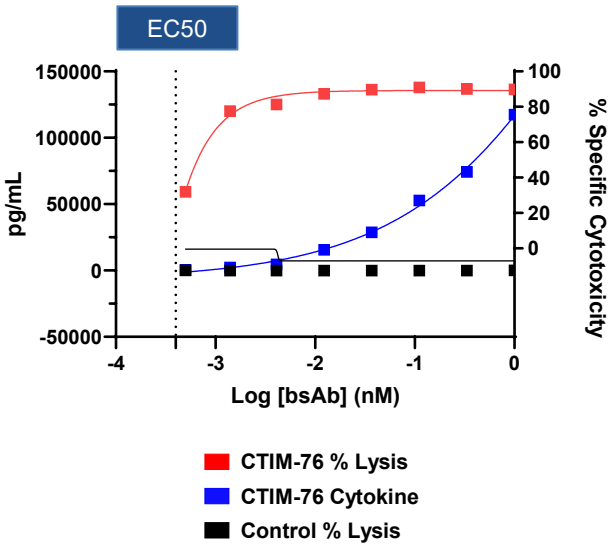
	K562-CLDN6	OV90	HEK
CLDN6 Expression	High	Medium	Low
CTIM-76 (EC50)	0.0004 nM	0.049 nM	2.79 nM

CTIM-76 has the Potential for a Wide Therapeutic Window

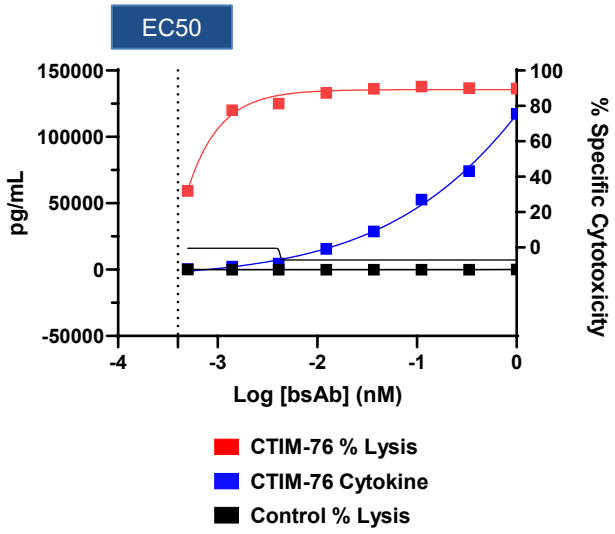
- Data supports potential to dose at levels that promote cancer cell killing but have manageable levels of free cytokine production, thereby potentially reducing the risk of cytokine release syndrome
- Cytokine production evaluated in exogenous (CLDN6-K562) cell line model at 48 hours
- Cytokine production happens well above the concentration of maximal killing (TDCC EC50 = 0.0004 nM)

Comparison of T cell-dependent cellular cytotoxicity (TDCC) to Cytokine Production

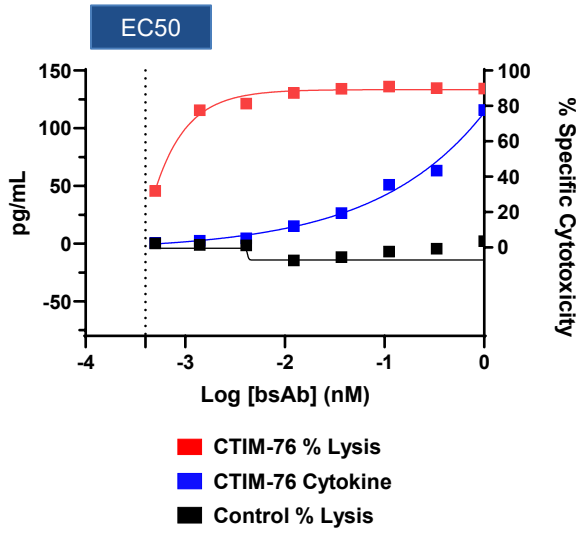
TDCC vs IFNg



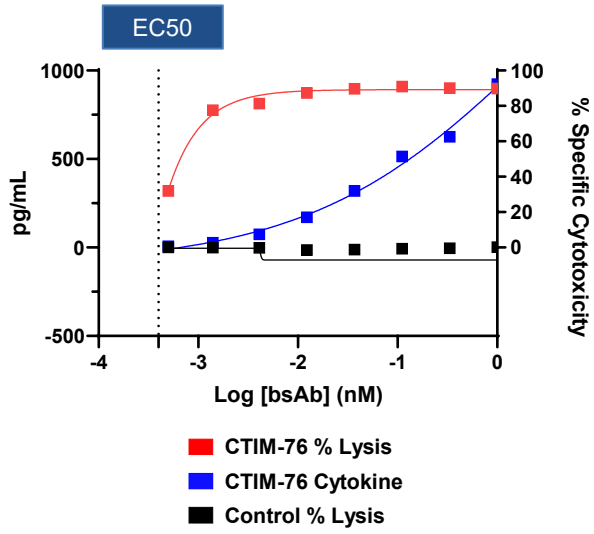
TDCC vs IL2



TDCC vs IL10



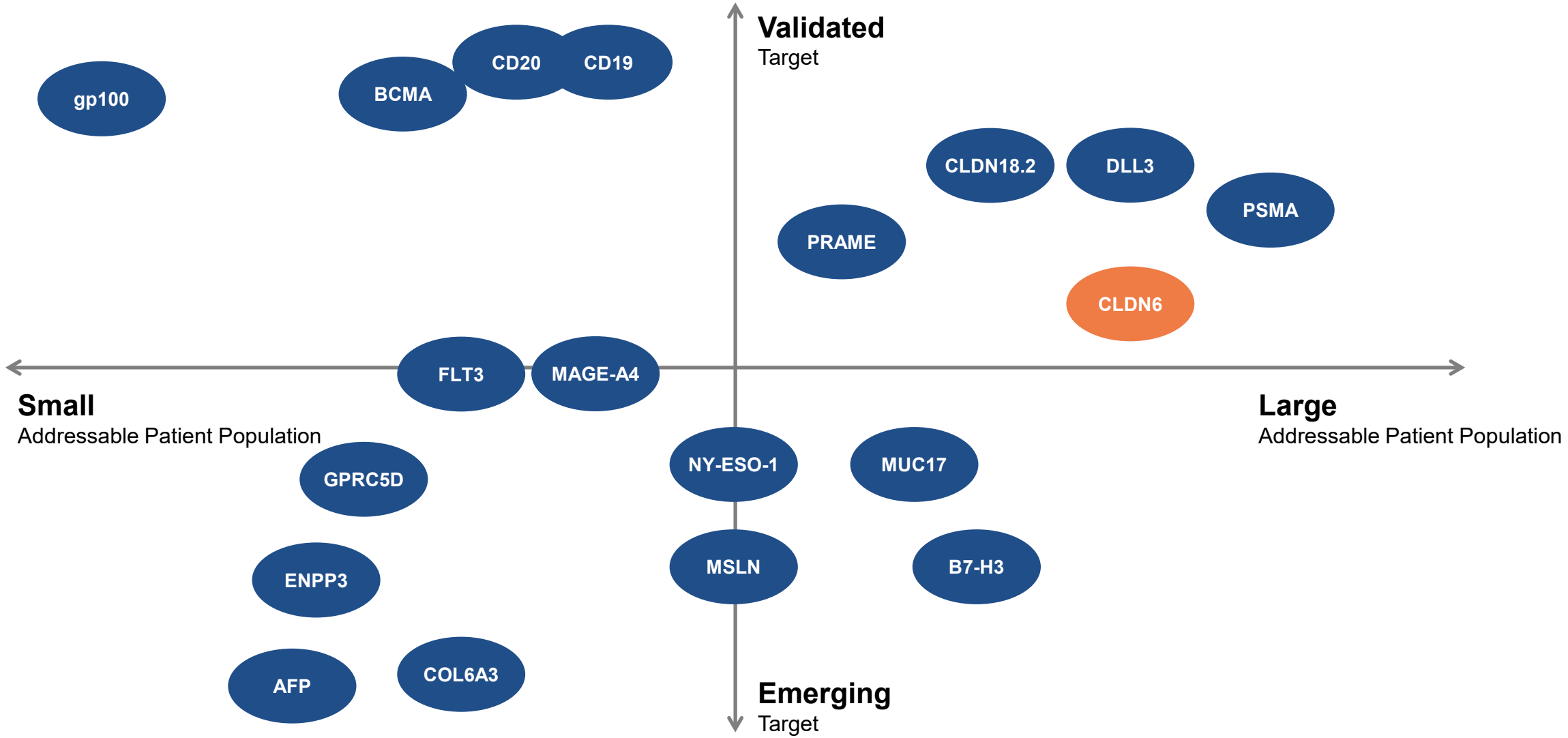
TDCC vs TNFα



Study Design: K562 cells stably over-expressing CLDN6 and luciferase were co-cultured with human T cells at an E:T ratio of 10:1 for 48 hours. Cytotoxicity was determined by luminescence imaging.

Competitive Landscape

Mapping the T-cell Directed Therapy Landscape[1]



1 Analysis based upon publicly available information and represents a non-head-to-head summary comparison

CLDN6 – Drug Development Strategy Comparison

CLDN6 is a tumor-associated antigen (TAA) for tumor-targeting therapeutics such as CAR-T and T cell engaging bispecific antibodies

Drug Development Strategy	CLDN6 Dependence / Rationale	Supporting Evidence
Monoclonal Antibody (mAb)	Receptor-mediated signaling	**Poor** Weak signaling dependence[1]
Bispecific Antibody (bsAb)	Cell surface antigen for T-cell targeting	**High** *In vivo* PoC + BNT211 clinical PoC[2,3]
Antibody-Drug Conjugate (ADC)	Receptor internalization	**Poor** Weak internalization[4]
CAR-T	Cell surface antigen for T-cell targeting	**High** BNT211 clinical PoC[3]

1 https://www.clinicaltrialsregister.eu/ctr-search/trial/2013-002755-15/results .
2 Context internal
3 Haanen J, et al. AACR Annual Meeting 2022; Oral presentation CT002.
4 Data courtesy of Integral Molecular and Dr. Andrew Tsourkas (UPenn)

CLDN6 Competitive Landscape[1]

Programs differentiated based upon treatment modality and selectivity for CLDN6 over CLDN9

	Preclinical	Phase 1
Antibody Drug Conjugate (ADC)	**GB-7008-01** CLDN6/CLDN9 + MMAE (*~1x, non-selective*) **UCLA-23-ADC** CLDN6 + MMAE (*~27x*)	**DS-9606a** CLDN6/CLDN9 + DXd (*~1x, non-selective*)
Bispecific Antibody	**XmAb541** 2+1 bsAb CLDN6xCD3 (*~10x*) **TJ-C64B** 2+2 bsAb CLDN6x4IBB (*not disclosed*) **CTIM-76** bsAb CLDN6xCD3 (*>1,000x*)	**SAIL66** bsAb CLDN6xCD3 (*~10x*) **BNT142** mRNA encoded BsAb CLDN6xCD3 (*~7x*) **AMG794** BiTE CLDN6xCD3 (*~630x*)
Cell Therapy		**BNT211** CAR-T + CARVac (*~7x*) **CLDN6-CAR-NK** CAR-NK + IL7 (*not disclosed*)

1 Analysis based on publicly available information compiled as of February 21, 2023

Potential for CTIM-76 to Separate From the Competition

	Company	Program (Development Stage)	Description / Details[3]
Active Programs	BioNTech	**BNT211:** CLDN6CAR-T + CARVac (Phase 1)	Initial data for BNT211 were presented April 2022 (AACR), with an update in Sept 2022 (ESMO). Received PRIME Designation for testicular cancer June 2022
		BNT142: CLDN6 mRNA encoded bsAb (Phase 1)	Initiated Phase 1 development for BNT142 in mid-2022
	Amgen	**AMG794:** CLDN6 BiTE (Phase 1)	AMG794 candidate were presented April 2022 (AACR), trial is not yet recruiting
	Guangzhou Medical University	**CLDN6-CAR-NK:** CAR-NK + multiple gene edits (Phase 1)	Engineered to express IL7/CCL19 and/or SCFVs against PD1/CTLA4/Lag3, initiated Phase 1 development in mid-2022
	Daiichi	**DS-9606a:** CLDN6/CLDN9 ADC (Phase 1)	Initiated Phase 1 development for DS-9606a in mid-2022
	Chugai	**SAIL66:** CLDN6 bsAb CLDN6xCD3 (Phase 1)	Initiated Phase 1 development for SAIL66 in Feb 2023
	I-Mab	**TJ-C64B:** CLDN6 bsAb CLDN6x4IBB (Preclinical)	Initial data presented April 2021 (AACR), IND filing is expected in 2H 2023
	Xencor	**XmAb541:** CLDN6 bsAb CLDN6xCD3 (Preclinical)	Initial data presented April 2021 (AACR), IND filing is expected in 2023
Notable Deprioritized Programs	Astellas/Ganymed	**IMAB027/ASP1650:** CLDN6 mAb (Phase 2)	Lack of single agent activity in Phase 2 trial relapse/refractory testicular germ cell tumors[1]
	Abbvie/Stemcentryx	**SC004:** CLDN6/CLDN9 ADC (Phase 1)	Dose-limiting toxicity (loss of hearing, diarrhea) attributed to CLDN9 binding observed in Phase 1 in patients with ovarian cancer[2]

1 Adra, Invest New Drugs, 2022
2 Hamilton, Cancer Res, 2020
3 Analysis based on publicly available information compiled as of February 21, 2023

Corporate

Experienced Leadership Team

Martin Lehr
CEO and Director

Praesidia BIOLOGICS
Cure Duchenne
OSAGE UNIVERSITY PARTNERS

Jennifer Minai, CPA
Chief Financial Officer

MILLENDO THERAPEUTICS
parexel
EY

Chris Beck, MBA
SVP Operations

Galera Therapeutics, Inc
Shire
MERCK

Alex Levit, Esq
Chief Legal Officer

optinose
teva
ReedSmith

Tarek Sahmoud, MD, PhD
Chief Medical Officer

NOVARTIS
H3 Biomedicine
Celgene

Priya Marreddy, MS
VP Clinical Operations

Spark THERAPEUTICS
teva
PRA Health Sciences

Focus on Execution

Experienced team with deep oncology experience

Our CMO led the clinical development of multiple blockbuster drugs including Kisqali, Arimidex, and Afinitor

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

Near-Term Milestones

Preclinical Update at AACR 2023

Strong Team

Deep Domain Experience, Track Record of Success

Financial Strength

Expected Cash Runway into late 2024

context therapeutics

Advancing Medicines
for Solid Tumors