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): January 4, 2023

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 January 4, 2023, Context Therapeutics Inc. (the "Company") issued a press release to provide 2023 corporate priorities and pipeline milestones. 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 January 4, 2023, the Company also updated its corporate presentation for use in meetings with investors, analysts and others. A copy of the corporate 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 9.01. Exhibits.

(d) Exhibits

Exhibit No.	**Description**
99.1	Press Release issued by Context Therapeutics Inc., dated January 4, 2023
99.2	Context Therapeutics Inc. Corporate Presentation - January 2023
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: January 4, 2023

Context Therapeutics Inc.

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

Context Therapeutics® Highlights 2023 Corporate Priorities and Pipeline Milestones

CTIM-76 nominated as Claudin 6 x CD3 bispecific antibody clinical candidate

Encouraging endometrial and breast cancer data in ongoing ONA-XR Phase 2 trials, with additional data updates expected in 2023

ELONA breast cancer trial open and enrolled first patient

PHILADELPHIA, PA— Jan. 4, 2023—Context Therapeutics Inc. (“Context” or the “Company”) (Nasdaq: CNTX), a clinical-stage biopharmaceutical company developing novel treatments for solid tumors, with a primary focus on female cancers, today provided 2022 year-end updates and corporate guidance for 2023.

"I am proud of the substantial progress the Context team made in 2022. We achieved key corporate milestones including nominating CTIM-76 as our Claudin 6 (CLDN6) bispecific antibody clinical candidate and delivering preliminary data in clinical trials of onapristone extended release (ONA-XR), our highly potent and selective progesterone receptor antagonist," said Martin Lehr, CEO of Context. "In 2023, we will continue to advance ONA-XR across the endometrial (OATH) and breast (SMILE and ELONA) cancer clinical trials. We expect to provide a clinical data update from the ongoing OATH Phase 2 trial in mid-2023, as well as a Phase 2 data update and Phase 1b data from the SMILE and ELONA breast cancer trials, respectively, in Q4 2023. In addition, we look forward to rapidly advancing CTIM-76 toward IND submission in Q1 2024."

Key Highlights

- **CTIM-76 nominated as CLDN6 x CD3 bispecific antibody clinical candidate**
  - During Q4 2022, Context presented preclinical data introducing CTIM-76 as a differentiated, potent, and selective CLDN6-directed immunotherapy. CLDN6 is an emerging, potentially high-value oncology target that is expressed in a broad range of cancers and CLDN6 expression is associated with a poor prognosis and diminished survival in cancer patients. The Company estimates that there are approximately 62,000 patients in the United States with CLDN6-positive metastatic cancers, including lung, ovarian, endometrial, gastric, and testicular cancers. Currently, there are no FDA-approved treatments targeting CLDN6. In cell-based assays, CTIM-76 was found to be over 1,000 times more selective for CLDN6 versus CLDN9, a structurally similar protein that unlike CLDN6 is associated with potential off-target side effects. Further, CTIM-76 was also found to be approximately 28 times more potent than a competing approach utilizing a bispecific T-cell engager (BiTE) format. These data were presented during a R&D webinar hosted by Context in December 2022. IND-enabling studies are scheduled for 2023 with an IND filing to support human clinical trials expected in Q1 2024.
- **ONA-XR ongoing Phase 2 trials show encouraging endometrial and breast cancer data**
  - **Endometrial cancer (OATH trial)**: Metastatic endometrial cancer is an aggressive cancer of the uterus that results in approximately 13,000 deaths per year in the United States. Current treatments are limited, with combination platinum and taxane chemotherapy being the standard of care. Clinician and patient feedback indicates a high unmet need for a novel therapeutic that provides chemotherapy-like efficacy but with fewer side effects. Initial data from a Phase 2 investigator-led clinical trial found that the combination of ONA-XR with anastrozole in progesterone receptor-positive (PR+) metastatic endometrial cancer demonstrated a 4-month progression free survival (PFS) rate of 77%, a 12-month PFS rate of 33%, and favorable safety and tolerability in patients who had failed at least one prior chemotherapy in the metastatic setting. Preliminary results suggest that ONA-XR exhibits a favorable efficacy and tolerability profile relative

to chemotherapy, the standard of care, which in a similar treatment setting demonstrated a 3.8-month median PFS in the KEYNOTE-775 Phase 3 trial[1]. In the KEYNOTE-775 trial, chemotherapy demonstrated a limited durability of effect as only 4% of patients treated with chemotherapy were progression free at 12 months, and chemotherapy resulted in significant toxicity with 72.9% of patients exhibiting a Grade 3 or higher adverse event. Initial clinical results from the endometrial trial were presented in Context's Q3 2022 earnings release and additional data are expected in mid-2023.
    - **Breast cancer (SMILE trial)**: Metastatic breast cancer results in approximately 43,250 deaths per year in the United States. Primary treatment in the metastatic setting is antiestrogen plus CDK4/6 inhibitor combination therapy. CDK4/6 resistance is a clinical challenge due to the activation of resistance mechanisms that limit the utility of current standard-of-care treatments, including fulvestrant, after prior CDK4/6 inhibitor exposure. Initial data from a Phase 2 investigator-led clinical trial found that the combination of ONA-XR with fulvestrant in estrogen receptor-positive (ER+), HER2- locally advanced or metastatic breast cancer demonstrated a 4-month PFS rate of 44%, and favorable safety and tolerability in patients who had failed prior CDK4/6 inhibitor therapy in the metastatic setting. Preliminary results suggest that ONA-XR in combination with fulvestrant exhibits a favorable efficacy and tolerability profile relative to fulvestrant alone, which in a similar treatment setting to the SMILE trial, fulvestrant demonstrated a 1.9-month median PFS in the EMERALD Phase 3 trial[2]. The initial clinical results of the SMILE trial were presented in December 2022 at the San Antonio Breast Cancer Symposium and additional data are expected in Q4 2023.
- **ELONA Phase 1b/2 breast cancer trial open and enrolled first patient**: In January 2023, Context enrolled the first patient in the ELONA study, an open-label, Phase 1b/2 breast cancer clinical trial being conducted in partnership with The Menarini Group ("Menarini"). The ELONA study is designed to explore the efficacy of ONA-XR in combination with elacestrant, Menarini's selective estrogen receptor degrader, in patients with locally advanced or metastatic breast cancer who have received prior treatment with a CDK4/6 inhibitor. In Menarini's recently completed EMERALD Phase 3 trial, elacestrant demonstrated a 0.9-month PFS improvement versus the standard-of-care fulvestrant (2.8 vs 1.9 months) in a similar treatment population and as a result may become the standard-of-care antiestrogen treatment[2]. Compared to elacestrant alone, Context believes that the combination of ONA-XR plus elacestrant may more completely inhibit progesterone and estrogen hormone signaling that is required for breast cancer growth and metastasis. Such a combination would potentially improve outcomes in patients without adding significant toxicity.

Cash Guidance

The Company had cash and cash equivalents of $39.4 million as of September 30, 2022. The Company expects its current level of cash and cash equivalents will enable the Company to fund its operations into Q1 2024.

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

References

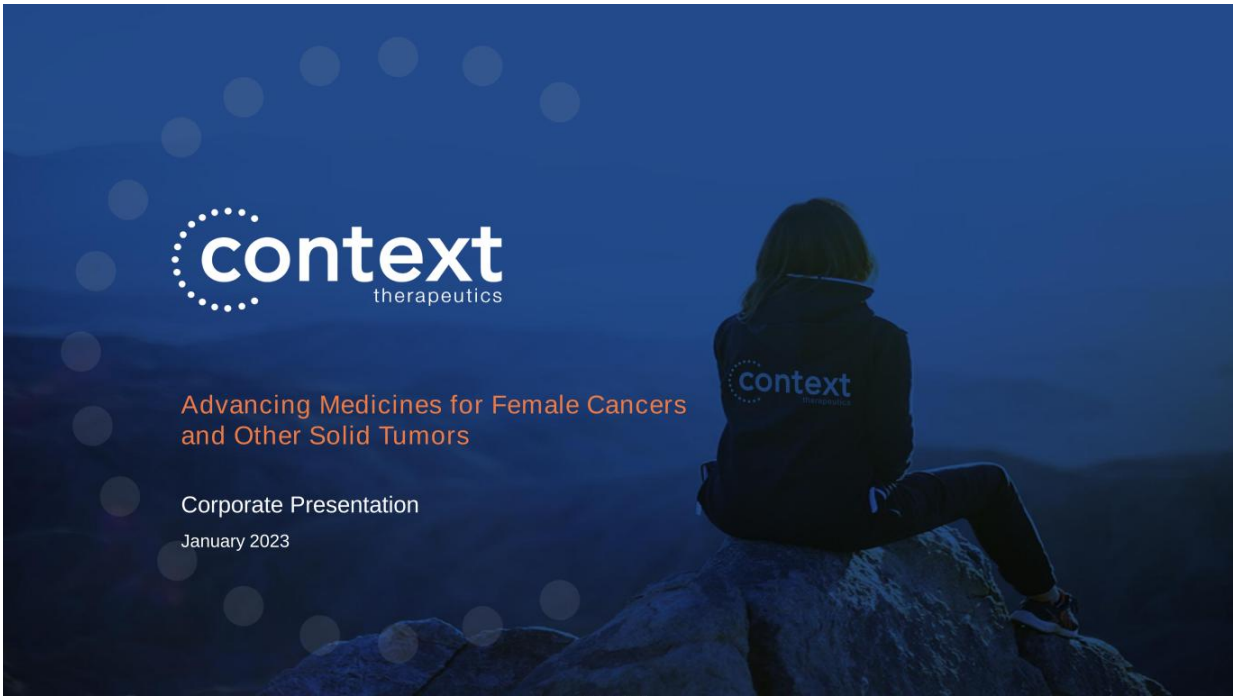
[1] Makker V, et al.; KEYNOTE-775 Investigators. Lenvatinib plus Pembrolizumab for Advanced Endometrial Cancer. N Engl J Med. 2022 Feb 3;386(5):437-448.

[2] Bidard FC, et al; EMERALD Investigators. Elacestrant Versus Standard Endocrine Therapy for Estrogen Receptor-Positive, Human Epidermal Growth Factor Receptor 2-Negative Advanced Breast Cancer: Results From the Randomized Phase III EMERALD Trial. J Clin Oncol. 2022 Oct 1;40(28):3246-3256.

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 expectation to provide a clinical data update from the OATH trial in mid-2023, as well as a Phase 2 data update from the SMILE trial and Phase 1b data for the ELONA trial in the fourth quarter of 2023, (ii) the expectation to have an IND submission for CTIM-76 in the first quarter of 2024, (iii) the selectivity, potency, and safety profile of CTIM-76, (iv) the timing, enrollment and results of our clinical trials, (v) the potential benefits and side effect profile of our product candidates, (vi) the likelihood data will support future development, and (vii) 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.

Media Contact:
Gina Cestari
6 Degrees
917-797-7904
gcestari@6degreespr.com

Investor Relations Contact:
Laine Yonker
Edison Group
lyonker@edisongroup.com


context
therapeutics
Advancing Medicines for Female Cancers
and Other Solid Tumors
Corporate Presentation
January 2023
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.

Context Therapeutics Overview

Our Mission	• Advancing medicines for solid tumors, with a primary focus on female cancers
CTIM-76 CLDN6 x CD3 bispecific antibody	• Claudin 6 (CLDN6) is uniquely expressed in a broad range of solid tumors, including ovarian and endometrial • CTIM-76 is Context's CLDN6 x CD3 bispecific antibody Development Candidate • CTIM-76 is selective for CLDN6 over other CLDN proteins, reducing the risk of potential off target side effects • IND submission on track for Q1 2024
ONA-XR oral PR antagonist	• ONA-XR is a novel, potentially first-in-class progesterone receptor (PR) antagonist • PR signaling drives metastasis and immune evasion in breast, endometrial, and ovarian cancer • Encouraging clinical activity and safety in ongoing Phase 2 endometrial cancer (post-chemotherapy) and breast cancer (post-CDK4/6 inhibitor) trials[1,2] • Clinical collaboration in metastatic breast cancer (post-CDK4/6 inhibitor) ongoing with the Menarini Group to evaluate combination of Menarini's novel selective estrogen receptor degrader, elacestrant, with ONA-XR
Cash Guidance	• Expected cash runway into Q1 2024

1 Data cut off as of September 30, 2022; preliminary raw data
2 Kamaraju, San Antonio Breast Cancer Symposium, 2022

Pipeline Highlights

Cancer	Clinical Indication	Preclinical	Phase 1 Clinical	Phase 2 Clinical	Milestones
CTIM-76 (CLDN6xCD3 bispecific antibody)					
	CLDN6-positive cancers				Candidate selection Q4 2022 ☑ IND submission Q1 2024
ONA-XR (PR antagonist)[1]					
Endometrial Cancer	Recurrent PR+ Endometrioid Combination with anastrozole in post-chemotherapy treated patients		Phase 2 Trial OATH Trial*		Initial data Q4 2022 ☑ Data update mid-2023
Breast Cancer	2L/3L ER+,PR+,HER2- Combination with elacestrant in post-CDK4/6 inhibitor treated patients		Phase 1b/2 ELONA Trial		Initiated Q4 2022 ☑ Phase 1b data Q4 2023
	2L/3L ER+,HER2- Combination with fulvestrant in post-CDK4/6 inhibitor treated patients		Phase 2 SMILE Trial*		Initial data Q4 2022 ☑ Data update Q4 2023

1 Tyligand Biosciences Ltd licensed rights to ONA-XR in China, HK, Macau
* Investigator Sponsored Trial

2022 Highlights and Future Milestones

CTIM-76	2H 2022	1H 2023	2H 2023	1H 2024
Candidate selection	✓			
Preclinical update		●		
IND submission				●

ONA-XR	2H 2022	1H 2023	2H 2023	1H 2024
Endometrial – OATH trial Phase 2 initial data	✓			
Endometrial – OATH trial Phase 2 data update		●		
Endometrial – OATH trial Phase 2 top line data			●	
Breast – ELONA trial Phase 1b data			●	
Breast – SMILE trial Phase 2 initial data	✓			
Breast – SMILE trial Phase 2 data update			●	
Breast – SMILE PK/PD data (^{18}F-FFNP)			●	


CTIM-76
CLDN6xCD3 bispecific antibody
context
therapeutics

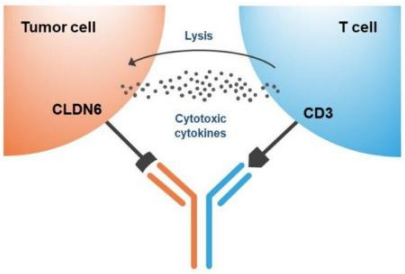
Emerging Role of Bispecific Antibodies in Treating Solid Tumors

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 Antibodies are a Hot Field for Drug Development

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



CLDN6 x CD3 bispecific antibody

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	WW	$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
Unmet Need	• Selectivity: limited off target effects • Potency: effective tumor killing • Safety: 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 United States in the Relapse/Refractory Setting

Initial indications of interest based on:

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

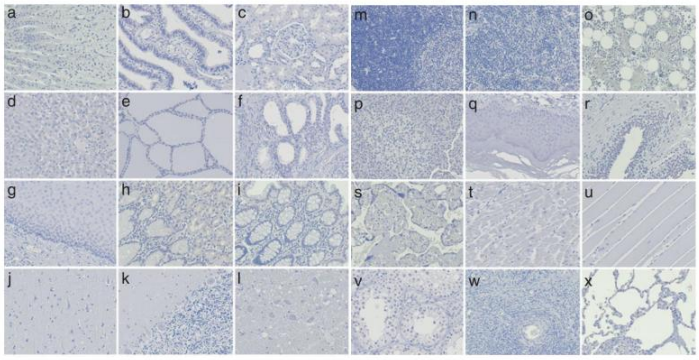
Selected Cancer indications	Incidence	Relapse / Remitting (R/R) Incidence	CLDN6 Positive	Patient Population Based on R/R Incidence
Testicular	9,910	400	95%[1]	380
Ovarian	19,900	12,800	54-55%[1,2]	6,982
NSCLC (lung)	201,229	110,653	6-50%[3,4,5]	35,221
Malignant Rhabdoid	50	500	29-44%[1,2,6,7]	183
Gastric (stomach)	26,380	11,090	13-55%[8,9]	3,771
Breast	290,600	43,800	2-41%[1,10,11]	9,417
Endometrial (uterus)	65,900	12,500	20-31%[1,12,13]	3,188
Glioma (brain)	19,000	10,000	21%[8]	2,100
Urothelial (bladder)	81,180	17,100	2-8%[1,13]	855
SCLC (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.

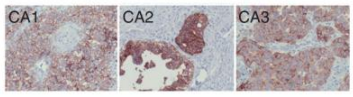
CLDN6 is Enriched in Cancer Cells vs. Non-Cancer Cells

Non-cancer, Healthy Cells



(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 Cells

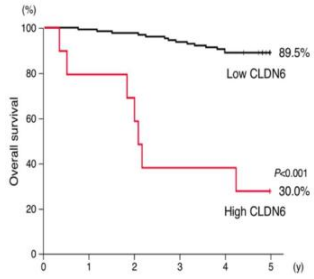


(CA1) testicular cancer, (CA2) ovarian cancer, and (CA3) lung cancer

Reinhard, Science, 2020

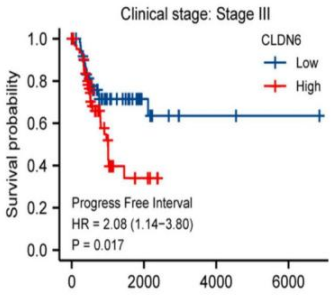
High CLDN6 Associated with a Worsened Prognosis in Cancer Patients

Endometrial Cancer[1]



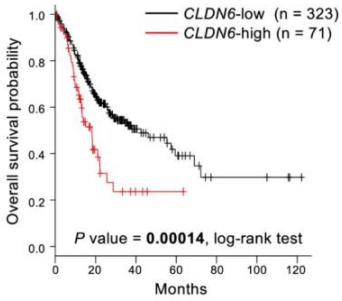
Overexpression of CLDN6 is associated with worse overall survival in endometrial cancer patients

Bladder Cancer[2]



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

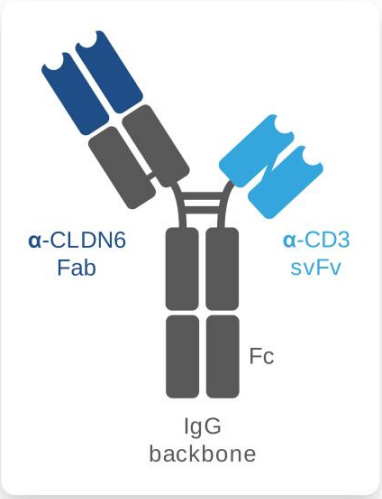
Stomach Cancer[3]



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 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 receptor. A mutation has been inserted into 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

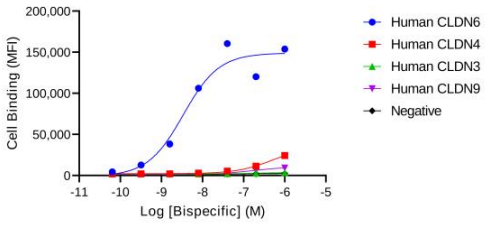
- T-cell dependent cellular cytotoxicity with no or minimal activation of circulating cytokines
- Humanized CLDN6 and CD3 binding domains

Ease of manufacturing

- IgG backbone is highly stable and enables high yield

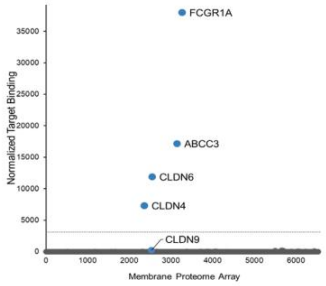
CTIM-76 Exhibits Excellent Selectivity and Specificity

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

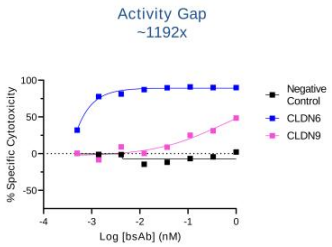


- IM301 Mab (CLDN6 Fab arm of CTIM-76) screened for specificity using Integral Molecular Membrane Proteome Array, consisting of ~6,000 human membrane proteins in their native state in unfixed cells
- IM301 Mab was cross-reactive for internal control FCGR1A (Fc gamma) and nonrelevant intracellular epitope of ABCC3

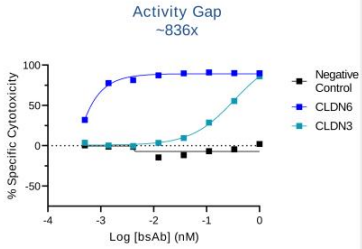
CTIM-76 Preferentially Targets CLDN6 Over Other Claudin Family Proteins

- 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

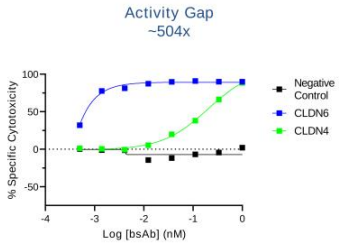
CLDN6:CLDN9



CLDN6:CLDN3



CLDN6:CLDN4



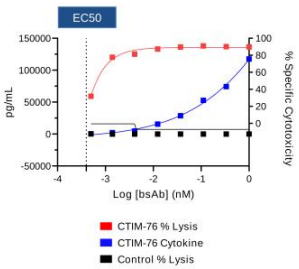
Study Design: K562 cells stably over-expressing CLDN3, CLDN4, CLDN6, or CLDN9 were co-cultured with human T-cells at an E:T ratio of 10:1 for 48 hours. Cytotoxicity was determined by luminescence imaging.

CTIM-76 has the Potential for a Wide Therapeutic Window

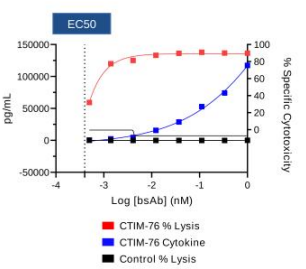
- Data supports potential to dose at levels that promote cancer cell killing but have manageable levels of free cytokine production, thereby potentially reducing the risk of cytokine release syndrome
- Cytokine production evaluated in exogenous (CLDN6-K562) cell line model at 48 hours
- Cytokine production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

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

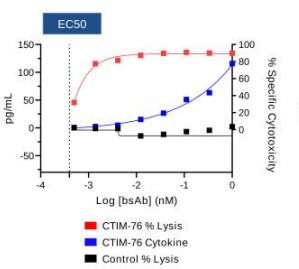
TDCC vs IFNg



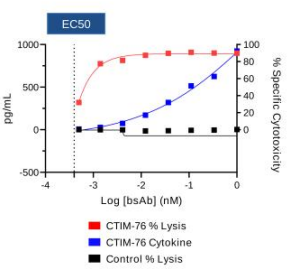
TDCC vs IL2



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.

CLDN6 Competitive Landscape[1]

	Candidate	IND	Phase 1
Antibody Drug Conjugate (ADC)	GB-7008-01 CLDN6/CLDN9 + MMAE UCLA-23-ADC CLDN6 + MMAE		DS-9606a CLDN6 + DXd
Bispecific Antibody	NBL028 Undisclosed 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 on publicly available information compiled as of January 1, 2023

Clinical Experience for CLDN6 Therapies is Nascent

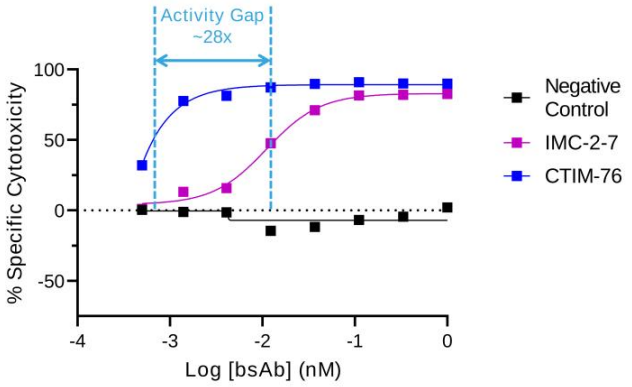
	Company	Program (Development Stage)	Description / Details[3]
Active Programs	BioNTech	BNT211: CLDN6CAR-T + CARVac (Phase 1)	Initial data for BNT211 were presented April 2022 (AACR), with an update in Sept 2022 (ESMO). Received PRIME Designation for testicular cancer June 2022
		BNT142: CLDN6 mRNA encoded 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	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 were presented April 2021 (AACR), IND filing is expected in 2H 2023
	Xencor	Undisclosed: CLDN6 bsAb CLDN6xCD3 (Preclinical)	Initial data were 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, potentially attributed to CLDN9 binding[2]

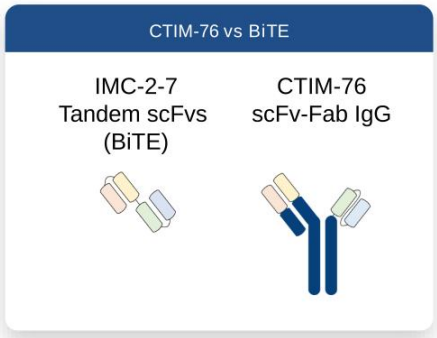
1 Adra, Invest New Drugs, 2022
2 Hamilton, Cancer Res, 2020

3 Analysis based on publicly available information compiled as of January 1, 2023

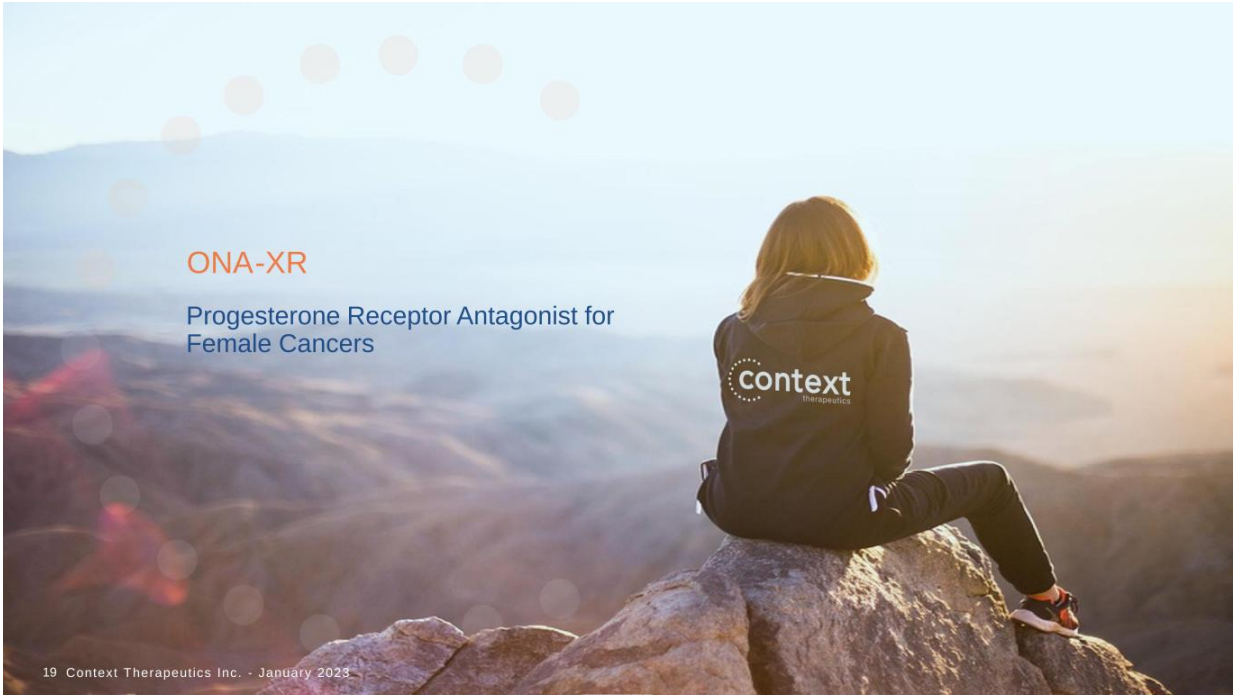
Role of Bispecific Format in Activity

CTIM-76 format demonstrates superior potency compared to a traditional BiTE molecule (e.g., AMG-794)



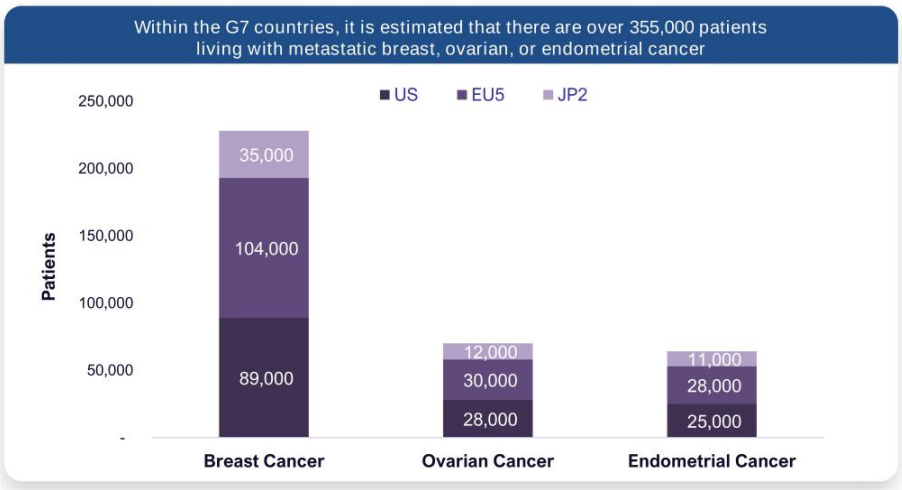


Study Design: K562 cells stably expressing CLDN6 and luciferase were co-cultured with human T-cells at an E:T ratio of 10:1 for 48 hours. Cytotoxicity was determined by luminescence imaging.


ONA-XR
Progesterone Receptor Antagonist for Female Cancers
context
therapeutics

Unmet Need in Female Cancers

Prevalence of Metastatic Female Cancers in EU5, Japan, and US



Source: secondary epidemiologic estimates, 2020 estimates

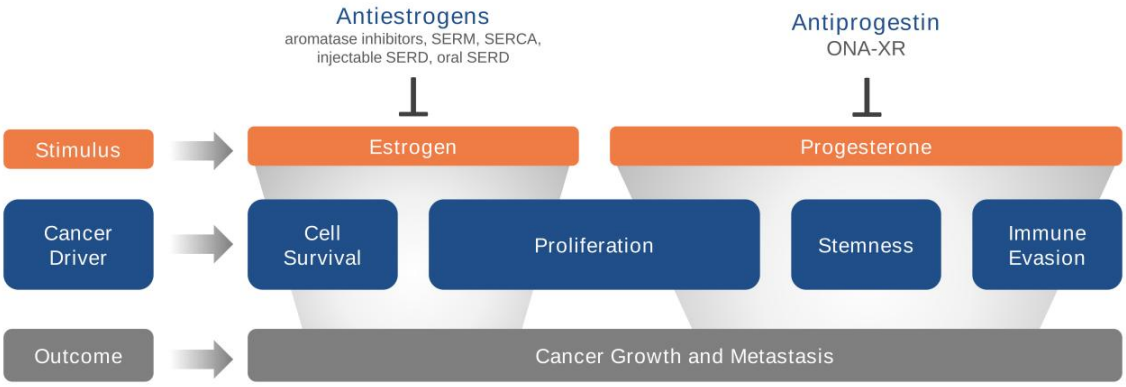
Onapristone Extended Release (ONA-XR)

- Progesterone Receptor (PR) oncogenic signaling is associated with female cancers and is a potential resistance mechanism to standard of care treatments including antiestrogens and CDK4/6 inhibitors
- Onapristone (ONA) is a progesterone receptor (PR) antagonist that suppresses PR oncogenic signaling
- Over 150 patients treated to date across female cancers
- Encouraging Phase 2 clinical data in ongoing breast (SMILE) and endometrial (OATH) cancer trials

Most Complete PR Antagonist	Easy Administration	Minimal Side Effects	Broad Activity	CNS Activity
Blocks both ligand-dependent and ligand-independent PR activation	Attractive pharmacokinetic profile; 50 mg orally administered at morning and night with or without food	Favorable clinical tolerability and safety as monotherapy and in combination with antiestrogens (anastrozole, fulvestrant)	Meaningful antitumor activity in both wild-type and mutant (ESR1, PIK3CA) preclinical models and durable benefit in clinical settings	Brain metastases are common with breast cancer; ONA-XR is CNS penetrant with demonstrated activity in nonclinical meningioma studies

Mechanism of Action

- Antiestrogen therapy is the backbone treatment for female cancers, whereas there are no FDA-approved antiprogestin therapies approved for cancer
- Estrogen and progesterone play unique roles in regulating the drivers of cancer growth and spread
- Combining antiestrogen and antiprogestin therapy may more completely block cancer drivers and ultimately improve patient outcomes



Completed Clinical Trials

Summary of select clinical trials evaluating onapristone with immediate (IR) or extended release (XR) formulation

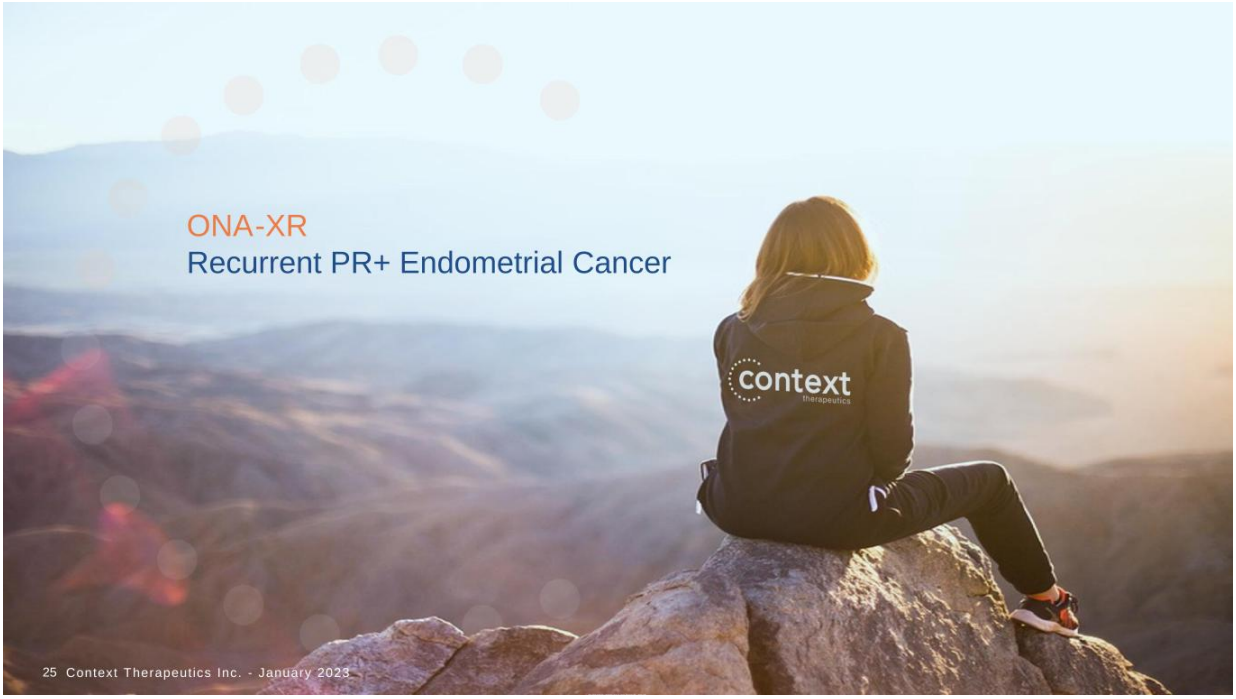
Onapristone Treatment	Stage	Patients (n)	Clinical Indication	Prior Treatments Median (range)	Biomarker	Data
IR (100 mg QD)	Ph 2	19	Breast Cancer First line (1L) advanced or metastatic	Hormone naïve		56% ORR[1] 67% CBR 14.0 month PFS
IR (100 mg QD)	Ph 2	101	Breast Cancer Second line (2L) advanced or metastatic	1 (1-2)		10% ORR[2] 48% CBR 4.0 month PFS
XR (50 mg BID)	Ph 2	14	Granulosa Cell Tumor of Ovary Advanced or Metastatic	4 (2-17)	PR+	35% CBR[3] 12 month PFS rate of 20%
XR (10-50 mg BID)	Ph 1	13	Ovarian Cancer Advanced or Metastatic	4 (2-10)	PR+	8% ORR[4] 6 month PFS rate of 31%
XR (10-50 mg BID)	Ph 1	20	Breast Cancer Advanced or Metastatic	9 (2-14)	PR+	25% DCR[4] 6 month PFS rate of 15%

IR = immediate release; XR = extended release
1 Robertson, Eur J Cancer, 1999
2 Jonat, Endocrine Therapy of Breast Cancer, 2002
3 Grisham, ASCO Annual Meeting 2022
4 Cottu, PLoS One, 2018

Key Ongoing Clinical Trials

Treatment	Clinical Indication	Stage	Patients (n)	Key Inclusion and Exclusion Criteria	Ongoing Trial Data	Completed Trials / Historical Data[2]
ONA-XR + Anastrozole[1]	Endometrial Cancer OATH Trial	Ph 2	25	• Must have received at least one prior treatment with a platinum plus taxane chemotherapy	• 12 patients enrolled • 4-month PFS rate of 77% • 12-month PFS rate of 33% • No treatment-related SAE	Chemotherapy (KEYNOTE-775)[3] • 3.8 month PFS • 72% Grade 3 or higher AE Anastrozole (PARAGON)[4] • 2.8 month PFS
ONA-XR + Fulvestrant[1]	Breast Cancer (2L/3L) SMILE Trial	Ph 2	39	• Must have received prior CDK4/6 inhibitor therapy • One line of prior chemotherapy in metastatic setting allowed	• 10 patients enrolled • 4-month PFS rate of 44% • No treatment-related SAE	Elacestrant (EMERALD)[6] • 2.8 month PFS Fulvestrant (EMERALD)[6] • 1.9 month PFS
ONA-XR + Elacestrant	Breast Cancer (2L/3L) ELONA Trial	Ph 1b/2	67	• Must have received prior CDK4/6 inhibitor therapy • ≥50% patients with ESR1 mutant • No prior chemotherapy in metastatic setting	• Initiated Q4 2022 • First patient enrolled Jan 2023 • Ph 1b data expected Q4 2023	Elacestrant (EMERALD)[6] • 2.8 month PFS Fulvestrant (EMERALD)[6] • 1.9 month PFS

1 Data cut off as of September 30, 2022; preliminary raw data
2 Analysis based upon publicly available information and represents a non-head-to-head summary comparison
3 Makker, NEJM, 2022
4 Mileshkin, Gyn Onc, 2019
5 Grisham, ASCO 2022
6 Bidard, JCO, 2022


ONA-XR
Recurrent PR+ Endometrial Cancer
context
therapeutics

Endometrial Cancer

- Endometrial cancer is the 4th most common cancer in women
  - Endometrial cancer is on the rise and is linked to obesity[1,2]
  - 12,500 patient deaths per year in the US[3]
  - Market is projected to grow from $1.5bn in 2020 to $5.1bn in 2029[5]
- Hormone signaling is a driver of endometrial cancer
  - Endometrial cancer is thought to be caused by excess hormone production that leads to endometrial hyperplasia and cancer
- Chemotherapy and surgery remain first-line treatments
  - First-line treatment includes surgical removal of uterus, ovaries, and fallopian tubes followed by platinum/taxane chemotherapy
  - PD-1 antibodies (Keytruda, Jemperli) were recently approved in MSI-H and dMMR genetic subpopulations post-chemotherapy (~13-30% of population)[5]
  - Lenvima + Keytruda combination therapy is approved post-chemotherapy, however, tolerability can be challenging for patients[6]
- Antiestrogen therapy is currently used off-label
  - Hormonal therapy is an alternative treatment for patients who wish to preserve their fertility, and for those with metastatic or recurrent disease without curative options

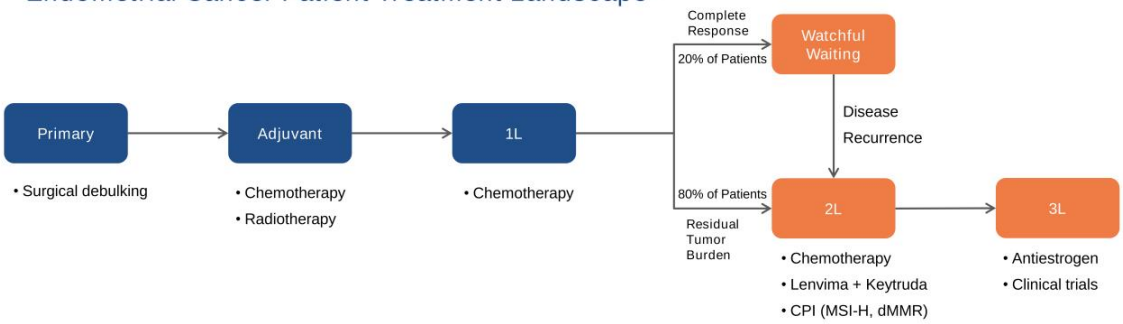
12,500 patients have recurrent endometrial cancer that cannot be fully removed via surgery [2]

34%

of endometrial cancer patients are PR+[4]

1 American Cancer Society, Endometrial Cancer Risk Factors. (accessed Nov. 4, 2022)
2 Epic Oncology (Incidence, 1st/ 2nd line treated); epic Oncology physician survey 2019
3 Nation Cancer Institute, Endometrial Cancer Incidence Rising in the US and Worldwide (accessed Nov. 4, 2022)
4 Høgdall, Oncol Rep, 2007
5 Vinuesa and Webster, Nat Rev Drug Disc, 2022
6 Makker, NEJM, 2022

Endometrial Cancer Patient Treatment Landscape[1]



1L First Line (1L)

- Standard of Care (SOC) is carboplatin + paclitaxel
- mPFS of ~12 months

2L Second Line (2L)

- Treatment goal is disease stabilization for 4-6 months
- Lenvima + Keytruda poor tolerability associated with high discontinuation rate in patients

M Maintenance Line

- No approved therapies
- Treatment goal is disease stabilization for ≥4 months and to provide a high quality of life

3L Third Line (3L)

- Limited treatment options

Potential Target Indications for ONA-XR

1 National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology. Uterine Neoplasms. v4.2021

ONA-XR + Anastrozole in PR+ Endometrial Cancer[1]

- Ongoing Phase 2 Trial
  - Investigator-initiated, open-label, multi-center trial (the “OATH” trial) evaluating ONA-XR 50 mg BID in combination with the antiestrogen anastrozole 1 mg QD administered orally to treat women with ER+/PR+ endometrial adenocarcinoma who have received at least one prior platinum/taxane-based chemotherapy regimen
  - Co-primary endpoints: 4-month PFS and ORR
  - Secondary endpoints: DCR, DoR, safety, and quality of life
- Efficacy
  - The study has enrolled 12 of 25 planned patients
  - 9 evaluable patients; completed at least one month of treatment
  - 4-month PFS rate was 77%
  - 12-month PFS rate was 33%
  - 7 patients remain on the trial
- Safety
  - There have been no treatment-related serious adverse events reported
- Updated data anticipated in mid-2023

Treatment Goal in Endometrial Cancer

We seek to deliver chemotherapy-like clinical activity without debilitating toxicity

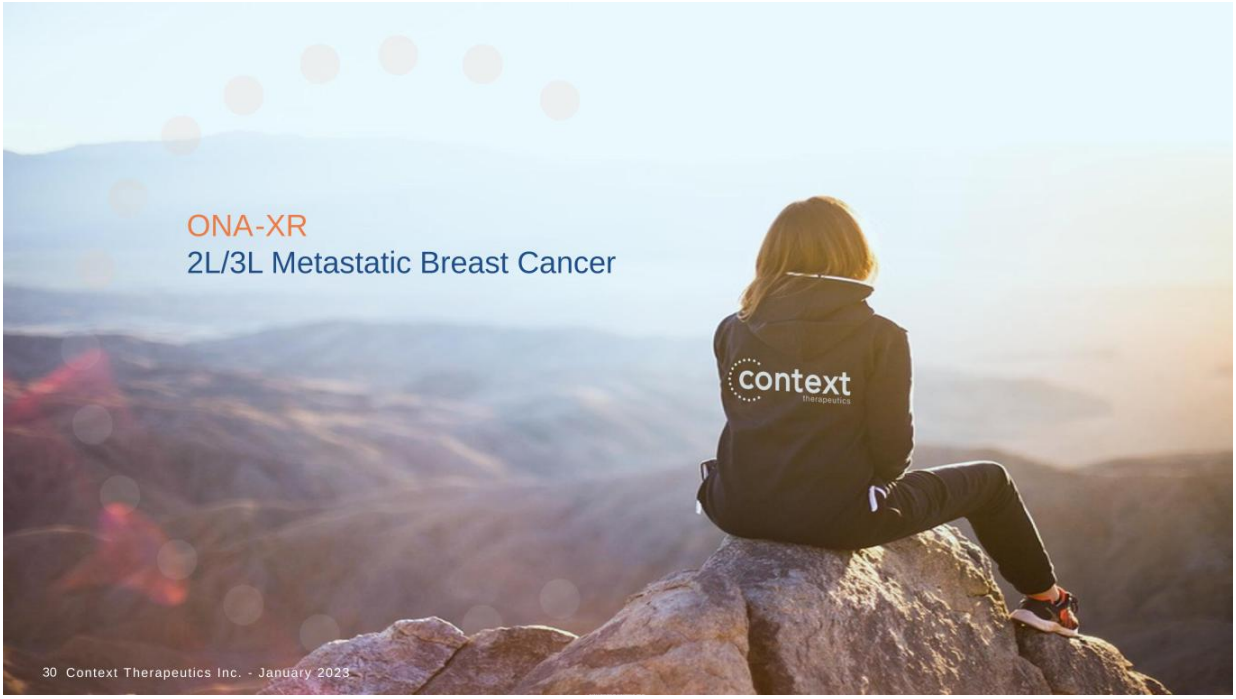
1 Data cut off as of September 30, 2022; preliminary raw data

Preliminary Data vs Historical Trials[1]

	ONA-XR + Anastrozole	ONA-XR	Anastrozole	Chemotherapy
Trial	OATH (ongoing)	Cottu 2018[2]	PARAGON 2019[3]	KEYNOTE-775 2022[4]
Patients (n)	12 (9 evaluable)	12	54	416
Lines of Prior Chemotherapy, n (%) 1 **≥2**	 8 (66) 4 (33)	 4 (33) 8 (66)	 50 (93) 4 (7)	 277 (67) 139 (33)
Treatment free interval (TFI) **≥6 months, n (%)**	4 (33)	1 (8)	36 (70)	ND
4-month PFS rate, n (%)	7 (77)	4 (33)	ND	ND
12-month PFS rate, n (%)	3 (33)	1 (8)	4 (7)	18 (4)
mPFS (95% CI), months	NE	2.0 (1.7-5.3)	2.7 (1.9-4.5)	3.8 (3.6-4.2)
Side Effects	Well tolerated	Well tolerated	Well tolerated	72% experienced Grade 3 or higher AE

1 Analysis based upon publicly available information and represents a non-head-to-head summary comparison. Data cut off as of September 30, 2022; preliminary raw data

2 Cottu, PLoS One, 2018
3 Mileshkin, Gyn Onc, 2019
4 Makker, NEJM, 2022


ONA-XR
2L/3L Metastatic Breast Cancer
context
therapeutics

Hormone Receptor-positive Breast Cancer

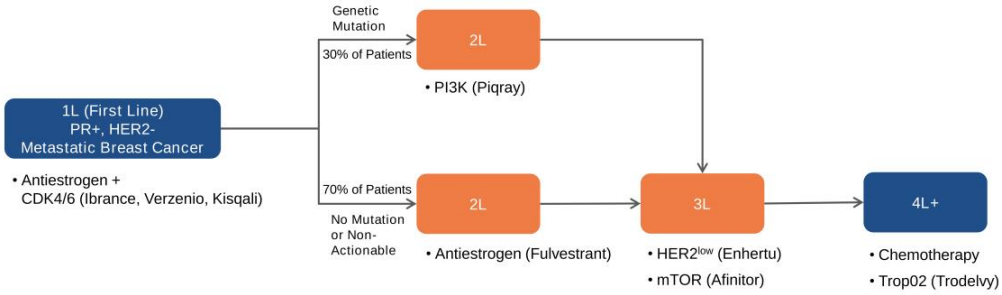
- Breast Cancer is the 2nd most common cancer in women
  - 2L/3L+ therapy, could represent a $3-5B U.S. segment of $20B endocrine therapy market
  - Potential to expand ONA-XR into earlier treatment lines
- Hormone signaling is a driver of breast cancer
  - Approximately 75% of breast cancer patients have hormone-driven, also known as hormone receptor-positive, breast cancer
  - For these patients, antiestrogen therapy is the backbone treatment due to excellent tolerability
- Antiestrogen + CDK4/6 inhibitor is first-line treatment in metastatic setting
  - Patients generally respond well to this treatment and are often on therapy for years
  - Upon first-line relapse (i.e., second-line), there are limited FDA approved treatment options for patients
- Second and third-line metastatic hormone-driven breast cancer is evolving
  - Potential FDA approvals in 2023 for new antiestrogen (elacestrant) and pan-AKT inhibitor (capivasertib)

~43,250 women succumb to metastatic breast cancer in the United States per year

~75%

of breast cancer patients are progesterone receptor positive (PR+)

ONA-XR has the Potential to be Used Across Many Lines of Treatment[1]



1L First Line

- Standard of Care (SOC) is CDK4/6 inhibitor plus antiestrogen
- mPFS of 14-18 months

2L Second Line

- Treatment goal is disease stabilization for >4 months
- Potential new treatments pending FDA approval include antiestrogen (elacestrant) and AKT inhibitor (capivasertib)

3L Third Line

- mTOR associated with significant side effects
- Enhertu anticipated to be approved in HER2^{low} and/or HER2-

Initial Target Indications for ONA-XR

4L Fourth Line

- Limited treatment options

1 National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology. Uterine Neoplasms. v4.2021

Our Development Strategy in 2L/3L HR+,HER2- Metastatic Breast Cancer

- Estimated 115,000 treatment eligible patients in United States and EU5
- Unmet need for new therapies that can improve antiestrogen response after CDK4/6 inhibitor therapy without adding significant toxicity
- New treatments, including antibody drug-conjugate (Enhertu) therapy, expected to be used once patients are no longer responsive to antihormonal therapy

Ongoing Context Clinical Trials in Post-CDK4/6 Treatment Line

	SMILE Trial	ELONA Trial
Patients (n)	39	67
Indication	2L/3L ER+,HER2- mBCa	2L/3L ER+,PR+, HER2- mBCa
Treatment	ONA-XR + fulvestrant	ONA-XR + elacestrant
Key Inclusion / Exclusion	• Must have received prior CDK4/6 inhibitor therapy • One line of prior chemotherapy in metastatic setting allowed	• Must have received prior CDK4/6 inhibitor therapy • ≥50% patients with ESR1 mutant • No prior chemotherapy in metastatic setting
Next Expected Data Milestone	Q4 2023	Q4 2023

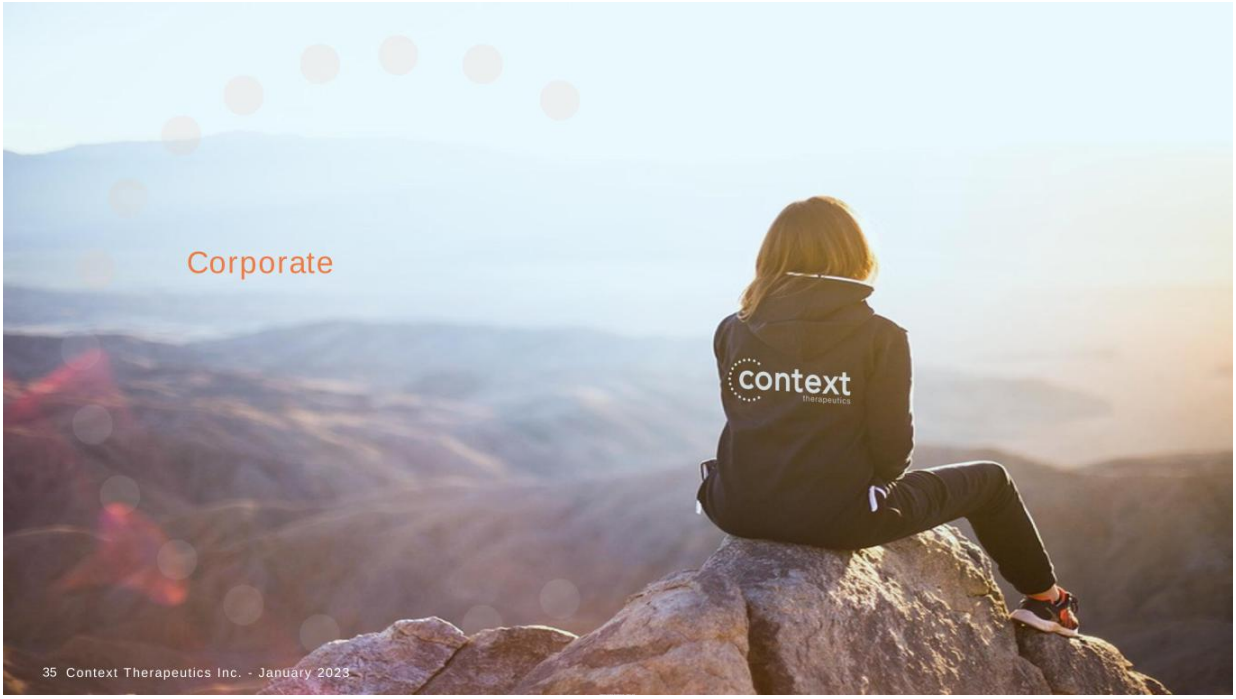
Preliminary Data vs Historical Trials[1]

	ONA-XR + Fulvestrant	Fulvestrant	Elacestrant
Trial	SMILE (ongoing)[2]	EMERALD 2021[3]	EMERALD 2021[3]
Patients (n)	10 (9 evaluable)	238	239
Key Demographics			
Prior CDK4/6 inhibitor	100%	100%	100%
ESR1 mutation	ND	48%	47%
4-month PFS rate, %	44.4	NE	NE
mPFS, months	Trial ongoing	1.91	2.79
Side Effects	Well tolerated	Well tolerated	Well tolerated

1 Analysis based upon publicly available information and represents a non-head-to-head summary comparison. Data cut off as of September 30, 2022; preliminary raw data

2 Kamaraju, SABCS 2022

3 Bardia, SABCS 2021


Corporate
context
therapeutics

Experienced Leadership Team

Martin Lehr
CEO and Director

Jennifer Minai, CPA
Chief Financial Officer

Chris Beck, MBA
SVP Operations

Alex Levit, Esq
Chief Legal Officer

Tarek Sahmoud, MD, PhD
Chief Medical Officer

Priya Marreddy, MS
VP Clinical Operations

Focus on Execution

Experienced team with deep oncology experience

Our CMO led the clinical development of multiple blockbuster drugs for female cancers, 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, Primary Focus on Female Cancers

High-Value Targets

Progesterone Receptor and Claudin 6

Near-Term Milestones

Multiple Data Readouts in 2023

Strong Team

Deep Domain Experience, Track Record of Success

Financial Strength

Expected Cash Runway into Q1 2024


context
therapeutics
Advancing Medicines For Female
Cancers and Other Solid Tumors
© Context Therapeutics 2023
context

Abbreviations

Clinical Trial Efficacy	
CBR (CR+PR+ **SD ≥6** mos)	Clinical benefit rate
CR	Complete response
DCR (CR+PR+ SD)	Disease control rate
DoR	Duration of response
mPFS	Median PFS
ORR (CR+PR)	Overall response rate
PFS	Progression free survival
SD	Stable disease
95% CI	95% confidence interval

Clinical Trial Safety	
AE	Adverse event
DLT	Dose-limiting toxicity
TRAE	Treatment-related adverse event
SAE	Serious adverse event

Diseases	
BC	Breast cancer
GCT	Granulosa cell tumor
NSCLC	Non-small cell lung cancer
SCLC	Small cell lung cancer

Other Terms	
1L	First Line
2L	Second Line
BID	Twice per day
CPI	Checkpoint inhibitor
dMMR	DNA mismatch repair
ER	Estrogen receptor
mAb	Monoclonal antibody
MSI-H	Microsatellite instability high
ND	Not determined
NE	Not evaluable
PK	Pharmacokinetics
PR	Progesterone receptor
QD	Once per day
QOL	Quality of life
SOC	Standard of care
TFI	Treatment free interval

Approved Drugs Mentioned	
Jemperli	Dostarlimab-gxly (GSK)
Lenvima	Lenvatinib (Eisai)
Keytruda	Pembrolizumab (Merck)

Medical Organizations / Conferences	
AACR	American Association for Cancer Research
ASCO	American Society of Clinical Oncology
ESMO	European Society for Medical Oncology
SABCS	San Antonio Breast Cancer Symposium