

# Initiation Report

CONTEXT THERAPEUTICS INC.



## Context Therapeutics Inc. – Innovative Novel Cancer Treatments for Women with Unique, Targeted Approaches

Context Therapeutics Inc. (NASDAQ: CNTX)

Share Price: \$0.85

Valuation: \$5.88



### Key Statistics

52 Week Range	\$0.60 - \$2.79
Avg. Volume (3 months)	2.08M
Shares Outstanding	15.97M
Market Capitalization	\$13.57M
EV/Revenue	n/a
Cash Balance*	\$39.43M
Analyst Coverage	4

\*Cash balance as of September 2022

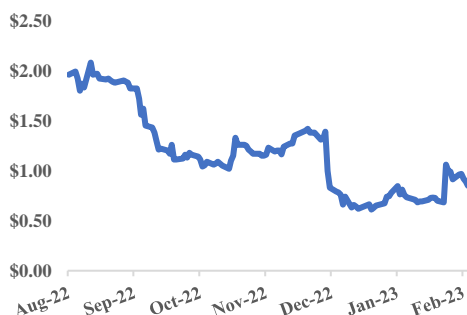
### Revenue (in \$mm)

Dec - FY	2021A	2022E	2023E
1Q	0.00	0.00	0.00
2Q	0.00	0.00	0.00
3Q	0.00	0.00	0.00
4Q	0.00	0.00	0.00
FY	0.00	0.00	0.00

### EPS (in \$)

Dec - FY	2021A	2022E	2023E
1Q	(2.55)	(0.22)	(0.34)
2Q	(14.18)	(0.25)	(0.36)
3Q	(4.00)	(0.24)	(0.40)
4Q	(0.30)	(0.33)	(0.45)
FY	(3.69)	(1.04)	(1.55)

### Stock Price Chart



## Investment Highlights

- Promising Pipeline of Novel Systemic Therapies:** Context Therapeutics has built a promising pipeline of novel systemic therapies for multiple solid cancer indications. The clinical stage candidate, onapristone extended-release (ONA-XR), is a complete PR antagonist that targets cancer indications where PR-mediated signaling contributes to resistance and disease progression. ONA-XR is being evaluated in combination with anti-estrogen drugs in hormone receptor-positive metastatic breast cancer and endometrial cancer. The extended-release formulation and pure antagonist properties of onapristone are expected to provide a balance between efficacy and toxicity, while overcoming drug resistance. The follow-on pipeline candidate CTIM-76 is a Claudin-6 (CLDN6) x CD3 bispecific antibody currently being evaluated in IND-enabling studies with an eventual goal of treating CLDN6-expressing cancers. CLDN6, an oncofetal tight junction protein, is highly expressed in different cancer cells, particularly testicular and ovarian, but lacks expression in healthy cells. Other clinical trial candidates such as BioNTech's CAR-T Candidate BNT211 have provided encouraging evidence of CLDN6 as an effective therapeutic target. The bispecific antibody approach of CTIM-76, accompanied by an ideal target (CLDN6), has shown high specificity and selectivity with optimal T-cell lysis (cancer cell apoptosis) and minimal off target inflammatory response in multiple in-vitro studies. We believe both candidates are being developed on a strong scientific foundation and have the potential to bring new drugs to market.
- Encouraging Clinical Early-Stage Results:** ONA-XR is currently being evaluated in combination with antiestrogen drug fulvestrant and recently FDA-approved only oral selective estrogen receptor degrader (SERD) elacestrant in patients with HR+, HER2- metastatic breast cancer for 2L/3L treatment. Preliminary results from the SMILE trial (ONA-XR + fulvestrant) have shown promising efficacy and tolerability. The ongoing SMILE trial found a 4-month progression-free survival rate of 44% (preliminary results) in patients with ER+, HER2- locally advanced or metastatic breast cancer. The ELONA trial (ONA-XR + elacestrant) has recently enrolled its first patient in Phase 1b/2 clinical trial. The complete PR antagonist is also being evaluated for PR+ recurrent endometrial cancer in combination with anastrozole (aromatase inhibitors) in Phase 2 clinical trial (OATH study). The ongoing OATH trial found a 4-month progression-free survival rate of 77% and a 12-month rate of 33% (preliminary results), with a favorable safety and tolerability profile. Even though a head-to-head comparison is not statistically perfect, ONA-XR's clinical results are encouraging when analyzed against standard of care chemotherapy or antiestrogen hormone therapy. The second candidate, CTIM-76, has yet to undergo clinical trials, but early results from cell-based assays are promising. The drug has demonstrated high selectivity and potency, being over 1,000 times more selective for CLDN6 compared to CLDN9 and about 28 times more effective than a conventional bispecific T-cell engager molecule. Although the results are not conclusive or all-encompassing, they suggest potential positive outcomes and significant potential for further development.
- Strong Scientific Background, Large Market, and Sound Financial Footing Supporting Valuation:** ONA-XR and CTIM-76 represent significant global opportunities and an unmet need in the treatment of solid tumors. Both medications are being progressed through the pipeline, with multiple clinical and pre-clinical data readouts expected to be released in 2023. The pipeline progress is further supported by a sound financial position as exhibited by the company having zero-debt and cash runway into Q1 2024. We have valued the company using a risk-adjusted DCF methodology, assuming a probability of success of 15% and a discount rate of 12.5%, yielding a value of \$93.82 million or \$5.88 per-share contingent on successful execution by the company.

## Company Description

Context Therapeutics is a clinical-stage biopharmaceutical company focused on developing treatments for female cancers in the U.S. Its lead product candidate is a selective antagonist of the progesterone receptor, and the company is also developing a CLDN6xCD3 bispecific antibody for redirecting T-cell-mediated lysis towards CLDN6 expressing cancer cells.

## Company Overview

Context Therapeutics Inc. (NASDAQ: CNTX), headquartered in Philadelphia, PA, is a clinical-stage biotechnology company developing advanced small-molecule and targeted therapy treatments with a primary focus on female cancers. According to WHO, breast cancer accounted for approximately 2.3 million cases in 2020, out of which 0.6 million died, making it the most diagnosed cancer world over. Gynecological cancer includes ovarian, cervical, endometrial, vaginal, and vulvar cancers, although uncommon, yet continue to be an important cause of cancer-related mortality in women worldwide. The company aims to target these cancers by leveraging its lead candidate, ONA-XR, in combination with FDA-approved anti-hormonal therapies. The lead candidate, onapristone extended-release (ONA-XR), is a novel, first-in-class small molecule investigational medicine that is a complete progesterone receptor (PR) antagonist currently under clinical trials. To date, over 150 patients with female cancers have been treated with ONA-XR. Additionally, Context's pipeline includes CTIM-76, a selective Claudin-6 (CLDN6) x CD3 bispecific antibody for CLDN 6-positive tumors.

*With a mission to advance medicines for solid tumors; and primary focus on female cancers, Context pipeline includes novel small molecule and bispecific antibody drug candidates that target cancer signaling pathways*

Cancer	Clinical Indication	Preclinical	Phase 1 Clinical	Phase 2 Clinical	Milestones
<b>CTIM-76 (CLDN6xCD3 bispecific antibody)</b>					
	CLDN6-positive cancers				Candidate selection Q4 2022 <input checked="" type="checkbox"/> Preclinical update Q2 2023 IND filing in Q1 2024
<b>ONA-XR (PR antagonist)<sup>1</sup></b>					
Endometrial Cancer	Recurrent PR+ Endometrioid Combination with anastrozole in post-chemotherapy treated patients				Initial data Q4 2022 <input checked="" type="checkbox"/> Data update Q2 2023
Breast Cancer	2L/3L ER+,PR+,HER2- Combination with ORSERDU (elacestrant) in post-CDK4/6 inhibitor treated patients				Initiated Q4 2022 <input checked="" type="checkbox"/> Phase 1b data Q4 2023
	2L/3L ER+,HER2- Combination with fulvestrant in post-CDK4/6 inhibitor treated patients				Initial data Q4 2022 <input checked="" type="checkbox"/> Data update Q4 2023

Exhibit 1: Context Therapeutics Pipeline. Source: Company Presentation

The wider acceptance of progesterone and progesterone receptor (PR) in cancer pathogenesis has led to increased interest in antiprogestins as a new type of hormone therapy for female cancers. PR is a protein found inside the cells of female reproductive tissue or some cancer cells, which plays a key role in the growth of cells by binding to the progesterone hormone in hormonally-regulated tissues such as the breast, ovaries, and endometrium (uterus). ONA-XR, as per pre-clinical and clinical trials, has exhibited anticancer activity by inhibiting PR binding to chromatin, downregulating cancer stem cell mobilization, and blocking immune evasion. Context is currently evaluating ONA-XR in a Phase 2 clinical trial in ER+, HER2- breast cancer and in recurrent PR+ endometrial cancer. The company has also initiated a Phase 1b/2 clinical trial evaluating ONA-XR in PR+, ER+, HER2- breast cancer in combination with the recently approved ORSERDU™ (elacestrant). The company is, additionally exploring the potential of CLDN6, a member of the Claudin family, as a promising target for the treatment of cancer. CLDN6 plays a critical role in the maintenance of tight junctions and cell adhesion in epithelial cells, making it a significant contributor to the progression of cancer. Context's research suggests that CTIM-76 is highly

selective of CLDN6 positive cancers. CTIM-76 is in pre-clinical development, and its investigative new drug (IND) application is on track, expecting submission in Q1 2024.

## Hormone Dependent Cancers: Mechanisms and Therapies

Hormones are natural chemical substances secreted by specific glands and are transported in tissue fluids to regulate the vital functions of the human body. The growth and development of various tissue are regulated by the secretion of hormones including reproductive tissues such as the breasts or ovaries. However, they are also responsible for the proliferation of multiple common cancers, such as breast, prostate, and gynecologic cancers, that further include cervical, ovarian, and uterine. Excessive hormonal stimulation and subsequent cell proliferation increase the risk of mutation, random genetic errors, and replication of those mutated cells. This distinctive underlying mechanism of carcinogenesis in hormone-driven cancers and the hormone’s ability to promote the development of cancer make them powerful carcinogens. Hormone-dependent cancers or hormone-sensitive cancers are identified by the presence of hormone receptors (commonly known as proteins) on cancer cells, which, when attached to specific hormones, leads to cancer proliferation and metastasis. Over 400,000 men and women were affected by hormonal cancers, and over 100,000 deaths occurred in 2018 in the United States alone.<sup>1</sup>

Cancer Type	5-Year Prevalence	Incidence	% Of HR+ Cases
Breast Cancer	1,070,703	253,465	<u>78%</u>
Endometrial Cancer	241,265	61,738	<u>64%</u>
Ovarian Cancer	72,013	23,820	<u>&gt;60%</u>
Cervical Cancer	43,175	13,545	<u>&gt;60%</u>

Exhibit 2: Female Hormone-Dirven Cancers. Source: Global Cancer Observatory, Diamond Equity Research (Prevalence and incidence 2020 data pertain to the U.S)

Breast and endometrial cancer are two of the most common female hormonal cancer with high hormone receptor positivity. In the past decade, there has been a marked improvement in the treatment of these cancers due to a deeper understanding of their molecular makeup. A multitude of new therapeutic options has become available, enhancing survival outcomes. However, these treatments have also brought forth more resistant and aggressive disease variants. The standard of care (SoC) first-line treatment options for hormone-driven cancers involve surgery, radiation therapy, followed by adjuvant chemotherapy and/or endocrine therapy depending on the cancer staging, progression, and biomarker profile. Recent advances in treatment modalities for HR+ (estrogen receptor and/or progesterone receptor) cancers include the development of multiple disease-modifying systemic treatments such as hormone therapies (SERMs and SERDs), targeted therapies (CDK4/6 inhibitors, mTOR inhibitors, PARP inhibitors), and immunotherapies. Even though there has been widespread use of hormone therapies and targeted therapies for the treatment of hormone-driven cancers in the recent past, a major drawback that has been researched and talked about is resistance to treatment and increased toxicity. Endocrine therapies have been found to lose effectiveness due to primary or acquired resistance, potentially leading to relapse, metastasis, and death. While most ER+ breast cancer may initially respond to endocrine treatment, 15-20% of tumors are intrinsically resistant to treatment, and another 30-40% acquire resistance

*Recent advancements in treating hormone-driven female cancers like breast and endometrial cancer have involved the use of hormone, targeted, and immunotherapies, but these treatments also come with challenges of resistance and higher toxicity*

<sup>1</sup> Ulm et al., Endocr Connect. 2019 Feb 1

to treatment over a period of many years.<sup>2</sup> The use of targeted therapies accompanied by endocrine therapies has been shown to improve efficacy but is also accompanied by an increase in the risk of complex and severe adverse events, however manageable. Results from the trials have shown that combining targeted agents with endocrine therapies substantially increases the incidence of grade 3-4 adverse events compared with conventional single-agent endocrine therapy.<sup>3</sup> The past decade has brought about a completely evolved treatment landscape that has improved patient outcomes, but there is still a high unmet medical need. Considering low five-year survival rates for metastasized tumors (exhibit 9), and a lack of effective balance between resistance and toxicity in current treatment options, there remains a need for therapies that can balance efficacy, resistance, and toxicity.

## Realizing The Role of Progesterone and Progesterone Receptor (PR)

Hormonal/endocrine therapy remains a mainstay treatment option for the majority of regional and metastasized/distant hormone-driven cancer. The use of antiestrogen and progestin drugs is highly prevalent as hormonal therapeutics. A bulk of research and FDA-approved drugs within the hormone therapy landscape have been concentrated around the inhibition of estrogen and estrogen receptor (ER) functioning while neglecting the role of progesterone and progesterone receptor (PR) in the pathogenesis and regulation of breast and gynecological cancers. Despite the fact that estrogen remains a major etiological factor driving cancer progression in up to 70% of female cancer cases, antiestrogen therapies have largely been held back owing to primary or acquired resistance mechanisms. Direct or indirect compensatory signaling mediated by the PR, mutations in estrogen receptor (ESR1), phosphatidylinositol 3-kinase (PI3K) gene mutations, growth factor signaling, and enrichment of cancer stem cells are a few of the resistance mechanisms limiting the uptake of antiestrogen therapies. Addressing the role of progesterone and progesterone receptors (PR) in tumorigenesis is crucial in creating a novel therapy enhancing efficacy that can overcome multiple resistance pathways.

Approximately ninety percent of all ER+ breast cancers are also positive for PR, and while selective ER modulators (SERMs) are routinely used as adjuvant therapy in women with PR+ breast cancers, relatively limited progress has been made in the development of effective PR-targeting therapies in the clinic. The role of progesterone and PR have been gaining attention as one of the critical regulators of disease initiation and progression in gynecological cancers, with [45%](#) of endometrial cancer cases being ER+ and PR+ and [35%](#) of ovarian cancer cases diagnosed as PR+. Recent studies have also considered the role of cross-talks between multiple steroid receptors (ER, PR, AR, and GR) in modulating each other's signaling with cascading implications on endocrine therapy response. Historically researched and early PR-targeted therapies have been found to lack receptor specificity and were accompanied by safety concerns relating to liver toxicity. Advancements within the antiprogestins landscape have been addressing the underlying issues with the creation of more potent and safer formulation alternatives. Currently, there aren't any FDA-approved antiprogestins for the treatment of cancer, while two antiprogestins have been approved for indications other than cancer.

*The role of progesterone and PR in tumorigenesis is gaining attention, with many cancers being positive for both ER and PR, and progress has been made in developing safer PR-targeted therapies, but currently, no FDA-approved antiprogestins exist for hormone-driven cancer*

<sup>2</sup> Lei JT et al., Breast. 2019 Nov

<sup>3</sup> Cazzaniga ME et al., Breast Cancer Res Treat. 2019 Aug

Drug	Company	Type	Indication
Mifepristone	Corcept Therapeutics	Mixed agonists/antagonists	Termination of Pregnancy* Cushing Syndrome*
Asoprisnil	AbbVie/TAP Pharmaceuticals	Mixed agonists/antagonists	Previously Studied for Uterine fibroids
Ulipristal acetate	Allergan/Gedeon Richter	Mixed agonists/antagonists	Emergency contraception* Uterine fibroids
Telapristone acetate	Repros Therapeutics Inc.	Mixed agonists/antagonists	Previously evaluated for breast cancer, endometriosis, and uterine fibroids.
Vilaprisan	Bayer	Mixed agonists/antagonists	Previously evaluated for Uterine fibroids.
Lonaprisan	Bayer	Pure progesterone antagonists	Previously evaluated for metastatic breast cancer.
Onapristone	Context Therapeutics	Pure progesterone antagonists	Currently being evaluated for metastatic breast cancer and endometrial cancer.

Exhibit 3: List of Select Antiprogestins. Source: Diamond Equity Research  
(\* Indicate US FDA Approved)

## Onapristone Extended Release (ONA-XR) - Antiprogestin Therapy for Female Cancers

Antiprogestins are considered promising investigational agents for the treatment of hormone-dependent female cancers. First developed in the 1980s as oral contraceptives, antiprogestins are trying to find their place as cancer therapeutics, with the role of progesterone in cancer pathogenesis becoming clearer. Context's lead pipeline candidate, Onapristone, is one such antiprogestin that has undergone multiple clinical trials in patients with hormone-driven cancers. The drug was initially developed by Schering AG as an immediate-release (IR) formulation (ONA-IR) in the 1990s and was initially evaluated as an oral contraceptive. The drug was later evaluated as a first-line endocrine therapy in patients with breast cancer. In two phase II studies, ONA-IR exhibited a 56% overall response rate and a 67% clinical benefit rate in patients with locally advanced, hormone therapy-naïve metastatic breast cancer, and a 10% overall response rate and a 49% clinical benefit rate in metastatic tamoxifen-resistant patients.<sup>4</sup> Even with strong efficacy data, the development of ONA-IR was discontinued due to liver test abnormalities and the perceived risk of drug-induced liver injury (DILI).

<sup>4</sup> Lewis, J.H et al., Drug Saf 43

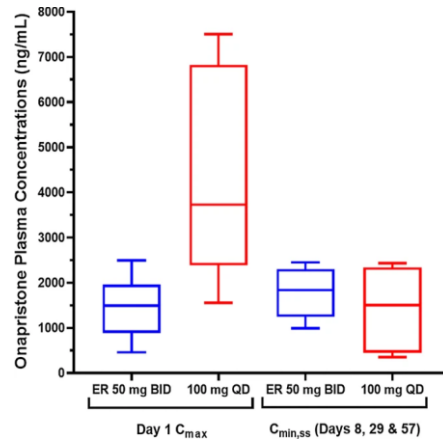


Exhibit 4: Onapristone IR vs. Onapristone ER Pharmacokinetics on Dosing Day 1 and at Steady State. Source: [Lewis et al.](#)

With renewed interest, Arno Therapeutics sought to develop an extended-release formulation of onapristone (ONA-XR) in an effort to reduce drug-related complications. Insights into the pharmacology and pharmacokinetic data suggested that liver enzyme elevation and the subsequent off-target toxicities were the results of increased and highly variable blood plasma concentration. A total of 88 patients with PR+ female cancers (endometrial, ovarian, and breast) and prostate cancer were administered ONA-XR in two Phase I/II studies with the primary goal of evaluating the hepatotoxic profile of the reformulated drug. The clinical trial indicated that the treatment was well tolerated, and only 6% of the patients exhibited liver-related adverse events or liver enzyme abnormalities without known liver metastasis. It should be noted that 83% of the patients were administered ONA-XR as a monotherapy treatment.

*Onapristone is a pure PR antagonist with unique structural properties, which may contribute to its high selectivity and target affinity as compared to other partial PR agonist anti-progestins*

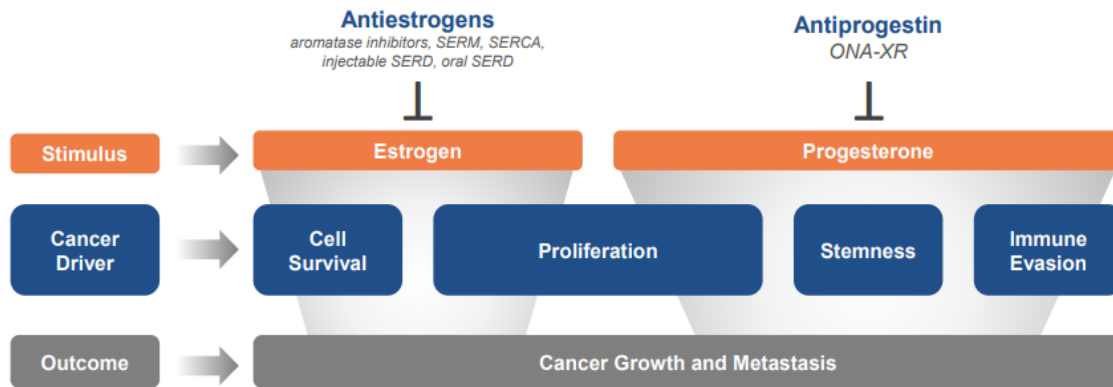


Exhibit 5: ONA-XR Mechanism of Action. Source: Company Presentation

The absence of approved treatments targeting progesterone receptor positive (PR+) cancers renders the disease a challenge in oncology. Nevertheless, evidence from preclinical studies and clinical trials suggests that onapristone extended-release (ONA-XR) holds potential as a promising therapeutic solution, characterized by its ability to impede PR from binding to chromatin, suppress the migration of cancer stem cells and impede immune evasion. Currently, ONA-XR is undergoing multiple mid-stage (Phase 1b/2 or Phase 2) clinical trials in metastatic breast cancer and endometrial cancer with the aim of guiding its potential advancement to Phase 3 development and FDA approval.

## Leveraging a Combination Therapy Approach

Context Therapeutics acquired ONA-XR in December 2017 and is currently evaluating the drug in combination with antiestrogen therapies in patients with HR+, HER2- metastatic breast cancer and recurrent PR+ endometrial cancer. Onapristone and antiprogestins, as a whole, have largely been evaluated in a monotherapy setting. The improved efficacy of antiestrogen therapy, when combined with targeted therapy, is evident and is widely used as a standard of care (SoC) therapy for metastatic breast cancer. The amalgamation of anticancer drugs enhances efficacy compared to the mono-therapy approach because it targets key pathways in a characteristically synergistic or additive manner.<sup>5</sup> Given the beneficial evidence and merit of combination therapy over monotherapy in treating cancer, it is likely that the current treatment landscape for hormone-driven breast and endometrial cancer can be improved with the addition of antiprogestins to the the current SoC. In a preclinical setting, the company evaluated the impact of complete hormone blockade via downregulation of estrogen receptor (ER) and progesterone receptor (PR) signaling pathways and their compensatory pathways, including CDK4/6 in PDX mouse models established from ER+ and PR+ bone metastasis of breast cancer.

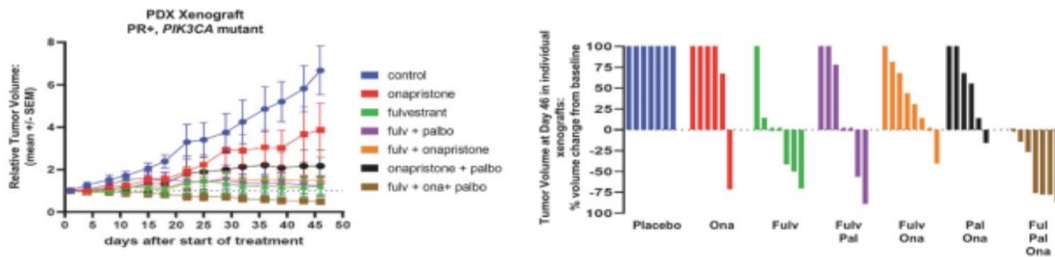


Exhibit 6: Merit of Combination Therapy in PDX Mouse Models. Source: Company Filings

The results were intuitive with treatment by a triple combination of onapristone + palbociclib (targeted therapy) + fulvestrant (antiestrogen), resulting in tumor growth inhibition of 92% which was far greater when compared to either of the drugs as monotherapy or in dual combination with each other.

## Hormone-Driven Metastatic Breast Cancer

Breast Cancer is one of the most [common](#) forms of cancer diagnosed among women and is the fourth leading cause of cancer-related death. The disease comprises a wide spectrum of tumors that are categorized into multiple subtypes depending on their hormone receptor positivity and genetic makeup that decides the future course of treatment. The most common subtype, HR+ HER2- breast cancer, accounts for approximately 68% of all breast cancer cases diagnosed. Despite advances in breast cancer screening, diagnosis, and treatment, nearly 12% of patients with a diagnosis of breast cancer eventually develop metastatic disease, or breast cancer, that has spread beyond the breast to other parts of the body.<sup>6</sup> Metastatic breast cancer is often associated with poor prognosis and low survival rates. The standard of care for HR+ HER2- metastatic breast cancer, which is also ONA-XR's primary indication, remains hormone therapy (tamoxifen, fulvestrant, or

<sup>5</sup> Bayat Mokhtari R et al., Oncotarget. 2017 Jun 6

<sup>6</sup> Peart O. Metastatic Breast Cancer. Radiol Technol. 2017 May



an aromatase inhibitor) combined with a targeted drug such as a CDK4/6 inhibitor, everolimus, or a PI3K inhibitor.

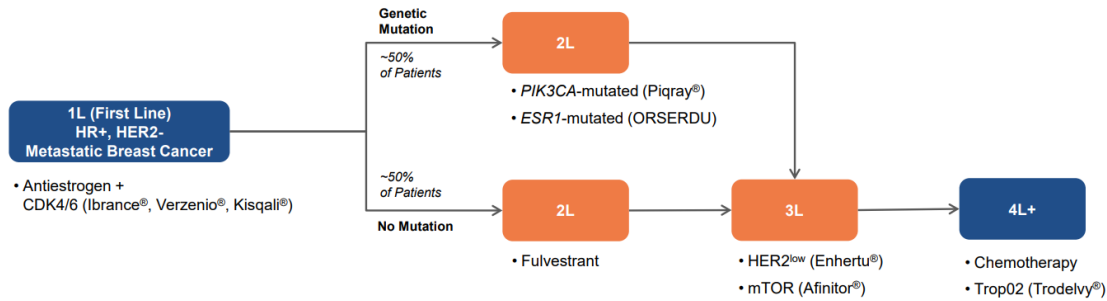


Exhibit 7: HR+ HER2- Treatment Landscape Source: Company Presentation

## ONA-XR’s Safety, Efficacy, and Future Development Strategy for Metastatic Breast Cancer

Context Therapeutics is evaluating ONA-XR in two clinical trials in combination with FDA-approved antiestrogen drugs as a second- and third-line treatment for hormone-driven metastatic breast cancer. The lead trial includes the study of ORSERDU™ (elacestrant) in combination with ONA-XR in patients with advanced/metastatic ER+, PR+, HER2- breast cancer. Furthermore, the ER+, HER2- metastatic breast cancer trial is targeted by ONA-XR and fulvestrant (antiestrogen drug) in patients who have already been treated with and progressed on antiestrogen and CDK4/6 inhibitors.

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

	Phase 2 SMILE Trial	Phase 1b/2 ELONA Trial
Patients (n)	39	67
Indication	2L/3L ER+,HER2- mBC	2L/3L ER+,PR+, HER2- mBC
Treatment	ONA-XR + fulvestrant	ONA-XR + ORSERDU (elacestrant)
Enrich for ESR1 Mutated	No	Yes
Prior Chemotherapy in Metastatic Setting	Yes	No
Prior CDK4/6 Inhibitor in Metastatic Setting	Required	Required
Next Expected Data Milestone	Q4 2023	Q4 2023

Exhibit 8: Clinical Trial Design for Metastatic Breast Cancer Source: Company Presentation

## The SMILE Study: Trial Design and Preliminary Results

The SMILE trial is a Phase II clinical study that aims to evaluate the safety and efficacy of the combination of onapristone and fulvestrant in treating ER+ and HER2- advanced or metastatic breast cancer in both men and women who have already progressed on first-line aromatase and CDK4/6 inhibitor treatments. The trial will enroll up to 39 patients, who will receive a twice-daily oral dose of 50 mg of onapristone and a 500 mg intramuscular injection of fulvestrant on days 1 and 15 of cycle 1, followed by injections every two weeks starting from day 1 of cycle 2 and once

every 28 days thereafter. The primary and secondary outcome measures include Objective Response Rate (ORR), Progression-Free Survival (PFS) Rate, Disease Control Rate (DCR), Time to Response, and the incidence of adverse events.

The preliminary trial results were presented at the 2022 San Antonio Breast Cancer Symposium® (SABCS®). The preliminary results presented from a Phase 2 clinical trial included nine evaluable subjects have shown that the combination therapy of ONA-XR and fulvestrant for treating ER+ and HER2- advanced or metastatic breast cancer has produced a 4-month progression-free survival (PFS) rate of 44%, with favorable safety and tolerability. The reported results, while preliminary, are considered promising given that the median PFS with fulvestrant treatment alone, following progression on CDK4/6 inhibitors, has previously been reported as only around two months in the underlying patient population. Furthermore, it should be noted that two other anti-progestins, mifepristone, and lonaprisan, have also been evaluated in PR+ metastatic breast cancer. Mifepristone reported an ORR of [11%](#) (n=28), and the lonaprisan trial reported an ORR of [0%](#) (n=68).

*The preliminary results indicate that ONA-XR combined with fulvestrant has a favorable efficacy and tolerability compared to fulvestrant alone*

### The ELONA Study: Trial Design

The ELONA study is a multicenter, Phase 1b/2 study of elacestrant in combination with ONA-XR in patients with advanced/metastatic ER+, PR+, HER2- breast cancer. The trial is conducted in partnership with Stemline Therapeutics, a wholly owned subsidiary of The Menarini Group, the developer of the first FDA-approved oral SERD, ORSERDU™ (elacestrant). The Phase 1b part of the trial is open-label and aims to determine the recommended Phase 2 dose (RP2D) of onapristone and elacestrant when administered together. The Phase 2 part of the trial will evaluate the efficacy and safety of this combination in patients with ER+, PR+, HER2- advanced/metastatic breast cancer. The trial is expected to enroll up to 67 participants who have previously been treated with a CDK4/6 inhibitor. The primary and secondary outcome measures include RP2D, the efficacy of elacestrant in combination with onapristone, and the incidence of adverse events.

ORSERDU™ (elacestrant) is the first oral SERD to gain FDA approval on the back of positive phase 3 trial results. The EMERALD trial assessed the efficacy of elacestrant, as monotherapy for ER+, HER2- metastatic breast cancer (mBC) patients. The study enrolled 477 patients, half of whom had ESR1 mutations, and compared elacestrant to the standard of care endocrine therapies including fulvestrant. The primary endpoint was PFS. The [trial results](#) showed a 30% reduction in the risk of progression or death with elacestrant compared to standard therapy for overall patients (PFS of 2.8 months vs. 1.9 months). The results were even more significant for patients with ESR1 mutations, with a 45% reduction in disease progression (PFS of 3.8 months vs. 1.9 months). ESR1 mutations are linked to endocrine therapy resistance and are common in mBC cases. Additionally, the study found that patients who received a longer duration of prior CDK4/6 inhibitor treatment had better outcomes with elacestrant. These findings suggest that elacestrant could potentially become a promising therapy and standard of care for ER+, HER2- mBC, particularly in patients with ESR1 mutations. The synergies created with the combination of ONA-XR plus elacestrant are likely to provide much more comprehensive and complete inhibition of estrogen and progesterone signaling pathways, thus potentially improving efficacy and patient outcomes.

*In clinical trials, elacestrant has demonstrated good bioavailability, engagement of the ER and the ability to cross the blood-brain barrier*

In the ELONA trial, The Menarini Group will supply elacestrant at no cost, while Context is sponsoring the ELONA trial. The company enrolled the first patient in the clinical trial study in January 2023, with further clinical updates expected during Q4 2023.

## Market Opportunity and Competitive Landscape

Breast cancer is a life-threatening disease that affects millions of women and some men worldwide. With increasing global incidence and death rates over the past three decades, there remains a high unmet need for more efficacious and safe treatments, especially for metastasized disease. Approximately 297,790 breast cancer cases are estimated to be diagnosed in the U.S. in 2023, accompanied by 43,700 deaths in women. Even after being the most diagnosed cancer, it remains the third leading cause of cancer-related deaths in the U.S. Overall 5-year survival for localized and regional breast cancer remains high (76%-100%), while for distant/metastatic breast cancer, the survival rate falls to as low as 12.0%.

Subtype	Localized	Regional	Distant
HR+/HER2-	100.0%	90.1%	31.9%
HR-/HER2-	91.3%	65.8%	12.0%
HR+/HER2+	98.8%	89.3%	46.0%
HR-/HER2+	97.3%	82.8%	38.8%
Unknown	96.1%	76.4%	15.6%
Total	99.1%	86.1%	30.0%

Exhibit 9: 5-year Survival Rate of Female Breast Cancer Subtypes. Source: [cancer.gov](https://www.cancer.gov)

An estimated 168,000 women are currently living with metastatic breast cancer in the U.S. Accounting for patients with ER+ HER2- patients (70%) and patients receiving 2L/3L patients, we believe the immediately addressable market for ONA-XR + fulvestrant is estimated at approximately 43,100 patients. For ONA-XR + elacestrant targeting PR+ ER+ HER2- metastatic breast cancer under the second and third line of treatment, the addressable estimated patients are approximately 13,800 (accounts for patients with ESR1 mutation as specified for elacestrant). In the past decade, targeted therapies such as CDK 4/6 inhibitors, PI3K inhibitors, and mTOR inhibitors have found their place within HR+ HER- metastatic breast cancer treatment landscape. Treatment with CDK 4/6 inhibitors has shown a significant improvement in progression-free survival, particularly in patients with visceral metastasis, endocrine sensitivity, and endocrine resistance, and has been widely used in combination with antiestrogen for 1L/2L treatment. Ibrance®, the only CDK 4/6 inhibitor that is FDA-approved for the treatment of HR+/HER2- mBC in combination with either an AI or fulvestrant regardless of menopausal status, generated global revenue of \$5.12 billion and domestic revenue (the U.S) of \$3.37 billion in 2022. Another FDA-approved CDK 4/6 inhibitor, Verzenio®, generated revenue of \$0.83 billion in the U.S. and \$1.35 billion across the globe in 2021. For 2L/3L patients with PIK3CA mutation, the preferred treatment option includes fulvestrant plus alpelisib (PI3K Inhibitor), and for wild-type patients, antiestrogen with or without everolimus (mTOR inhibitors). The only FDA-approved therapy developed for the approximately 40% of HR+/HER2- advanced breast cancer patients who have a PIK3CA mutation, Piqray® generated revenue of \$0.4 billion in 2022. Multiple novel therapies are currently being evaluated in a clinical trial, including oral SERDs, SARMS, and AR antagonists, with some of them showing excellent efficacy when compared to SoC antiestrogen

therapy, while there aren't any other antiprogestins currently in a clinical trial for hormone-driven metastatic breast cancer. Competition is further intensifying as additional targeted therapies continue to gain traction with the recent approval of AstraZeneca-Daiichi Sankyo's [Enhertu](#)<sup>®</sup> and Gilead's [Trodelvy](#)<sup>®</sup>.

Drug	Type	Stage	Past Results
Giredestrant	Oral SERD	Phase III	The <a href="#">phase 2</a> acelERA BC study indicated a median PFS with giredestrant (n = 151) was 5.6 months vs. 5.4 months with PCET (n = 152) in ER+ HER2- mBC. The 6-month PFS rates in the investigative and control arms were 46.8% and 39.6%, respectively. In ESR1 mutated patients, the median PFS with giredestrant (n = 51) was <b>5.3 months</b> vs. <b>3.5 months</b> with PCET (n=39). The study failed to meet the primary endpoint of improving PFS.
Camizestrant	Oral SERD	Phase III	The <a href="#">phase 2</a> SERENA trial showed that two doses of single-agent camizestrant (AZD9833) improved progression-free survival compared to standard-of-care fulvestrant (Faslodex) in patients with ER+ advanced breast cancer. The trial included three dose levels of camizestrant and a fulvestrant cohort. The median PFS was <b>7.2 months</b> for the 75 mg dose, <b>7.7 months</b> for the 150 mg dose, and <b>3.7 months</b> for the fulvestrant. Meet the primary endpoint of improving PFS.
H3B-6545	Oral SERCA	Phase I/II	The <a href="#">phase I/II</a> trial of H3B-6545, a selective estrogen receptor covalent antagonist, showed an ORR of 17% in 94 patients with metastatic ER-positive breast cancer refractory to endocrine therapy. The trial had a median PFS of <b>5.1 months</b> , and the treatment was well tolerated, with anemia, nausea, and diarrhea as the most common adverse events. The drug showed greater antitumor activity in patients with Y537S clonal mutations, with an ORR of 30% and median PFS of 7.3 months.
Enobosarm	Oral SARM	Phase III	The <a href="#">phase 2</a> trial investigated the efficacy and safety of enobosarm in 136 postmenopausal women with AR-positive, ER-positive, HER2-negative metastatic breast cancer (MBC) who had progressed after multiple lines of endocrine therapy. The trial found that the clinical benefit rate (CBR) at 24 weeks was 32% in the 9-mg group and 29% in the 18-mg group. An exploratory analysis showed a correlation between radiographic progression-free survival and the degree of AR nuclei staining. The median PFS was <b>5.5 months</b> in patients with over 40% AR staining compared to <b>2.75 months</b> in those with less.

Exhibit 10: Select Novel Therapies in Clinical Development for Hormone-Driven Metastatic Breast Cancer. Source: Diamond Equity Research

## Hormone-Driven Recurrent Endometrial Cancer

Endometrial cancer, or cancer of the corpus uteri, is one of the prevailing gynecological malignancies that arise from the epithelial lining of the uterine cavity. Long-lasting imbalances in hormonal exposure, where there is excessive estrogen and inadequate progesterone acting upon the endometrial tissue, is hypothesized to be a driver of endometrial cancer initiation and proliferation. The malignancy is categorized based on hormonal dependency, progression, and clinical behavior. Type 1 endometrioid carcinoma accounts for 80% of cases with high dependence on estrogen accompanied by favorable prognosis, while type 2 non-endometrioid are less common and more aggressive. Because of progesterone's ability to antagonize proliferation and promote atrophy of the endometrium, progesterone, and its derivatives have been used successfully as therapeutics to treat endometrial hyperplasias and early-stage cancers. A majority

of endometrial cancer cases (80%) are diagnosed in early stages and are treated with surgery, radiation, and chemotherapy. Endometrial cancer often has a good prognosis if diagnosed in its early stages, with a 5-year survival rate being more than 90%. For patients diagnosed with recurrent or metastatic diseases, outcomes are less favorable with the 5-year survival rate dropping to 20%. The standard treatment options for recurrent or metastatic diseases include combination platinum plus taxane chemotherapy and immunotherapy, including Jemperli® and Keytruda® as monotherapies for dMMR or MSI mutated endometrial cancer. Keytruda® also has an additional indication for use in combination with Lenvima® (partnered with Eisai) in previously treated endometrial cancer without dMMR. While not approved in endometrial cancer, antiestrogen therapy is often used in younger patients who seek fertility preservation or for patients who cannot tolerate cytotoxic therapy.

## ONA-XR and Anastrozole in PR+ Endometrial Cancer

Context is evaluating onapristone extended releases in combination with anastrozole (antiestrogen - aromatase inhibitor) on the same premise of bringing about complete blockage of estrogen and progesterone signaling pathway. The combination hormone therapy is currently being evaluated in phase 2 clinical trials in patients with HR+ endometrial cancer.

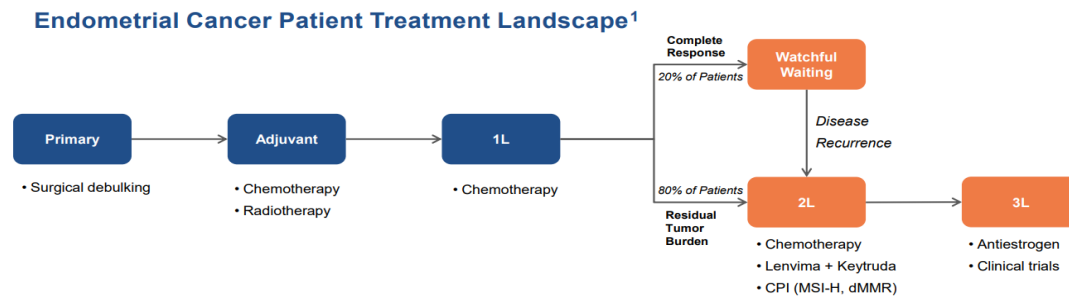


Exhibit 11: Endometrial Cancer Treatment Landscape. Source: Company Presentation

## OATH Study: Trial Design and Early Efficacy Data

The OATH Study is a Phase 2 clinical trial in partnership with Jefferson Health, aimed at evaluating the effectiveness of the combination therapy of ONA-XR 50mg twice daily and anastrozole 1mg daily in women with hormone receptor-positive (ER+ and PR+) endometrial cancer who have previously undergone a failed front-line treatment with a platinum/taxane-based chemotherapy regimen. The trial is projected to enroll 25 participants, and its primary and secondary outcome measures encompass the objective response rate (ORR), progression-free survival (PFS), and disease control rate, as well as assessing the safety and tolerability of the therapy regimen.

During the fourth quarter of 2022, the company released preliminary results from its ongoing OATH study. Twelve patients had enrolled in the trial, with nine being eligible for evaluation. The preliminary 4-month progression-free survival (PFS) rate was reported at 77.7%, and the 12-month PFS rate was 33%, with no treatment-related adverse events observed. Recently the company announced that two patients achieved a confirmed partial response (PR) among the first

*Preliminary results of the ONA-XR and ANA combination therapy show improved performance in terms of efficacy and manageable side effects*

12 patients (9 evaluable) enrolled in the clinical trial. Additionally, the preliminary data indicated an overall response rate (ORR) of 22% (refer exhibit 12). These encouraging efficacy data, combined with a favorable safety profile, strengthen confidence in the clinical profile of ONA-XR. For comparison, the historical 4-month PFS for ONA-XR as monotherapy was 33% (n=4), 31% (n=17) for anastrozole, and 42% (n=174) for chemotherapy. Studies on progestins as a first-line treatment for metastatic or recurrent endometrial cancer showed an overall response rate of 23.3%, with a median PFS of 2.9 months and median overall survival (OS) of 9.2 months.<sup>7</sup> Additionally, systemic therapies particularly immunotherapy (Keytruda® + Lenvima®) has exhibited high clinical efficacy as shown by 4-month PFS rate of 67% (n=278) but has also been associated with poor tolerability and significant debilitating side effects.

The combination therapy (ONA-XR + anastrozole) is expected to offer favourable efficacy and safety compared to other treatments. While a direct comparison may not be ideal due to differences in study design, dosage, and patient population, these initial results provide evidence of the potential for the ONA-XR and anastrozole combination therapy to capture a significant market opportunity. The company is expected to provide a further clinical trial update by mid-2023.

	ONA-XR + Anastrozole	ONA-XR	Anastrozole	Chemotherapy	Lenvima + Keytruda
<b>Trial</b>	OATH (ongoing)	Context Phase 1 <sup>2</sup>	PARAGON <sup>3</sup>	KEYNOTE-775 <sup>4</sup>	KEYNOTE-775
<b>Patients (n)</b>	12 (9 evaluable)	12	54	416	411
<b>Lines of Prior Chemotherapy, n (%)</b>					
1	8 (67)	4 (33)	50 (93)	277 (67)	324 (79)
≥2	4 (33)	8 (66)	4 (7)	139 (33)	87 (21)
<b>4-month PFS rate, n (%)</b>	7 (77)	4 (33)	17 (31)	174 (42) <sup>4</sup>	278 (67) <sup>4</sup>
<b>ORR, n (%)</b>	2 (22)	0 (0)	2 (4)	61 (14)	131 (32)
<b>mPFS (95% CI), months</b>	Trial ongoing	2.0 (1.7-5.3)	2.7 (1.9-4.5)	3.8 (3.6-4.2)	7.2 (5.7-7.6)
<b>Side Effects</b>	Well tolerated; mainly Grade 1 or 2 AE; 0% discontinuation rate	Well tolerated; mainly Grade 1 or 2 AE	Well tolerated; mainly Grade 1 or 2 AE	73% experienced Grade 3 or higher AE; 8% discontinuation rate	89% experienced Grade 3 or higher AE; 33% discontinuation rate

ONA-XR + Anastrozole  
early signs of clinical activity

Significant adverse events (AE) leading  
to high treatment discontinuation rate

Exhibit 12: Clinical Trial Result Comparison. Source: Company Presentation

## Market Opportunity and Competitive Overview

It is estimated that over 60,000 new cases of endometrial cancer will be diagnosed in the U.S., mainly affecting postmenopausal women. The 5-year survival rate for this cancer is 84%, but for those with recurrent or metastatic disease, it decreases to 20%. The three-year prevalence of endometrial cancer is estimated to be 241,625, with the risk of relapse at 10-15% for early-stage diseases and 40%-70% for advanced stages.<sup>8 9</sup> Of the patients experiencing recurrence, 64% occur within two years, while 87% occur within three years of the first follow-up. Approximately 64%

<sup>7</sup> Helen et al., American Society of Clinical Oncology Educational Book 2020

<sup>8</sup> Global Cancer Observatory

<sup>9</sup> Francesca et al., Critical Reviews in Oncology/Hematology, Volume 180, 2022,

of endometrial cancer cases are hormone receptor-positive (HR+), and [49%](#) are progesterone receptor-positive (PR+). Based on these figures, we estimate that approximately 13,800 patients in the U.S. could benefit from the combination therapy of ONA-XR and anastrozole.

Patients with metastatic or recurrent endometrial cancer are currently treated with a combination of surgical procedures, radiation therapy, and systemic therapies. These systemic therapies include chemotherapy, hormone therapy, and immunotherapy. The standard first-line treatment for this type of cancer is the use of carboplatin and paclitaxel (platinum-based chemotherapy), which has been shown to have a response rate between 40% and 62% with median OS times of 13 to 29 months.<sup>10</sup> For some patients, hormone therapy, specifically megestrol acetate, may be used as a first-line treatment. In recent years, immunotherapy has emerged as a promising option for treating advanced/metastatic endometrial cancer in later lines of treatment. The FDA approved Keytruda<sup>®</sup> (pembrolizumab) as a single-agent treatment for endometrial cancer patients who have a high level of microsatellite instability (MSI-H) or deficient mismatch repair (dMMR) following the failure of previous systemic therapy in May 2017. In September 2019, the approval was extended to include the combination therapy of Keytruda<sup>®</sup> (pembrolizumab) and lenvatinib for women who do not have MSI-H or have MMR-proficient endometrial cancer. In April 2021, FDA approved another Immunotherapy, Jemperli<sup>®</sup> (dostarlimab-gxly), a programmed death receptor-1 (PD-1) blocking antibody for the treatment of adult patients previously progressed on platinum-containing regimen and with mismatch repair-deficient (dMMR) recurrent or advanced endometrial cancer. Both [Jemperli<sup>®</sup>](#) and [Keytruda<sup>®</sup>](#) are currently targeting the first-line treatment for advanced/metastatic endometrial cancer in combination with chemotherapy and have recently announced positive results showing statistically significant improvement in progression-free survival.

## Therapeutic Application of Bispecific Antibodies (BsAbs)

Bispecific antibodies, also known as BsAbs, is a type of artificially made protein that possess dual binding sites, which can target two distinct antigens or two separate epitopes on a single antigen. This unique feature makes them more effective than monoclonal antibodies (MoAbs) in providing clinical therapeutic effects, and they have a wide range of applications, including tumor immunotherapy and the treatment of other diseases. Because of its dual specificity, the bispecific antibodies can support redirecting T cells to tumor cells, blocking two different signaling pathways simultaneously, dual targeting different disease mediators, and delivering payloads to targeted sites.

The recent advancements in antibody or protein engineering and recombinant DNA technology have allowed the establishment of various platforms for generating different types of BsAbs based on novel strategies. Currently, there are nine bispecific antibodies approved worldwide, more than 180 BsAbs are in preclinical development, and over 50 BsAbs have been investigated in clinical trials. Catumaxomab, blinatumomab, and emicizumab are the only commercially available BsAbs, out of which catumaxomab and blinatumomab are the two U.S. FDA-approved bispecific antibody products that are expected to fuel the growth of the bispecific antibodies market. While

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<sup>10</sup> Halla K et al., J Adv Pract Oncol. 2022 Jan

blinatumomab and emicizumab are used in the treatments of relapsed leukemia and hemophilia A, respectively, catumaxomab is the only approved BsAb used for treating solid tumors. Catumaxomab (brand name Removab™), initially approved in 2009, is a trifunctional bispecific monoclonal antibody that treats malignantly caused ascites from solid tumors by targeting EpCAM and CD3. Catumaxomab brings cancer cells, T cells, and other immune cells together and triggers the activation of these immune cells, leading to the destruction of the cancer cells through the immune system. This process is self-sufficient, as there is no need for further activation of immune cells to eliminate the tumor. However, due to commercial reasons, Catumaxomab was voluntarily withdrawn from the market by its manufacturer in 2017.

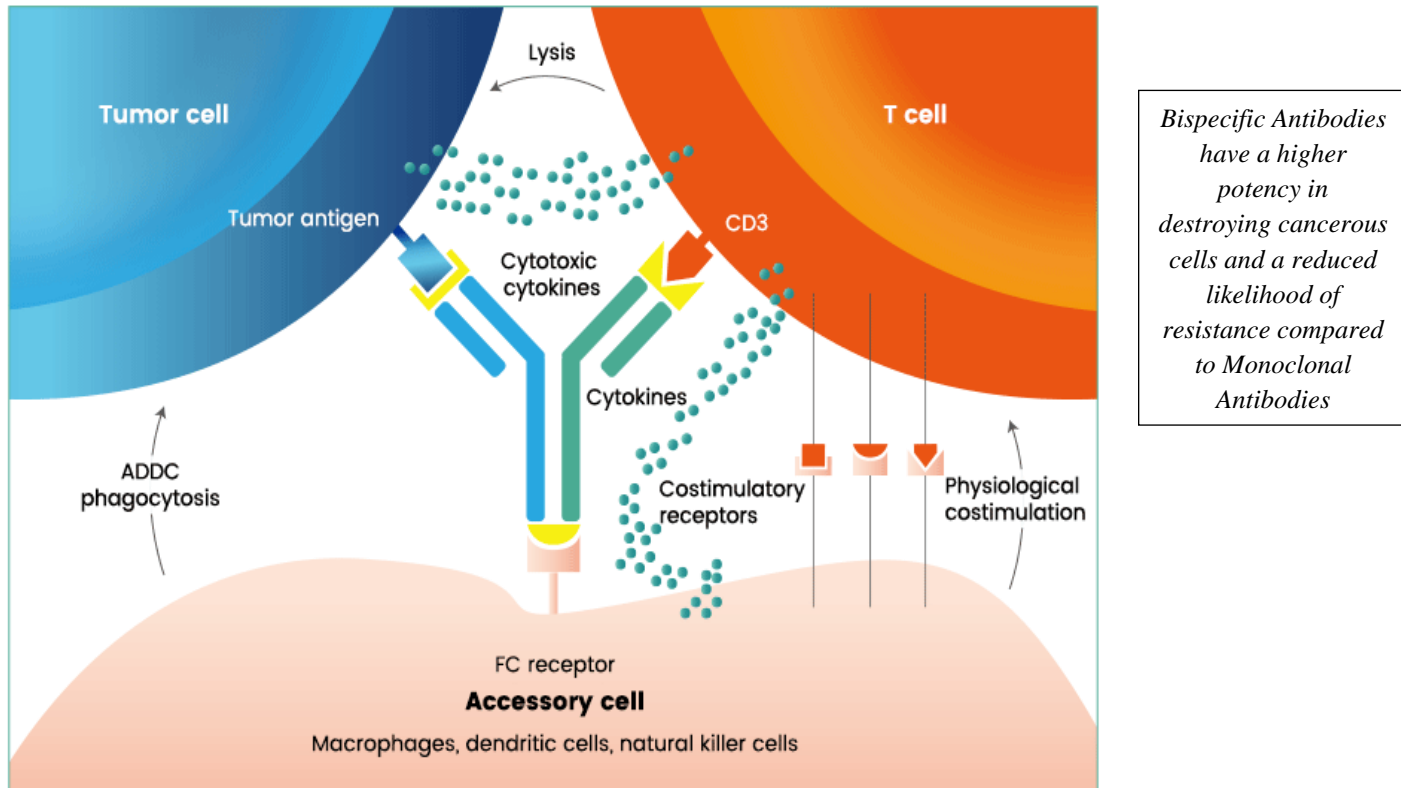


Exhibit 13: How do Bispecific Monoclonal Antibodies Work? Source: Sino Biological

One of the main advantages of BsAbs compared to MoAbs is their superior cytotoxic effects and a lower rate of resistance due to the matched targeting of two different antigens, especially in the context of tumors and infections. Unlike normal antibodies, in which both arms recognize the same antigen, these bispecific antibodies can recognize two different antigens with each arm. CD3-bispecific antibodies, for example, work by attaching to both a tumor cell and a T cell at the same time. This creates a connection between the two cells, which leads to T-cell activation and the release of substances that can kill the tumor cells. The Knobs-into-Holes technology, which emerged in 1996, paved the way for the development of BsAbs, and with the continuous evolution of antibody engineering and biology, their potential applications have become diverse and flexible.



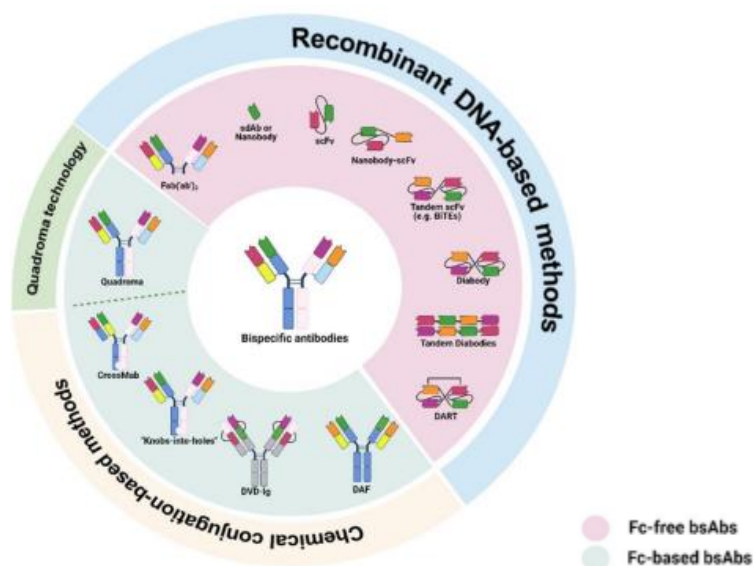


Exhibit 14: Classical Molecular Platform of BsAbs and Representative Antibodies. Source: Jiabing Ma et al.

BsAbs play a crucial role in targeted cancer therapy by precisely targeting and reactivating immune cells, regulating their activation, fine-tuning their fate and function, and improving their tolerance, thus overcoming the hurdles of “on-target off-tumor” toxicities. Over 86% of BsAbs developed to date are used in cancer treatment, and the half-life of these molecules varies with their molecular size. The multivalent targeting of CD3 by BsAbs has been found to be more effective than single-targeting strategies such as 1+1, and the selection of antibodies with different affinities for CD3 and tumor-associated antigens (TAAs) can also greatly impact their effectiveness. Studies on animals have shown that using CD3 bsAbs might be effective in treating solid tumors.<sup>11</sup> These studies have found that using CD3 bsAbs can lead to an increase in the number of T cells in the tumor and create a more active environment within the tumor. However, it's not clear yet if this is because of more T cells entering the tumor, fewer T cells leaving the tumor, or if the bsAbs make the existing T cells grow more. Early results from human trials with CD3 bsAbs are starting to show promise against solid tumors.

The future of Bispecific Antibodies (BsAbs) will see advancements in the selection of targets, the pairing of multiple targets, the use of innovative platforms, and new shapes or configurations.<sup>12</sup> Additionally, they will be combined with existing biological drugs, immunotherapies, and physical and chemical treatments to create more effective therapies. BsAbs are poised to become a new focus of medical and biological research and development. Context Therapeutics has initiated developments on its CTIM-76 technology which is a CLDN6 x CD3 bispecific antibody program to target Claudin-6 (CLDN6) positive solid tumors.

<sup>11</sup> Alison Crawford et al., Mol Cancer Ther 1 August 2021

<sup>12</sup> Jiabing Ma et al., Front. Immunol., 05 May 2021

## CTIM-76: CLDN6xCD3 Bispecific Antibody Program

According to World Cancer Research Fund International, there were more than 2,206,000 new cases of Non-Small Cell Lung Cancer (NSCLC) and more than 313,000 new cases of ovarian cancer in 2020. There is increasing attention towards using antibody-based approaches, such as bispecific antibodies, antibody-drug conjugates, and CAR-T cells, for solid tumors. However, finding suitable tumor-specific targets that do not harm healthy tissue remains a difficult task. Claudin-6 (CLDN6), a tight junction protein, has been confirmed as a target for the treatment of various solid tumor types such as ovarian, endometrial, testicular, and gastric. CLDN6 is a protein found only in tumors and is present in large amounts on the surface of many cancers in adults and children. Its expression is unique to cancer cells and is not found in normal, healthy tissue. The Claudin multigene family encodes tetraspan membrane proteins that are crucial structural and functional components of tight junctions, which have important roles in regulating paracellular permeability and maintaining cell polarity in epithelial and endothelial cell sheets. The Claudin family is made up of 24 known transmembrane proteins, each with a unique pattern of presence in specific tissues and during different stages of development. High expression of CLDN6 is associated with a worsened prognosis in cancer patients.

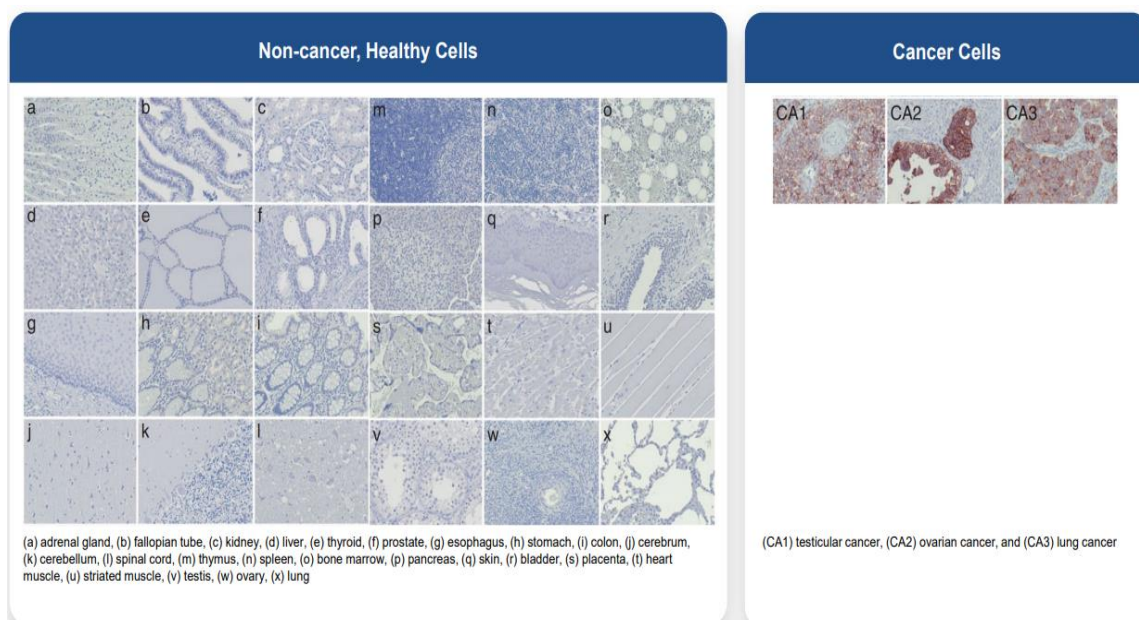


Exhibit 15: CLDN6 is Enriched in Cancer Cells vs. Non-Cancer Cells. Source: Investor Presentation

Targeting CLDN6 with therapeutic monoclonal antibodies (MAbs) is challenging due to the presence of numerous related family members and the requirement for high specificity. Of the 24 human CLDN family members, most are widely expressed and highly conserved. Existing CLDN6 MAbs in development have shown binding to other CLDN family members, leading to their termination.<sup>13</sup> CLDN6 is similar in appearance to other claudins, particularly CLDN9, which is found in healthy cells. Context and its collaborator Integral Molecular have been able to isolate

<sup>13</sup> <https://www.cusabio.com/c-21073.html>

and optimize rare antibodies against CLDN6 that do not cross-react with other CLDN family members.

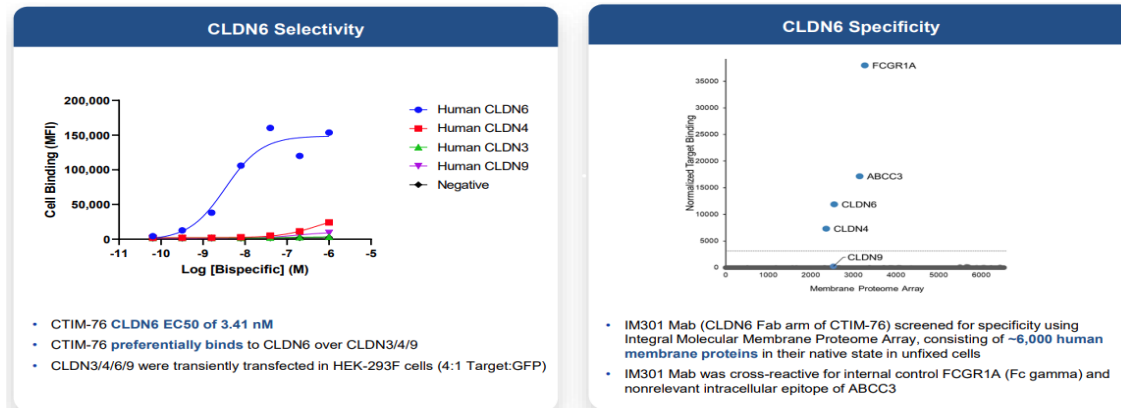
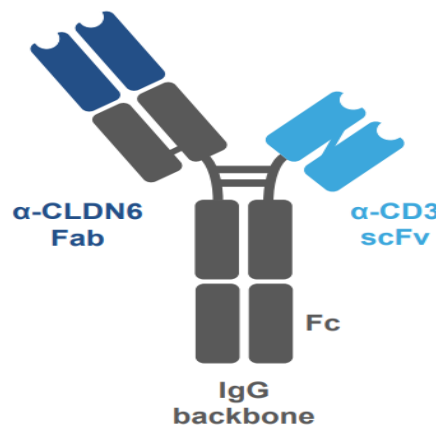


Exhibit 16: CTIM-76 shows excellent selectivity and specificity for CLDN6. Source: Investor Presentation

CTIM-76 has a potentially broad therapeutic window, with a highly selective CLDN6 binding fragment antibody-binding (Fab) arm and an immunostimulatory CD3 binding single-chain fragment variable (scFv) domain that is designed to be functionally monovalent to minimize the chance of aberrant T-cell activation, potentially improving its safety profile. The fragment crystallizable region (Fc region in the image below) is the end part of an antibody that connects with Fc receptors, which are cell surface receptors. A mutation has been introduced into the Fc domain to suppress its function and prevent T-cell activation by Fc-gamma receptor-positive cells.



*CTIM-76 effectively targets and destroys CLDN6+ cancer cells while sparing normal cells and triggers cytotoxic T cell activation without inducing unwanted cytokine release*

Exhibit 17: CTIM-76: Claudin-6 x CD3 Bispecific Antibody Source: Company Presentation

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, thereby reducing the risk of cytokine release syndrome. In-vitro studies show that CTIM-76 therapy may have the benefits of easy dosing and a low risk of causing an immune response. It can also be manufactured in large amounts to treat a large number of patients who may be eligible for the therapy. Additionally, the antibody is easily manufactured due to its stable and high-yielding IgG backbone.

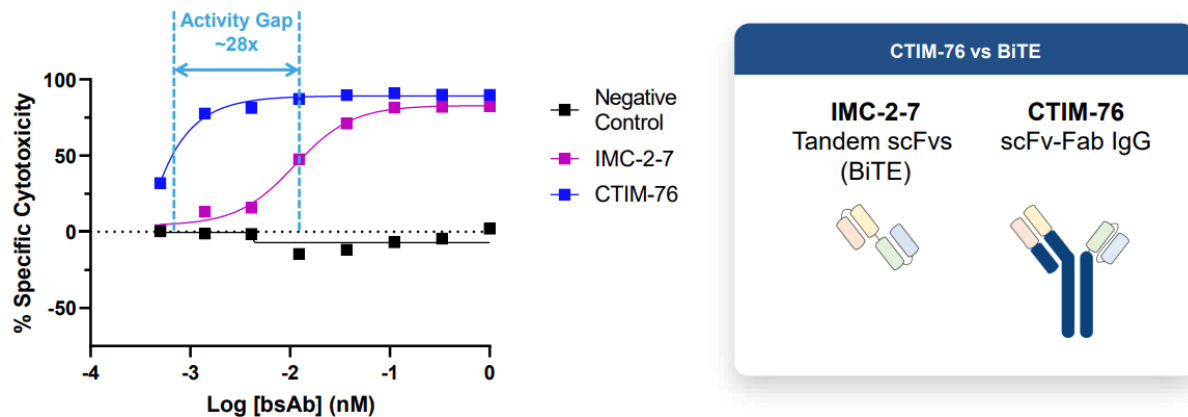


Exhibit 18: Comparing CTIM-76 Potency To That of BiTE Molecule. Source: Investor Presentation

CTIM-76 CLDN6 binding and cancer lysis were further evaluated in multiple in-vitro studies. Both CTIM-76 and a bi-specific T-cell engager antibody (IMC-2-7) were tested against CLDN6 expressing K562 cell line. CTIM-76 successfully induced a superior cytotoxic T-cell response at a similar level of dosage, demonstrating approximately 28 times more potency compared to a traditional BiTE molecule.

Context Therapeutics has collaborated with Lonza, a global development and manufacturing partner to the pharma, biotech, and nutrition industries, to manufacture Context's CTIM-76. Under the agreement, Lonza will be responsible for conducting manufacturability evaluations, constructing genes and cell lines, and developing production processes. By partnering with Lonza, known for its expertise in developing and producing complex proteins, and its regulatory knowledge and extensive manufacturing network, Context seeks to take advantage of these capabilities.

### Market Sizing and Competitive Landscape

According to publicly available estimates, CLDN6 is highly expressed in multiple cancer indications providing a wide use case for CLDN6 targeting therapies. The expression level of CLDN6 is significantly higher (>50%) in ovarian and testicular compared to other malignancies. Context estimates that approximately 62,500 cases have been reported in the US in either relapsed or refractory incidences making CLDN6 a favorable target for systemic cancer therapy in the future. The initial indication of interest is based on its CLDN6 prevalence, prognostic significance, and observed clinical responses.

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

Exhibit 19: CLDN6 Prevalence in Various Indications. Source: Company Presentation

The table shows the status of various bispecific antibody programs being studied by different institutes. A comparison was made between Context's internally developed CLDN6 monoclonal antibodies and those from BioNTech and Xencor in vitro, revealing that Context's selectivity for CLDN6:9 was 100x, compared to BioNTech's 7x and Xencor's 10x. These results should be viewed cautiously as these weren't head-to-head trial comparisons but rather data gathered from publicly available reports of independent trials or meta-analyses of clinical trials. Although BioNTech's and Xencor's products are not meant to compete with CLDN6xCD3 bsAb, comparing their symptomatic results is useful to understand their adoption as therapies. Several institutes and corporations, including UCLA, Daiichi-Sankyo, Guangzhou Medical University, and Shanghai GeneChem Co. Inc., are running more programs to use CLDN6 as a target for tumor therapies using antibody-drug conjugate and cell therapy methods. Although CLDN 6 shows great potential in cancer treatment therapies, its clinical data are in the very nascent stage, with the majority of the programs currently in phase 1 or preclinical trials, thereby providing limited but encouraging evidence of the successful development of CLDN6 targeting therapies.

Company Name	Bispecific Antibody	Stage
NovaRock Biotherapeutics	<i>NBL028:CLDN6x4IBB</i>	Preclinical
Xencor	<i>XmAb541: CLDN6xCD3</i>	Preclinical
I-MAB Biopharma	<i>TJ-46CB: CLDN6x4IBB</i>	Preclinical
Amgen	<i>AMG794: CLDN6xCD3</i>	Phase 1
BioNTech	<i>BNT142: CLDN6xCD3</i>	Phase 1
Context Therapeutics	<i>CTIM-76: CLDN6xCD3</i>	Preclinical

Exhibit 20: Select CLDN6 Bispecific Anti-bodies. Source: Company

## Management Overview

### **Martin Lehr - Co-founder and CEO**

Martin Lehr is the CEO and co-founder of Context Therapeutics. He also serves on the boards of Praesidia Biologics and CureDuchenne Ventures. Before that, he was part of the founding team at Osage University Partners, a VC fund focused on academic spinouts from leading research institutions. Martin is also a director of BioBreak, a biotech executive peer network with over 2,500 active members across the US, and a member of the advisory board for Life Science Cares and Life Science Leader magazine. He previously conducted research at Sloan Kettering Institute in DNA repair and at the Children's Hospital of Philadelphia in thrombosis and hemostasis. He holds an M.A. in Biotechnology from Columbia University and a B.A. in Economics from the University of Pennsylvania.

### **Christopher Beck, MBA - Senior Vice President, Operations**

Christopher Beck is the Senior Vice President of Operations at Context Therapeutics. With over 30 years of experience in various Pharmaceutical and Biotech companies, Mr. Beck is a pharmaceutical leader with a proven track record in strategy execution and program management capabilities. His earlier works include designing and implementing an operations management methodology that drove execution across R&D, CMC, and commercial functions at Galera Therapeutics, where he was designated as Vice President, Program Management. Mr. Beck has also worked with many startup companies as V.P. of program management. He also held program management leadership positions at Shire Pharmaceuticals, Merck and Co., and AstraZeneca. On the academic front, Mr. Beck is a B.S. in Business Administration from Drexel University and obtained an MBA from Pennsylvania State University.

### **Alex Levit, Esq. - Chief Legal Officer**

Alex Levit joined Context Therapeutics in April 2021 as the Chief Legal Officer and Corporate Secretary. Before that, he served as Vice President, Deputy General Counsel, and Assistant Corporate Secretary of OptiNose (NASDAQ: OPTN) and was the Associate General Counsel at Teva Pharmaceuticals (TLV: TEVA) from 2010 to 2017. During his tenure at OptiNose and Teva, he negotiated diverse inbound and outbound licenses, collaborations, M&A, and supply agreements. At OptiNose, he also managed various public and private financing transactions. Prior to Teva, he worked as a corporate and life sciences attorney at the law firm Reed Smith LLP. Levit also sits on the board of Strados Labs, a medical device company. He holds a JD from Temple University's Beasley School of Law and a BA in Labor & Industrial Relations from Pennsylvania State University, where he graduated from the Schreyer Honors College.

### **Priya Marreddy - Vice President, Clinical Operations**

Ms. Marreddy joined Context Therapeutics in April 2022 as the VP of Clinical Operations. With over 20 years of experience in Clinical Development and Operations, she has worked across multiple therapeutic areas at large and mid-sized pharmaceutical and biotech companies, CROs,

and startups, where she directed multinational, cross-functional teams in the strategy, design, and execution of global clinical development plans and the implementation of best clinical practices and quality improvement. Before joining Context, she served as the Head of Clinical Operations at Rafael Pharmaceuticals (now Cornerstone Research), where she established and led the Clinical Operations team in planning and conducting clinical trials for rare cancers. Ms. Marreddy holds an undergraduate degree from George Washington University and a Master's Degree in Molecular Biotechnology from the University of Pennsylvania.

#### **Jennifer Minai-Azary, CPA- Chief Financial Officer**

Jennifer Minai-Azary holds the position of Chief Financial Officer at Context Therapeutics. She has over 20 years of finance and accounting experience leading finance teams lately within the life sciences industry. She also serves on the board of directors of KAHR Medical Ltd. Before joining the company, Ms. Minai was the CFO at Millendo Therapeutics, a publicly-traded biopharmaceutical company. Additionally, she served as the Vice President of Finance at Millendo and held various finance positions, where she oversaw the financial reporting, accounting, treasury, tax, and risk management functions and also participated in several financing transactions and company mergers. She began her career at Ernst & Young holding positions of increasing responsibility, managing financial statement audits for both publicly-traded and privately-held clients in diverse industries. She holds a Master of Accounting and a B.B.A. from the University of Michigan and is a certified public accountant.

#### **Tarek Sahmoud, M.D., Ph.D. - Chief Medical Officer**

Dr. Tarek Sahmoud holds the position of consulting Chief Medical Officer at Context Therapeutics. With over 25 years of experience in oncology drug development and medical affairs, he also holds senior clinical development positions at Celgene, Novartis, and AstraZeneca, and most recently, as CMO of H3 Biomedicines. Throughout his career, Tarek has played a leading or supportive role in the global drug development programs for multiple novel oncology drugs across various indications, including adjuvant breast cancer (Arimidex<sup>®</sup>) and hormone receptor-positive breast cancer (Kisqali<sup>®</sup> and Afinitor<sup>®</sup>), leading to successful global registrations. Dr. Sahmoud obtained his medical degree from Cairo University Medical School, Egypt, and has a Ph.D. in biostatistics from University Bordeaux II, France.

#### **Richard Berman - Chairman of the Board**

Richard Berman is the Chairman of the Board of Context Therapeutics with over 35 years of experience in venture capital, senior management, and M&A. Previously, he worked at Goldman Sachs and was Senior Vice President at Bankers Trust Company, where he started the M&A and Leveraged Buyout Departments. He has served as a director or officer for over a dozen companies in the past 5 years, and over the last decade, he's been on the board of 5 one billion-dollar companies. He created the largest battery firm, helped develop SoHo in NYC, and advised on \$4B M&A deals, closing 300 transactions. Berman is a past Director of the Stern School of Business of NYU, where he obtained his B.S. and M.B.A. degrees, and has U.S. and foreign law degrees from Boston College and the Hague Academy of International Law, respectively.

## Financial Positioning

Context Therapeutics boast a robust financial position with a zero-debt and sufficient capital to support its operations and progress its clinical pipeline into Q1 2024 based on guidance. As of Q3 2022, the company reported a cash balance of \$39.4 million and negligible interest-bearing liability on its balance sheet. The company's past four quarters' average operating cash burn rate was approximately \$3.5 million. As the company progresses with its ONA-XR clinical trials and with CTIM-76 entering clinical trials next year, we expect a significant increase in operating cash burn. We estimate an operating cash burn of \$23.4 million for FY 2023e and \$31.2 million for FY 2024e. We expect the company may raise additional capital during late 2023 or early 2024.

Year-end 31 Dec. (in \$mm)	2020A	2021A	2022E	2023E	2024E
<b>INCOME STATEMENT</b>					
Revenue	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00
Gross Profit	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00
EBITDA	(\$2.57)	(\$10.53)	(\$16.80)	(\$24.94)	(\$33.42)
Depreciation & Amortization	\$0.00	\$0.00	(\$0.01)	(\$0.01)	(\$0.01)
EBIT	(\$2.57)	(\$10.53)	(\$16.80)	(\$24.95)	(\$33.42)
Interest Income/Expense	(\$0.66)	(\$0.06)	\$0.28	\$0.24	\$0.08
Profit Before Tax (PBT)	\$6.64	(\$10.46)	(\$16.53)	(\$24.71)	(\$33.34)
Profit After Tax (PAT)	\$6.64	(\$10.46)	(\$16.53)	(\$24.71)	(\$33.34)
Basic Shares Outstanding (M)	0.35	2.83	15.97	15.97	23.95
EPS - basic	\$19.07	(\$3.69)	(\$1.04)	(\$1.55)	(\$1.39)
<b>BALANCE SHEET</b>					
Cash and cash equivalents	\$0.29	\$49.64	\$34.53	\$11.15	\$44.94
Other current assets	\$0.01	\$1.62	\$3.56	\$3.73	\$3.55
Total current assets	\$0.30	\$51.26	\$38.08	\$14.88	\$48.48
Non-current assets	\$0.17	\$0.05	\$0.14	\$0.13	\$0.13
<b>Total Assets</b>	<b>\$0.47</b>	<b>\$51.31</b>	<b>\$38.22</b>	<b>\$15.02</b>	<b>\$48.61</b>
Short-term borrowing	\$5.88	\$0.00	\$0.00	\$0.00	\$0.00
Other current liabilities	\$3.66	\$3.03	\$5.16	\$5.41	\$5.68
Total current liabilities	\$9.55	\$3.03	\$5.16	\$5.41	\$5.68
Long-term borrowing	\$0.07	\$0.00	\$0.00	\$0.00	\$0.00
Other non-current liabilities	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00
Total liabilities	\$9.62	\$3.03	\$5.16	\$5.41	\$5.68
Total Equity	(\$9.15)	\$48.27	\$33.07	\$9.61	\$42.93
<b>Total Liabilities &amp; Equity</b>	<b>\$0.47</b>	<b>\$51.31</b>	<b>\$38.22</b>	<b>\$15.02</b>	<b>\$48.61</b>

Exhibit 21: Income Statement Snapshot. Source: Diamond Equity Research

## Valuation

We have valued Context Therapeutics using risk-adjusted DCF as our preferred methodology. Our valuation incorporates ONA-XR's three clinical indications that are currently in human clinical trials. Given the lack of information regarding potential indications that CTIM-76 might target and its pre-IND stage, we have refrained from incorporating it into our valuation approach. We have assumed potential commercialization for ONA-XR in the United States, EU5 countries, and Japan. We will take into consideration ROW and other significant geographies as soon as additional information becomes available. Considering similarities in ONA-XR's mechanism of action between breast and endometrial cancers, as well as Onapristone's previous clinical experience in both gynecological and breast cancers, we believe it's reasonable to assign a 15%



probability of success for all its three indications. Furthermore, our pricing assumptions are based on other competing drugs, primarily targeted therapies [Ibrance](#)<sup>®</sup>, [Verzenio](#)<sup>®</sup>, and [Piqray](#)<sup>®</sup>, that are currently being used as 1L/2L treatment for metastatic breast cancer in combination with antiestrogen drugs. We have assumed a monthly treatment cost of \$14,000 and assumed 9-month treatment cycle for breast cancer and 8-month treatment cycles for endometrial cancer. Our pricing estimates for endometrial cancer are in similar line with what is established for breast cancer. Our revenue projection takes into account the 2034 expiration year of the patent for ONA-XR. We have discounted the cash flows assuming a discount rate of 12.5%

Based on our estimates and assumptions, we valued Context Therapeutics at \$93.82 million or \$5.88 per-share contingent on successful execution by the company.

Therapy	Cancer Indication	Probability	Stage	Commercialization Year
ONA-XR + Anastrozole	PR+ Endometrial Cancer	15%	Phase 2	2026
ONA-XR + Fulvestrant	ER+, HER2- Breast Cancer	15%	Phase 2	2026
ONA-XR + Elecestrant	ER+, PR+, HER2- Breast Cancer	15%	Phase 1b/2	2027

		Approaches (in \$ mm)	Value (USD)	Weight	Wtd. Value (USD)
<b>Calculated Equity Value (\$mm)</b>		DCF	\$93.93	90%	\$84.54
Enterprise Value	\$54.58	GPCM	\$92.87	10%	\$9.29
- Debt and Preferred Stock	\$0.08	GTM	-	0%	\$0.00
+ Cash	\$39.43	<b>Wtd. Avg. Equity Value (USD)</b>			<b>\$93.82</b>
Net Debt	\$39.35	<b>No of Diluted Shares Outstanding</b>			<b>15.97</b>
Equity Value	<b>\$93.93</b>	<b>Intrinsic Value Per Share</b>			<b>\$5.88</b>

Company Name	Ticker	Price	Currency	Country	Mkt Cap.	P/B*	P/R&D*
Arvinas Inc.	ARVN	\$35	USD	US	\$1,884	3.00x	6.76x
Merus N.V.	MRUS	\$17	USD	NL	\$764	2.60x	6.01x
Zymeworks Inc.	ZYME	\$10	USD	CA	\$633	3.50x	3.00x
Celcuity Inc.	CELC	\$10	USD	US	\$413	9.50x	13.70x
Puma Biotechnology Inc.	PBYI	\$5	USD	US	\$209	9.50x	3.98x
Olema Pharmaceuticals Inc.	OLMA	\$5	USD	US	\$182	0.80x	2.37x
Atossa Therapeutics Inc.	ATOS	\$1	USD	US	\$104	0.80x	8.02x
Ambrx Biopharma Inc.	AMAM	\$2	USD	US	\$69	0.50x	1.06x
Xencor Inc.	XNCR	\$37	USD	US	\$2,194	3.00x	11.02x
<b>Median</b>						<b>3.00x</b>	<b>6.01x</b>
<b>Mean</b>						<b>3.69x</b>	<b>6.21x</b>

Exhibit 22: Valuation Snapshot (in \$mm). Source: Diamond Equity Research  
(\*P/B and P/R&D are based on LTM values)

## Risks Profile

- **Clinical Development Risks:** The success of the company heavily relies on the success of the CTIM-76 and ONA-XR clinical trials. They may face risks with the emergence of pandemics, epidemics, or outbreaks. It is also important to note that clinical trials are expensive, time-consuming, and difficult to plan and implement, all with the risk of an uncertain outcome. Context Therapeutics products are based on novel technologies, which make it difficult to predict the cost, timing, and results of product candidates. Other parts of the trial process, such as patient retention, are also complicated and could be disrupted by negative externalities.
- **Financial/Dilution Risks:** Context Therapeutics has a limited operating history, is not profitable yet, and might never achieve or sustain profitability. Even if CTIM-76 and ONA-XR are successful, they will need further financing to develop new products. This runs the risk of dilution. There is also the risk of concentrating scarce resources on a product candidate that fails to yield returns and fails to capitalize on a profitable drug.
- **Regulatory Risks:** Any disruptions in the FDA or other authorities, domestic or foreign, could impact development and commercialization. FDA and other regulatory processes are lengthy, costly, uncertain, and time-consuming. Serious side effects or other adverse findings might emerge after final approval leading to discontinuation of the product, losing approval on all products, or if discovered after marketing approval, it could lead to the loss of marketing authorizations on their other product candidates. Besides regulatory approvals for product candidates, there are the regulatory requirements required for continued marketing.
- **Commercialization Risks:** Context Therapeutics has never commercialized a product, so it is difficult to determine the viability of a new product. The market opportunity for CTIM-76 and ONA-XR might also be smaller than anticipated. The company faces competition from other biotech and pharma companies. They may also face early generic drug competition for female cancer and other solid tumors drugs.
- **Counterparty Risks:** Counterparties such as employees and independent contractors such as clinical trial sites, principal investigators, contract research organizations (CROs), consultants, contract manufacturing organizations (CMOs), and other third parties could engage in malpractices, renege on the terms of their contract, etc. and lead to a major operational loss and hindrance to development. Furthermore, the number and nature of collaborations could harm potential partnerships, and any loss of relationships would significantly deter business.

*This list of risk factors is not comprehensive. For a full list, please refer to Context Therapeutics' latest prospectus and/or annual filings.*

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