UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 OR 15(d)
of The Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): November 29, 2022

Context Therapeutics Inc.
(Exact name of registrant as specified in its charter)

Delaware	001-40654	86-3738787
(State of other jurisdiction of incorporation)	(Commission File Number)	(I.R.S. Employer Identification No.)

2001 Market Street, Suite 3915, Unit#15
Philadelphia, Pennsylvania 19103
(Address of principal executive offices including zip code)

(267) 225-7416
(Registrant's telephone number, including area code)

Not Applicable
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Title of each class	Trading Symbol	Name of exchange on which registered
Common Stock $0.001 par value per share	**CNTX**	**The Nasdaq Stock Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01. Regulation FD Disclosure.

On November 29, 2022, Context Therapeutics Inc. issued a press release announcing the selection of CTIM-76, its lead clinical development candidate to target Claudin 6 (CLDN6) positive cancers, and that the Company would be holding a webinar on December 1, 2022 regarding CTIM-76. A copy of the press release is filed as Exhibit 99.1 to this Current Report on Form 8-K and incorporated herein by reference.

On December 1, 2022, the Company will be presenting information during the webinar regarding the identification of CTIM-76. A copy of the presentation is filed as Exhibit 99.2 to this Current Report on Form 8-K and incorporated herein by reference.

The information in this Item 7.01 and Exhibits 99.1 and 99.2 attached hereto are being furnished and shall not be deemed "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, regardless of any general incorporation language in such filing.

Item 8.01. Other Events.

On November 29, 2022, Context Therapeutics Inc. issued a press release announcing the selection of CTIM-76, a T cell-engaging bispecific antibody, as the Company's lead clinical development candidate to target Claudin 6 (CLDN6) positive cancers, resulting from the Company's research collaboration and licensing agreement with Integral Molecular.

Item 9.01. Exhibits.

(d) Exhibits

Exhibit No.	**Description**
99.1	Press Release issued by Context Therapeutics Inc., dated November 29, 2022
99.2	Context Therapeutics Inc. CTIM-76 presentation, dated December 1, 2022
104	Cover Page Interactive Data File (embedded within the inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Dated: December 1, 2022

Context Therapeutics Inc.

By: /s/ Martin A. Lehr
Name: Martin A. Lehr
Title: Chief Executive Officer

Context Therapeutics® Nominates CTIM-76 Bispecific Antibody Candidate to Develop Treatment for Claudin 6-Positive Solid Tumors

CTIM-76 named as lead candidate to target Claudin 6 positive cancers

IND submission expected in Q1 2024

Context to host webinar on Thursday, December 1, 2022, at 11 a.m. ET

PHILADELPHIA, PA — November 29, 2022—Context Therapeutics Inc. ("Context" or the "Company") (Nasdaq: CNTX), a women's oncology company developing novel treatments for breast and gynecologic cancers, today announced the selection of CTIM-76, a T cell-engaging bispecific antibody, as its lead clinical development candidate to target Claudin 6 (CLDN6) positive cancers, resulting from its research collaboration and licensing agreement with Integral Molecular.

CLDN6 is differentially expressed on cancer cells with no or very low expression in normal, healthy tissue. CLDN6-enriched cancers include ovarian, endometrial, testicular, and gastric, among others. With the potential to reach a large patient population and selective expression on cancer cells, CLDN6 has emerged as an exciting drug target.

Context's lead candidate, CTIM-76, is a CLDN6 x CD3 bispecific antibody that incorporates a highly selective CLDN6 binding arm and a CD3 binding single-chain Fv domain in an IgG format with a silenced Fc that is designed to be functionally monovalent to avoid aberrant T-cell activation and to enhance the safety profile. Research has demonstrated that CTIM-76 is potent with specific lysis of CLDN6+ cancer cells over normal cells and can activate cytotoxic T cells without concomitant activation of free cytokines – critical determinants of immunotherapy safety and activity. Preclinical studies suggest the potential for convenient dosing with low immunogenicity risk and manufacturing can be scalable to address the significant number of patients who are potentially eligible for CTIM-76 therapy.

"This year has been marked by several exciting and significant milestones for Context, culminating in naming our lead CLDN6 clinical development candidate, CTIM-76, a bispecific antibody showing high selectivity for CLDN6," said Martin Lehr, CEO of Context Therapeutics. "We selected this bispecific based on the specificity which suggests its potential to address the need for potent therapeutic modalities for cancer without compromising patient safety. With the selection of CTIM-76 as our lead CLDN6 candidate, we are well-positioned to rapidly advance our clinical development plan in CLDN6-positive tumors including, but not limited to, ovarian cancer. We have initiated IND-enabling studies and expect to submit our Investigational New Drug Application (IND) for CTIM-76 to the U.S. Food and Drug Administration in Q1 2024."

"Despite being an attractive target, therapeutic monoclonal antibodies (MAbs) targeting CLDN6 are difficult to discover due to an abundance of closely related family members and an absolute need for high specificity. Context and Integral Molecular have been able to isolate and optimize rare antibodies against CLDN6 that do not cross-react with other CLDN family members," said Joseph Rucker, Ph.D., VP of R&D at Integral Molecular.

R&D Webinar
On Thursday, December 1, 2022, at 11 a.m. ET, members of the Context team, including management, and Integral Molecular will host a webinar to discuss the selection process and

nomination of CTIM-76. There will be a question-and-answer period following the formal presentation. To register for the webinar, please visit https://edisongroup.zoom.us/webinar/register/WN_Am1qwkDwRiSYJm51SpP-TQ.

About Context Therapeutics®
Context Therapeutics Inc. (Nasdaq: CNTX) is a clinical-stage biopharmaceutical company committed to advancing medicines for female cancers. The Company's pipeline includes small molecule and bispecific antibody drug candidates that target cancer signaling pathways. Onapristone extended release (ONA-XR), a novel, first-in-class potent and selective progesterone receptor antagonist, is currently in three Phase 2 clinical trials and one Phase 1b/2 clinical trial in hormone-driven breast, ovarian, and endometrial cancers. Context is also developing CTIM-76, a selective Claudin 6 (CLDN6) x CD3 bispecific antibody for CLDN6 positive tumors, currently in preclinical development. Context is headquartered in Philadelphia. For more information, please visit www.contexttherapeutics.com or follow the Company on Twitter and LinkedIn.

Forward-looking Statements
This press release contains "forward-looking statements" that involve substantial risks and uncertainties for purposes of the safe harbor provided by the Private Securities Litigation Reform Act of 1995. Any statements, other than statements of historical fact, included in this press release regarding strategy, future operations, prospects, plans and objectives of management, including words such as "may," "will," "expect," "anticipate," "plan," "intend," and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) are forward-looking statements. These include, without limitation, statements regarding (i) the selectivity, dosing convenience, potency, binding, scalable manufacturing, and safety profile of CTIM-76, (ii) the expectation to have an IND submission for CTIM-76 in the first quarter of 2024, (iii) the results of our IND-enabling studies and clinical trials, (iv) the potential benefits of our product candidates, (v) the likelihood data will support future development, and (vi) the likelihood of obtaining regulatory approval of our product candidates. Forward-looking statements in this release involve substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by the forward-looking statements, and we, therefore cannot assure you that our plans, intentions, expectations or strategies will be attained or achieved. Other factors that may cause actual results to differ from those expressed or implied in the forward-looking statements in this press release are discussed in our filings with the U.S. Securities and Exchange Commission, including the section titled "Risk Factors" contained therein. Except as otherwise required by law, we disclaim any intention or obligation to update or revise any forward-looking statements, which speak only as of the date they were made, whether as a result of new information, future events or circumstances or otherwise.

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context
therapeutics
Identification of CTIM-76,
a CLDN6 x CD3 bispecific antibody
December 1, 2022
context

Forward Looking Statement

Except for statements of historical fact, any information contained in this presentation may be a forward-looking statement that reflects the Company's current views about future events and are subject to risks, uncertainties, assumptions and changes in circumstances that may cause events or the Company's actual activities or results to differ significantly from those expressed in any forward-looking statement. In some cases, you can identify forward-looking statements by terminology such as "may", "will", "should", "plan", "predict", "expect," "estimate," "anticipate," "intend," "goal," "strategy," "believe," "could", "would", "potential", "project", "continue" and similar expressions and variations thereof.

Forward-looking statements may include statements regarding the Company's business strategy, cash flows and funding status, potential growth opportunities, clinical development activities, the timing and results of preclinical research, clinical trials and potential regulatory approval and commercialization of product candidates.

Although the Company believes that the expectations reflected in such forward-looking statements are reasonable, the Company cannot guarantee future events, results, actions, levels of activity, performance or achievements.

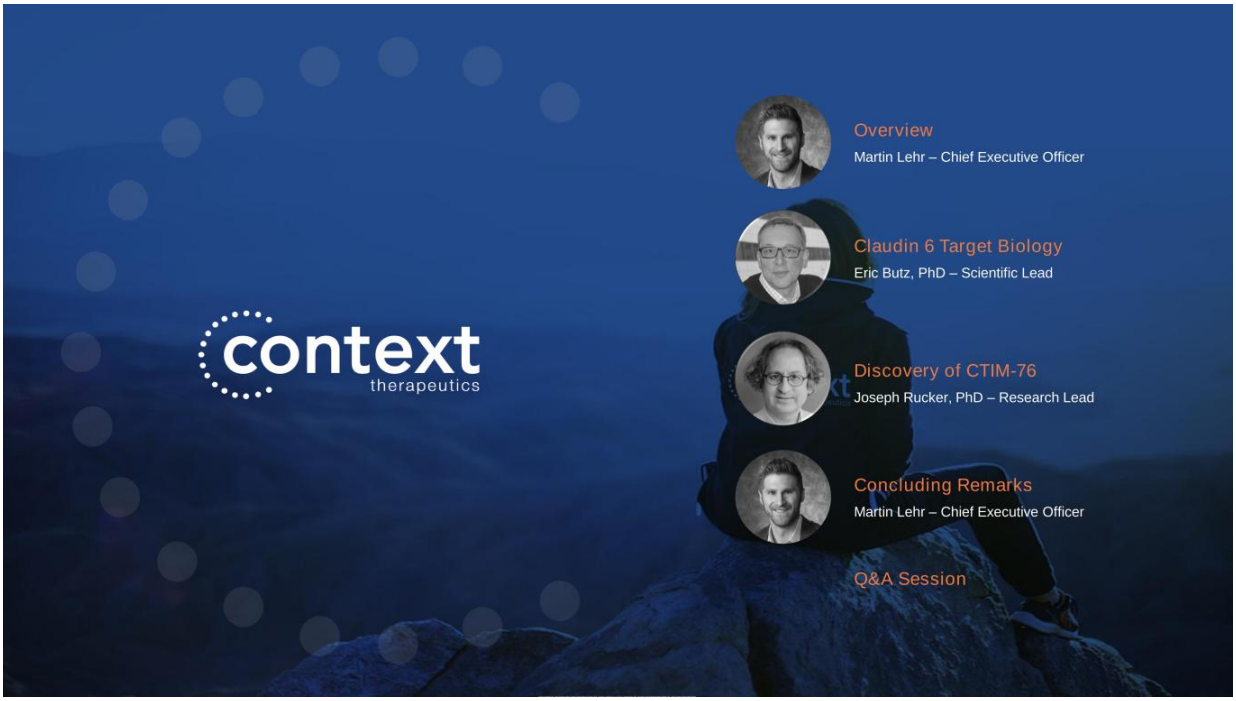
These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including those described under the heading "Risk Factors" in documents the Company has filed with the SEC. These forward-looking statements speak only as of the date of this presentation and the Company undertakes no obligation to revise or update any forward-looking statements to reflect events or circumstances after the date hereof.

Important Notice and Disclaimers

Certain information contained in this Presentation relates to or is based on studies, publications, surveys and other data obtained from third-party sources and the Company's own internal estimates and research. While the Company believes these third-party sources to be reliable as of the date of this Presentation, it has not independently verified, and makes no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. In addition, all of the market data included in this Presentation involves a number of assumptions and limitations, and there can be no guarantee as to the accuracy or reliability of such assumptions.

This presentation discusses product candidates that are under clinical study and which have not yet been approved for marketing by the U.S. Food and Drug Administration. No representation is made as to the safety or effectiveness of these product candidates for the use for which such product candidates are being studied. While the Company believes its internal research is reliable, such research has not been verified by any independent source. All the scientific and clinical data presented within this presentation are – by definition prior to completion of the clinical trial and a clinical study report – preliminary in nature and subject to further quality checks including customary source data verification.

The trademarks included herein are the property of the owners thereof and are used for reference purposes only. Such use should not be construed as an endorsement of such products.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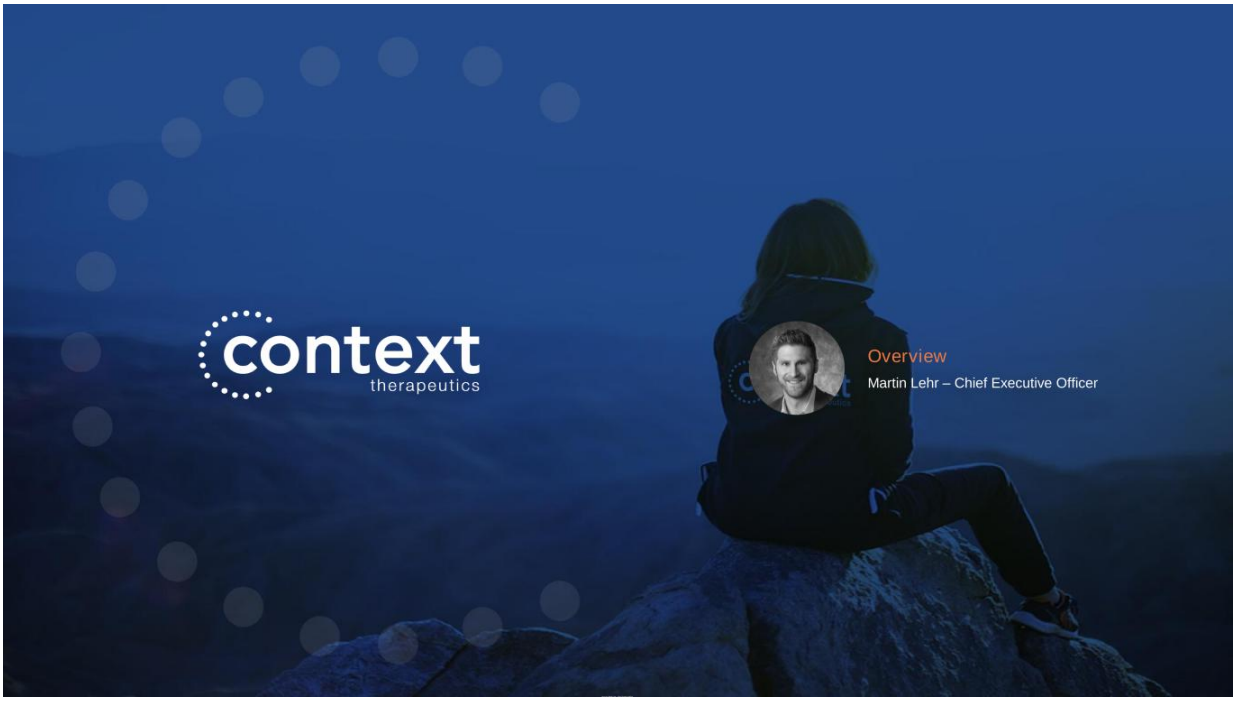
therapeutics
Overview
Martin Lehr – Chief Executive Officer
Claudin 6 Target Biology
Eric Butz, PhD – Scientific Lead
Discovery of CTIM-76
Joseph Rucker, PhD – Research Lead
Concluding Remarks
Martin Lehr – Chief Executive Officer
Q&A Session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therapeutics
Overview
Martin Lehr – Chief Executive Officer

Context Therapeutics Overview

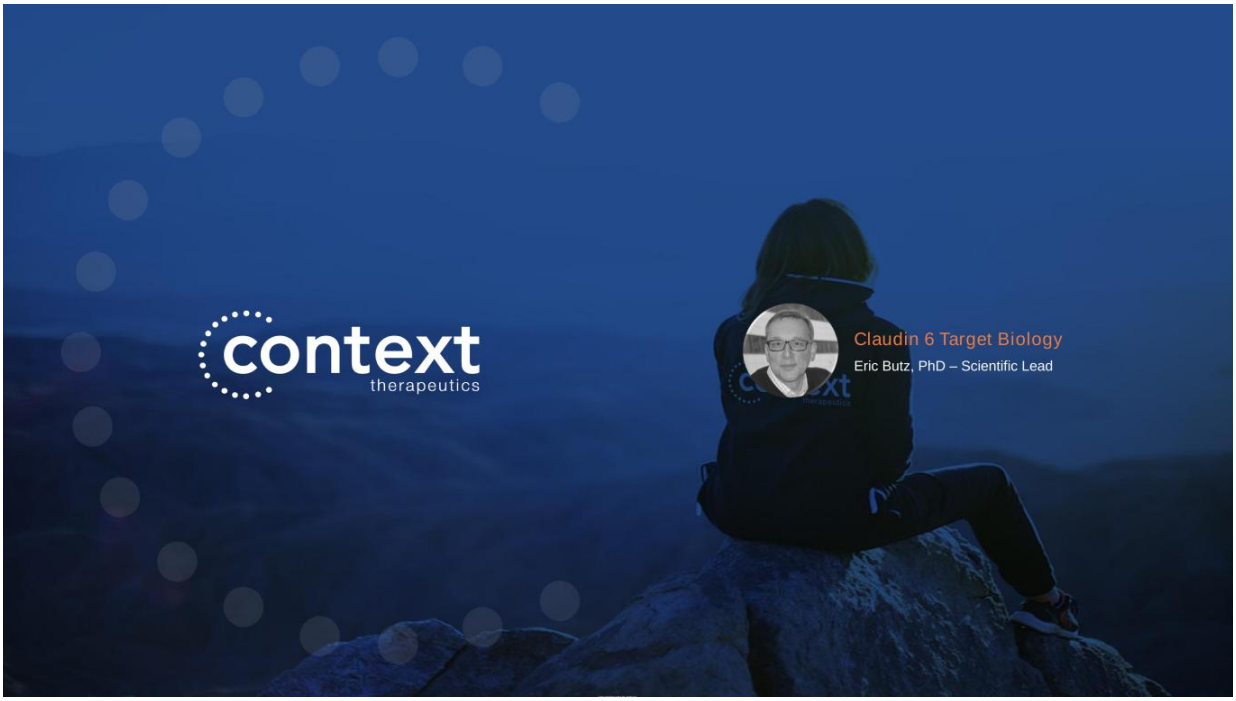
Focus on **Women's Oncology**	• Unmet clinical need in breast, ovarian, and endometrial cancers
ONA-XR oral PR antagonist	• ONA-XR is a novel, potentially first-in-class progesterone receptor (PR) antagonist • Endometrial cancer Phase 2 trial initial data reports 4-month PFS rate of 77%[1] • Breast cancer SMILE trial initial data to be presented Dec. 7 at San Antonio Breast Cancer Symposium • Breast cancer ELONA trial Phase 1b data expected Q4 2023
CTIM-76 CLDN6 x CD3 bispecific antibody	• Claudin 6 (CLDN6) is uniquely expressed in certain adult and pediatric cancers • CTIM-76 is Context's CLDN6 x CD3 bispecific antibody Development Candidate • IND submission on track for Q1 2024
Cash Guidance	• Expected cash runway into Q1 2024

1 Data cut off as of September 30, 2022; preliminary raw data

Pipeline

Cancer	Clinical Indication	Preclinical	Phase 1 Clinical	Phase 2 Clinical	Milestones
ONA-XR (PR antagonist)[1]					
Breast Cancer	2L/3L ER+,PR+,HER2- Combination w/ elacestrant		Phase 1b/2 ELONA Trial		Initiated Q4 2022 ☑ Phase 1b data Q4 2023
	2L/3L ER+,PR+,HER2- Combination w/ fulvestrant		*Phase 2 SMILE Trial		Initial data Dec 2022
Endometrial Cancer	Recurrent PR+ Endometrioid Combination w/ anastrozole		*Phase 2 Trial		Initial data Q4 2022 ☑ Data update mid-2023
Ovarian Cancer	Recurrent PR+ Granulosa Cell Tumor Combination w/ anastrozole		*Phase 2 Trial		Initial data Q4 2022 ☑ Data update mid-2023
CTIM-76 (CLDN6xCD3 bispecific antibody)					
	CLDN6-positive cancers				Candidate selection Q4 2022 ☑ IND submission Q1 2024

1 Tyligand Biosciences Ltd licensed rights to ONA-XR in China, HK, Macau
* Investigator Sponsored Trial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Claudin 6 Target Biology
Eric Butz, PhD – Scientific Lead

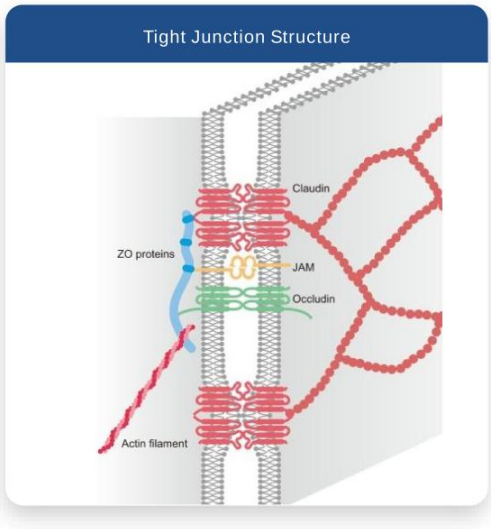
Claudin 6 (CLDN6) is an Emerging Oncology Target

Opportunity	• CLDN6 is a tumor-specific protein that is present at high surface density across certain 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 • Antigen binding region is highly conserved with CLDN3, CLDN4, and CLDN9 • CLDN6 selectivity is required to avoid off-target liabilities identified in murine knockout studies with CLDN3 (pancreas), CLDN4 (kidney, pancreas), and CLDN9 (ear, gut)
Target Validation	• BNT211 CAR-T establishes Proof of Concept[2]: – Novel CAR-T + mRNA vaccine evaluated in Phase 1 dose-escalation study in CLDN6+ solid tumors – 50% response rate (ORR) in second dosing cohort
Unmet Need	• Selectivity: preferentially target CLDN6 over other CLDN proteins • Potency: specific lysis of CLDN6+ cancer cells over normal cells • Safety: activation of cytotoxic T cells without concomitant activation of free cytokines • Manufacturability: scalable process and on-demand therapy

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

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



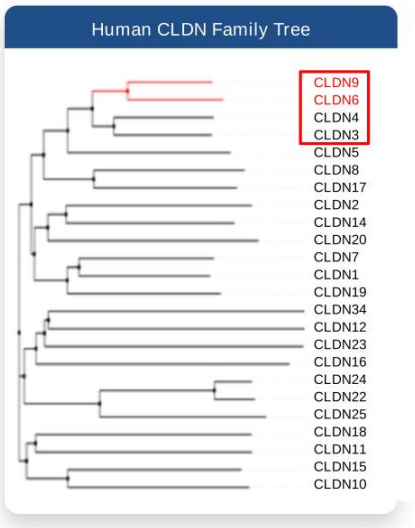
Otani, Trends in Cell Biology, 2020

Many CLDN Proteins are Associated with Disease

CLDN	Disease
CLDN 1	Colitis, skin permeability
CLDN 2	Colorectal cancer, IBD
CLDN 3	Psoriasis, ovarian cancer
CLDN 4	Diabetes, ovarian cancer
CLDN 5	Cerebral edema, depression
CLDN 6	Multiple cancers
CLDN 7	Colon cancer
CLDN 9	Hearing loss

CLDN	Disease
CLDN 11	Myelin dysfunction
CLDN 14	Kidney stones, hearing loss
CLDN 15	Celiac
CLDN 16	Hypercalcinuria
CLDN 17	Renal dysfunction
CLDN 18.2	Gastric cancer
CLDN 19	Renal dysfunction, vision loss

The Challenge: developing a highly selective CLDN6 antibody



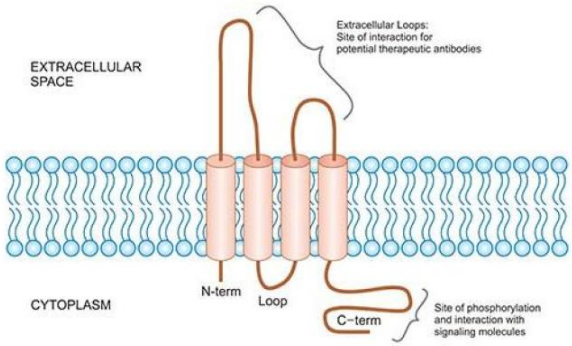
- CLDN6 antigen is conformationally-dependent, which limits access to antibody-antigen binding
- Antigen binding region is highly conserved with CLDN3, CLDN4, and CLDN9, making target selectivity a challenge[1]
- CLDN6 selectivity is required to avoid off-target liabilities identified in murine knockout 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, Considered Favorable Candidates for Immunotherapy

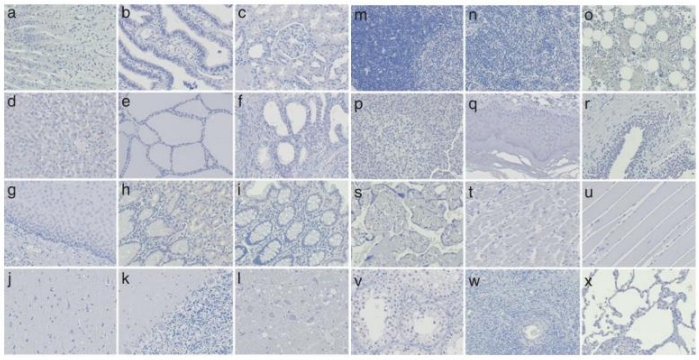
CLDN6 Biology

- 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



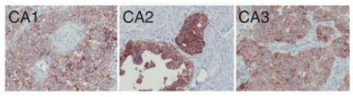
CLDN6 is Selectively Expressed on Cancer Cells

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

Cancer Tissue



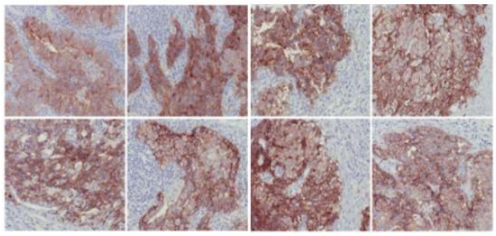
(CA1) testicular cancer, (CA2) ovarian cancer, and (CA3) lung cancer

Reinhard, Science, 2020

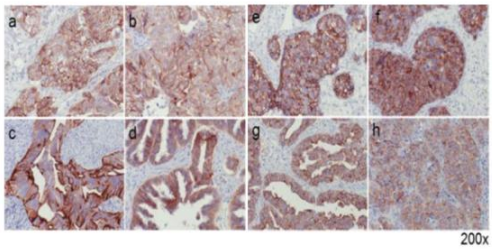
CLDN6 Exhibits High, Homogeneous Expression on Cancer Cells

Consistent expression makes CLDN6 a promising tumor associated antigen (TAA) for immunotherapy

Testicular Cancer



Ovarian Cancer



- CLDN6 protein expression in testicular and ovarian tumors each from eight different patients analyzed by IHC
- Testicular: all embryonal carcinoma
- Ovarian: (a) adenocarcinoma, (b,c,e-h) serous cystadenocarcinoma, (d) papillary serous cystadenocarcinoma

Reinhard, Science, 2020

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 or Rare Pediatric Designation

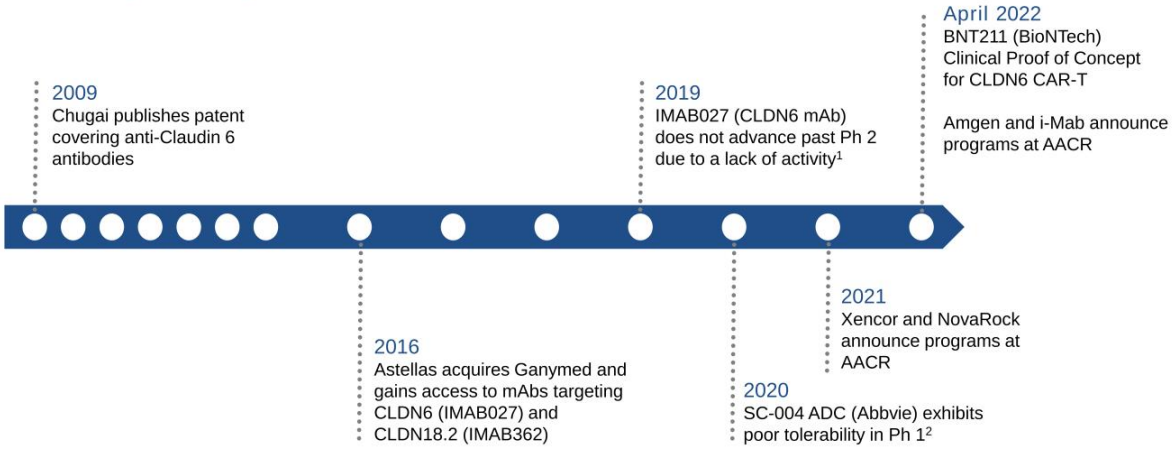
Selected Cancer indications	Incidence	R/R Incidence	CLDN6 Positive	Patient Population Based on R/R Incidence
Testicular	9,910	400	95%[1]	380
Ovarian	19,900	12,800	54-55%[1,2]	6,982
NSCLC	201,229	110,653	6-50%[3,4,5]	35,221
Malignant Rhabdoid	50	500	29-44%[1,2,6,7]	183
Gastric	26,380	11,090	13-55%[8,9]	3,771
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
SCLC	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.

Key Developments in CLDN6 R&D Timeline

R&D activity has recently accelerated



1 https://www.clinicaltrialsregister.eu/ctr-search/trial/2013-002755-15/results
2 Hamilton et al, AACR, Virtual: 2020

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 is Not Ideally Suited for Conventional mAb or ADC Therapy

CLDN6 has weak signaling activity and poor internalization

CLDN6 mAb Exhibits Weak Monotherapy Activity[1]

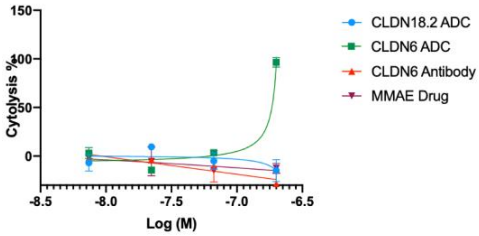
IMAB027 Phase 1 Dose Escalation Trial

IMAB027 Treatment	Stage 1/2 1-1000 mg/m^2	Stage 2 100 mg/m^2	Stage 2 300 mg/m^2	Stage 2 600 mg/m^2	Stage 2 1000 mg/m^2
Patients (n)	2	10	10	10	9
CR (n)	0	0	0	0	0
PR (n)	0	0	1	0	0
SD (n)	0	1	3	3	7

- 41 patients with recurrent ovarian cancer were treated with IMAB027 in a Phase 1 dose escalation trial
- 1 PR and 14 SD noted
- IMAB027 was well tolerated

CLDN6 Does Not Rapidly Internalize[2]

OVCAR3 Cell Killing Assay



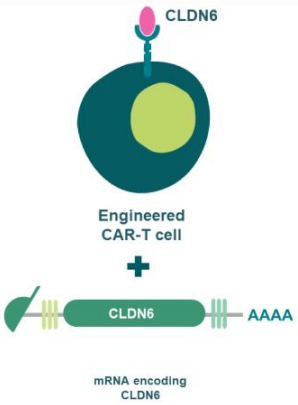
- CLDN6 and CLDN18.2 antibodies from Integral Molecular were converted to ADC utilizing MMAE payload
- ADC constructs evaluated in OVCAR3 cell killing assay
- CLDN6 ADC cell killing achieved only at supratherapeutic doses

1 https://www.clinicaltrialsregister.eu/ctr-search/trial/2013-002755-15/results
2 Data courtesy of Integral Molecular and Dr. Andrew Tsourkas (UPenn)

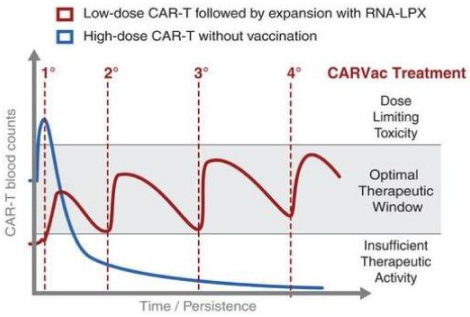
CLDN6 is an Ideal Tumor Associated Antigen for T-cell Targeting

BNT211 (BioNTech) demonstrates preliminary clinical proof of concept

BNT211 CAR-T + CLDN6 CARVac



CARVac mRNA Vaccine Strategy



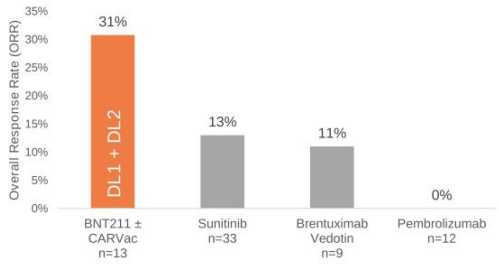
- CARVac intended to drive in vivo expansion, persistence, and efficacy of CAR-T
- Strategy intended to minimize number of CAR-T cells infused and offset cytokine storm risk

Reinhard, Science 2020

BNT211 ± CARVac Exhibited Activity Across CLDN6+ Advanced Cancers

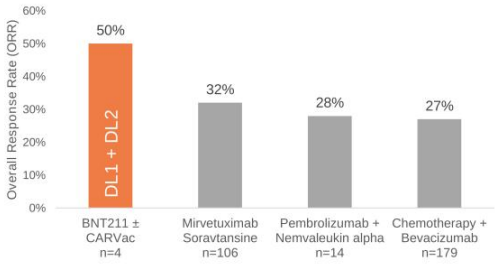
Initial clinical efficacy benchmarked to standard of care or emerging treatments

Testicular Cancer



- DL1 + DL2: 13 testicular cancer patients received BNT211 ± CARVac across DL1 ($1x10^7$ cells) and DL2 ($1x10^8$ cells) for a response rate of 31%
- DL2 only: Seven (7) testicular cancer patients received the second BNT211 dose level (DL2) after lymphodepletion with four (4) patients responding, including one complete response (CR), for a response rate of 57%

Ovarian Cancer



- DL1 + DL2: 4 ovarian cancer patients received BNT211 ± CARVac for a response rate of 50%
- DL2 only: Two (2) ovarian cancer patients received the second BNT211 dose level (DL2) after lymphodepletion with both patients responding for a response rate of 100%

Testicular: Haanen 2022, Oechsle 2011, Adra 2018, Necchi 2016
Ovarian: Haanen 2022, Matulonis 2022, Pujade-Lauraine 2014, Vaishampayan 2022

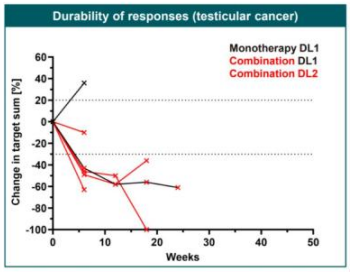
Limitations of CLDN6 CAR-T + CARVac Approach

Limited Dose Sparing[1,2]

Target	Asset	Ph 1 Dose Range	RP2D
CLDN6	BNT211	$1x10^7$ to $1x10^9$ cells	TBD
CLDN18.2	CT041	$2.5x10^8$ to $5x10^8$ cells	2.5×10^8 cells

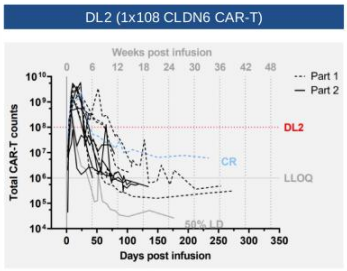
- BNT211 + CARVac T-cell infusion is consistent with similar CAR-T products
- Without CAR-T dose sparing, patients may be exposed to high dose CAR-T side effects, including neurologic and hepatic

Limited Durability[1]



- CAR-T activity in solid tumors is often limited by a weak durability of response
- BNT211 + CARVac exhibits a limited durability of response in advanced solid tumors

Limited T Cell Persistence[1]



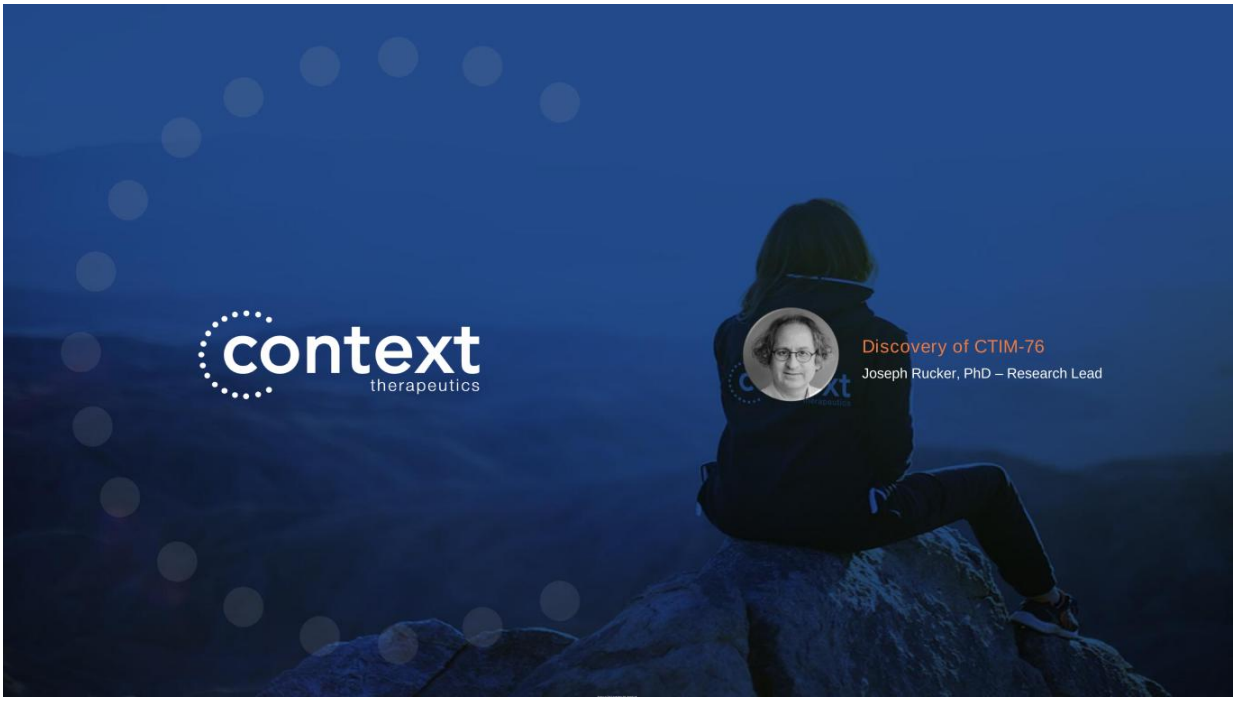
- CARVac is intended to enhance T-cell persistence
- Preliminary findings indicate that CARVac provides limited enhancement of T-cell persistence

1 Haanen J, et al. AACR Annual Meeting 2022; Oral presentation CT002.
2 Qi C, et a. ESMO Annual Meeting 2021; Oral Presentation Virtual.
RP2D = recommended Phase 2 dose

CTIM-76 Differentiation[1]

	BNT211 + CARVac	CTIM-76
Administration	Complex + In-Patient Hospital administered autologous cell therapy in combination with repeat mRNA vaccination utilizing lipid nanoparticle carrier	Easy + Out-Patient Outpatient infusion every 2-4 weeks based on IgG backbone
Lymphodepletion	Required	None
Treatment Durability	Weak T cell persistence	Fully stimulated T cell
Selectivity and Safety	Elevated transaminase and lipase	Selective for CLDN6

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


context
therapeutics
Discovery of CTIM-76
Joseph Rucker, PhD – Research Lead

Bispecific Antibody Considerations

Candidates evaluated based on a range of scaffolds, CLDN6, and T-cell engagers

CLDN6 Targeting Arm

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

CD3 Targeting Arm

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

Bispecific Scaffolds

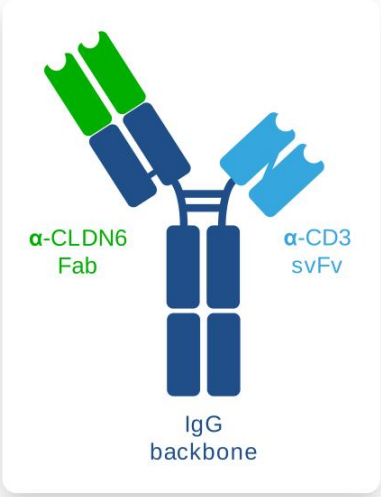
- Multiple formats evaluated

Other Factors

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

NHP = non-human primate

CTIM-76 Nominated as Development Candidate



Wide therapeutic window

- Highly selective CLDN6 binding Fab arm
- CD3 binding single-chain Fv domain is designed to be functionally monovalent to avoid aberrant T-cell activation, potentially enhancing safety profile
- Silenced Fc domain to 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

Identification of CLDN6-targeting Arm

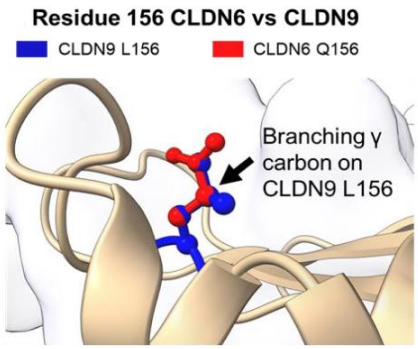
The Problem

- The extracellular binding region of CLDN6 is highly conserved with CLDN3 (78% homology), CLDN4 (81%), and CLDN9 (96%)
- Antigen is conformationally dependent, which limits conventional antibody discovery methods
- Human CLDNs share approximately 95% extracellular sequence homology with their mouse counterparts, necessitating the use of divergent species for immunization

Our Solution

- Using discovery strategies tailored to complex membrane proteins at our partner, Integral Molecular, we isolated and characterized rare antibodies with picomolar affinity and specificity for CLDN6
- Epitope mapping at single-atom resolution identified steric hindrance near the γ-carbon of residue 156 as critical for discriminating CLDN6 versus CLDN9 binding[1]

CLDN6 Monospecificity Challenge[1]

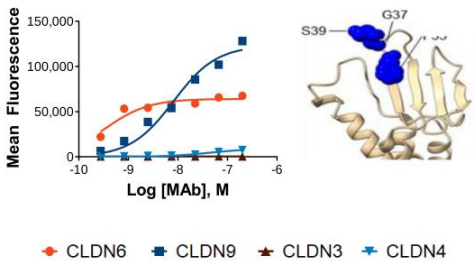


1 Screnci, iScience, 2022

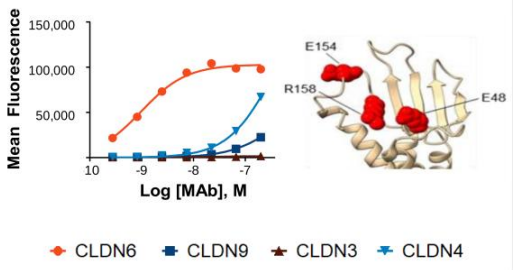
Identification of Selective CLDN6 MAbs

- 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



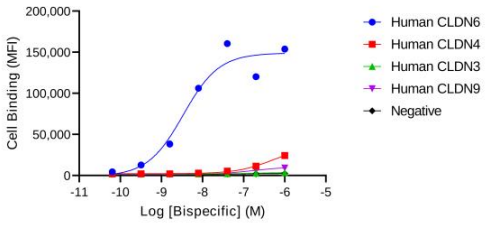
IM301



1 Screnci, iScience, 2022

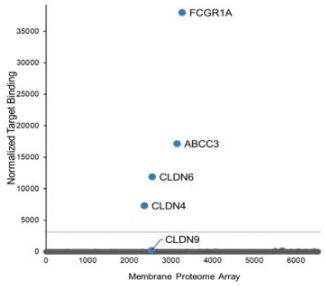
CTIM-76 Exhibits Excellent Selectivity and Specificity

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)

CLDN6 Specificity

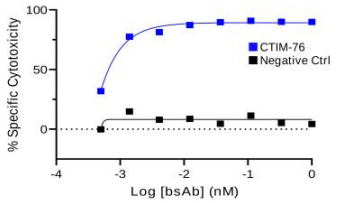


- IM301 Mab screened for specificity using Integral Molecular Membrane Proteome Array, consisting of ~6,000 human membrane proteins in their native state in unfixed cells
- IM301 Mab was cross-reactive for internal control FCGR1A (Fc gamma) and intracellular epitope of ABCC3

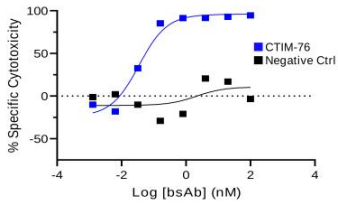
Specific Lysis

T-cell mediated cell killing is dependent on CLDN6 expression

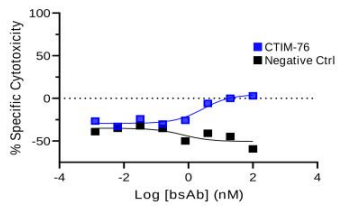
K562-CLDN6 Cell Line



OV90 Cell Line



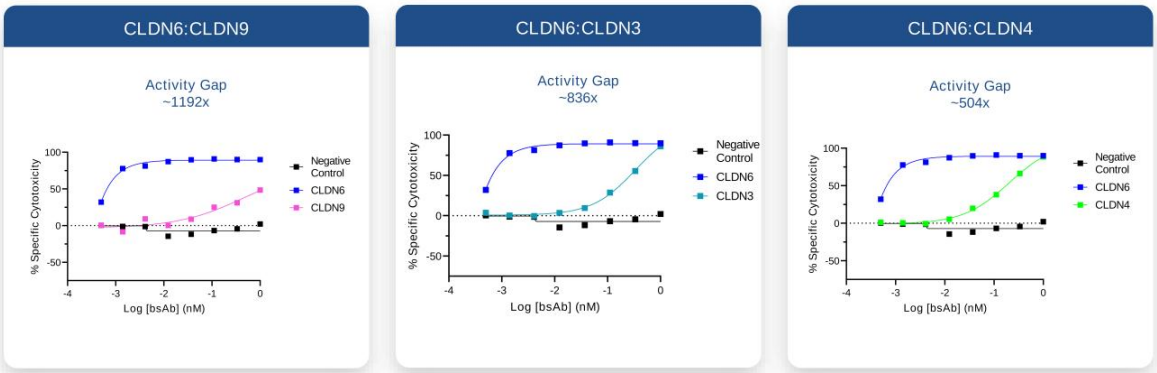
HEK Cell Line



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

CTIM-76 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 that have <85% homology in the extracellular loops

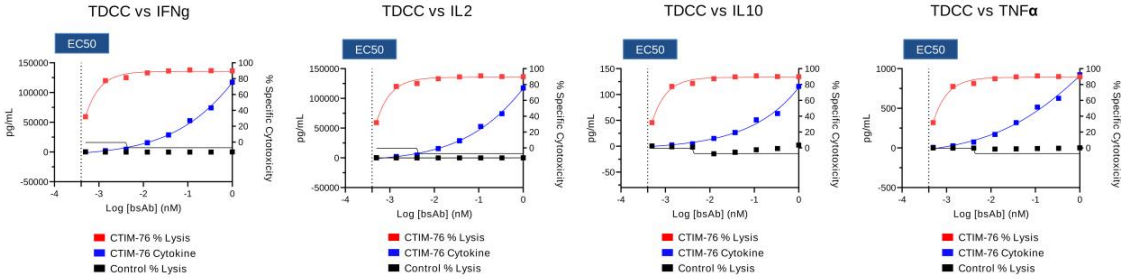


Study Design: K562 cells stably over-expressing CLDN3, CLDN4, CLDN6, or CLDN9 were co-cultured with human T-cells at an E:T ratio of 10:1 for 48 hours. Cytotoxicity was determined by luminescence imaging.

CTIM-76 has the Potential for a Wide Therapeutic Window

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

Comparison of **T cell-dependent cellular cytotoxicity (TDCC) to cytokine production in CLDN6-K562 cell line**

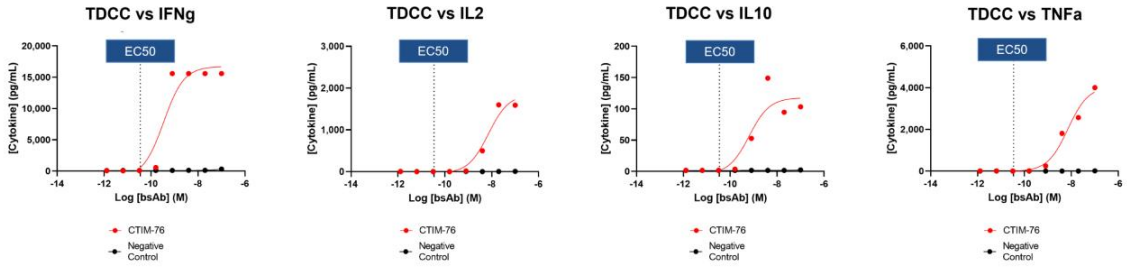


Study Design: K562 cells stably over-expressing CLDN6 and luciferase were co-cultured with human T cells at an E:T ratio of 10:1 for 48 hours. Cytotoxicity was determined by luminescence imaging.

CTIM-76 Exhibits Ideal Immunomodulatory Properties

- Exogenous (CLDN6-K562) results replicated in endogenous (OV90) cell line model
- Cytokine production happens well above the concentration of maximal killing (EC50 = 0.049 nM) in OV90 cells at 48 hours

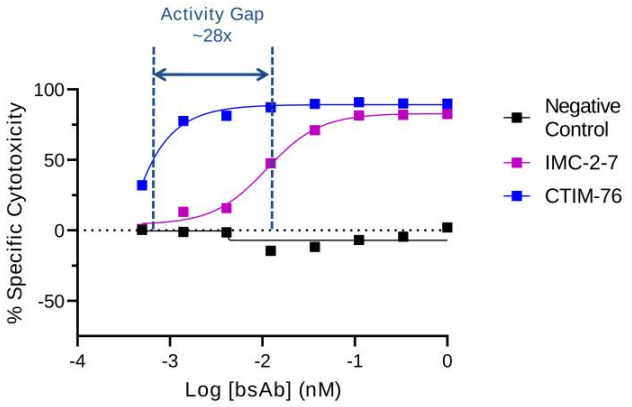
Comparison of **T cell-dependent cellular cytotoxicity (TDCC) to cytokine production in OV90 cell line**

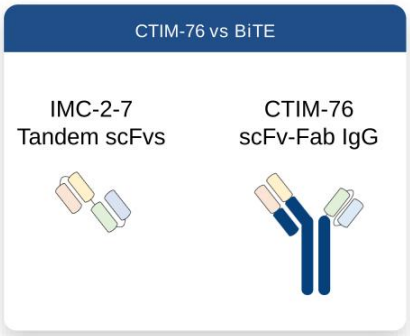


Study Design:OV90 cells stably expressing luciferase were co-cultured with human T cells at an E:T ratio of 10:1 for 48 hours. Cytotoxicity was determined by luminescence imaging.

Role of Bispecific Format in Activity

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





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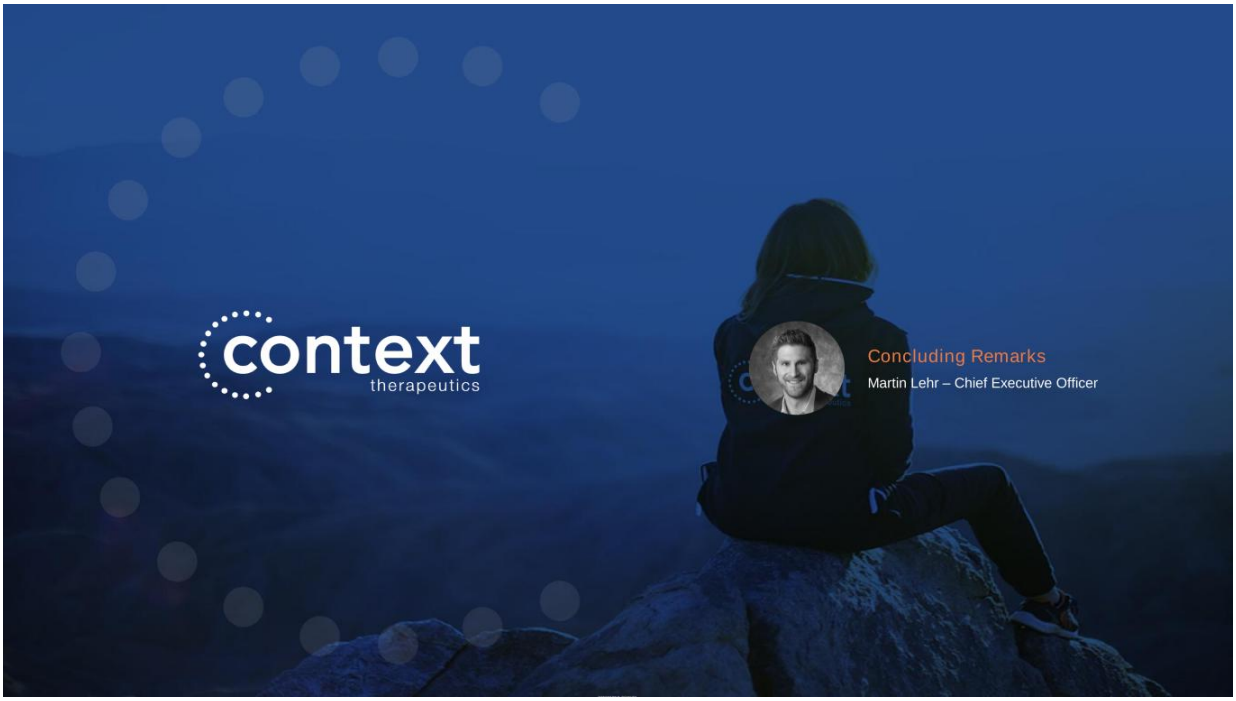
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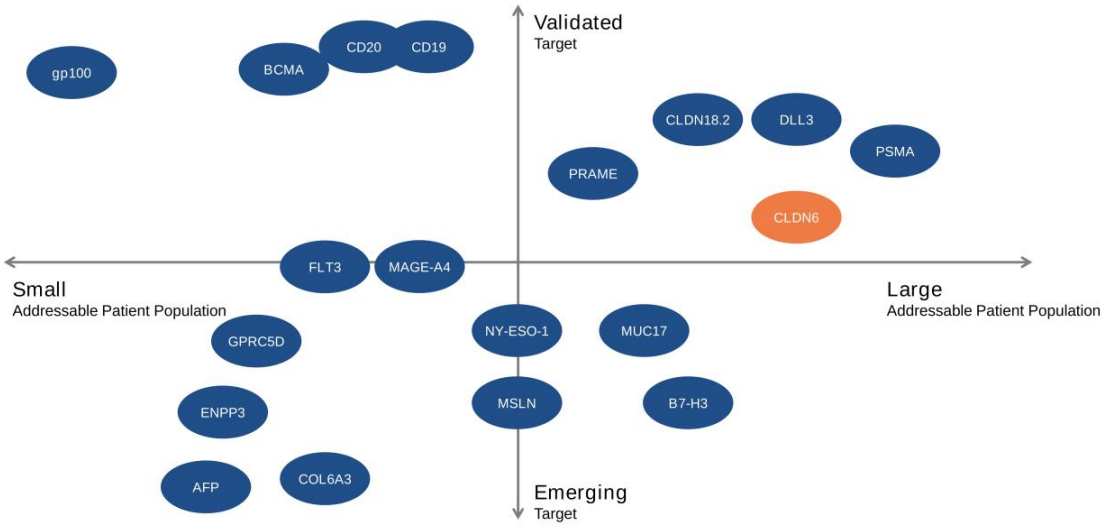
Concluding Remarks
Martin Lehr – Chief Executive Officer

CLDN6 is an Exciting Cancer Target Within the T-cell Directed Therapy Landscape[1]



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

Competitive Landscape[1]

	Candidate	IND	Phase 1
ADC	GB-7008-01 CLDN6/CLDN9 + MMAE UCLA-23-ADC CLDN6 + MMAE		DS-9606a CLDN6 + DXd
Bispecific Antibody	NBL028 Fc Engineered CLDN6x4IBB Undisclosed 2+1 bsAb CLDN6xCD3 CTIM-76 bsAb CLDN6xCD3 TJ-46CB 2+2 bsAb CLDN6x4IBB		AMG794 BiTE CLDN6xCD3 BNT142 mRNA encoded BsAb CLDN6xCD3
Cell Therapy			CAR-NK CAR-NK + IL7 secreting vector BNT211 CAR-T + CARVac

1 Analysis based upon publicly available information

Clinical Experience for CLDN6 Therapies is Nascent

	Company	Program	Description / Details[3]
Active Programs	BioNTech	BNT211: CLDN6CAR-T + CARVac (Phase 1)	Initial data for BNT211 was 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 was presented April 2022 (AACR), trial is not yet recruiting
	Guangzhou Medical University	Undisclosed: 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 + DXd (Phase 1)	Initiated Phase 1 development for DS-9606a in mid-2022
	I-Mab	TJ-46CB: CLDN6 bsAb CLDN6x4IBB (Preclinical)	Initial data was presented April 2021 (AACR), IND filing is expected in 2H 2023
	Xencor	Undisclosed: CLDN6 bsAb CLDN6xCD3 (Preclinical)	Initial data was presented April 2021 (AACR), no timeline to IND provided
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: CLDN6/9 ADC (Phase 1)	Dose-limiting toxicity 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 November 28, 2022

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

Licensee	Licensor	Target	Asset	Stage	Geography	Upfront ($M)	Milestones ($M)
TeneoTwo	AstraZeneca	CD19	TNB-486	Phase 1	WW	$100	$1,165
Macrogenics	Gilead	CD123	MGD024	IND	WW	$60	$1,700
LAVA	Seagen	EGFR	LAVA-1223	Preclinical	WW	$50	$650
Kelun	Merck	Claudin 18.2	SKB315	Preclinical	WW (ex-China)	$35	$910
CSPC	Elevation	Claudin 18.2	STSA1801	Preclinical	WW (ex-China)	$27	$148
LaNova	Turning Point / BMS	Claudin 18.2	LM-302	IND	WW (ex-China, Korea)	$25	$575
Harbour	AstraZeneca	Claudin 18.2	HBM7022	Preclinical	WW	$25	$350

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

Next Steps and Summary

Encouraging efficacy signals

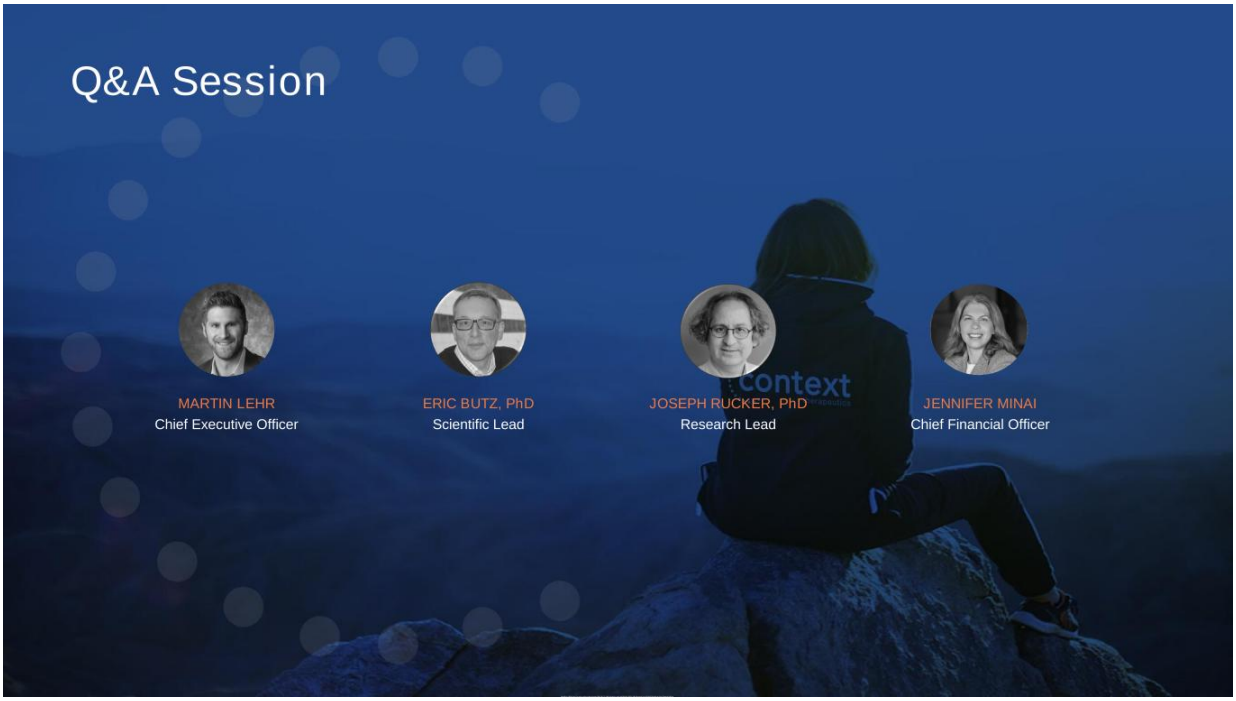
- CLDN6-selective activity across binding and cytotoxicity

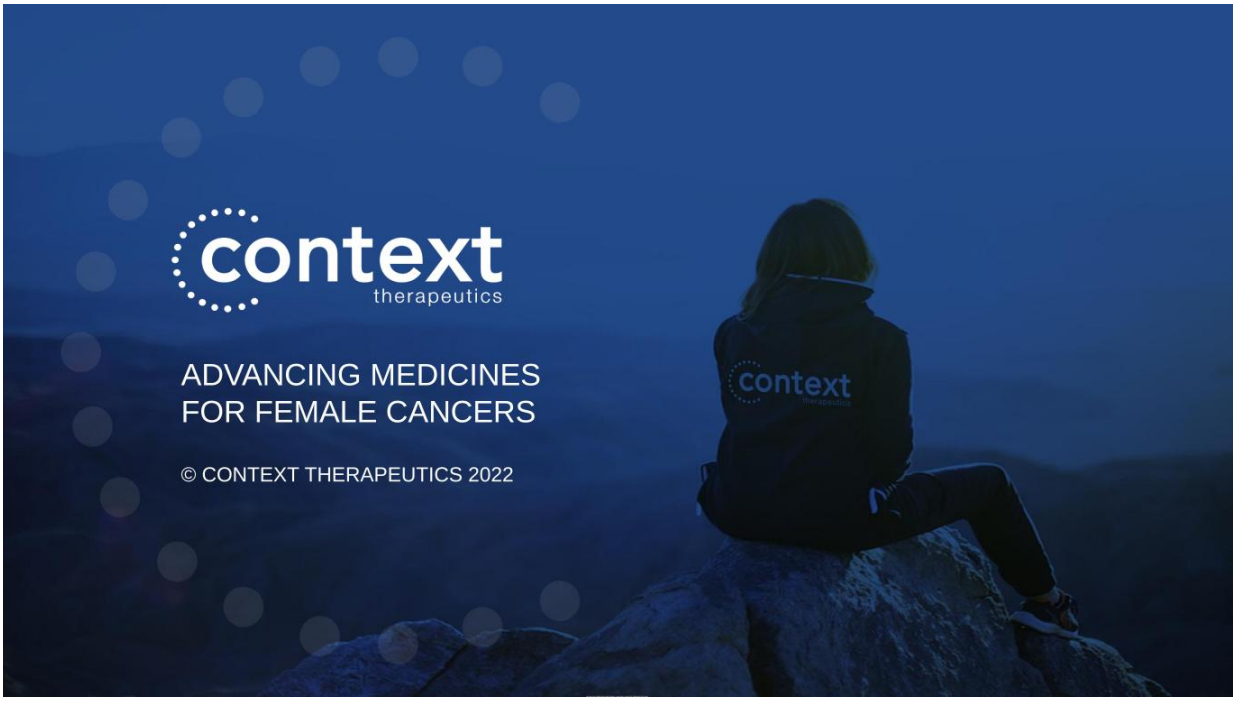
Well tolerated

- Preferential cytotoxicity over activation of free circulating cytokines
- PK consistent with IgG backbone
- No significant safety findings to date

On track for IND submission in Q1 2024

- Lonza selected as GMP manufacturing partner


Q&A Session
MARTIN LEHR
Chief Executive Officer
ERIC BUTZ, PhD
Scientific Lead
JOSEPH RUCKER, PhD
Research Lead
JENNIFER MINAI
Chief Financial Officer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