Filed Pursuant to Rule 433 of the Securities Act of 1933
Issuer Free Writing Prospectus dated September 10, 2021
Relating to the Preliminary Prospectus dated September 10, 2021
Registration Statement File No. 333-256572

context therapeutics

Advancing Medicines For Female Cancers

Context Therapeutics Inc.

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.

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Free Writing Prospectus

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The Company has filed with the SEC a registration statement (File No. 333-256572) including a preliminary prospectus for the offering to which this presentation relates, but such registration statement has not been declared effective.

Before you invest, you should read the preliminary prospectus in that registration statement, including the “Risk Factors” set forth therein, and the documents filed as exhibits to the registration statement for more complete information about the Company and the offering. You may access these documents for free by visiting EDGAR on the SEC website at www.sec.gov.

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Copies of the preliminary prospectus may be obtained for free by visiting EDGAR on the SEC web site at www.sec.gov or by contacting ThinkEquity LLC, 17 State Street, 22nd Floor, New York, NY 10004, by telephone at (877) 436-3673 or by email at prospectus@think-equity.com.

Offering Summary

Issuer	Context Therapeutics Inc.
Listing	CNTX (NASDAQ Capital Markets)
Proposed Aggregate Offering[1]	$19,500,000
Price Range	$12.00-$14.00 per share
Shares Offered	1,500,000
Pre-IPO Common Shares Outstanding as converted[2]	5,437,190
Use of Proceeds	Advancing clinical development of ONA-XR, our lead PR antagonist for PR+ solid tumors, preclinical advancement of Claudin 6 bispecific, R&D working capital, general corporate
Sole Book-Runner	ThinkEquity

(1) Anticipated gross proceeds are assuming a $13.00 initial public offering price, which is the midpoint of the range included on the cover page of the preliminary prospectus and the sale of 1,500,000 shares of common stock
(2) Common stock share total is as of September 1, 2021, after giving pro forma affect to the conversion of all outstanding shares of preferred stock and the conversion of certain warrants immediately prior to the completion of the initial public offering.

Executive Summary

Our Focus	→ Women's oncology
Lead Asset: ONA-XR	→ Onapristone extended release (ONA-XR) is a progesterone receptor (PR) antagonist → PR oncogenic signaling associated with breast, ovarian, and endometrial cancer
Value Proposition	→ PR antagonism (PRA) is a new treatment modality → Large market opportunity for PRA when used in combination with standard of care therapies
Focus on Execution	→ ONA-XR in multiple clinical trials: • Three Phase 2 trials • One Phase 1b/2 trial • Two Phase 0 biomarker studies
Path Forward	→ ONA-XR has been administered in over 128 subjects-to-date • Appears to be well tolerated and shows efficacy supporting continued development • Straightforward clinical development plan

Progesterone Receptors Antagonism: Ready for Prime Time

There is heightened interest in PR antagonists (PRAs) for treating hormone-dependent cancers due to new mechanistic understandings of PR oncogenic signaling

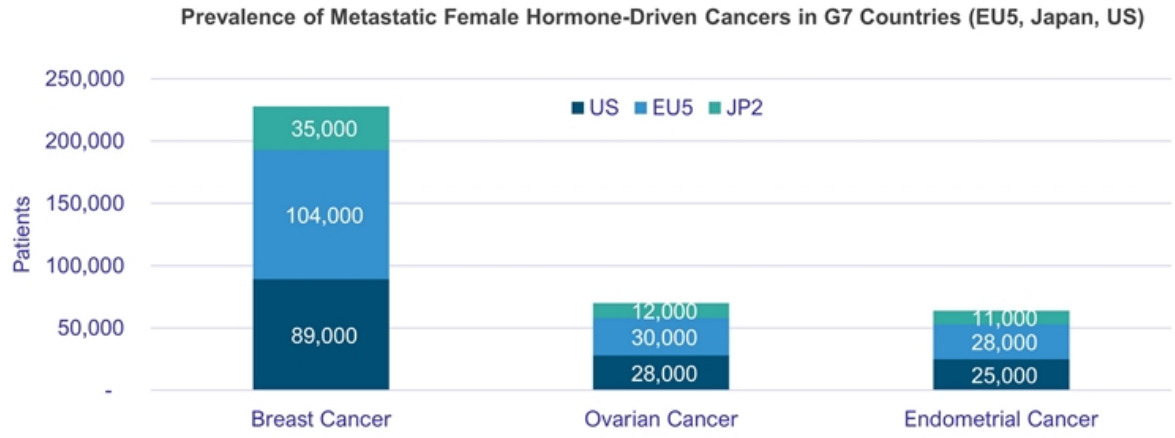
Development of PRAs hindered by PK issues, poor selectivity, and mixed agonist/antagonist properties

ONA-XR addresses prior limitations of PRAs

ONA-XR is an opportunity to realize the potential of progesterone receptor antagonists in oncology

Market Opportunity for Lead Program (ONA-XR)

- We target large, underserved markets
- Within the G7 countries, over 355,000 patients are living with metastatic breast, ovarian, or endometrial cancer
- Based upon published data, up to 70% of these patients are potentially eligible for ONA-XR treatment



*Source: secondary epidemiologic estimates, 2020 estimates

Recent Drug Launches

- Since 2012, there have been 5 major drug approvals, as shown below, for hormone-dependent breast cancer
- We believe that ONA-XR will be additive or synergistic with these recently approved drugs, leading to a billion-dollar plus peak sales potential

Highest projected or historical annual peak sales for currently marketed products in breast cancer; includes historical years for drug classes with generic competition; based on data from EvaluatePharma as of July 2020

Focus on Execution

- We believe that clinical development of ONA-XR is primarily a function of exacting clinical execution
- Context has an experienced management team
- 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

Management

Martin Lehr
CEO and Director

- Independent Director, Praesidia Biologics
- Director, CureDuchenne Ventures
- Senior Associate, Osage University Partners

Tarek Sahmoud, MD, PhD
Chief Medical Officer

- President, OncoStrategy LLC
- CMO, H3 Biomedicines
- SVP, Celgene
- SVP, Novartis Oncology

Evan Dick, PhD
SVP R&D

- SVP, Aclaris Therapeutics
- SVP, Ralexar Therapeutics
- SVP, Ceptaris Therapeutics
- SVP, Ception Therapeutics

Bill Rencher, PhD
Head of CMC and Regulatory

- President, Drug Development Solutions LLC
- Senior Director, Fulcrum Pharma Dev
- Director, CONRAD Program
- Assoc. Director, Schering Plough

Eileen Kittrick, CPA
Controller

- Controller, Genova Group
- Sr Dir, Siegfried Group
- Auditor, Lindquist & Joyce

Alex Levit, Esq
Chief Legal Officer

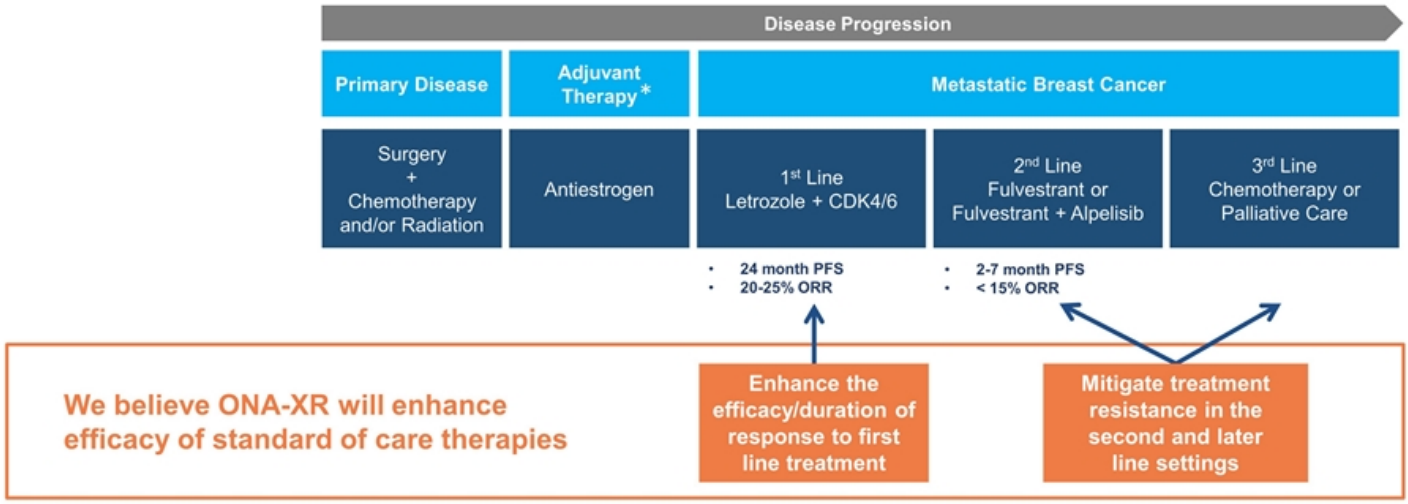
- Deputy GC, OptiNose
- Associate GC, Teva
- Associate, Reed Smith

ONA-XR

Progesterone Receptor Antagonist

ONA-XR is Being Developed to Enhance SOC Efficacy in Hormone-dependent Breast Cancer

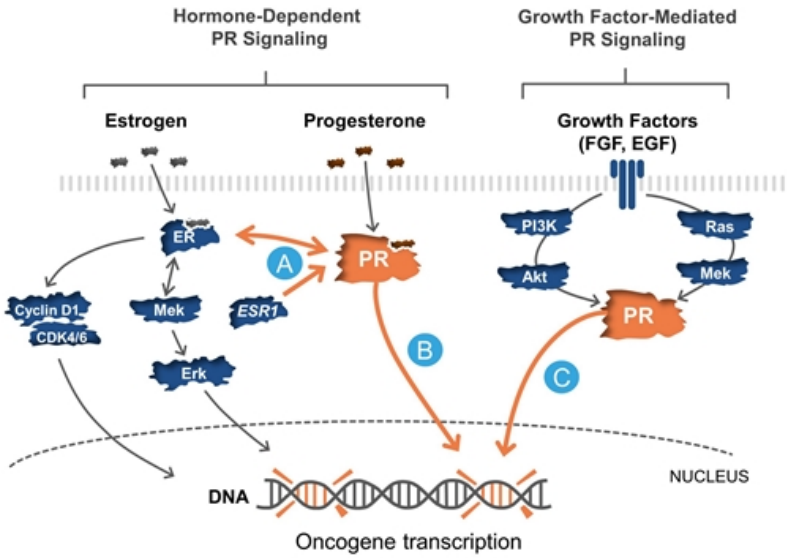
- The current standard of care (SOC) for **primary**, hormone-dependent breast cancer (ER+,PR+,HER2-) is **antiestrogen** therapy
- The current 1st line SOC treatment for **metastatic** breast cancer is **antiestrogen** therapy ***plus*** a **CDK4/6 inhibitor**[1]
- Current therapeutic options are limited for patients whose disease continues to progress after 1st line therapy[2]
- ONA-XR has the potential to enhance the efficacy of 1st line therapy, as well as that of 2nd line and later line treatments



* Adjuvant therapy is therapy that is given in addition to the primary or initial therapy to maximize its effectiveness.

[1] Rugo, JCO, 2016
[2] Clarke, Mol and Cell Endo, 2015

Progesterone Receptor (PR) Signaling is Oncogenic



Oncogenic PR signaling is associated with:

- Cancer initiation[1]
- Metastatic spread[2]
- Resistance to current therapies[2,3]

Oncogenic PR signaling can be driven by:

- A Wild-type or mutant estrogen receptor (ER) receptor activity
- B Progesterone-mediated signaling
- C Growth factor-mediated signaling

Onapristone blocks all forms of PR signaling

[1] Knutson, J Hem Onc, 2017
[2] Dwyer, Metastasis, 2021
[3] Lopez-Knowles, BJC, 2018

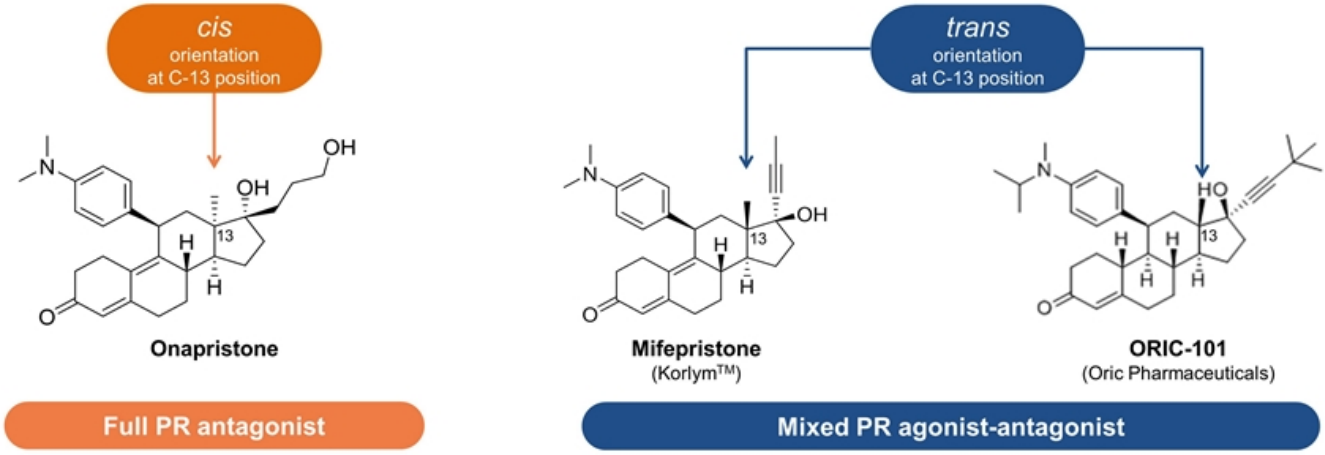
Stereochemical Basis of Onapristone's Full PR Antagonism

→ Onapristone is the only full PR antagonist (PRA) from among all clinically evaluated PRAs

- Full PR antagonism means it exhibits no PR agonist activity

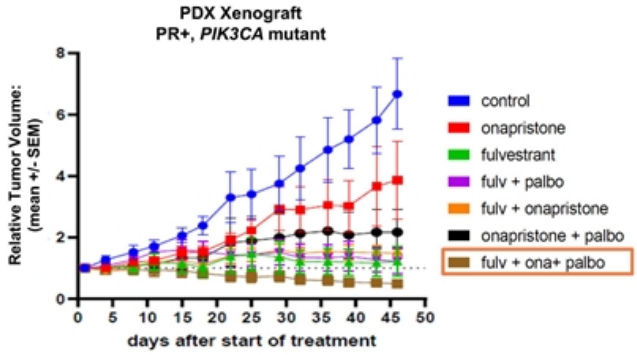
→ Onapristone's full PRA activity is attributed, in part, to a unique spatial orientation or "stereochemistry"

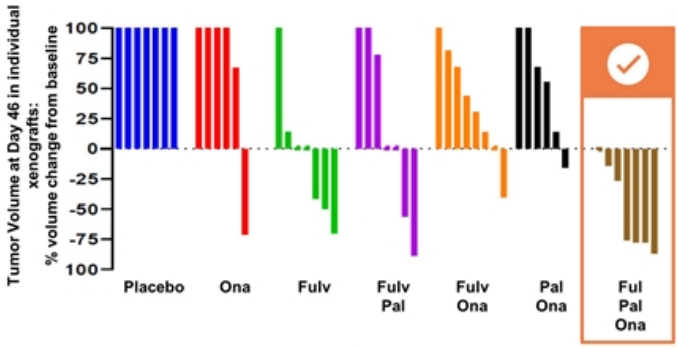
- The methyl group at the C-13 position is in a ***cis*** orientation for ONA compared to a ***trans*** orientation for all other drugs in its class



Patient-Derived Xenograft Data

Addition of onapristone to standard of care drugs enhanced tumor regression





Triplet treatment: fulvestrant, onapristone, palbociclib

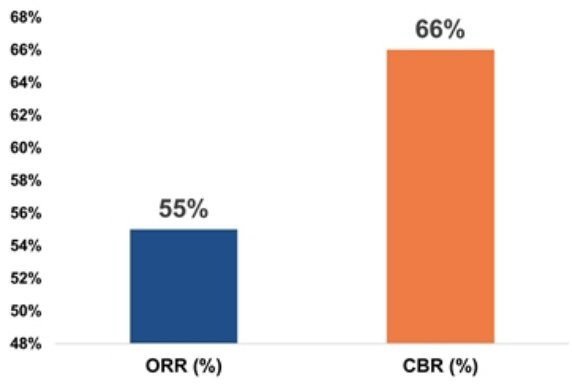
→ Onapristone, in triplet with standard of care drugs, produced a statistically significant enhancement of tumor regression compared to monotherapy and combination arms

→ Patient-derived xenograft (PDX) data supports the clinical evaluation of ONA-XR in combination with CDK4/6 inhibitors plus antiestrogen therapy

Maragoni et al, Unpublished, 2021
Ona = onapristone; Fulv = fulvestrant; Pal = Palbociclib
Relative tumor volume = $100(V_f - V_i)/V_i$ where V_i = initial tumor volume and V_f = final tumor volume

Promising Evidence of Clinical Efficacy as a First-Line Rx in Breast Cancer

Onapristone Immediate Release (ONA-IR) as First Line Therapy



overall response rate (ORR) and clinical benefit rate (CBR) in locally advanced or metastatic breast cancer [1]

→ Onapristone in an immediate release formulation (ONA-IR) had a meaningful impact on treatment of hormone-dependent breast cancer

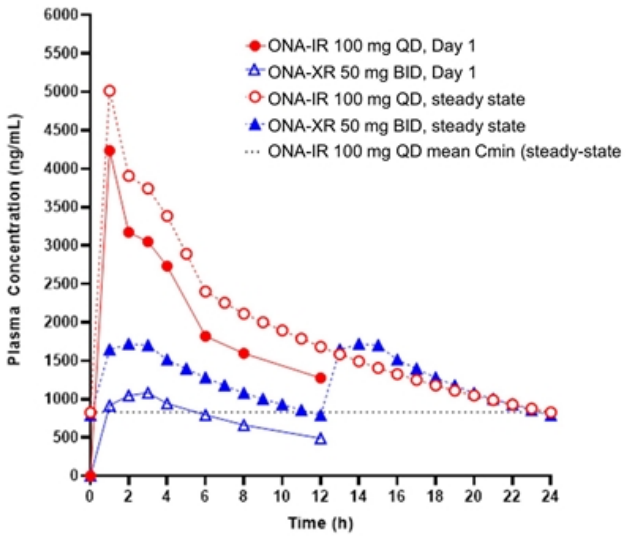
→ In 1999, Robertson et al reported that ONA-IR showed promising efficacy as a first line therapy for localized or metastatic breast cancer, but with "…transient liver function test abnormalities"[1]

→ ONA-XR was designed to minimize liver function test abnormalities and enable onapristone to be evaluated again, for efficacy/safety in hormone-dependent cancers

[1] Robertson, Eur J Cancer, 1999
ORR = overall response rate; CBR = clinical benefit rate

ONA-XR Was Designed to Improve Therapeutic Window of ONA-IR

ONA-XR versus ONA-IR: plasma onapristone concentrations at Day 1 and at steady-state[1]



→ PK dataset enabled a direct comparison between C_{max} and steady-state trough concentrations (C_{min-ss}) ONA-IR 100mg QD and ONA-XR 50mg BID

→ Dosing with ONA-XR resulted in a steady-state C_{max} almost 3X lower than for ONA-IR

→ Steady-state C_{min} was similar for both onapristone formulations

Compared to ONA-IR, ONA-XR has:

- Lower peak drug concentration (C_{max}) to improve tolerability
- Similar trough drug concentration (C_{min}) to maintain target coverage and efficacy

[1] Lewis, Drug Safety, July 2020

ONA-XR Evaluation in Breast Cancer Trials

Treatment Line	Context Trial	Trial Status	Estimated Patients (US)*	Standard of Care (SOC)	Medical Need
Adjuvant (after primary disease treatment)	**Window of Opportunity**[1]	Enrollment Completed; Presentation Q4 2021	>>250,000	Antiestrogen	Enhance antiestrogen potency; decrease progression to TNBC
First-Line Metastatic	**1L ER+,PR+,HER2- (ctDNA^{high})**[2]	Enrolling Patients	75,000	Antiestrogen + CDK4/6i	Identify and treat 20% of patients who are at high risk of early relapse
Second / Third Line Metastatic	**2L/3L ER+,PR+,HER2- (post-CDK4/6i)**[3]	Enrolling Patients	35,000	Fulvestrant or Fulvestrant + PI3Ka	Weak tumor response to current SOC

Our breast cancer trials build upon positive Phase 1-2 data from ONA-IR trials

(1) NCT04142892; (2) NCT04872608; (3) NCT04738292
*Source: secondary epidemiologic estimates, 2020 estimates

ONA-XR Evaluation in Gynecologic Trials

Cancer	Context Trial	Trial Status	Estimated Patients (US)*	Standard of Care (SOC)	Medical Need
Recurrent Endometrial	Combination with Anastrozole in PR+ patients[1]	Enrolling Patients	25,000	Lenvima + Keytruda	Limited treatment options after recurrence
Recurrent Granulosa Cell Tumor of Ovary	Combination with Anastrozole in PR+ patients[2]	Monotherapy Phase Complete; Combination Study Enrolling Patients	5,000	Physician's Choice	No FDA approved products in recurrent setting

Focused on gynecologic malignancies where PR is a known driver

(1) NCT04719273; (2) NCT03909152
*Source: secondary epidemiologic estimates, 2020 estimates

Granulosa Cell Tumor (GCT) of Ovary: A White Space Opportunity

- **GCT of Ovary are Rare Tumors**
  - Estimated 5,000 patients with recurrent disease in US[3]
  - Almost 100% are progesterone receptor (PR) positive[1,2]

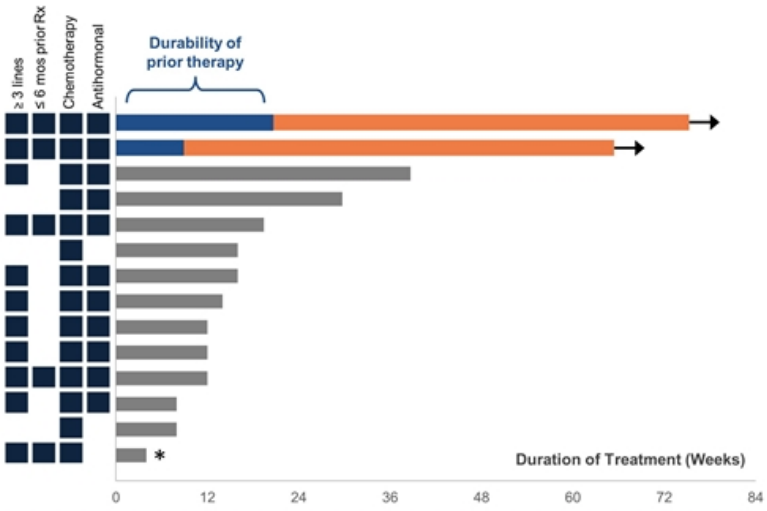
- **Current Treatment Options are Limited**
  - Primary treatment is cytoreductive surgery and platinum-based chemotherapy[3]
  - No FDA approved treatments for recurrent GCT[3]
  - Antiestrogen use is common, but rarely results in tumor shrinkage[4]

- **Program Status and Next Steps**
  - **Completed enrollment** of **late line** patients with ONA-XR monotherapy (n = 14 patients)
  - **Ongoing treatment** of **early line** patients with ONA-XR plus antiestrogen therapy (n = 25 patients)

Context has the only open clinical trial in the United States

[1] Puechl, Gynecol. Oncol.,2019
[2] Schumer, Gynecol. Oncol.,2003
[3] Farinola, Int. J. Gynecol. Pathol.,2007
[4] Banerjee, JCO, 2018

ONA-XR in Late Line Granulosa Cell Tumors of the Ovary



Durability of Prior Therapy

- Letrozole + ketoconazole (5 mos)
- Lupron + Cyclophosphamide (2 mos)
- Anastrozole (7 mos)
- Letrozole (7 mos)
- Letrozole (3 mos)
- Carboplatin + Gemcitibine (4 mos)
- Anastrozole (100 mos)
- Lupron (23 mos)
- Tamoxifen + Megace (7 mos)
- Letrozole (6 mos)
- Doxil (2 mos)
- Bevacizumab (7 mos)
- Carboplatin + Taxol (5 mos)
- Etopside (2 mos)

Prior Therapies	%, Median (Range)
Overall	4 (1-17)
Chemotherapy	1.5 (1-8)
Antiestrogen	2.5 (0-11)

Prior Response	% (n)
Treatment Free Interval	
< 6 months	93% (13)
6-12 months	0% (0)
> 12 months	7% (1)

Response	% (n)
Stable Disease	64% (9)
Progressive Disease	29% (4)
Not Assessed	7% (1)

Overall Durability	% (n)
Pts on study ≥ 16 weeks	42% (6)
Pts on study ≥ 24 weeks	29% (4)

Late line data supports evaluating ONA-XR earlier in patient treatment

- → Two patients remain on therapy with stable disease
- → 64% of patients had stable disease
- → Excellent safety and tolerability

* Progression due to disease-related AE
Data Cutoff August 2, 2021

Summary

ONA-XR

- ONA-XR is the only full progesterone receptor (PR) antagonist in clinical development
- Clinical activity established with ONA-IR, new data emerging with ONA-XR
- ONA-XR has superior safety profile to ONA-IR
- IP protection through at least 2034

Market Opportunity

- Hormone-dependent cancer (breast, ovarian, endometrial) are large and growing markets
- Progesterone receptor antagonism (PRA) represents a new approach
- PRA may be used alone or in combination to enhance the efficacy/durability of therapeutics used as the standard of care

Value Creation

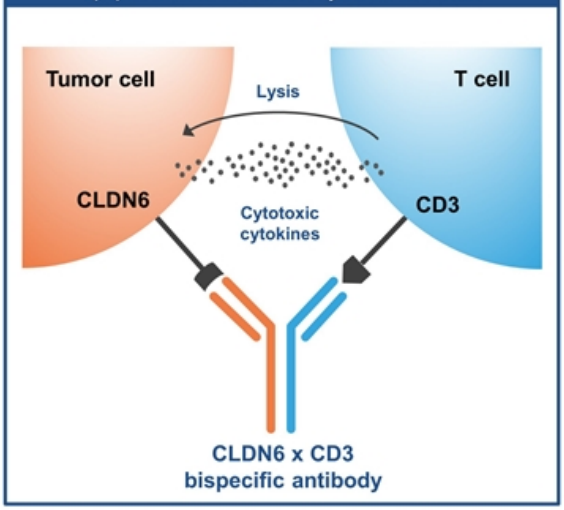
- Three Phase 2 trials
- One Phase 1b/2 trial
- Two Phase 0 biomarker trials
- Incorporation of ctDNA for an early read on clinical response to ONA-XR

Claudin 6 Program

CLDN6 x CD3 Bispecific Antibody

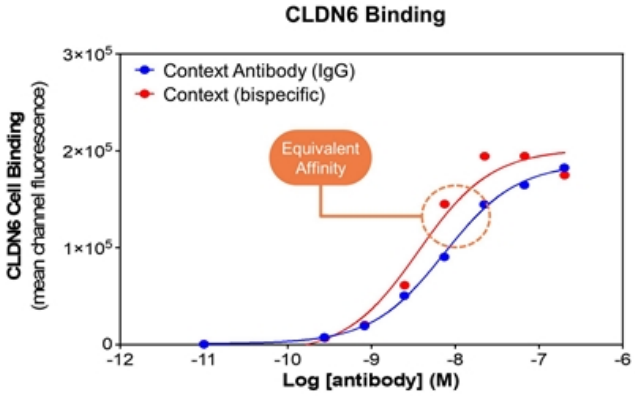
- **A "pure" cancer target**
  - Claudin-6 (CLDN6) is an oncofetal protein expressed in several tumor types, but NOT in normal adult tissues
- **Claudin-6 is expressed in ovarian, endometrial, lung, and gastric cancers**
- **Target selectivity is a challenge – and a differentiator in the field**
  - CLDN6 is structurally similar to CLDN9, differing by only 3 amino acids in the extracellular domain
  - Target selectivity is paramount, because CLDN9 is required for normal hearing and maintenance of the gut[1,2]
- **Precedent for targeting a claudin-family oncofetal protein**
  - CLDN18.2 is, like CLDN6, a oncofetal protein. In adults, CLDN18.2 is expressed in gastric and pancreatic adenocarcinomas, but otherwise limited to the epithelium of the stomach
  - Strong results treating gastric cancers with naked anti-CLDN18.2, as well as CLDN18.2-based bispecific antibodies has led to an expansion to 24 clinical trials
  - The technical principles for targeting CLDN6 are very similar to those for targeting CLDN18.2

The bispecific antibody simultaneously binds to a CLDN6-expressing tumor cell and a cytotoxic T-cell. This brings the T-cell into close proximity to the tumor cell, triggering tumor cell apoptosis via the release of cytotoxic elements.

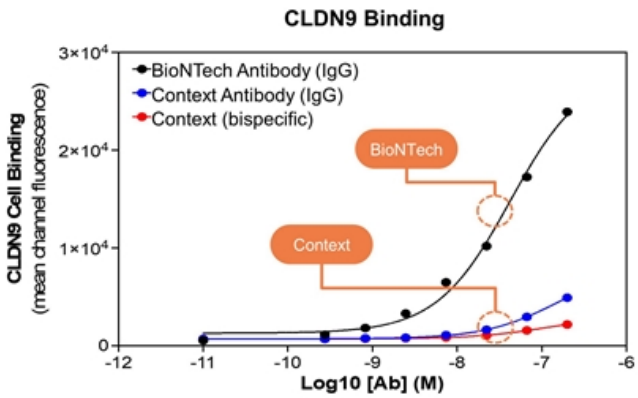


[1] Sineni, Hum Genet, 2019
[2] Vecchio, PNAS, 2019

CLDN6 x CD3 Bispecific Retains Selectivity of Parental mAb



Anti-CLDN6 mAb *versus* CLDN6xCD3 bispecific antibody: binding to CLDN6-expressing cells



Anti-CLDN6 mAbs *versus* CLDN6xCD3 bispecific antibody: binding to CLDN9-expressing cells

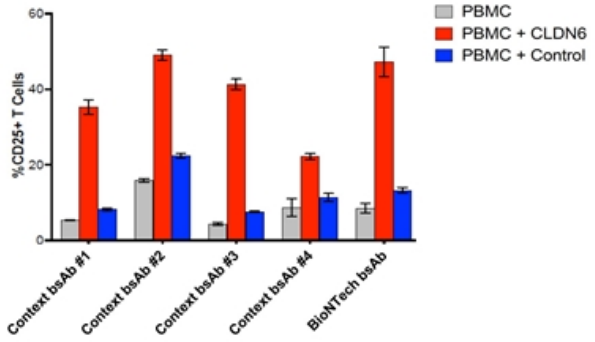
→ **CLDN6 binding affinity of bispecific *is not significantly different* from its parental anti-CLDN6 mAb**

→ **CLDN9 binding of Context bispecific *is not significantly different* from that of its parent anti-CLDN6 mAb**

→ **BioNTech mAb shows *higher* CLDN9 binding than either the parent Context mAb or the Context bispecific antibody**

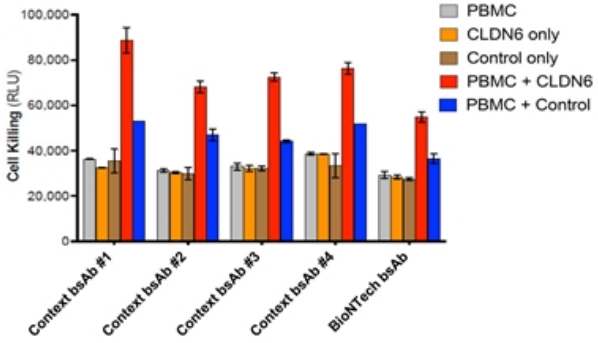
Context Bispecifics Activate T Cells Against CLDN6+ Cells

T Cell Activation



- Context bispecifics activate T-cells as determined by T-cell expression of CD25
- Background activation (PBMCs alone) is not significantly different from PBMCs plus a control bispecific
- Significant activation is seen in the presence of PBMCs plus either Context CLDN6xCD3 bispecifics or the BioNTech bispecific (red bars)

T Cell Dependent Cytotoxicity



- Context bispecifics drive T-cell dependent cytotoxicity
- Background cytotoxicity (PBMCs alone) is not significantly different from the several controls
- Significant cytotoxicity is seen in the presence of PBMCs plus either Context CLDN6xCD3 bispecifics or the BioNTech bispecific (red bars)

Context CLDN6-selective bispecifics induce T-cell activation and T-cell mediated cytotoxicity against CLDN6-expressing cells

Study Design: formats all contain same CD3 arms; activity measured after 72 hours

Competitive Landscape/Advantage

- Context anti-CLDN6 binding is at least 10x more selective vs. CLDN9 than competitive anti-CLDN6 mAbs and bispecifics
- CLDN6:CLDN9 binding selectivity is a critical safety factor for CLDN6-targeted bispecific antibodies

	Context	Xencor	BioNTech
Program	Confidential	Confidential	BNT211 BNT142
Antibody Format	CLDN6xCD3 Bispecific	CLDN6xCD3 Bispecific	CLDN6 CAR-T, CLDN6xCD3 (bi(sFc))
Stage	Preclinical	Preclinical	Phase 1, Phase 1
Status	Active	Active	Active[2]
Selectivity CLDN6:9	**>100x**	**10x[1]**	**7x**

The Company has performed head-to-head *in vitro* studies comparing BioNTech CLDN6 monoclonal antibodies. These antibodies were derived from publicly available reports published independent of the Company and may differ in material ways from the actual antibody that is in development.

(1) Faber et al., Proceedings: AACR Annual Meeting 2021; April 9-14, 2021
(2) BNT211: NCT04503278; BNT142 Ph 1 initiation 2H 2021 (ref: BioNTech Corp Presentation June 1, 2021)

Summary

- **Claudin-6 is a tumor-specific protein in adults**
- **Integrating Claudin-6 binding with the CD3 T-cell engager couples immunotherapy to tumor specific targeting**
- **Opportunity to be 1st/2nd in market based on current competition**
- **Entering IND-enabling studies in 2022**

Corporate

Pipeline

Cancer	Clinical Indication	Research	Phase 1	Phase 2	Phase 3	Upcoming Milestones	FDA Fast Track
ONA-XR (PR antagonist)[1]							
Breast Cancer	1L ER+,PR+,HER2- ctDNA^{high}			Phase 1b/2 Trial		• First patient Q3 2021 • Phase 1b data 1H 2022	
	2L/3L ER+,PR+,HER2- Post-CDK4/6 inhibitor			Phase 2 Trial		• First patient Q3 2021 • Preliminary data 2H 2022	
Ovarian Cancer	Recurrent PR+ Granulosa Cell			Phase 2 Trial		• Preliminary data Mid 2022	✓
Endometrial Cancer	Recurrent PR+ Endometrioid			Phase 2 Trial		• Preliminary data 2H 2022	
CLDN6xCD3 bispecific antibody							
	Ovarian & Endometrial Cancer					• IND enabling studies 2022	

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

Anticipated Use of Proceeds: $15.9 million(1)

	Activity	Description	Capital Allocation(2)
	**Clinical Development**	ONA-XR development, including our three ongoing Phase 2 trials and our ongoing Phase 1b/2 trial	~$7.4 million
	**Preclinical Development**	CLDN6xCD3 bsAb development	~3.5 million
	**General Corporate and Working Capital**	Corporate expenses	~$5.0 million

(1) Anticipated net proceeds are assuming a $13.00 initial public offering price, which is the midpoint of the price range included on the cover page of the preliminary prospectus and the sale of 1,500,00 shares of common stock, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

(2) Our expected use of gross proceeds represents our intentions based upon our current plans and business conditions. However, we cannot predict with certainty all of the particular uses for the net proceeds or the amounts that we will actually spend on the uses set forth above.

Upcoming Milestones

ONA-XR	Q3 2021	Q4 2021	1H 2022	2H 2022
Breast – 1L (ctDNA enriched) Phase 1b trial update			●	
Breast – 2L/3L (post-CDK4/6) Phase 2 trial update				●
Breast – Window of Opportunity data presentation		●		
Breast – PDX mechanism of action data	●			
Granulosa Cell – monotherapy Phase 2 trial update	●			
Granulosa Cell – combination Phase 2 trial update				●
Endometrial – Phase 2 trial update			●	

Claudin 6	Q3 2021	Q4 2021	1H 2022	2H 2022
Nominate clinical development candidate				●

Cap Table

Capitalization	
Common Stock[1]	**5,437,190**
Options[2]	**436,437**
Fully Diluted Common	**5,873,627**

Valuation

Valuation drivers are:

ONA-XR
Multiple Phase 2 trial readouts

Claudin 6
Precision medicine meets immunotherapy

Business Development
Opportunistic pipeline expansion

Experienced Team
Multiple FDA approvals in female cancers

(1) Common stock share total is as of September 1, 2021, after giving pro forma effect to the conversion of all outstanding shares of preferred stock and the conversion of certain warrants immediately prior to the completion of the initial public offering.
(2) Shares of common stock subject to options is as of September 1, 2021. The weighted average exercise of such option is $2.69 per share.

Investment Highlights

Large Unmet Need	Female Cancers
High Value Targets	Progesterone Receptor and Claudin 6
Lead Product Candidate	ONA-XR Being Evaluated in Multiple Phase 2 Trials
Strong Team	Deep Domain Experience, Track Record of Success
Near-Term Milestones	Multiple Data Readouts in 2022

context therapeutics

Advancing Medicines for Female Cancers

Appendix

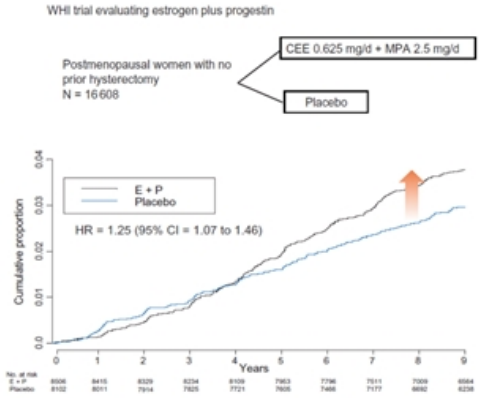
Abbreviations

AR	Androgen Receptor
ctDNA	Circulating tumor DNA
ER	Estrogen receptor
ESR1	Estrogen receptor 1 gene
Ful	Fulvestrant
GR	Glucocorticoid Receptor
MAPK	Mitogen activated protein kinase
mBCa	Metastatic breast cancer
ONA-IR	Onapristone immediate release
ONA-XR	Onapristone extended release
ORR	Overall response rate
PFS	Progression free survival
PR	Progesterone receptor
PR+	Progesterone receptor positive
SERD	Selective estrogen receptor degrader
SoC	Standard of Care
WT	Wild type

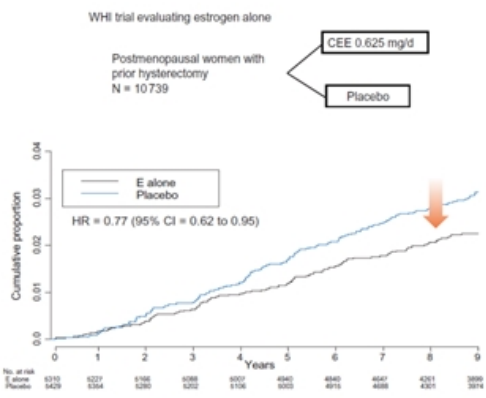
Epidemiologic Evidence: Progesterone Increases Breast Cancer Risk

Progesterone promotes oncogenic progression and maintenance of stem cells, creating a reservoir of pre-malignant cells to seed metastasis. Initial evidence for this tumorigenic role is derived from longitudinal studies of the use of hormone replacement therapy in menopausal women. These studies determined that estrogen was correlated with a 23% decrease in cancer risk, whereas progesterone was correlated with a 25% increase in cancer risk (Horwitz 2008, Anderson 2012). **The conclusion of this finding is that blocking progesterone function via anti-progestin therapy may be beneficial in cancer patients.**

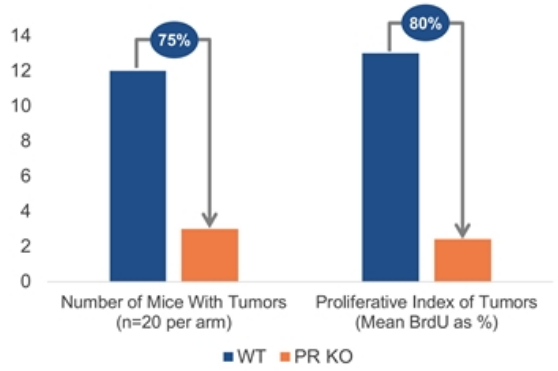
Estrogen + Progestin HRT
25% increase cancer risk



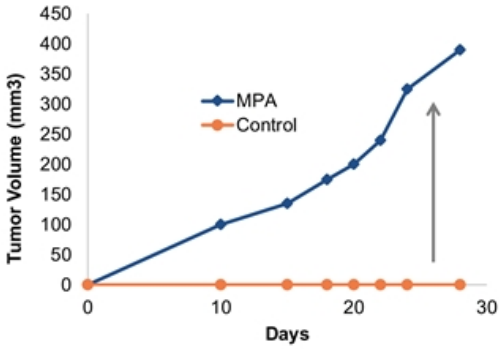
Estrogen HRT
23% decrease cancer risk



Target Validation: In Vivo Models



Progesterone Receptor Knockout (PR KO) Inhibits Tumors
Carcinogen treated, 7,12 dimethylbenz(*a*)anthracene (DMBA), pituitary-isografted mice, there was a marked reduction in mammary tumor incidence at week 44 in PRKO mice as compared with isogenic wild types (WT).
(Adapted from Lydon)



Progesterone Stimulates Tumors
Progestin-induced mammary carcinomas were subcutaneously transplanted into the flank of female BALB/c mice treated or non-treated with synthetic progesterone - medroxyprogesterone acetate (MPA).
(Adapted from Lanari)

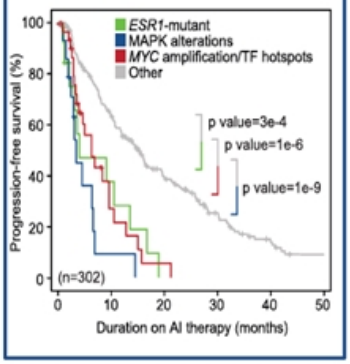
Progesterone Receptor Regulates Tumor Growth

Lydon, Cancer Research, 1999
Lanari, Endocrine-Related Cancer, 2009

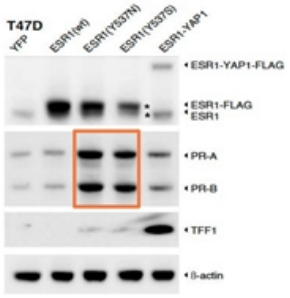
ONA-XR Active in Hard-to-Treat *ESR1* Mutations

- 20-35% of ER+,PR+,HER2- metastatic breast tumors are *ESR1* mutated (hyperactive estrogen receptor) [1,2]
- Estrogen receptor mutations are associated with resistance to anti-estrogen + CDK4/6i therapy[1,2]
- ESR1 mutations stimulate PR expression and induce PR activity[3]

Mechanisms of Resistance

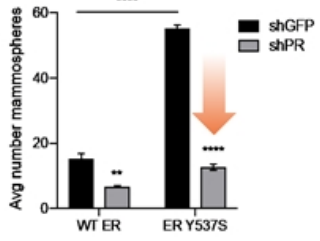


ESR1 Mutations Stimulate PR



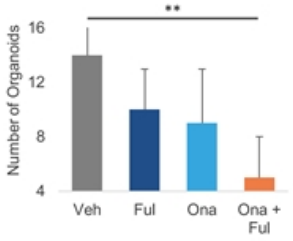
T47D cells stably transduced with ESR WT and point mutants and were grown in CSS medium for 8 days, followed by western blot

ESR1 Mutants Require PR for Growth



MCF7 WT and MCF7 ESR1:Y537S^{hom} were stimulated with estradiol and treated with vehicle (shGFP) or treatment (shPR) for 5 days

Synergy in *ESR1* Mutant Model



Patient-derived ER+,PR+ / ESR1mutant organoids (WHIM20), stimulated with estradiol (E2) and treated with onapristone (100nM), fulvestrant (100nm), or both for 5 days

[1] ESR1 Mut: Bartels, Mod Path, 2018; Lopez-Knowles, BJC, 2018
[2] MAPK: Razavi, Cancer Cell, 2018; de Leeuw, Clin Cancer Res, 2018
[3] PR Activity: Lopez-Knowles, BJC, 2018; Li, Cell Reports, 2013

Onapristone Clinical Experience

Antiprogestin	Stage	Patients (n)	Clinical Indication	Prior Treatments Median (Range)	Biomarker	Data	Reference
Onapristone IR (100mg QD)	Phase 2	19	Breast Cancer Locally Advanced or Metastatic	Hormone naïve		**56% ORR, 17.5-month DoR** **67% CBR** **14.0 month PFS**	Robertson 1999
Onapristone IR (100mg QD)	Phase 2	101	Breast Cancer Metastatic	1 (1-2)		**10% ORR** **48% CBR** **4.0 month PFS**	Jonat 2002
Onapristone XR (50mg BID)	Phase 2	14	Granulosa Cell Tumor of Ovary Metastatic	4 (2-17)	PR+	***57% DCR** ***21% 6-month PFS**	Ongoing
Onapristone IR (10 - 50mg BID) ±Abiraterone	Phase 1b/2	36	Castrate Resistant Prostate Cancer Active progression on Abiraterone	2 (1-4)	PR+	**ONA-XR (10-50 mg)** **2.8 month PFS** **ONA-XR (50 mg) + Abiraterone** **4.4 month PFS**	Jayaram 2017
Onapristone XR (10 - 50mg BID)	Phase 1	20	Breast Cancer Metastatic	9 (2-14)	PR+	**25% DCR** **15% 6-month PFS**	Cottu 2018
Onapristone XR (10 - 50mg BID)	Phase 1	13	Ovarian Cancer Metastatic	4 (2-10)	PR+	**8% ORR** **31% 6-month PFS**	Cottu 2018

* = immature data
IR = immediate release; XR = extended release

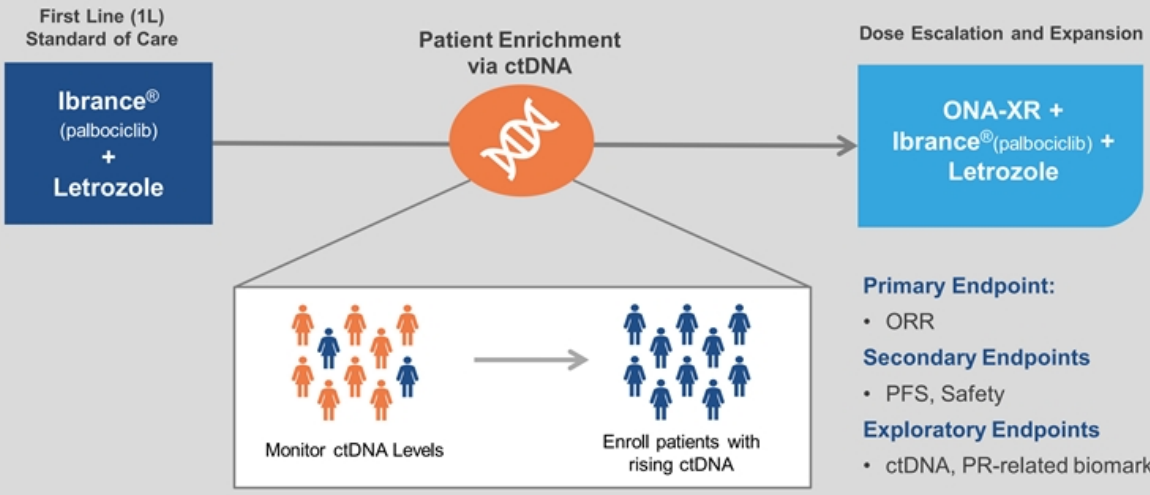
ONA-XR: Summary of Cumulative Serious Adverse Events*

System Organ Class Preferred Term	Overall (N=128) n (%)	10mg BID (N=16) n (%)	20mg BID (N=18) n (%)	30mg BID (N=15) n (%)	40mg BID (N=14) n (%)	50mg BID (N=47) n (%)*	100mg QD (N=6) n (%)
Any Serious TEAE	**34 (27)**	**7 (44)**	**7 (39)**	**6 (40)**	**3 (21)**	**9 (19)**	**1 (17)**
Ascites	2 (2)	0	0	0	1 (7)	1 (2)	0
Vomiting	2 (2)	0	1 (6)	1 (7)	0	0	0
Chest pain	2 (2)	0	1 (6)	0	1 (7)	0	0
Pneumonia	2 (2)	0	0	2 (13)	0	0	0
Femur fracture	2 (2)	0	0	1 (7)	0	1 (2)	0
Anemia	1 (1)	0	0	0	0	0	1 (17)
Atrial fibrillation	1 (1)	0	0	0	0	1 (2)	0
Syncope	1 (1)	0	0	0	0	1 (2)	0
Retinal artery occlusion	1 (1)	0	1 (6)	0	0	0	0
Abdominal pain upper	1 (1)	1 (6)	0	0	0	0	0
Upper gastrointestinal hemorrhage	1 (1)	0	0	1 (7)	0	0	0
Volvulus	1 (1)	0	0	0	0	1 (2)	0
Death	1 (1)	0	0	0	0	1 (2)	0
Pyrexia	1 (1)	0	1 (6)	0	0	0	0
Portal vein thrombosis	1 (1)	1 (6)	0	0	0	0	0
Abdominal wall abscess	1 (1)	1 (6)	0	0	0	0	0
Post procedural cellulitis	1 (1)	0	0	0	1 (7)	0	0
Pyelonephritis	1 (1)	0	0	0	0	0	1 (17)
Sepsis	1 (1)	0	0	0	0	1 (2)	0
Aspartate aminotransferase increased	1 (1)	1 (6)	0	0	0	0	0
Hypercalcaemia	1 (1)	0	0	0	1 (7)	0	0
Hyperkalaemia	1 (1)	0	0	0	1 (7)	0	0
Hyponatraemia	1 (1)	0	0	0	1 (7)	0	0
Hydronephrosis	1 (1)	0	0	0	0	0	**1 (17)**
Urinary retention	**1 (1)**	**0**	**0**	**1 (7)**	**0**	**0**	**0**

* As of Dec 31, 2020

First Line Metastatic Breast Cancer[1]

Phase 1b/2 Adaptive Trial utilizing ctDNA for Selection of Patients Who Are at High Risk of Early Relapse



Primary Endpoint:

- ORR

Secondary Endpoints

- PFS, Safety

Exploratory Endpoints

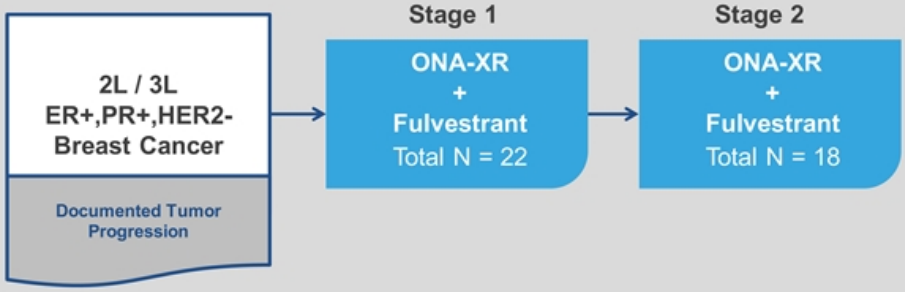
- ctDNA, PR-related biomarkers

Potential Whitespace Opportunity Within 1L HR+,HER2- mBCa

[1] NCT04872608

Second / Third Line Metastatic Breast Cancer[1]

Phase 2 Trial Evaluating Complete Hormone Blockade in Women Who Progressed on Prior Therapy in the Metastatic Setting



Endpoints:

- Primary: ORR
- Secondary: ctDNA, PFS, safety

Subgroup Analysis

- *ESR1* and *PIK3CA* mutations
- PR-related biomarkers

Intended to Establish Combination Synergy After Failure of CDK4/6 and/or PI3Kα Inhibitors

[1] NCT04738292

Pharmacodynamic Studies

Study	Target Deliverables
[1]Radiolabeled Progesterone ([18]F-FFNP PET) Uptake in Tumors	• Target engagement • Confirmation of recommended phase 2 dose (RP2D) • Drug distribution
[2] Window of Opportunity in primary breast cancer	• On-target drug effects

Studies Seek to Confirm Target Engagement and On-target Drug Effects

[1] NCT04738292; [2] NCT04142892

Partnerships

Worldwide Exclusive License to CDLN6 Antibody in Bispecific Format

- Integral Molecular to design and optimize CLDN6 x CD3 bispecific antibody
- Context to fund all development and commercial activities
- Integral received upfront payment and is eligible to receive future milestones and royalties

CMC Partnership and Out-licensing of Rights to ONA-XR in Greater China

- Tyligand designed and optimized a novel onapristone manufacturing process
- Tyligand received license to ONA-XR in Greater China

Value-Creating Partnerships

Expands Pipeline | **Capital Efficient** | **Mutually Beneficial Economics**