EDISON

Context Therapeutics

Development update

Promising combination therapy for ONA-XR

Pharma and biotech

Context Therapeutics announced plans to collaborate with the Menarini Group to study ONA-XR in combination with elacestrant, an oral selective estrogen receptor degrader (SERD) for the treatment of second/third-line HR+/HER2- metastatic breast cancer (mBC) patients. The Phase Ib/II study (ELONA trial) is expected to commence from Q422. This is a key development as elacestrant is the first oral SERD to demonstrate higher efficacy than fulvestrant (standard of care) in Phase III studies. Fulvestrant is an injectable SERD and we believe an oral formulation within this drug class would improve patient adherence. Greater efficacies are often observed in combinational oncology therapies, so we believe the upcoming ONA-XR/elacestrant trial is an encouraging clinical advancement. ONA-XR has previously shown promising preclinical data in combination with anti-estrogen therapy. We value an incremental contribution of $1.1/share from this program.

Year end	Revenue ($m)	PBT* ($m)	EPS* ($)	DPS ($)	P/E (x)	Yield (%)
12/20	0.0	(3.2)	(9.28)	0.0	N/A	N/A
12/21	0.0	(10.6)	(3.74)	0.0	N/A	N/A
12/22e	0.0	(21.9)	(1.37)	0.0	N/A	N/A
12/23e	0.0	(34.2)	(2.14)	0.0	N/A	N/A

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

Elacestrant leads the pack in oral SERDs

While several oral SERDs are in mid-to-late-stage clinical development, we believe elacestrant is the frontrunner, having reported positive top-line data from its Phase III EMERALD study in December 2021. The study met both primary endpoints, demonstrating a 30% reduction in the risk of disease progression or death versus standard of care endocrine therapy in the overall population (p=0.0018) and 45% reduction in patients with estrogen receptor 1 (*ESR1*) mutations (p=0.0005). Menarini filed a new drug application (NDA) for elacestrant in June 2022 and recently announced its plans to pursue combination studies for elacestrant under the hypothesis that a broader targeting (than just estrogen receptors) would likely improve efficacy and thereby progression-free survival (PFS) in patients.

ONA-XR elacestrant study design

The upcoming trial will be a Phase Ib/II proof-of-concept study (Context-sponsored trial with Menarini contributing the elacestrant at no cost) and is expected to recruit up to 73 patients who have progressed on first-line treatment (≥50% of the selected patient population will have the *ESR1* mutation). The primary endpoint will be overall response rate, while PFS and the clinical benefit rate will be secondary endpoints.

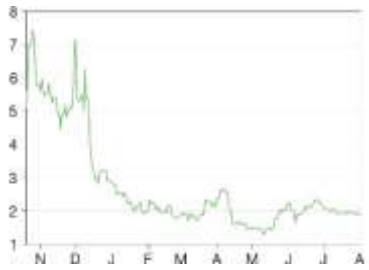
Valuation: $151.0m or $9.46 per basic share

We have updated our valuation to include the upcoming ONA-XR elacestrant program. The target population has been kept in line with the ongoing combination study with fulvestrant, but we assume peak penetration of 7.5% and a 10% probability of success. The program has added roughly $1.1/share to our valuation and shortens the cash runway to Q423 (from Q124). We now estimate the need to raise $10m in FY23 and a further $160m between FY24 and FY26 before reaching profitability in FY27.

2 August 2022

Price	**$1.89**
Market cap	**$30m**
Net cash ($m) at 31 March 2022	45.7
Shares in issue	15.97m
Free float	67%
Code	CNTX
Primary exchange	Nasdaq
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	(8.3)	26.8	N/A
Rel (local)	(14.8)	28.0	N/A
52-week high/low		$7.45	$1.29

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 the Phase II PR+ recurrent endometrial cancer trial is expected in H222. The other asset is a bi-specific monoclonal antibody, CLDN6xCD3, currently undergoing preclinical development.

Next events

Recurrent endometrial cancer updates	H222
Development candidate for CLDN6xCD3	Q422
1st-line HR+/HER2- mBCa (ctDNA enriched) Phase Ib trial update	Mid-2023

Analysts

Soo Romanoff +44 (0)20 3077 5700

Jyoti Prakash, CFA +44 (0)20 3077 5700

heathcare@edisongroup.com

Edison profile page

Menarini agreement broadens market potential

Despite ongoing R&D efforts, the treatment landscape for advanced hormone-driven cancers remains restricted. Currently approved endocrine therapies only target estrogen, which allows tumorigenic activity mediated by other pathways to continue unchecked. Studies indicate that a combination therapy may improve the efficacy of anti-estrogens, resulting in better treatment outcomes. Context has been exploring this unmet need to develop its PR antagonist ONA-XR as a combination therapy with anti-estrogens. One of the ongoing studies being undertaken by Context is a Phase II clinical trial in HR+/HER2- mBC along with the standard of care (SoC), fulvestrant, which, as noted earlier, is a SERD available only in the injectable form and is associated with side effects such as liver damage. The newer-generation oral SERDs, several of which are under later-stage clinical development, are being proposed as more convenient and safer oral alternatives to fulvestrant, although we note the possible regulatory resistance stemming from lower-priced generic versions of the injectable formulation.

Elacestrant leading the oral SERDs race

The global SERD market is estimated to reach $4.1bn by 2030, the bulk of which we expect to be made up of oral SERDs. While several oral SERDs targeting second-line HR+/HER2- mBC are currently in advanced stage clinical development, elacestrant is the first oral SERD to demonstrate a statistically significant and clinically meaningful improvement in PFS versus the SoC endocrine therapy, while early category leaders Sanofi and Roche have fallen short of meeting the primary endpoint (Exhibit 1).

Exhibit 1: Selected oral SERDs in late-stage clinical development for previously treated HR+/HER2- mBC

Drug	Company	Development phase	Indication	Comparator	Prior CDK4/6 use	Trial participants selected for *ESR1* mutation	Comments
Elacestrant	Menarini/ Radius Health	NDA	Second-line, postmenopausal mBC	Faslodex or aromatase inhibitor	Mandatory	Yes	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). New drug application (NDA) filed in June 2022 with FDA decision expected in 2023.
Camizestrant	AstraZeneca	Phase III	Second-line, postmenopausal mBC	Faslodex	Not mandatory	Unclear	Data from the pivotal Phase III SERENA-2 study expected to read out in September 2022.
Imlunestrant	Lilly	Phase III	Second-line, postmenopausal mBC	Faslodex or aromatase inhibitor	Not mandatory	Unclear	Data from the pivotal Phase III EMBER-3 study expected to read out in June 2023.
Giredestrant	Roche	Phase II	Second/third-line pre/peri/ postmenopausal mBC	Faslodex or aromatase inhibitor	Not mandatory	No	Failed to meet the primary end (PFS in all-comers) point in the Phase II acelERA study. Positive signal seen in cases with *ESR1* mutation. Roche is continuing to study the drug as a first line and adjuvant treatment in separate studies.
Amcenestrant	Sanofi	Phase II	Second-line mBC	Faslodex or aromatase inhibitor	Required for some cohorts	No	Failed to meet the primary end (PFS in all-comers) point in the Phase II AMEERA-3 study. Sanofi is continuing to study the drug as a first line and adjuvant treatment in separate late-stage studies.

Source: Evaluate Pharma, Edison Investment Research

ESR1 mutation cohort likely to be the biggest beneficiary

The Phase III EMERALD trial was a randomized, open-label, active-controlled study evaluating elacestrant as second/third-line monotherapy in estrogen receptor+(ER+)/HER2- mBC patients. The study enrolled 477 patients (~50% had *ESR1* mutations) who had received prior treatment with one or two lines of endocrine therapy, including a CDK 4/6 inhibitor. Patients in the study were randomized to receive either elacestrant or the investigator's choice of an approved hormonal agent. The primary endpoint of the study was PFS in the overall patient population and in patients with *ESR1* mutations. Secondary endpoints included evaluation of overall survival (OS), objective response rate (ORR), and duration of response (DOR).

The study met its primary endpoint, demonstrating a 30% reduction in the risk of disease progression or death versus SoC in all-comers (PFS of 2.79 months versus 1.91months for the control group; p=0.0018). More notably, the corresponding figure stood at 45% for patients with *ESR1* mutations (PFS of 3.78 months versus 1.87 months for the control group; p=0.0005), which is believed to have driven the positive results for all comers. We highlight that *ESR1* mutations are associated with endocrine therapy resistance and, while rarely present in primary tumors, are relatively common in metastatic HR+/HER2- cancers (10–50% of cases[1]). Some observers consider that the failure of Sanofi and Roche's candidates could have resulted from their lack of *ESR1* selectivity in the study design. We therefore expect the *ESR1* mutation cohort to be the most likely target population for new oral SERDs under development.

The Phase Ib/II ELONA study design

The upcoming trial will be a Phase Ib/II proof -of-concept study to evaluate the efficacy and tolerability of ONA-XR + elacestrant combination treatment in patients who have progressed on first-line antiestrogen + CDK4/6 inhibitor therapy. The patients cannot have received prior chemotherapy in the metastatic setting. Notably ≥ 50% of the selected patient population will carry the *ESR1* mutation. The trial is expected to recruit up to 73 participants across 16–19 sites in the United States and will be sponsored by Context, with Menarini providing elacestrant clinical trial material free of cost. The Phase Ib dose escalation portion will evaluate four cohorts of ONA-XR plus elacestrant and Phase II will evaluate up to 45 patients. The primary endpoint will be objective response rate (ORR), while PFS and clinical benefit rate (CBR) will be secondary endpoints. The trial is expected to commence in Q422 and Context and Menarini will form a joint committee to review the results.

Valuation

We include the upcoming ONA-XR elacestrant program in our valuation but keep our assumptions conservative. While the target population (c 35,000 progesterone receptor positive (PR+)/HER2- mBC patients seeking second/third-line treatment in the US) has been kept in line with the ongoing combination study with fulvestrant, we incorporate a lower peak penetration (7.5% versus 10%) due to the likelihood of the combination benefiting the *ESR1* subset the most (c 40% of the total target population according to Context). We have also assumed a probability of success of 10%, which is in line with the standard figure ascribed to Phase Ib/II studies. Overall, the program adds an incremental $1.1/share to our valuation. The cash runway, however, shortens to Q423 (from Q124) to account for the increased spending given the trial will be sponsored by Context. We now estimate the need to raise $10m in FY23 and an additional $160m between FY24 and FY26

1 Zundelevich, A., Dadiani, M., Kahana-Edwin, S. et al. *ESR1 mutations are frequent in newly diagnosed metastatic and loco-regional recurrence of endocrine-treated breast cancer and carry worse prognosis. Breast Cancer (2020)*

(previously $110m) before reaching profitability in FY27 (this assumes that Context self-commercializes in the US). We show the raises as illustrative debt, as per Edison methodology. However, we note that, given fulvestrant and elacestrant are both SERDs, Context is likely to pursue only one of the two programs for further clinical studies, based on data from the Phase II trials. We also believe that a positive result from the Phase Ib/II combination study could lead to potential licensing partnerships in the future for ONA-XR.

Exhibit 2: Context Therapeutics valuation (risk-adjusted NPV)

Program	Indication	Status	Probability of success	Launch year	Peak sales ($m)	Economics	Risked NPV ($m)
ONA-XR	Second-line HR+/HER2- mBC (in combination with fulvestrant)	Phase II	15%	2026	498	US (fully owned) Europe (out-licensed)	40.7
	First-line escalation therapy for HR+/HER2- mBC (ctDNA+)	Phase Ib	7.5%	2027	222	US (fully owned) Europe (out-licensed)	7.0
	Second-third line HR+/HER2- mBC (in combination with elacestrant)	Phase Ib/II	10%	2028	498	US (fully owned) Europe (out-licensed)	17.5
	Recurrent PR+ endometrial cancer	Phase II	10%	2027	583	US (fully owned) Europe (out-licensed)	28.5
	Advanced GCT of the ovary	Phase II	10%	2027	292	US (fully owned) Europe (out-licensed)	11.5
Net cash (at the end of Q122) $m							45.7
Total firm value							**151.0**
Total basic shares (m)							16.0
Value per basic share ($)							**9.46**
Total diluted shares (m)							2.1
Value per diluted share ($)							**8.37**

Source: Edison Investment Research

Exhibit 3: Financial summary

$000s	2020	2021	2022e	2023e	2024e
Year end 31 December	US GAAP	US GAAP	US GAAP	US GAAP	US GAAP
INCOME STATEMENT					
Revenue	0	0	0	0	0
Cost of Sales	0	0	0	0	0
Gross Profit	0	0	0	0	0
Research and Development Expenses	(1,642)	(6,893)	(13,536)	(21,654)	(35,546)
Sales, General and Administrative Expenses	(931)	(3,633)	(8,356)	(12,534)	(13,787)
EBITDA	(2,572)	(10,526)	(21,892)	(34,188)	(49,333)
Operating profit (before amort. and excepts.)	(2,572)	(10,526)	(21,892)	(34,188)	(49,333)
Amortization of acquired intangibles	0	0	0	0	0
Exceptionals	0	0	0	0	0
Share-based payments	0	0	0	0	0
Reported operating profit	(2,572)	(10,526)	(21,892)	(34,188)	(49,333)
Net Interest	(661)	(64)	0	0	0
Joint ventures & associates (post tax)	0	0	0	0	0
Exceptionals	9,878	133	0	0	0
Profit Before Tax (norm)	(3,233)	(10,590)	(21,892)	(34,188)	(49,333)
Profit Before Tax (reported)	6,644	(10,457)	(21,892)	(34,188)	(49,333)
Reported tax	0	0	0	0	0
Profit After Tax (norm)	(3,233)	(10,590)	(21,892)	(34,188)	(49,333)
Profit After Tax (reported)	6,644	(10,457)	(21,892)	(34,188)	(49,333)
Minority interests	0	0	0	0	0
Discontinued operations	0	0	0	0	0
Net income (normalized)	(3,233)	(10,590)	(21,892)	(34,188)	(49,333)
Net income (reported)	6,644	(10,457)	(21,892)	(34,188)	(49,333)
Average Number of Shares Outstanding (m)	0	3	16	16	16
EPS - basic normalized ($)	(9.28)	(3.74)	(1.37)	(2.14)	(3.09)
EPS - normalized fully diluted ($)	(9.28)	(3.74)	(1.37)	(2.14)	(3.09)
EPS - basic reported ($)	19.07	(3.69)	(1.37)	(2.14)	(3.09)
Dividend ($)	0	0	0	0	0
BALANCE SHEET					
Fixed Assets	118	0	0	0	0
Intangible Assets	0	0	0	0	0
Tangible Assets	0	0	0	0	0
Investments & other	118	0	0	0	0
Current Assets	350	51,306	32,689	9,481	20,674
Stocks	0	0	0	0	0
Debtors	0	0	0	0	0
Cash & cash equivalents	341	49,686	32,041	8,833	20,026
Other	9	1,620	648	648	648
Current Liabilities	(9,548)	(3,033)	(6,309)	(7,289)	(7,815)
Creditors	(2,708)	(1,826)	(3,798)	(4,152)	(4,194)
Tax and social security	0	0	0	0	0
Short term borrowings	(5,884)	0	0	0	0
Other	(956)	(1,207)	(2,511)	(3,137)	(3,621)
Long Term Liabilities	(69)	0	0	(10,000)	(70,000)
Long term borrowings	(69)	0	0	(10,000)	(70,000)
Other long-term liabilities	0	0	0	0	0
Net Assets	(9,150)	48,272	26,380	(7,807)	(57,141)
Convertible preferred stock	(7,771)	0	0	0	0
Minority interests	0	0	0	0	0
Shareholders' equity	(16,921)	48,272	26,380	(7,807)	(57,141)
CASH FLOW					
Operating Cash Flow	(2,572)	(10,526)	(21,892)	(34,188)	(49,333)
Working capital	1,318	(2,225)	4,248	980	526
Exceptional & other	219	3,951	0	0	0
Tax	0	0	0	0	0
Net operating cash flow	(1,035)	(8,799)	(17,644)	(33,208)	(48,807)
Capex	0	(250)	0	0	0
Acquisitions/disposals	0	0	0	0	0
Net interest	0	0	0	0	0
Equity financing	0	58,394	0	0	0
Dividends	0	0	0	0	0
Other	0	0	0	0	0
Net Cash Flow	(1,035)	49,345	(17,644)	(33,208)	(48,807)
Opening net debt/(cash)	21,742	13,384	(49,686)	(32,041)	1,167
FX	0	0	0	0	0
Other non-cash movements	9,393	13,725	0	0	0
Closing net debt/(cash)	13,384	(49,686)	(32,041)	1,167	49,974

Source: Context Therapeutics reports, Edison Investment Research

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
1,185 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