EDISON

Context Therapeutics

Q322 update

Period marked by readouts and pipeline progress

Pharma and biotech

Context Therapeutics' Q322 report focused on pipeline progress, reporting interim data from two Phase II trials (advanced endometrial and ovarian cancer). Preliminary data from the former (ONA-XR+anastrozole) was encouraging, with a four-month PFS of 77.7%, superior to historical data from either drug alone, although we note that the small sample size limits our ability to draw definitive conclusions. Q322 operating performance was in line with expectations, with R&D expenses of $2.1m. We anticipate that these will rise further in Q422 following initiation of the Phase Ib/II ELONA trial in November 2022. Based on our cash burn projections, the period-end cash balance of $39.4m should be sufficient to fund operations into Q124, in line with management guidance. We view the forthcoming readout from the Phase II trial in HR+/HER2- metastatic breast cancer (mBC) as the next key catalyst for the company. We reduce our valuation slightly to $9.18/share on lower net debt.

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	(18.1)	(1.13)	0.0	N/A	N/A
12/23e	0.0	(27.4)	(1.72)	0.0	N/A	N/A

Note: *PBT and EPS are normalized, excluding amortization of acquired intangibles, exceptional items and share-based payments.

Encouraging preliminary data in endometrial cancer

The treatment landscape for recurrent endometrial cancer remains underserved despite ongoing development efforts. While checkpoint inhibitors (Keytruda, Jemperli) are only effective in a subset of patients – those with the MSI-H or dMMR mutations (16–31% of all endometrial cancers) – the recently approved combination treatment, Lenvima+Keytruda, while effective, is associated with serious side effects. The ONA-XR+anastrozole combination treatment has reported a strong safety profile and superior efficacy over its individual constituents, although the small sample size limits absolute comparability. If replicated in larger, randomized trials, these results could translate into a sizeable market opportunity.

Elacestrant combination enters the clinic

Commencement of the Phase Ib/II ELONA trial (ONA-XR+elacestrant) in November 2022 was a major post-period development for Context. As a reminder, elacestrant (developed by the Menarini Group) is the first oral selective estrogen receptor degrader (SERD) to demonstrate better efficacy than fulvestrant (standard of care) in Phase III studies, with the FDA decision on approval expected in February 2023. We continue to view the combination trial as an encouraging pipeline advancement and key value proposition for the company (Phase Ib data expected in Q423).

Valuation: $146.5m or $9.18 per basic share

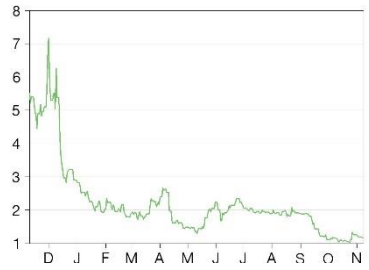
We have updated our estimates for the Q322 results and period-end net cash position. Overall, we reduce our valuation slightly to $146.5m ($9.18/share) from $150m ($9.39/share). The current cash balance should fund operations into Q124, although we estimate the need to raise $140m between FY24 and FY26 (assuming self-commercialization) before reaching profitability in FY27.

10 November 2022

Price	**$1.17**
Market cap	**$19m**

Net cash ($m) at 30 September 2022	39.4
Shares in issue	15.97m
Free float	67%
Code	CNTX
Primary exchange	Nasdaq
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	(0.9)	(37.8)	(79.5)
Rel (local)	(3.7)	(31.6)	(74.3)
52-week high/low		$7.16	$1.02

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 and one Phase Ib/II clinical trial in hormone-driven breast, endometrial and ovarian cancer. The other asset is a bi-specific monoclonal antibody, CLDN6xCD3, currently undergoing preclinical development, with the final clinical candidate expected to be finalized by December 2022.

Next events

Data readouts from the Phase II study in HR+/HER2- mBC (ONA-XR+fulvestrant)	December 2022
Development candidate for CLDN6xCD3	December 2022

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Edison profile page

Pipeline gaining traction

Recent months have been marked by notable pipeline development activity by Context, as it signed a collaboration deal with Menarini, reported preliminary data from two Phase II investigator-sponsored trials (endometrial cancer and granulosa cell tumor (GCT) of the ovary) and made progress in finalizing its CLDN6 clinical candidate (see Exhibit 1 for an overview of Context's ongoing clinical trials).

Exhibit 1: Context's ONA-XR clinical trials

Treatment	Stage	Patients (n)	Clinical Indication	Biomarker	Key Inclusion and Exclusion Criteria	Collaborator	Data Update[1]
ONA-XR + Anastrozole	Ph 2	25	Endometrial Cancer	PR+	• Must have received at least one prior treatment with a platinum/taxane chemotherapy	Jefferson	• 12 patients enrolled • 4-month PFS rate of 77% • No treatment-related SAE
ONA-XR + Anastrozole	Ph 2	25	Granulosa Cell Tumor of the Ovary	PR+	• Must have received at least one prior chemotherapy regimen	Memorial Sloan Kettering Cancer Center	• 14 patients enrolled • No treatment-related SAE
ONA-XR + Fulvestrant	Ph 2	39	Breast Cancer (2L/3L) SMILE Trial	PR+	• Must have received prior CDK4/6 inhibitor therapy • One line of prior chemotherapy in metastatic setting allowed	Carbone Cancer Center, University of Wisconsin School of Medicine and Public Health	
ONA-XR + Elacestrant	Ph 1b/2	67	Breast Cancer (2L/3L) ELONA Trial	PR+	• Must have received prior CDK4/6 inhibitor therapy • ≥50% patients with ESR1 mutant • No prior chemotherapy in metastatic setting	MENARINI group	

Source: Context Therapeutics corporate presentation, November 2022

Preliminary data from the remaining Phase II trial in second/third-line HR+/HER2- mBC (SMILE study; ONA-XR+fulvestrant) are expected in December 2022 and we see this as the next catalyst for the company. The results may also have a bearing on the recently initiated ELONA trial (given that elacestrant is an oral SERD challenging the standard-of-care fulvestrant, which is an injectable SERD) and should therefore be of particular interest to the market. Phase Ib data from the ELONA trial (please see our update note published on 2 August for more details) are expected in Q423 and could be another major infection point for Context.

Endometrial cancer: An untapped space

Despite the hormonal origins of endometrial cancer, anti-hormone therapies have, to date, been unsuccessful in delivering meaningful benefits to patients with advanced disease (unlike in breast cancer). We note that the only hormonal therapy currently approved for recurrent endometrial tumors is the progestin, megestrol acetate, which has shown a 20–30% response rate in metastatic patients. Antiestrogens such as tamoxifen and aromatase inhibitors have only shown modest improvement in smaller studies, although this could be partially attributable to lack of patient selectivity.

More recently, the FDA has given the green light to two checkpoint inhibitors – Jemperli (April 2021) and Keytruda (March 2022) as monotherapies and Keytruda+Lenvima (accelerated approval in September 2019, full approval in July 2021) as combination treatment – although all of have certain limitations. While the checkpoint inhibitors only work for a subset of patients (those with the microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) mutations; collectively 16–31% of all advanced endometrial cancer cases), the combination treatment is associated with serious side effects, most notably hypertension, resulting in 30% of patients discontinuing treatment.

Context is developing ONA-XR as a combination therapy with antiestrogens for this indication based on the same principle as the one Context is applying in breast cancer, to potentially improve treatment outcomes by achieving complete hormone blockage.

Positive early data from the ONWARD 221 Phase II trial in advanced endometrial cancer

In our view, the key highlight of the Q322 release was the encouraging preliminary data presented by the company from its ongoing Phase II trial in recurrent endometrial cancer. As a reminder, the study (ONWARD 221) is an open-label, single-arm, investigator-sponsored trial evaluating ONA-XR (50mg BID) in combination with antiestrogen anastrozole in women with progesterone receptor positive (PR+) metastatic endometrial cancer after progression on at least one prior line of chemotherapy. The first patient was dosed in May 2021 and the study aims to enroll 25 patients across three sites in the United States. The primary endpoints are four-month progression-free survival (PFS) and objective response rate (ORR).

As of 30 September 2022, 12 patients have been enrolled in the trial and the reported PFS data relates to nine evaluable patients. The reported four-month PFS of 77.7% (12-month PFS of 33%; n=3) is encouraging and superior to results from previous standalone trials (see Exhibit 2), although larger data sets are needed to confirm the initial findings. We also note that potential variations in study designs, dosages, patient population and cohort size mean that the data may not be strictly comparable on a head-to-head basis. Nevertheless, we see this as an early validation of ONA-XR's potential and combination approach which, if replicated in the full data set following complete enrolment and in subsequent larger, randomized studies, could translate to significant market potential. We expect further clarity on this when Context presents additional data in mid-2023.

Exhibit 2: ONWARD 221 preliminary data benchmarked against standalone treatments

	ONA-XR + Anastrozole	ONA-XR	Anastrozole
Trial	Schilder (ongoing)[1]	Cottu 2018[2]	PARAGON 2019[3]
Patients (n)	12 (9 evaluable)	12	54
Lines of Prior Chemotherapy, n (%) 1 ≥2	 8 (66) 4 (33)	 4 (33) 8 (66)	 50 (93) 4 (7)
Treatment free interval (TFI) ≥6 months, n (%)	4 (33)	1 (8)	36 (70)
4-month PFS rate, n (%)	7 (77)	4 (33)	ND
12-month PFS rate, n (%)	3 (33)	1 (8)	4 (7)
mPFS (95% CI), months	NE	2.0 (1.7 5.3)	2.7 (1.9 4.5)
Side Effects	Well tolerated	Well tolerated	Well tolerated

Source: Context Therapeutics corporate presentation, November 2022. Notes: 1. Data as of 30 September 2022. 2. Cottu, PloS one, 2018. 3. Mileshkin, Gyn Onc, 2019

Additional data from the ONWARD 220 Phase II trial in GCT of the ovary

In addition to initial data from the Phase II endometrial cancer, Context also reported updated data from the ongoing basket study evaluating ONA-XR both as monotherapy and in combination with anastrozole in women with PR+ advanced GCT of the ovary (cohort 1 and cohort 4, respectively). The 84-week study was designed as a Simon two-stage study with both cohorts recruiting 14 patients in stage 1. The criterion to move to stage 2 was overall response (complete or partial) from at least one of the 14 patients. Data from cohort 1 (a monotherapy arm, which commenced

enrollment in May 2019) was presented by the company at the American Society of Clinical Oncology in June 2022, reporting 12-month PFS of 20.1% and a clinical benefit rate (stable disease) of 35.7%. However, the ORR cut-off required to progress to stage 2 was not met and therefore we do not expect the company to pursue this indication as a monotherapy.

The combination arm of the study (cohort 4) initiated recruitment in 2021 and has completed enrollment of the 14th patient according to the latest information provided by the company. As with cohort 1, the criterion to advance to stage 2 will be objective response from at least one of the 14 patients and it is unclear as of now if the combination treatment has been able to meet this requirement. Seven patients remain on the trial. We expect the combination treatment to deliver incremental efficacy versus monotherapy and await further data from the company on this (expected in mid-2023). We highlight that more than 95% of GCT tumors are PR+, making them a potentially attractive therapeutic target for anti-progestin therapies. Moreover, these tumors are characterized by very few mutations, limiting the applicability of targeted treatments. With no currently approved treatments in the recurrent setting for this indication, the market opportunity for any new treatments remains high, in our view. We note that the FDA granted the fast-track designation for ONA-XR in PR+ ovarian cancer in August 2020, highlighting the significant unmet need in the space.

Q322 financials

Context reported a net loss of $3.9m in Q322, significantly higher than the corresponding figure of $1.4m in Q321, driven by higher R&D and G&A expenses attributable to ongoing clinical trials and preclinical development efforts. Q322 R&D expenses stood at $2.1m versus $0.7m in Q321 ($1.5m in Q222) and we expect this figure to increase further in Q422 with the initiation of the Phase Ib ELONA trial (sponsored by Context). We note that the company has recently announced cost-cutting measures, deprioritizing discretionary R&D on preclinical activities and focusing entirely on the current developmental pipeline. G&A expenses during the quarter were $2.0m (in line with the previous quarter but higher than the $0.8m recorded in Q321) due to higher headcount and insurance and professional fees. We have made slight adjustments to our FY22–24 forecasts based on the Q322 results.

Period-end cash was $39.4m which, based on our cash burn projections, should be sufficient to fund operations into Q124, past key milestones such as interim data from the ELONA trial (Q423) and IND submission for the CLDN6 program (Q124). Assuming self-commercialization, we estimate the need to raise a further $140m between FY24 and FY26 (lower than our previous estimate of $160m due to the announced cost-savings initiatives) before reaching profitability in FY27, contingent on its programs receiving market approval. We show the raises as illustrative debt, according to Edison methodology. We also believe that a positive result from the ongoing combination studies could lead to potential licensing partnerships in the future for ONA-XR.

Valuation

We make minor adjustments to our estimates to factor in the Q322 performance and a slightly lower period-end net cash figure ($39.4m versus $42.9 in Q222). Overall, our valuation reduces slightly to $146.5m ($9.18/share) from $150m ($9.39/share) previously.

Exhibit 3: 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)	41.4
	First-line escalation therapy for HR+/HER2- mBC (ctDNA+)	Phase Ib	7.5%	2027	222	US (fully owned) Europe (out-licensed)	7.4
	Second-third line HR+/HER2- mBC (in combination with elacestrant)	Phase Ib/II	10%	2028	374	US (fully owned) Europe (out-licensed)	17.5
	Recurrent PR+ endometrial cancer	Phase II	10%	2027	583	US (fully owned) Europe (out-licensed)	29.1
	Advanced GCT of the ovary	Phase II	10%	2027	292	US (fully owned) Europe (out-licensed)	11.9
Net cash (at the end of Q322) $m							39.4
Total firm value							146.5
Total basic shares (m)							16.0
Value per basic share ($)							9.18
Total diluted shares (m)							1.9
Value per diluted share ($)							8.18

Source: Edison Investment Research

Exhibit 4: Financial summary

$000s	2020	2021	2022e	2023e	2024e
31-December	US GAAP	US GAAP	US GAAP	US GAAP	US GAAP
INCOME STATEMENT					
Revenue	0	0	0	0	0
Cost of Sales	0	0	0	0	0
Gross Profit	0	0	0	0	0
Research and Development Expenses	(1,642)	(6,893)	(9,718)	(14,881)	(20,289)
Sales, General and Administrative Expenses	(931)	(3,633)	(8,356)	(12,534)	(13,787)
EBITDA	(2,572)	(10,526)	(18,074)	(27,415)	(34,076)
Operating profit (before amort. and excepts.)	(2,572)	(10,526)	(18,074)	(27,415)	(34,076)
Amortization of acquired intangibles	0	0	0	0	0
Exceptionals	0	0	0	0	0
Share-based payments	0	0	0	0	0
Reported operating profit	(2,572)	(10,526)	(18,074)	(27,415)	(34,076)
Net Interest	(661)	(64)	0	0	0
Joint ventures & associates (post tax)	0	0	0	0	0
Exceptionals	9,878	133	0	0	0
Profit Before Tax (norm)	(3,233)	(10,590)	(18,074)	(27,415)	(34,076)
Profit Before Tax (reported)	6,644	(10,457)	(18,074)	(27,415)	(34,076)
Reported tax	0	0	0	0	0
Profit After Tax (norm)	(3,233)	(10,590)	(18,074)	(27,415)	(34,076)
Profit After Tax (reported)	6,644	(10,457)	(18,074)	(27,415)	(34,076)
Minority interests	0	0	0	0	0
Discontinued operations	0	0	0	0	0
Net income (normalized)	(3,233)	(10,590)	(18,074)	(27,415)	(34,076)
Net income (reported)	6,644	(10,457)	(18,074)	(27,415)	(34,076)
Average Number of Shares Outstanding (m)	0	3	16	16	16
EPS - basic normalized ($)	(9.28)	(3.74)	(1.13)	(1.72)	(2.13)
EPS - normalized fully diluted (c)	(928.15)	(373.72)	(113.20)	(171.71)	(213.43)
EPS - basic reported ($)	19.07	(3.69)	(1.13)	(1.72)	(2.13)
Dividend ($)	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	35,407	8,629	4,106
Stocks	0	0	0	0	0
Debtors	0	0	0	0	0
Cash & cash equivalents	341	49,686	34,759	7,980	3,458
Other	9	1,620	648	648	648
Current Liabilities	(9,548)	(3,033)	(5,209)	(5,845)	(5,398)
Creditors	(2,708)	(1,826)	(3,136)	(3,330)	(2,897)
Tax and social security	0	0	0	0	0
Short term borrowings	(5,884)	0	0	0	0
Other	(956)	(1,207)	(2,073)	(2,515)	(2,501)
Long Term Liabilities	(69)	0	0	0	(30,000)
Long term borrowings	(69)	0	0	0	(30,000)
Other long-term liabilities	0	0	0	0	0
Net Assets	(9,150)	48,272	30,198	2,784	(31,292)
Convertible preferred stock	(7,771)	0	0	0	0
Minority interests	0	0	0	0	0
Shareholders' equity	(16,921)	48,272	30,198	2,784	(31,292)
CASH FLOW					
Operating Cash Flow	(2,572)	(10,526)	(18,074)	(27,415)	(34,076)
Working capital	1,318	(2,225)	3,147	636	(447)
Exceptional & other	219	3,951	0	0	0
Tax	0	0	0	0	0
Net operating cash flow	(1,035)	(8,799)	(14,926)	(26,779)	(34,522)
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	(14,926)	(26,779)	(34,522)
Opening net debt/(cash)	21,742	13,384	(49,686)	(34,759)	(7,980)
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)	(34,759)	(7,980)	26,542

Source: Company reports, Edison Investment Research

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