EDISON

Context Therapeutics

Initiation of coverage

Women's oncology play with a novel pipeline

Pharma & biotech

Context Therapeutics is a Nasdaq-listed biopharma company developing novel therapeutics focused on women's oncology indications. Lead program onapristone extended release (ONA-XR) is a potential first-in-class progesterone receptor (PR) antagonist being evaluated in several mid-stage clinical programs in advanced breast, endometrial and ovarian cancer, all areas with significant unmet need. In-licensing a bi-specific monoclonal antibody, CLDN6Xcd3, in April 2021 has added another (preclinical) novel compound to the pipeline. With multiple data readouts expected in 2022, we foresee several inflection points in the coming months. We initiate coverage with a valuation of $134.9m or $8.45/share.

Year end	Revenue ($m)	PBT* ($m)	EPS* ($)	DPS ($)	P/E (x)	Yield (%)
12/19	0.0	(6.5)	(20.11)	0.0	N/A	N/A
12/20	0.0	(3.2)	(9.28)	0.0	N/A	N/A
12/21e	0.0	(10.6)	(2.49)	0.0	N/A	N/A
12/22e	0.0	(17.5)	(1.10)	0.0	N/A	N/A

Note: *PBT and EPS are normalized, excluding exceptional items.

ONA-XR has first-in-class potential

ONA-XR is the only pure PR antagonist in clinical development for hormone-driven cancers and comes with preliminary clinical validation, based on previous studies assessing the immediate release (IR) version of the drug. While development of the IR version was marred by hepatotoxicity concerns, Context's extended-release alternative is formulated to provide a more balanced systemic exposure. We estimate a combined peak sales potential of c $1bn for the drug in the US alone.

Multiple data readouts in 2022

The company recently reported positive data from its Phase 0 'window of opportunity' study, analyzing ONA-XR in primary breast cancer. With another four, albeit small, clinical trials ongoing (including three Phase II trials in HR+/HER2- metastatic breast cancer (Mbc), recurrent endometrial cancer and granulosa cell tumor of the ovary) and expected to release interim/preliminary data starting in mid-2022, we see several catalysts for the company in the coming months.

CLDN6Xcd3: A promising addition to the pipeline

CLDN6, a protein coding gene, part of the claudin family of tight junction proteins, is enriched in several cancer cells (rarely in healthy tissue), but accurate selectivity remains a challenge. Context's bispecific antibody claims more than 10x selectivity than competitors and potentially improved efficacy through CD3 facilitated T-cell recruitment. IND-enabling studies are planned for 2022.

Valuation: $134.9m or $8.45 per basic share

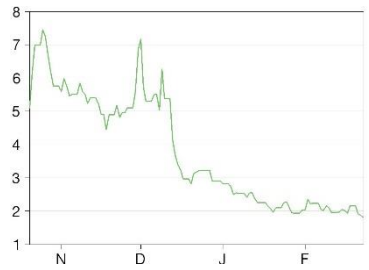
Our current valuation (using a risk-adjusted net present value model, NPV) is wholly attributable to ONA-XR's four programs under clinical development. CLDN6Xcd3 could add further upside on successful clinical transition. Estimated end-Q421 cash of c $48m should extend the runway into 2024, but we project another $110m raise (shown as illustrative debt) before reaching profitability in 2027.

24 February 2022

Price	**$1.82**
Market cap	**$29m**

Est. net cash ($m) at 31 December 2021	48.0
Shares in issue	15.97m
Free float	67%
Code	CNTX
Primary exchange	Nasdaq
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	(13.8)	(62.4)	N/A
Rel (local)	(10.3)	(58.3)	N/A
52-week high/low		$7.45	$1.81

Business description

Context Therapeutics is a clinical stage women's oncology company. Lead candidate ONA-XR is a 'full' progesterone receptor antagonist currently being evaluated in three Phase II clinical trials in hormone-driven breast, endometrial and ovarian cancer. Preliminary data from at least one trial are expected in mid-2022. The other asset is a bi-specific monoclonal antibody, CLDN6Xcd3, currently undergoing preclinical development.

Next events

ONA-XR endometrial cancer Phase II preliminary data	Mid-2022
ONA-XR second line HR+HER2- Mbc Phase II preliminary data	H222

Analyst

Jyoti Prakash, CFA +91 98 188 0393

heathcare@edisongroup.com

Edison profile page

Context TherapeuticsContext Therapeutics is a research client of Edison Investment

Investment summary

Company description: Focus on women's oncology indications

Context Therapeutics is a clinical-stage, US-headquartered biopharmaceutical company focused on developing therapeutics for cancers that mainly affect women. The company was formed in 2015 and listed on the Nasdaq in October 2021. Its lead asset ONA-XR is an extended-release version of the PR antagonist onapristone, the only 'full' PR antagonist (no agonist activity) to be tested in humans to date, to our knowledge. The drug is being evaluated as a combination therapy in hormone-driven cancers affecting women, including hormone receptor-positive (HR+)/human epidermal growth factor receptor 2 negative (HER2-) Mbc (Phase II trials in second/third-line treatment and Phase Ib/II trials as first-line escalation therapy for a subset of patients), recurrent endometrial (uterine) cancer (Phase II) and a rare form of ovarian cancer termed granulosa cell tumor (GCT) of the ovary (Phase II). Data readouts are expected from mid-2022 across all programs. The second asset is a bispecific monoclonal antibody (BsAb) CLDN6Xcd3, which is designed to facilitate T-cell mediated destruction of CLDN6 expressing malignant cells (by attaching to both the CD3 protein on cytotoxic T-cells and also on CLDN6 expressing cells, in particular in ovarian and endometrial tumors). The company is planning IND-enabling studies in 2022.

Financials: Funded into 2024

Context is currently at the pre-revenue stage and has, until now, funded its operations through capital-raising. It raised $28.8m in gross proceeds from its October 2021 initial public offering (IPO) and a subsequent $31.5m private placement in December. Based on our cash burn projections, the company is capitalized into 2024 but would need to raise an additional c $110m before reaching profitability in 2027 (by which time we estimate all three Phase II programs will have reached the market). We have modelled a $40m fund-raise as illustrative debt in both FY24 and FY25, with an additional $30m in FY26. This assumes that Context will continue to hold commercialization rights in the US, but the European operations would be out-licensed to a partner at the conclusion of Phase III studies.

Valuation: $134.9m or $8.45 per basic share

We value Context Therapeutics at $134.9m or $8.45 per basic share using a risk-adjusted NPV model focusing strictly on the four ONA-XR clinical programs. We attribute a 15% and 7.5% probability of success to the two Mbc programs (Phase II second/third-line Mbc and Phase Ib first-line escalation study, respectively) and a 10% probability of success to the other Phase II programs (recurrent endometrial cancer and GCT) due to the higher risk associated, according to our assessment. We estimate c $1bn in peak sales from all four programs combined in the US, including more than $300m each from the second/third-line Mbc and recurrent endometrial cancer programs. As CLDN6Xcd3 is preclinical, it is excluded from our valuation, but could add to the upside on successful clinical transition.

Sensitivities: Relying on ONA-XR

Context is exposed to clinical, regulatory and commercialization risks typical of all biopharma companies. In our view, the primary sensitivity is the dependence on a single asset (ONA-XR) to drive the bulk of the valuation. Key data readouts for all four clinical programs are expected in 2022 and will dictate the direction of the company's future plans. The ongoing trials are fairly small, open-label studies and the results may need to be replicated in larger randomized studies to meet the stringent regulatory hurdles in the highly competitive oncology space. Reliance on third-party contractors for drug development/clinical trials is another key risk as it affects the company's ability to maintain adequate control over quality and progress. Intellectual property risk is another

sensitivity as ONA-XR's patent (2034 expiry) is limited to the extended-release formulation and related uses (the underlying drug onapristone is off-patent), which could potentially be challenged by competitors developing other formulations of the drug. Additional risk comes from potential dilution as independent clinical development and commercialization plans in the US, if actioned, would require the company to raise significant capital, possibly through equity issues. It is also possible that, given the large size of the targeted indications (particularly breast cancers), Context may be required to carry out larger studies than we anticipate, possibly delaying registration and market launch compared to our estimates, and materially increasing our funding assumptions. Developing out-licensing opportunities in other geographies will also be critical.

Company description: Optimizing the oncology opportunity

Context Therapeutics is a US-based drug development company with a focus on women's oncology indications such as breast, endometrial and ovarian cancer. The company was formed in 2015 and listed on the Nasdaq in October 2021. Context operates an asset-light model, employing a core team of five to seven people and outsourcing its development and laboratory activities to third-party providers. It is not currently engaged in drug discovery, instead seeking to identify and onboard novel assets from late preclinical to Phase II and develop them through the clinical stages with the aim of potentially commercializing them.

Context's core pipeline drug is ONA-XR, which is an extended-release version of pure PR antagonist onapristone. The drug has had an eventful journey since its original development by Schering in the mid-1990s for potential use as an anti-endocrine treatment for breast cancer, as an oral contraceptive and a treatment for benign gynecological disorders uterine leiomyoma and endometriosis. While initial efficacy data from the first Phase II studies in Mbc were encouraging (objective response rate of 56%), the trial was halted prematurely over liver toxicity concerns. In 2012, the worldwide licence to the drug was acquired by Arno Therapeutics, which developed an extended-release version under the premise that a slower-releasing, more balanced systemic distribution should be able to counteract any off-target toxicity issues. Subsequent safety studies (two Phase I/II studies involving patients with breast, ovarian, endometrial and prostate cancer) showed reduced risk of hepatotoxicity with the extended-release version, supporting further clinical evaluation of the drug. Context eventually acquired ONA-XR in December 2017 for an undisclosed consideration, following Arno's decision to go into liquidation. The company holds patents involving ONA-XR's composition, formulation and related methods of use (patent expiry in 2034).

ONA-XR is currently being evaluated in four separate clinical trials in hormone-dependent cancers, including three Phase II studies and one Phase Ib/II study:

- Phase II: second-line treatment for HR+/HER2[1]- Mbc, in combination with anti-estrogen drug Faslodex (fulvestrant) for patients who have progressed on the first-line treatment standard of care (SoC) anti-estrogen therapy (aromatase inhibitors) +CDK4/6 inhibitors (SMILE study).
- Phase II: treatment for recurrent/metastatic PR+ endometrial cancer in combination with aromatase inhibitor Arimidex (anastrozole) (ONWARD 221 study).
- Phase II: treatment for PR+ advanced GCT of the ovary in combination with aromatase inhibitor Arimidex (anastrozole); this program holds the FDA fast track designation (ONWARD 220 study).

1 HER2 is a tyrosine kinase protein and oncogene that is overexpressed in about 20% of breast cancers. These are termed HER2+ breast cancers.

- Phase Ib: first-line escalation treatment for HR+/HER2- Mbc, for a subset of patients (c 20%) who do not show a clinical response to the SoC (aromatase inhibitor letrozole/Femara and CDK inhibitor palbociclib/Ibrance) after six months of treatment.

All four trials are expected to read out in 2022 (starting in mid-2022), making the next few months extremely crucial for the company. We note that each of the trials is an investigator-sponsored, open-label, single-arm, non-randomized trial recruiting a small number of patients (20–40 subjects), which comes with the benefit of materially reduced costs compared with trials conducted by contract research organizations (CROs). However, the flip side is reduced control and possible investigator bias.

The second asset is a BsAb CLDN6Xcd3, in-licensed from Integral Molecular in April 2021 for an upfront payment of c $3.1m ($2.8m paid as equity), as well as potential development and regulatory milestones totaling $55.3m, potential sales milestones of $130m and tiered royalties of up to 12% of net sales. CLDN6 is a member of the claudin family of tight junction proteins. It is expressed in several malignant tumors but rarely in healthy tissues, making it a potentially suitable target for therapeutic intervention. However, development had been hampered by difficulty in selectively targeting the protein due to its close similarity with CLDN4 and CLDN9, which are expressed in healthy cells. Context claims that its antibody solution is highly specific to CLDN6 (at least 10x times higher selectively compared with other competing products under development, according to management). Moreover, by developing a bi-specific antibody, where one arm of the Y-shaped antibody will bind to CLDN6 and the other arm will dock with CD3 (expressed on cytotoxic immune T-cells), the company is aiming for the T-cells to move closer to the cancer cells to maximize their cytotoxic effect on the tumor, in effect enhancing the efficacy of the drug. BsAbs are a new class of therapeutics, and only three assets are currently approved and marketed in this category. Context's R&D pipeline is shown in Exhibit 1 below.

Exhibit 1: Context's therapeutic's 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			• Phase 1b data Mid 2022	
	2L/3L ER+,PR+,HER2- Post-CDK4/6 inhibitor		Phase 2 Trial			• Preliminary data 2H 2022	
Ovarian Cancer	Recurrent PR+ Granulosa Cell		Phase 2 Trial			• Preliminary data 2H 2022	✓
Endometrial Cancer	Recurrent PR+ Endometrioid		Phase 2 Trial			• Preliminary data Mid 2022	
CLDN6xCD3 bispecific antibody							
	Ovarian & Endometrial Cancer					• IND enabling studies 2022	

Source: Context Therapeutics

Targeting underserved, hormone-driven cancers

A hormone-sensitive/hormone-dependent cancer is a type of malignancy that is dependent on hormones for growth and/or survival. In females, these hormones are estrogen and progesterone (produced by the ovaries in premenopausal women and by certain other tissues, such as fat and skin, in both premenopausal and postmenopausal women). Hormone-driven tumors express a type

of protein called hormone receptors, in this case estrogen receptors (ERs) and PRs, which become activated on binding with estrogen and progesterone respectively, leading to the growth, proliferation and metastases in cancers that affect women. According to the American Cancer Society, there were around 284,200 breast cancer cases, 66,570 endometrial cancer cases and 21,410 ovarian cancer cases in the US in 2021. More than 70% of these are known to be hormone-driven (Soo Youn Bae et. Al, Maria C. DeLeon et.al, Fang Shen et. Al), translating into a combined c 260,000 newly diagnosed cases in the United States in 2021. Context estimates that over 355,000 patients are living with hormone-dependent metastatic breast, ovarian or endometrial cancer in G7 countries alone.

The SoC treatment for primary (localized) tumors is surgical resection with or without radiation therapy. This may be followed up by adjuvant chemotherapy and/or anti-hormone/endocrine therapies (only approved in hormone receptor positive (HR+) breast cancer; discussed in more detail later), depending on the tumor grade and progression at initial diagnosis. The five-year survival rate remains high for localized/regional tumors following treatment, ranging from c 93/75% in ovarian cancer to 100/90% for HR+/HER2- breast cancer, respectively, according to the National Cancer Institute (see Exhibit 2). Despite the early success, between 10% and 30% of tumors recur or eventually metastasize. Notwithstanding the recent advances in new therapeutic treatments, hormone-driven cancers, in the metastatic setting, remain a high unmet medical need, as evidenced by the materially lower five-year survival rates for distant/metastasized tumors. One case in point is HR+/HER2- breast cancer where, despite having the best prognosis for localized tumors, the five-year survival rate for metastatic tumors tends to be lower than HER2+ tumors.

Exhibit 2: Selected cancer-types and survival rates

Type	Five-year survival (localized)	Five-year survival (regional)	Five-year survival (distant/metastatic)
HR+/HER2- breast cancer	100.0%	89.9%	**30.6%**
HR+/HER2+ breast cancer	98.9%	89.4%	44.7%
HR-/HER2+ breast cancer	96.7%	82.0%	37.9%
Triple negative breast cancer (TNBC)	91.2%	65.4%	12.2%
Endometrial cancer	94.9%	69.3%	**17.8%**
Ovarian cancer	92.6%	74.8%	**30.3%**

Source: National Cancer Institute

As highlighted above, the treatment landscape for advanced hormone-driven cancers remains limited. While anti-endocrine therapy seems an intuitive choice given the hormonal foundation of these tumors, its application has been restricted to breast cancer (as both monotherapy and combination therapy alongside targeted treatments such as CDK4/6 and PI3K inhibitors), with only off-label usage in the other hormone-driven indications. Another critical shortcoming is that the currently approved endocrine therapies only target the hormone estrogen (Exhibit 3), which allows progesterone/PR-mediated tumorigenic activity to continue unchecked.

Exhibit 3: Approved anti-estrogen therapies in metastatic breast cancer

Treatment class	Mechanism of action	Approved drugs	Administration	Initial FDA approval
Aromatase inhibitors (Ais)	Blocks the enzyme aromatase, which converts androgens into estrogen, to reduce levels of circulating estrogen. Ais are unable to prevent the ovaries from making estrogen, restricting their usage to postmenopausal women with breast cancer.	Arimidex (anastrozole)	Oral	1995
		Femara (letrozole)	Oral	1998
		Aromasin (exemestane)	Oral	1999
Selective estrogen receptor modulators (SERMs)	Blocks the binding of estrogen to its receptor by attaching to the estrogen receptor instead. If estrogen is not attached to a breast cell, the cell does not receive estrogen's signals to grow and multiply. SERMs act as ER antagonists in breast cancer but may act as ER agonists in other tissues. SERMs can be used in both premenopausal and postmenopausal cases	Tamoxifen	Oral	1977
Selective estrogen receptor degraders (SERDs)	Similar mechanism to SERMs but SERDs are full antagonists that degrade/downregulate the ER. Can be used in both premenopausal and postmenopausal cases	Faslodex (fulvestrant)	Injectable	2002

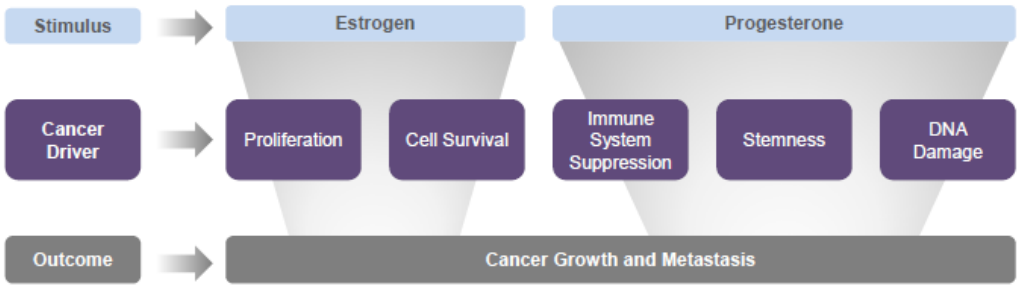
Source: Edison Investment Research

While anti-estrogen therapies have remained the treatment of choice in recurrent/metastatic HR+/HER2- breast cancer, 15–20% of tumors are believed to be intrinsically resistant (de novo resistance) to this treatment and another 30–40% of patients become refractory or acquire resistance to the treatment over a period of time.[2] Mutations in the estrogen receptor (ER) (in particular estrogen receptor 1-ESR1), compensatory PR-mediated signaling and crosstalk with other signaling pathways and/or growth factors have been established as some of the reasons for this resistance. Overcoming this limitation remains a major challenge, highlighting the need to develop more optimal combination therapeutic strategies. Targeting the PR (c 75% of ER expressing tumors express PR as well) could therefore be a promising add-on/combination therapy to the current SoC in terms of enhancing the efficacy and duration of response to current treatments, as well as mitigating the impact of acquired resistance to them.

In gynecological cancers (endometrial and ovarian cancers), despite the high prevalence of ER/PR expression (60–80% of cases), it has been challenging for anti-estrogens to gain a foothold given their limited and variable clinical activity reported as single-agent therapies.[3] Studies indicate that a combination therapy may improve the efficacy of anti-estrogens, resulting in better treatment outcomes. Context is exploring this unmet need to develop its PR antagonist ONA-XR as a combination therapy with anti-estrogens (Exhibit 4).

Exhibit 3: Context's clinical development strategy for ONA-XR

Blocking cancer growth by combining antiestrogen and antiprogestin therapies



Source: Context Therapeutics corporate presentation

Uptake of anti-progestins hindered by toxicity concerns

Similar to ER, PR is expressed in both normal cells and certain hormone-driven malignant tissues. PR is activated by binding with progesterone (one of the two female hormones produced by the ovaries, playing an important role in regulating the female menstrual cycle and pregnancy). The activated PR then binds with other PRs (called dimerization), following which it translocates to the cell nucleus where it regulates the transcription of various genes. However, progress in developing a therapeutic in this class has been hindered by a scarcity of selective and potent PR-targeting (anti-progestin) drugs under development. Only two PR antagonists have been approved for humans to date. Moreover, all approved drugs show partial PR agonist activity, with ONA-XR being the only selective/full PR antagonist under clinical development, to our knowledge. Other than selectivity, toxicity also remains an overriding concern (Exhibit 5 below gives some examples), impeding the development in this therapeutic class and highlighting the need to develop safer alternatives.

2 Lei, Jonathan T et al. Endocrine therapy resistance: new insights. *Breast. 2019*

3 Van Weelden WJ et al. Anti-estrogen Treatment in Endometrial Cancer: A Systematic Review. 2019

Exhibit 5: Antiprogestins clinical programs

Drug	Company	Indications	Agonist/ antagonist activity	Comments
Mifepristone	Corcept Therapeutics	Medical abortion (marketed) Cushing's syndrome (marketed) Metastatic HER2- breast cancer (Phase II) Metastatic glucocorticoid receptor positive TNBC (Phase II) Castration-resistant prostate cancer (Phase II)	Partial agonist	First PR antagonist to gain FDA approval in 2000. Currently being evaluated as combination therapy for HER2- Mbc and glucocorticoid receptor positive TNBC with pembrolizumab (Keytruda) and nab-paclitaxel (abraxane), respectively.
Ulipristal acetate	Allergan/ Gedeon Richter	Uterine fibroids (marketed – EU)	Partial agonist	Licence temporarily suspended in March 2020 on liver injury concerns. Suspension subsequently lifted but with stringent restrictions on usage.
Vilaprisan	Bayer	Uterine fibroids (Phase III – on hold) Endometriosis (Phase II – on hold)	Partial agonist	Trials put on hold following concerning data from animal toxicology studies.
Onapristone	Context Therapeutics	HR+/HER2- Mbc (Phase II) Endometrial cancer (Phase II) Granulosa cell tumor (Phase II)	Full antagonist	Development of the IR version halted due to liver toxicity concerns. Extended-release version designed to tackle the issue.

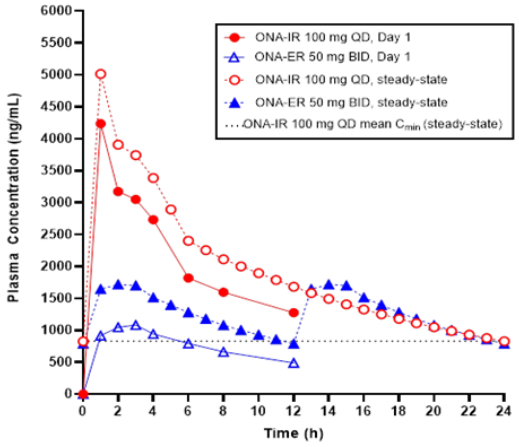
Source: Context Therapeutics, Edison Investment Research

ONA-XR: A potentially potent solution, albeit with history

Context's lead program is ONA-XR, an extended-release version of the PR antagonist, onapristone. Onapristone, in its IR formulation, was originally developed by **Schering** (now part of Bayer) in the 1990s as an oral contraceptive and potential treatment for gynecological disorders (uterine fibroids, endometriosis). The drug was later evaluated in a Phase II clinical trial as first-line therapy in postmenopausal patients with primary breast cancer (dosage: 100mg/day). The study reported strong efficacy data (an objective response rate of 56%, similar to tamoxifen, the only approved anti-estrogen treatment at that time) but was terminated prematurely (only 19 of the planned 30 patients recruited) due to liver function abnormalities in some patients.

Development was subsequently revived by **Arno Therapeutics**, which in-licensed the product in 2012 and developed an extended-release version on grounds that the off-target toxicity stemmed from high blood plasma concentrations of the drug, which can be mitigated by the more stable bioavailability of an extended-release formulation (50mg twice-daily dosing), see Exhibit 6.

Exhibit 4: Pharmacokinetic comparison of ONA-XR versus ONA-IR



Source: Context Therapeutics. Note: Dosing with ONA-XR resulted in a 3x lower maximum steady-state blood plasma concentration than ONA-IR while matching minimum plasma concentration levels.

The safety profile of ONA-XR was established from evaluating data from 88 subjects across the two Phase I/II studies undertaken by Arno in PR+ recurrent/metastatic female cancers (breast, ovarian and endometrial) and prostate cancer, which highlighted that there were no concerning toxicity issues (elevated liver markers were observed in 20% of patients with liver metastasis but in only 6.3% of patients without liver metastasis). We highlight that while there were no major safety issues

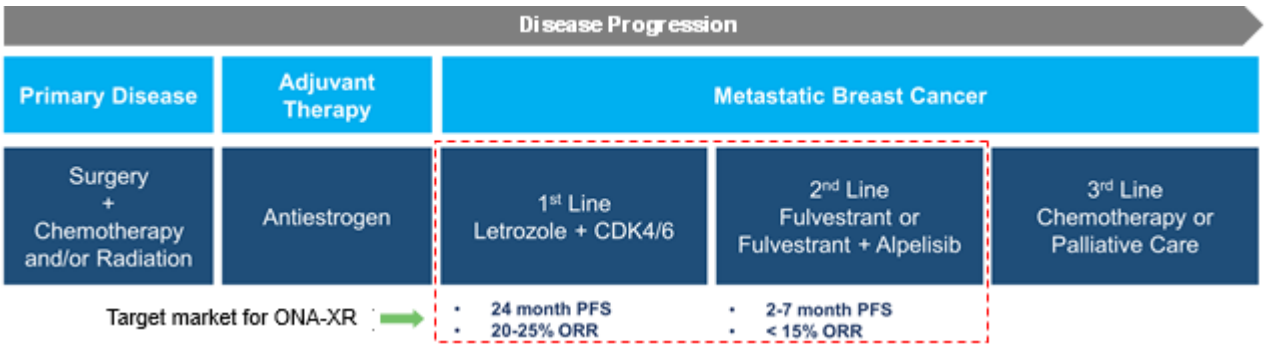
arising from the trials, preliminary efficacy data from the female cancer study were less encouraging (one partial response and eight patients with stable disease after 24 weeks; total cohort size of 52).[4] However, since the study was not designed to evaluate efficacy, it is difficult to draw firm conclusions from the available data or extend the results to other studies. Moreover, the study assessed ONA-XR as monotherapy, which may not be indicative of the drug's efficacy as a combination treatment.

Context Therapeutics acquired ONA-XR in December 2017 for an undisclosed consideration following Arno's decision to liquidate its assets. Context is evaluating ONA-XR as an add-on treatment to SoC (in contrast to Arno, which assessed the drug as a standalone treatment/monotherapy) across four indications (first-line escalation and second-line Mbc, endometrial cancer and GCT of the ovary). All programs are currently recruiting patients in mid-stage proof-of-concept studies expected to report preliminary readouts later this year. We discuss the company's clinical programs in the next section.

HR+/HER2- breast cancer – the core focus

HR+ breast cancer is the core disease area focus for ONA-XR and the one indication where anti-endocrine therapy is well established as the treatment of choice in the adjuvant (additional treatment following primary treatment to lower the risk of the cancer recurring) as well as metastatic setting. Non-resectable, recurrent or metastatic tumors of this class are typically treated initially with anti-estrogens (see Exhibit 3) either as monotherapy or combination therapy with CDK4/6 inhibitors, a new class of targeted therapies first approved in 2015. Currently approved drugs in the CDK4/6 class include Ibrance (palbociclib, Pfizer), Kisqali (ribociclib, Novartis) and Verzenio (abemaciclib, Eli Lilly). Ibrance, the first drug to be approved in this category, holds upwards of 80% market share and recorded $5.4bn of sales in 2020, which speaks to the size and scope of this market. Other approved targeted therapies include the PI3K inhibitor Piqray (alpelisib, Novartis) and the Mtor inhibitor Afinitor (everolimus, Novartis), which are used in later lines of treatment.

Exhibit 5: HR+/HER- breast cancer treatment landscape



Source: Context Therapeutics

Context's development of ONA-XR is based on the premise that enhanced outcomes in HR+/HER- Mbc can be achieved through complete hormone blockade via downregulation of ER and PR signaling pathways as well as their compensatory pathways, such as CDK4/6 and PI3K. ONA-XR is therefore being proposed as a triplet treatment in the first-line escalation setting (for a subset of patients likely to be non-responsive to current SoC, discussed below), as well as a combination treatment with anti-estrogens in the second-line setting. This assertion is supported by in vivo data

4 Cottu, Paul H et al. Phase I study of onapristone, a type I antiprogestin, in female patients with previously treated recurrent or metastatic progesterone receptor-expressing cancers. PloS one. *2018*

from an animal study[5] (using patient-derived tumor cells in a xenograft model), which showed that onapristone in triple combination (with fulvestrant and palbociclib) produced a statistically significant tumor growth inhibition (92%) versus onapristone monotherapy (42%) and onapristone/palbociclib dual combination (67%) arms.

'Window of opportunity' data encouraging in primary disease

In October 2021, the company reported positive data from a three-week Phase 0 'window of opportunity' study assessing ONA-XR as a neoadjuvant treatment in postmenopausal patients with PR+ early/primary breast cancer. The study was an open-label, single-arm, multi-center trial conducted by the Spanish cancer research group SOLTI, enrolling 10 patients with HR+/HER2- tumors with levels of the cell proliferation marker Ki-67 at >10%. The primary endpoint was complete cell cycle response (CCCR), which translates to a Ki-67 value of ≤2.7%. While no patients achieved a CCCR, Ki-67 expression decreased in six patients, remained stable in one patient and increased in three patients. The key takeaway from the study was the high correlation observed between PR expression and Ki-67 decline – the mean Ki67 decline of 25.23% was reported for patients with baseline PR expression ≥90% (n=4) versus 2.54% growth in cases with PR of <90% (n=6). However, we add the caveat that it is unclear whether a 25% decline in Ki-67 would be clinically meaningful, particularly given the small sample size. Another observation highlighted by Context was that the tumors treated with ONA-XR appeared to show more anti-estrogen sensitivity following treatment, implying an increased chance of response to anti-estrogen therapy when used in combination with ONA-XR. This provides an early rationale for ONA-XR as a potential therapeutic option as adjuvant therapy in early breast cancer, but the results would need to be reproduced in larger trials to establish efficacy. It is prudent to highlight here that regulatory requirements for approval in early breast cancer are likely to be more stringent due to its 'curative-intent' setting. A case in point has been the shortage of new therapeutic approvals in the adjuvant setting in HR+/HER2- breast cancer with the CDK4/6 inhibitor Verzenio the first treatment to be approved in this category (for a subset of early breast cancer patients at high risk of recurrence and a Ki-67 score of ≥20%) in more than two decades (approved in October 2021).

Trial design for ongoing clinical studies in HR+/HER2- Mbc

The first ongoing clinical program is a Phase II investigator-sponsored trial evaluating ONA-XR in combination with Faslodex (fulvestrant) in second-line HR+/HER2- Mbc (the SMILE study). The trial commenced in 2021 and is designed to be an open-label, single-arm, multi-center study assessing the effect of ONA-XR plus fulvestrant following progression on first-line SoC (aromatase inhibitor plus CDK4/6 inhibitor). The study is sponsored by the Wisconsin Oncology Network and will enroll up to 39 patients across four trial sites in the US (the first patient was dosed in October 2021). The primary endpoint will be overall response rate (ORR), which is the proportion of patients with a complete or partial tumor response. Secondary endpoints will include duration of tumor response, progression-free survival (PFS), disease control rate, time to response and incidence of adverse events. Preliminary data from the study are expected to be reported in H222.

The second clinical trial is an open-label pilot Phase Ib/II study evaluating ONA-XR as escalation therapy for first-line HR+HER2- Mbc patients who do not achieve molecular complete response (Mcr) after six months of treatment with SoC Ibrance (palbociclib) and Femara (letrozole). These cases are termed primary endocrine resistant or biochemically recurrent, defined as circulating tumor DNA (ctDNA) positive. A key molecular mechanism of endocrine resistance is believed to be mutations in the ER coding gene, ESR1, which is rare in primary breast cancer but has a high prevalence in patients with Mbc who have previously received endocrine treatment. It is estimated

[5] Context Therapeutics prospectus. 16 December 2021. Pages 72–73.

that c 20% of patients[6] undergoing first-line treatment would fall under this category and will be the target subset for ONA-XR in the first-line setting. The study commenced in 2021 and is being sponsored by the Memorial Sloan Kettering Cancer Center and will enroll up to 28 patients across seven trial sites in the US. The primary objective of the trial will be the recommended Phase II dose for ONA-XR in this setting. Phase Ib data from the study are expected in mid-2022.

Market opportunity and competitive landscape

We expect the biggest market opportunity for Context to come from ONA-XR as a second-line treatment, in combination with the current SoC. We estimate c 46,500 HR+/HER2- patients eligible for second-line treatment in the US by 2026 (expected time of initial market launch), of which 75% are estimated to be PR+, taking the target population to 35,000 patients per year. The corresponding figure in Europe stands at 37,000. We project market approval in 2026 following Phase III trials in 2023–25 and a peak penetration rate of 10%. We estimate a list price of $10,000 per monthly cycle (eight cycles per year) with a net/gross discount of 30% in the US and 60% in Europe (we have factored in a 5% annual price increment). By way of reference, the currently approved CDK4/6 inhibitors as well as the PIK3CA inhibitor, Piqray, come with a list price in the range of $13,000–15,000 per monthly cycle. We expect ONA-XR peak sales to reach c $300m in the US by patent expiry in 2034 (c $200m in Europe). As a reference, the aromatase inhibitors, Femara and Arimidex, and the SERD Faslodex all recorded peak sales of more than $1bn globally ($1.4bn, $1.9bn and $1.03bn, respectively) before going off-patent.

In the first-line escalation setting, we estimate c 45,000 patients seeking treatment in the US (46,000 in Europe), 80% of which will be PR+ and ONA-XR will target a subset of c 20% of these patients. The number of monthly cycles has been assumed at 12 in the first-line setting. Peak penetration is estimated to be 15%, which translates to peak sales potential of $140m and $85m in the US and Europe, respectively.

In terms of the competitive landscape, while ONA-XR continues to be the only PR antagonist in clinical development for breast cancer to our knowledge, competition from the newer-generation oral SERDs and other emerging drug classes (such as anti-androgens) cannot be ruled out. A number of oral SERDs are currently in late-stage clinical development (note that the only currently approved SERD, fulvestrant, is an injectable formulation). The front runner is Elacestrant (developed by Radius Health and out-licensed to Menarini), which recently reported top-line data from its pivotal Phase III trial where it met both primary endpoints, including strong efficacy signals against the ESR1 mutation. Exhibit 8 presents a list of selected SERD clinical programs.

Exhibit 6: Selected oral SERDs in late-stage clinical development

Drug	Company	Development phase	Indication	Comparator	Prior CDK4/6 use	Comments
Elacestrant	Radius Health/ Menarini	Phase III	Second-line, postmenopausal Mbc	Faslodex or aromatase inhibitor	Mandatory	Top-line data from pivotal Phase III EMERALD trial presented in December 2021. Trial met both primary endpoints (PFS as monotherapy vs SoC endocrine therapy in overall population and PFS versus SoC in ESR1 population). Regulator filing expected in 2022.
Giredestrant	Roche	Phase III	Second/third-line, pre/peri/ postmenopausal Mbc	Faslodex or aromatase inhibitor	Not mandatory	Data from the pivotal Phase III acelERA study expected to read out in H122
Camizestrant	AstraZeneca	Phase III	Second-line, postmenopausal Mbc	Faslodex	Not mandatory	Data from the pivotal Phase III SERENA-2 study expected to read out in early 2022
Amcenestrant	Sanofi	Phase III	Second-line Mbc	Faslodex or aromatase inhibitor	Required for some cohorts	Data from the pivotal Phase III AMEERA-3 study expected to read out in early 2022

Source: Evaluate Pharma, Edison Investment Research

6 Harrod, A., Fulton, J., Nguyen, V. et al. Genomic modelling of the ESR1 Y537S mutation for evaluating function and new therapeutic approaches for metastatic breast cancer. *Oncogene*

Gynecological cancers: Additional shots on goal

Context is also evaluating ONA-XR in two other hormone-driven indications: endometrial cancer and GCT of the ovary. The American Cancer Society estimates that there were 65,570 and 21,410 cases of endometrial and ovarian cancer reported in the US in 2021. Maximal surgical debulking and platinum chemotherapy are the cornerstone treatments for primary gynecologic cancers, but relapse rates are as high as 20–25% for early-stage disease and 70% for advanced tumors due to acquired resistance to platinum-based chemotherapy. Although the prognosis remains good for patients diagnosed with early-stage disease, options have been limited and prognosis is short for those diagnosed with recurrent or metastatic disease.

Recurrent metastatic endometrial cancer

Endometrial cancers are divided into two subtypes:

- Type I (accounting for c 80% of cases) are typically lower grade (grades I and II) and hormone-driven. We expect recurrent/metastatic cases from this cohort to be the target for ONA-XR.
- Type II (c 20% of cases) are higher grade (grades III and IV), but are not generally hormone-driven.

75% of endometrial cancers are diagnosed at an early stage and are typically curable with surgery and platinum chemotherapy. The only hormonal therapy approved for recurrent endometrial tumors is the progestin, megestrol acetate, which has shown a 20–30% response rate in metastatic patients.[7] Anti-estrogens such as tamoxifen and aromatase inhibitors have only shown modest improvement in smaller studies, although this can be partially attributable to lack of patient selectivity. More recently, the FDA has given the green light to two targeted therapies – Keytruda+Lenvima (accelerated approval in September 2019, full approval in July 2021) and Jemperli in April 2021 for a subset of patients with the deficient mismatch repair (Dmmr) genetic mutation (known to affect 25–30% of patients with advanced endometrial cancer).

Context is developing ONA-XR as a combination therapy with anti-estrogens on the same principle as in the case of breast cancer, to potentially improve treatment outcomes by achieving complete hormone blockage. We assess a higher development risk for ONA-XR in this indication, although on the upside, positive development would mean a potentially rewarding outcome.

Phase II clinical trial (ONWARD 221) design

The study is an open-label, single-arm, investigator-sponsored trial evaluating ONA-XR in combination with anti-estrogen Arimidex (anastrozole) in women with PR+ metastatic endometrial cancer after progression on at least one prior line of chemotherapy. The trial commenced in 2020 (first patient dosed in May 2021) and will enroll 25 patients across three sites in the US. The study sponsor is Thomas Jefferson University. The primary endpoint will be ORR. Secondary endpoints include duration of response, clinical benefit rate and PFS. Preliminary data from the study are expected to be reported in mid-2022.

Recurrent granulosa cell tumor of the ovary

GCT of the ovary is a rare form of ovarian cancer, accounting for less than 5% of all ovarian malignancies. According to the American Cancer Society, there were an estimated 235,081 women living with ovarian cancer in the US in 2018. Almost 50% of these are estimated to be metastatic/recurrent cases, which translates to c 5,000–6,000 cases of recurrent GCT in the US. Context estimates that there are c 5,000 patients with recurrent disease in both the US and Europe. More than 95% of GCT tumors are believed to be PR+ (50% ER+), making them an attractive

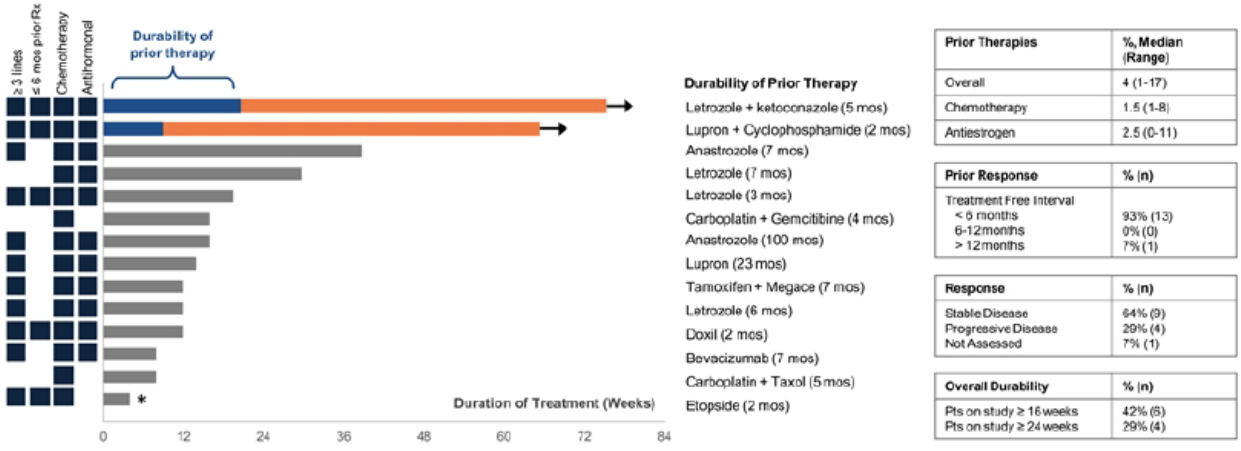
7 Wen, Wei et al. Pterostilbene, a natural phenolic compound, synergizes the antineoplastic effects of megestrol acetate in endometrial cancer. Scientific reports October 2017.

therapeutic target for anti-progestin therapies. Platinum-based chemotherapy is recommended as first-line treatment in the metastatic setting, followed by either further chemotherapy, antihormonal treatments or cytoreductive surgery on disease progression. As these tumors show few mutations, the applicability of targeted treatments is limited. There are currently no FDA-approved treatments in the recurrent setting for this indication. Context received FDA fast track designation for ONA-XR in PR+ ovarian cancer in August 2020, highlighting the significant unmet need in the space.

Phase II clinical trial (ONWARD 220) design

ONA-XR's Phase II study in GCT has been conducted in two parts. Part one (part of a basket study) evaluated the therapeutic benefits of ONA-XR as monotherapy in late-line patients (ie patients who have had multiple prior lines of treatment) over an 84-week study duration. Fourteen patients with PR+ GCT of the ovary were enrolled in the trial (which commenced in May 2019), with 13 completing at least one full cycle of treatment. While no participant reported complete or partial response (data released at the end of 2020), 64% (9/14) of patients experienced stable disease (SD) including four patients (29%) having clinical benefit (ie SD) lasting 24 weeks. Two patients remained on treatment after 12 months (Exhibit 9).

Exhibit 7: ONA-XR data in late-line granulosa cell tumor of the ovary



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)

Source: Context Therapeutics

Based on monotherapy data, Context initiated a second part of the study in 2021, an open-label trial to evaluate the efficacy and safety of ONA-XR as a combination treatment (along with the anti-estrogen Arimidex (anastrozole) in women with PR+ advanced GCT of the ovary (early-line, ie first- or second-line therapy). This study is sponsored by the Memorial Sloan Kettering Cancer Center and will enroll up to 25 patients across seven sites in the US. The primary endpoint of the study will be ORR and the secondary endpoints will include duration of response, clinical benefit and PFS. Preliminary data from the study are expected in H222.

Market estimates

For recurrent endometrial cancer, we estimate 35,000 recurrent/metastatic cases in the US per year, of which 60% will be PR+, taking the target population for ONA-XR to c 21,500 (the corresponding figures is c 27,000 for Europe due to the relatively larger number of endometrial cancer cases in the region). We project peak penetration at 10% on approval, but assign a slightly lower 10% probability of success (versus 15% for the Phase II study in Mbc) as we see a higher risk profile in this indication. We estimate 12-month cycles of ONA-XR per patient, per year.

For GCT of the ovary, we estimate a target patient population of 5,000 and 7,500 in the US and Europe, respectively. Given there are no FDA-approved therapies in the space, we project peak penetration of 20% but with a 10% probability of success.

CLDN6Xcd3 bispecific antibody

The second asset in Context's portfolio is a preclinical stage BsAb targeting the oncofetal antigen, claudin-6 (CLDN6). CLDN6 is a member of the claudin family of tight junction proteins (24 members in humans), which play an important role in cell polarity, permeability and adhesion, and participate in the regulation of cell proliferation and differentiation. A unique aspect of CLDN6 is that it has been found to be upregulated in several malignant tumors such as endometrial, ovarian, lung and gastric cancers, but is rarely expressed in adult healthy tissues. However, the expression appears to be heterogeneous across cancer subtypes and seems directly related to tumor grade (the higher the grade, the higher the CLDN6 enrichment). Importantly, studies have indicated that higher levels of CLDN6 expression lead to poorer prognosis in terms of overall survival (OS) and PFS. A 2020 study assessing CLDN6 expression in endometrial cancer tissue resected from patients concluded that the five-year survival rate in the high CLDN6 expression group stood at 30% compared to 90% for the low expression group.[8] This could make CLDN6 an attractive therapeutic target for these indications.

While several pharmaceutical companies are developing CLDN6 targeting antibodies, development has been stymied by challenges in accurate selectivity due to CLDN6's close resemblance to other claudins, in particular CLDN9, which is present in healthy cells. CLDN9, which differs from CLDN6 by only three amino acids in the extracellular domain, is crucial to maintaining normal hearing and a healthy gut, highlighting the importance of accurate targeting. Context asserts that its mAb exhibits best-in-class selectivity, at least 10x higher than its closest competitors (see Exhibit 10).

Exhibit 10: Claudin-6 development programs

Company	Program name	Antibody format	Development Phase	Indications	CLDN6/9 selectivity*	Comments
Clinical development						
Astellas Pharma	ASP1650	mAb	Phase II (abandoned)	Testicular cancer, germ cell tumors	7x	Discontinued after Phase II studies due to lack of clinical benefit
BioNTech	BNT211	CLDN6 CAR-T	Phase I/II (active)	Relapsed or refractory advanced solid tumors	7x	Encouraging preliminary efficacy data presented from Phase I study in November 2021
AbbVie	SC-004	Antibody drug conjugate	Phase II (abandoned)	Endometrial cancer; fallopian tube cancer; ovarian cancer; peritoneal cancer	1x	Discontinued after Phase II studies (study data unavailable)
BioNTech	BNT142	CLDN6Xcd3 bispecific antibody	Phase I ready	Multiple solid tumors	7x	Phase I studies expected to commence in H122
Preclinical						
Context Therapeutics	N/D	CLDN6Xcd3 bispecific antibody	Preclinical (active)	Gynecological cancers	>100x	IND-enabling studies expected to commence in 2022
Xencor	N/D	CLDN6Xcd3 bispecific antibody	Preclinical (active)	Ovarian cancer	10x	Reported positive preclinical data at American Association for Cancer Research (AACR) conference in April 2021; timeline for clinical progression not disclosed
Chugai	N/D	mAb	Discovery	N/A	5x	Details unavailable
University of California, Los Angeles	AB3	TBD	Discovery	N/A	N/A	Details unavailable
NovaRock	N/D	CLDN6x41BB bispecific antibody	Discovery	N/A	N/A	Details unavailable

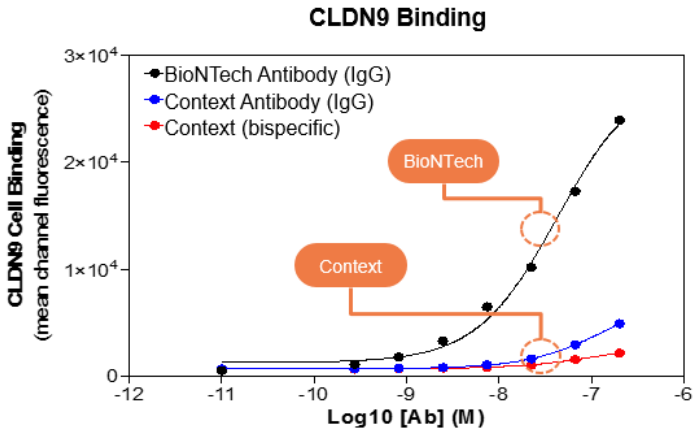
Source: Context Therapeutics, Edison Investment Research. Note: *Selectivity data as analyzed by Context Therapeutics.

BioNTech, the leader in this category with its CLDN6 CAR-T asset, recently presented some encouraging early preliminary efficacy data from its Phase I study. Eight patients (testicular, ovarian and endometrial, as well as soft tissue sarcoma) were treated across two dose levels with no dose-limiting toxicities or adverse events. Following six weeks of treatment, data were available for 5/8

8 Manabu Kojima et al. Aberrant claudin-6–adhesion signal promotes endometrial cancer progression via estrogen receptor. *bioRxiv - Cancer Biology*. 2020

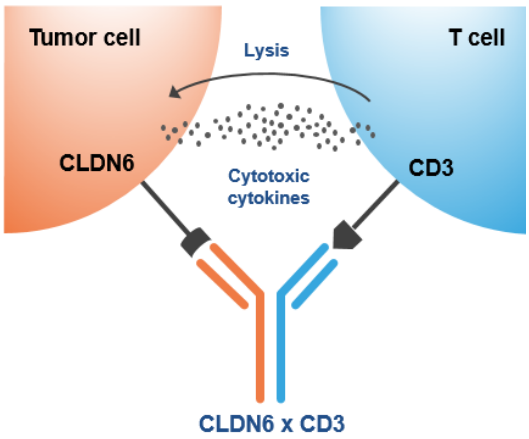
patients, four of which reported stable disease. More importantly, three patients showed initial tumor shrinkage (-18%, -21% and -27%, respectively). We see this as a potentially positive read-across for Context, albeit based on very early clinical data. A head-to-head comparison conducted by Context with BioNTech's CLDN6 mAb suggested a significantly lower binding to CLDN9 by Context's mAb, potentially indicating a superior safety profile (Exhibit 11). Furthermore, by developing a BsAb, one domain of which attaches to the CLDN6 antigen on tumor cells and the other to CD3 protein expressed on cytotoxic T-cells, the drug aims to effectively recruit the immune system (by bringing the cytotoxic T-cell in close proximity to the tumor cell), in theory enhancing the efficacy of the treatment (Exhibit 12). We note that there are several BsAbs with a likely similar mechanism of action in preclinical development, although it appears that only BioNTech's candidate BNT142 is ahead of Context's, with Phase I studies planned for H122. However, Context asserts that superior selectivity, if reproduced in clinical studies, could potentially offer an advantage.

Exhibit 11: CLDN9 binding of Context's versus BioNTech's mAb



Source: Context Therapeutics

Exhibit 12: Context's BsAb structure



Source: Context Therapeutics

Context plans to commence IND-enabling studies for its CLDN6Xcd3 candidate in 2022, with advancement to the clinic anticipated in 2023. Its licensing partner, Integral Molecular, will be eligible to receive development, regulatory and sales milestone payments and high single-digit to low double-digit percentage royalties on net sales. Given the lack of homogeneity across tumor types (a 2016 study reported significant differences in CLDN6 expression between different histological tumor subtypes of endometrial cancer, ranging from 20.5% in adenocarcinomas to 83.3% of serous carcinoma patients), further analysis/data would be required to accurately ascertain the target market and potential for Context's CLDN6 asset. Based on very preliminary estimates, we anticipate peak sales potential could exceed $500m, although we add the caveat that this is subject to high variability. However, we currently do not include this asset in our valuation of Context (according to Edison's standard practice of only valuing clinical-stage assets). Successful clinical progression would likely add materially to our valuation.

The bispecific antibody market

Unlike the monoclonal antibody landscape, which is already well established, the market for bispecific counterparts is fairly nascent with only three therapies currently approved, two of which are targeting indications in the oncology space: Blincyto (blinatumomab) and Rybrevant (amivantamab). The third approved drug is Hemlibra (emicizumab) for hemophilia A, which recorded $2.4bn in sales in 9M21 and is projected to report peak sales of more than $5bn, according to EvaluatePharma.

Exhibit 13: Selected bispecific antibodies (approved and in late-stage development)

Drug	Developer	Target	Indications	Phase	Latest sales ($m)
Blincyto	Amgen	CD19 x CD3	Leukemia	Approved (2014)	$340m (9M21)
Hemlibra	Genentech/Roche	Factor Ixa x Factor X	Hemophilia A	Approved (2017)	$2.4bn (9M21)
Rybrevant	Johnson & Johnson	EGFR x Cmet	Lung cancer	Approved (2021)	N/A
Mosunetuzumab	Roche	CD20 x CD3	Lymphoma	Phase III	N/A
Glofitamab	Roche	CD20 x CD3	Lymphoma	Phase III	N/A
Epcoritamab	AbbVie, Genmab	CD20 x CD3	Lymphoma, Leukemia	Phase III	N/A

Source: Evaluate Pharma, Edison Investment Research

Sensitivities

We believe that the bulk of risk for Context is related to development as our valuation case for the company rests entirely on ONA-XR and its successful development across the four indications being tested. All four programs are expected to read out in 2022, which means the next few months are pivotal to the company's future direction. The basis for the hypothesis of ONA-XR's efficacy is a Phase II study conducted by Schering in 1994, which evaluated the drug's IR version, so it is uncertain whether the results will be mirrored in the trials assessing the current XR version. We also highlight that the ongoing clinical trials are fairly small, open-label studies with small patient populations, and the robustness of the data/results will need to be tested in larger randomized studies to meet the stringent regulatory hurdles in the highly competitive oncology space. Our valuation model assumes that the Phase III/pivotal clinical studies will recruit less than 150–200 participants and achieve a registration-enabling endpoint in less than three years. However, given the large size of the targeted indications (particularly breast cancers), Context may be required to carry out larger studies, possibly delaying registration and market launch compared to our estimates, and materially increasing our funding assumptions.

Another risk is the reliance on third-party contractors for drug development/clinical trials as it affects the company's ability to maintain adequate control over quality and progress, eg investigator-sponsored clinical trials, which can be associated with investigator bias and reduced control over study timelines. However, we note that this risk is counterbalanced by the company freeing up internal resources and reduced cost.

Additional risk comes from potential dilution as independent clinical development and commercialization plans in the US will require Context to raise significant capital. Timely and adequate access to funds will be crucial to progressing the pipeline through clinical studies, as well as marketing the assets on approval. If the company chooses to out-license, its ability to identify and realize strategic partnerships will be critical. Successful execution of a deal will depend on a multitude of factors, primarily the strength of clinical data.

Intellectual property risk should also be highlighted. While Context holds patent rights to ONA-XR's formulation, composition and related use until 2034, the underlying molecule is off-patent and ONA-XR could be challenged by other formulations developed by competitors. However, ONA-XR's first-mover advantage in this space (as it is the only drug in its category currently in clinical trials) should give Context the FDA's standard five-year marketing exclusivity following approval (until 2031/32 based on our estimate of a 2026/27 launch across indications), which in our opinion mitigates some of this risk. Competition is an ever-present risk as well. The oncology space is dominated by big pharma and there are several assets in development targeting the same therapeutic indication. While ONA-XR is the only PR antagonist in clinical trials, it may still face competition from new-generation anti-estrogens (such as oral SERDs) and other classes of drug such as anti-androgens. ONA-XR would need to show tangible improvement in clinical outcomes to create a meaningful market for its product.

Valuation

We have valued Context at $134.9m ($8.45 per basic share) using a risk-adjusted NPV approach, individually forecasting the free cash flows from the company's clinical programs and discounting them back to ascertain their current value. Our forecasts assume internal development in the US and out-licensing in Europe following completion of Phase III clinical trials. Due to lack of visibility on out-licensing deal terms, we currently incorporate only sales royalties from Europe (assuming c 15% of sales). We are also not factoring in contribution from other geographies in our model at this stage. This is conditional and we will update as further information becomes available. Our valuation considers only the company's clinical-stage programs, ie those involving ONA-XR across its target four indications. The other asset, the CLDN6 targeting BsAb, will likely be included in our valuation provided it transitions to the clinic, with a corresponding revision in our estimates for the company.

We have allocated appropriate probabilities of success to each program based on its clinical stage, as well as our assessment of the potential risk in that indication. All programs are modelled to 2040, with peak sales estimated to be achieved in 2034 (patent expiry) and a steady y-o-y decline in sales thereafter. The success probabilities for each program are based on standard industry criteria for each stage of the clinical development process, but are flexed to reflect the inherent risks of the individual program, the indication targeted and the trial design. We use a 12.5% discount rate, which is our standard rate for clinical-stage assets.

Exhibit 14: Context Therapeutics Rnpv valuation

Program	Indication	Status	Probability of success	Launch year	Peak sales ($m)	Economics	Rnpv ($m)
ONA-XR	Second-line HR+/HER2- Mbc	Phase II	15%	2026	498	US (fully owned) Europe (out-licensed)	39.5
	First-line escalation therapy for HR+/HER2- Mbc (ctDNA+)	Phase Ib	7.5%	2027	222	US (fully owned) Europe (out-licensed)	7.1
	Recurrent PR+ endometrial cancer	Phase II	10%	2027	583	US (fully owned) Europe (out-licensed)	28.7
	Advanced GCT of the ovary	Phase II	10%	2027	292	US (fully owned) Europe (out-licensed)	11.7
Net cash (Q421e) $m							48.0
Total firm value							**134.9**
Total basic shares (m)							16.0
Value per basic share ($)							**8.45**
Total diluted shares (m)							2.0
Value per diluted share ($)							**7.52**

Source: Edison Investment Research

Financials

Context is currently at the pre-revenue stage and has been relying on capital-raising to fund its operations. Prior to its IPO in October 2021, the company had raised more than $25m in funds (since inception) through convertible debt and preferred stock issues (all convertibles and preferred shares were converted to ordinary shares prior to the IPO). Its net cash position at the end of September 2021 stood at $419k. The company raised $28.8m in gross proceeds from the IPO and the cash position was bolstered further by a subsequent private $31.5m (gross) placement in December, bringing a handful of institutional investors on board (who together currently hold >20% equity in the company). We estimate a cash balance at the end of FY21 of c $48m. We assume the company will undertake complete development and commercialization of its programs in the US while the European operations will be out-licensed following the conclusion of the Phase III clinical

trials. Based on our cash burn projections ($6.2m, $11.0m and $24.8m in FY21, FY22 and FY23 respectively), Context looks to be well capitalized into 2024. However, we estimate that it would need to raise another c $110m before reaching profitability in 2027 (by which time we expect all three current Phase II stage programs to hit the market). We have modelled the required fund-raising as illustrative debt according to Edison policy ($40m each in FY24 and FY25 and an additional $30m in FY26).

In terms of operating performance, Context reported an operating loss of $7.4m in the first nine months of FY21 (9M21), significantly higher than the corresponding figure of $1.8m in 9M20. This can be attributed to a one-off expense related to the upfront payment for in-licensing the CLDN6Xcd3 asset ($3.1m recorded as acquired in-process R&D), as well as higher internal R&D and G&A expenses related to the initiation of Phase II trials. The adjusted net loss came in at $7.5m versus $2.4m in 9M20. We note that the company reported a net profit of $7.4m in 9M20, but this includes the non-cash contribution from the change in fair value of promissory notes ($9.8m). We expect R&D and other operating costs to continue to rise over the next few years as the pipeline progresses through the clinic. We project the FY21 and FY22 operating loss to come in at $10.5m and $18.5m respectively with materially higher figures in FY23 and FY24 ($25.7m and $42.9m, respectively) as the programs undergo Phase III trials (see Exhibit 15). We expect the company to become profitable in 2027 contingent on its programs receiving market approval.

Exhibit 15: ONA-XR modelling assumptions

Indication	Stage	Assumptions
Second/third-line HR+/HER2- Mbc	Phase II	Target population: PR+ Mbc cases seeking second-line treatment (c 35,000 per year US, c 37,000 per year Europe). Peak penetration: 10% based on current assessment. Pricing: $10,000 per monthly cycle growing by 5% pa (eight cycles required per year), gross/net discount: 30% in the US, 60% in Europe. Peak sales potential: $300m in the US, $200m in Europe. R&D: 39 patients in Phase II trials lasting 2022. Assumed 200 patients in Phase III trials at $50k each + $2m overhead lasting until 2025. COGS: 20% of sales. SG&A: $8–10m pa. Tax: 21% US corporate tax rate. Probability of success: 15%. Market entry in 2026.
First-line escalation treatment for HR+/HER2- Mbc	Phase Ib	Target population: PR+ Mbc cases seeking first-line treatment who remain unresponsive to SoC following six months of treatment (estimated to be c 20% of patients (c 6,600 and c7,000 patients per year in the US and Europe, respectively). Peak penetration: 15% based on current assessment. Pricing: $10,000 per monthly cycle growing 5% pa (12 cycles required per year), gross/net discount: 30% in the US, 60% in Europe. Peak sales potential: $140m in the US, $85m in Europe. R&D: 28 patients in Phase 1b/II trials lasting 2023. Assumed 150 patients in Phase III trials at $50k each + $2m overhead lasting until 2026. COGS: 20% of sales. SG&A: $8–10m pa. Tax: 21% US corporate tax rate. Probability of success: 7.5%. Market entry in 2027.
Recurrent endometrial cancer	Phase II	Target population: PR+ recurrent endometrial cancer cases (c 21,500 and c 27,000 patients per year in the US and Europe, respectively). Peak penetration: 10% based on current assessment. Pricing: $10,000 per monthly cycle growing 5% pa (12 cycles required per year), gross/net discount: 30% in the US, 60% in Europe. Peak sales potential: $340m in the US, $240m in Europe. R&D: 25 patients in Phase II trials lasting 2023. Assumed 200 patients in Phase III trials at $50k each + $2m overhead lasting until 2026. COGS: 20% of sales. SG&A: $8–10m per year. Tax: 21% US corporate tax rate. Probability of success: 10%. Market entry in 2027.
Granulosa cell tumor of the ovary	Phase II	Target population: PR+ GCT of the ovary cases (c 5,000 and c 7,500 patients in the US and Europe). Peak penetration: 20% based on high unmet need, no currently approved therapies. Pricing: $10,000 per monthly cycle growing 5% pa (12 cycles required per year), gross/net discount: 30% in the US, 60% in Europe. Peak sales potential: $155m in the US, $140m in Europe. R&D: 43 patients in Phase II trials lasting 2023. Assumed 150 patients in Phase III trials at $50k each + $2m overhead lasting until 2026. COGS: 20% of sales. SG&A: $8–10m per year. Tax: 21% US corporate tax rate. Probability of success: 10%. Market entry in 2027.

Source: Edison Investment Research

Exhibit 16: Financial summary

$'000s	2019	2020	2021e	2022e	2023e
31-December	US GAAP	US GAAP	US GAAP	US GAAP	US GAAP
INCOME STATEMENT					
Revenue	0.0	0.0	0.0	0.0	0.0
Cost of Sales	0.0	0.0	0.0	0.0	0.0
Gross Profit	0.0	0.0	0.0	0.0	0.0
Research and Development Expenses	(2,411.9)	(1,641.5)	(7,692.1)	(14,823.7)	(20,874.7)
Sales, General and Administrative Expenses	(2,965.2)	(930.7)	(2,828.8)	(3,677.4)	(4,780.7)
EBITDA	(5,377.1)	(2,572.2)	(10,520.9)	(18,501.2)	(25,655.4)
Normalized operating profit	(5,377.1)	(2,572.2)	(10,520.9)	(18,501.2)	(25,655.4)
Amortization of acquired intangibles	0.0	0.0	0.0	0.0	0.0
Exceptionals	0.0	0.0	0.0	0.0	0.0
Share-based payments	0.0	0.0	0.0	0.0	0.0
Reported operating profit	(5,377.1)	(2,572.2)	(10,520.9)	(18,501.2)	(25,655.4)
Net Interest	(1,100.4)	(661.2)	(64.6)	959.0	739.3
Joint ventures & associates (post tax)	0.0	0.0	0.0	0.0	0.0
Exceptionals	93.4	9,877.9	133.5	0.0	0.0
Profit Before Tax (norm)	(6,477.5)	(3,233.4)	(10,585.5)	(17,542.1)	(24,916.1)
Profit Before Tax (reported)	(6,384.2)	6,644.5	(10,452.0)	(17,542.1)	(24,916.1)
Reported tax	0.0	0.0	0.0	0.0	0.0
Profit After Tax (norm)	(6,477.5)	(3,233.4)	(10,585.5)	(17,542.1)	(24,916.1)
Profit After Tax (reported)	(6,384.2)	6,644.5	(10,452.0)	(17,542.1)	(24,916.1)
Minority interests	0.0	0.0	0.0	0.0	0.0
Discontinued operations	0.0	0.0	0.0	0.0	0.0
Net income (normalised)	(6,477.5)	(3,233.4)	(10,585.5)	(17,542.1)	(24,916.1)
Net income (reported)	(6,384.2)	6,644.5	(10,452.0)	(17,542.1)	(24,916.1)
Basic average number of shares outstanding (m)	0.3	0.3	4.3	16.0	16.0
EPS – basic normalised ($)	(20.11)	(9.28)	(2.49)	(1.10)	(1.56)
EPS – diluted normalised ($)	(20.11)	(9.28)	(2.49)	(1.10)	(1.56)
EPS – basic reported ($)	(19.82)	19.07	(2.45)	(1.10)	(1.56)
Dividend ($)	0.00	0.00	0.00	0.00	0.00
BALANCE SHEET					
Fixed Assets	33.9	117.6	364.4	72.9	72.9
Intangible Assets	0.0	0.0	0.0	0.0	0.0
Tangible Assets	0.0	0.0	0.0	0.0	0.0
Investments & other	33.9	117.6	364.4	72.9	72.9
Current Assets	239.6	349.7	47,988.6	37,029.7	12,302.4
Stocks	0.0	0.0	0.0	0.0	0.0
Debtors	0.0	0.0	0.0	0.0	0.0
Cash & cash equivalents	226.6	341.0	47,952.4	36,966.1	12,214.1
Other	13.0	8.7	36.2	63.6	88.2
Current Liabilities	(24,108.3)	(9,548.2)	(8,679.2)	(15,262.4)	(15,451.1)
Creditors	(2,067.9)	(2,707.9)	(6,070.3)	(10,674.6)	(10,361.7)
Tax and social security	0.0	0.0	0.0	0.0	0.0
Short term borrowings	(21,842.9)	(5,884.3)	0.0	0.0	0.0
Other	(197.5)	(956.0)	(2,608.9)	(4,587.8)	(5,089.4)
Long Term Liabilities	0.0	(69.0)	0.0	0.0	0.0
Long term borrowings	0.0	(69.0)	0.0	0.0	0.0
Other long-term liabilities	0.0	0.0	0.0	0.0	0.0
Net Assets	(23,834.8)	(9,149.9)	39,673.7	21,840.2	(3,075.9)
Convertible preferred stock	(126.0)	(7,771.2)	0.0	0.0	0.0
Minority interests	0.0	0.0	0.0	0.0	0.0
Shareholders' equity	(23,960.8)	(16,921.1)	39,673.7	21,840.2	(3,075.9)
CASH FLOW					
Op Cash Flow before WC and tax	(5,377.1)	(2,572.2)	(10,520.9)	(18,501.2)	(25,655.4)
Working capital	561.8	1,318.3	4,252.8	6,555.8	164.1
Exceptional & other	1,979.3	219.2	68.9	959.0	739.3
Tax	0.0	0.0	0.0	0.0	0.0
Net operating cash flow	(2,836.1)	(1,034.6)	(6,199.3)	(10,986.3)	(24,751.9)
Capex	0.0	0.0	0.0	0.0	0.0
Equity financing	0.0	0.0	53,732.5	0.0	0.0
Dividends	0.0	0.0	0.0	0.0	0.0
Other	0.0	0.0	0.0	0.0	0.0
Net Cash Flow	(2,836.1)	(1,034.6)	47,533.2	(10,986.3)	(24,751.9)
Opening net debt/(cash)	1,105.3	21,742.3	13,383.5	(47,952.4)	(36,966.1)
FX	0.0	0.0	0.0	0.0	0.0
Other non-cash movements	(17,800.9)	9,393.4	13,802.7	0.0	0.0
Closing net debt/(cash)	21,742.3	13,383.5	(47,952.4)	(36,966.1)	(12,214.1)

Source: Context Therapeutics reports, Edison Investment Research

Contact details	Revenue by geography
2001 Market Street Suite 3915, Unit 15 Philadelphia, PA 19103 United States +1 267 225 7416 www.contexttherapeutics.com/	N/A

Management team

CEO: Martin Lehr	CFO: Jennifer Minai-Azary
Martin Lehr is co-founder and CEO of Context Therapeutics. In addition, he serves on the boards of Praesidia Biologics and CureDuchenne Ventures. Previously, he was part of the founding team at Osage University Partners, a venture capital fund focused on academic spin-outs from established research institutions. Prior to Osage, Martin conducted research at the Sloan Kettering Institute in DNA repair and at the Children's Hospital of Philadelphia in thrombosis and hemostasis. He is a director of BioBreak, a biotech executive peer networking group with over 2,500 active members across the United States, and an advisory board member of Life Science Cares and Life Science Leader magazine. Martin has an MA in Biotechnology from Columbia University and a BA in Economics from the University of Pennsylvania.	Jennifer Minai-Azary joined Context in November 2021 as CFO. She brings more than 20 years of finance and accounting experience and has spent the past few years in senior finance roles in the life sciences industry. Prior to joining Context, Jennifer served as CFO of Millendo Therapeutics, a publicly traded biopharmaceutical company. She also served as VP of finance, as well as in other finance roles at Millendo, where she was responsible for the financial reporting, accounting, treasury, tax and risk management functions. Before that, she served as director of technical accounting at PAREXEL International. Jennifer has a Master of Accounting and a BBA from the University of Michigan and is a certified public accountant.
CMO (consulting): Tarek Sahmoud, MD, PhD	
Dr Tarek Sahmoud is president of OncoStrategy, a boutique clinical development consultancy, and consulting CMO to Context Therapeutics. He has more than 25 years of experience in oncology drug development and medical affairs, most recently as CMO of H3 Biomedicines. Tarek also held senior clinical development positions at Celgene, Novartis and AstraZeneca.	

Principal shareholders	(%)
Sabby Management, LLC	7.71
Kepos Capital	6.26
Martin Lehr	5.70
AIGH Capital Management	4.78
Seth Lehr	4.34
Altium Capital Management	3.09
Integral Molecular	2.62

General disclaimer and copyright

This report has been commissioned by Context Therapeutics and prepared and issued by Edison, in consideration of a fee payable by Context Therapeutics. Edison Investment Research standard fees are £60,000 pa for the production and broad dissemination of a detailed note (Outlook) following by regular (typically quarterly) update notes. Fees are paid upfront in cash without recourse. Edison may seek additional fees for the provision of roadshows and related IR services for the client but does not get remunerated for any investment banking services. We never take payment in stock, options or warrants for any of our services.

Accuracy of content: All information used in the publication of this report has been compiled from publicly available sources that are believed to be reliable, however we do not guarantee the accuracy or completeness of this report and have not sought for this information to be independently verified. Opinions contained in this report represent those of the research department of Edison at the time of publication. Forward-looking information or statements in this report contain information that is based on assumptions, forecasts of future results, estimates of amounts not yet determinable, and therefore involve known and unknown risks, uncertainties and other factors which may cause the actual results, performance or achievements of their subject matter to be materially different from current expectations.

Exclusion of Liability: To the fullest extent allowed by law, Edison shall not be liable for any direct, indirect or consequential losses, loss of profits, damages, costs or expenses incurred or suffered by you arising out or in connection with the access to, use of or reliance on any information contained on this note.

No personalised advice: The information that we provide should not be construed in any manner whatsoever as, personalised advice. Also, the information provided by us should not be construed by any subscriber or prospective subscriber as Edison's solicitation to effect, or attempt to effect, any transaction in a security. The securities described in the report may not be eligible for sale in all jurisdictions or to certain categories of investors.

Investment in securities mentioned: Edison has a restrictive policy relating to personal dealing and conflicts of interest. Edison Group does not conduct any investment business and, accordingly, does not itself hold any positions in the securities mentioned in this report. However, the respective directors, officers, employees and contractors of Edison may have a position in any or related securities mentioned in this report, subject to Edison's policies on personal dealing and conflicts of interest.

Australia

Edison Investment Research Pty Ltd (Edison AU) is the Australian subsidiary of Edison. Edison AU is a Corporate Authorised Representative (1252501) of Crown Wealth Group Pty Ltd who holds an Australian Financial Services Licence (Number: 494274). This research is issued in Australia by Edison AU and any access to it, is intended only for "wholesale clients" within the meaning of the Corporations Act 2001 of Australia. Any advice given by Edison AU is general advice only and does not take into account your personal circumstances, needs or objectives. You should, before acting on this advice, consider the appropriateness of the advice, having regard to your objectives, financial situation and needs. If our advice relates to the acquisition, or possible acquisition, of a particular financial product you should read any relevant Product Disclosure Statement or like instrument.

New Zealand

The research in this document is intended for New Zealand resident professional financial advisers or brokers (for use in their roles as financial advisers or brokers) and habitual investors who are "wholesale clients" for the purpose of the Financial Advisers Act 2008 (FAA) (as described in sections 5(c) (1)(a), (b) and (c) of the FAA). This is not a solicitation or inducement to buy, sell, subscribe, or underwrite any securities mentioned or in the topic of this document. For the purpose of the FAA, the content of this report is of a general nature, is intended as a source of general information only and is not intended to constitute a recommendation or opinion in relation to acquiring or disposing (including refraining from acquiring or disposing) of securities. The distribution of this document is not a "personalised service" and, to the extent that it contains any financial advice, is intended only as a "class service" provided by Edison within the meaning of the FAA (i.e. without taking into account the particular financial situation or goals of any person). As such, it should not be relied upon in making an investment decision.

United Kingdom

This document is prepared and provided by Edison for information purposes only and should not be construed as an offer or solicitation for investment in any securities mentioned or in the topic of this document. A marketing communication under FCA Rules, this document has not been prepared in accordance with the legal requirements designed to promote the independence of investment research and is not subject to any prohibition on dealing ahead of the dissemination of investment research.

This Communication is being distributed in the United Kingdom and is directed only at (i) persons having professional experience in matters relating to investments, i.e. investment professionals within the meaning of Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the "FPO") (ii) high net-worth companies, unincorporated associations or other bodies within the meaning of Article 49 of the FPO and (iii) persons to whom it is otherwise lawful to distribute it. The investment or investment activity to which this document relates is available only to such persons. It is not intended that this document be distributed or passed on, directly or indirectly, to any other class of persons and in any event and under no circumstances should persons of any other description rely on or act upon the contents of this document.

This Communication is being supplied to you solely for your information and may not be reproduced by, further distributed to or published in whole or in part by, any other person.

United States

Edison relies upon the "publishers' exclusion" from the definition of investment adviser under Section 202(a)(11) of the Investment Advisers Act of 1940 and corresponding state securities laws. This report is a bona fide publication of general and regular circulation offering impersonal investment-related advice, not tailored to a specific investment portfolio or the needs of current and/or prospective subscribers. As such, Edison does not offer or provide personal advice and the research provided is for informational purposes only. No mention of a particular security in this report constitutes a recommendation to buy, sell or hold that or any security, or that any particular security, portfolio of securities, transaction or investment strategy is suitable for any specific person.

Frankfurt +49 (0)69 78 8076 960
Schumannstrasse 34b
60325 Frankfurt
Germany

London +44 (0)20 3077 5700
280 High Holborn
London, WC1V 7EE
United Kingdom

New York +1 646 653 7026
1185 Avenue of the Americas
3rd Floor, New York, NY 10036
United States of America

Sydney +61 (0)2 8249 8342
Level 4, Office 1205
95 Pitt Street, Sydney
NSW 2000, Australia