EDISON

Cantargia

Company update

Sentiment affected, but fundamentals robust

Pharma & biotech

Novartis reported negative data from its Phase III CANOPY-2 trial for canakinumab in 2nd/3rd-line NSCLC; canakinumab targets the same IL-1 pathway as CAN04, but in a more restricted way. This has triggered negative sentiment towards Cantargia's share price. However, we note that the readout coincided with the ongoing correction in the European and US biotechnology subsectors as well as in the broader technology sector. Starting in mid-February 2021, the biotechnology indexes retreated by as much as 15%, which continues to keep pressure on Cantargia's share price. Ultimately, we believe CAN04 is differentiated and Novartis's results should add to the data that will help Cantargia define CAN04's positioning. We value Cantargia at SEK6.86bn or SEK68.5/share.

Year end	Revenue (SEKm)	PBT* (SEKm)	EPS* (SEK)	DPS (SEK)	P/E (x)	Yield (%)
12/19	0.0	(110.8)	(1.56)	0.0	N/A	N/A
12/20	0.0	(173.1)	(1.94)	0.0	N/A	N/A
12/21e	0.0	(276.3)	(2.76)	0.0	N/A	N/A
12/22e	0.0	(297.1)	(2.97)	0.0	N/A	N/A

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

CANOPY-2 data negative, but not definitive for CAN04

While disappointing, Novartis's Phase III CANOPY-2 trial readout is just the first of the three CANOPY trials in lung cancer patients. The CANOPY-2 trial enrolled the most advanced patients, while the other two are in earlier settings. As a reminder, Novartis engaged in this large Phase III programme in NSCLC after it found an efficacy signal in a large cardiovascular outcomes study in an unrelated area. This particular six-year Phase III study CANTOS (n = 10,061; our analysis is in the initiation report) showed that canakinumab reduced lung cancer incidence by 67% (p<0.0001) and mortality by 77% (p = 0.0002). So, in a way this was even earlier setting than in the CANOPY trials and can be perceived as cancer prevention. To this end, Novartis recently initiated a Phase II Can-Prevent-Lung trial.

CAN04 is significantly different from canakinumab

Novartis's canakinumab targets IL-1beta, while CAN04 targets the downstream IL-1RAP, which means CAN04 blocks signalling from both IL-1beta and IL-1alpha, potentially allowing for more comprehensive IL-1 pathway signalling control. In addition, CAN04 has so-called Antibody-Dependent Cellular Cytotoxicity (ADCC) effect, which further differentiates the mechanism of action. The CANFOUR trial is evaluating CAN04 in an earlier stage setting of NSCLC than CANOPY-2 and in a different combination with chemotherapy (cisplatin plus gemcitabine). So, Cantargia's CAN04 and the R&D programmer are both significantly differentiated.

Valuation: SEK6.86bn or SEK68.5/share

We value Cantargia at SEK6.86bn or SEK68.5/share, versus SEK5.93bn or SEK65.1/share previously. We have rolled our model forward, incorporated the December 2020 capital raise and increased near-term R&D spend in line with company guidance. Potential use of CAN04 in NSCLC contributes c 35% of our valuation and, while we acknowledge sentiment has been knocked by the CANOPY-2 data, because of the differences described above we do not feel this currently necessitates a fundamental change to our assumptions.

6 April 2021

Price	**SEK31.3**
Market cap	**SEK3.1bn**

Net cash and short-term investments (SEKm) at end-2020	903.3
Shares in issue	100.2m
Free float	99%
Code	CANT
Primary exchange	Nasdaq Stockholm
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	(35.9)	(51.6)	101.9
Rel (local)	(40.0)	(57.4)	21.9
52-week high/low	SEK69.7	SEK16.3	

Business description

Cantargia is a clinical-stage biotechnology company based in Sweden, established in 2009. It is developing two assets against IL1RAP, CAN04 and CAN10. CAN04 is being studied in several solid tumours with a main focus on NSCLC and pancreatic cancer. The most advanced trial is in Phase II.

Next events

Phase IIa CANFOUR efficacy data for CAN04 in PDAC and NSCLC	2021
Phase Ib ICI combination data (CAN04+pembrolizumab)	H221
Final analysis from Novartis's Phase III CANOPY-1 trial in 1L NSCLC	H221

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Edison profile page

More data from Novartis this year

The CANOPY-2 study was investigating canakinumab in second- or third-line patients with non-small cell lung cancer (NSCLC), patients who are heavily pre-treated having progressed while on or after previous platinum-based chemotherapy and PD-(L)1 inhibitor immunotherapy. In this setting it did not show a significant improvement in overall survival (OS). However, this outcome could be a result of the trial design, that is too advanced second- or third-line treatment; or the docetaxel chemotherapy was not the optimal combination. Or it could indicate the drug's mechanism of action (ie targeting IL-1beta) was not sufficient. More detailed analysis by Novartis is expected to be presented at an upcoming conference, which we believe could potentially be either at ASCO 2021 (3–7 June), WCLC 2021 (8–14 September) or ESMO 2021 (17–21 September).

Cantargia's CAN04 and the lead Phase II CANFOUR trial are both significantly differentiated. Recall, Novartis' canakinumab targets IL-1beta, while CAN04 targets the downstream IL-1RAP, which means CAN04 blocks signalling from both IL-1beta and IL-1alpha, potentially allowing for more comprehensive IL-1 pathway signalling control. CAN04 also has the ADCC effect, which further differentiates its mechanism of action from canakinumab.

The CANFOUR trial is evaluating CAN04 in an earlier-stage setting of NSCLC than CANOPY-2, recruiting first-line NSCLC patients receiving cisplatin plus gemcitabine or second-line after relapse post checkpoint inhibitor therapy. The final analysis from this trial is expected **during 2021**, which could demonstrate the potential benefits of CAN04's differentiated mechanism.

Because of these differences, CAN04's late-stage development will be based on the data from the CANFOUR trial. Novartis's CANOPY studies will provide valuable information of how to position CAN04, but do not invalidate the IL-1 axis theory in cancer, in our view. Upcoming data from Novartis's Phase III CANOPY-1 trial is the next key focus (**expected H221**). CANOPY-1 is investigating canakinumab as part of a first-line combination with anti-PD-1 pembrolizumab and chemotherapy in treatment-naïve NSCLC patients. If the data are again negative, this could further affect the sentiment (but would not invalidate the IL-1 axis theory). If the data are positive, we believe the rebound would be sharp.

Exhibit 1: Summary of key lung cancer trials for Novartis's canakinumab and Cantargia's CAN04

Pharmacological class/target	Product (generic name)	Current development status of oncology indications	Notes
Anti-IL-1β Mab Novartis	Ilaris (canakinumab)	Phase III in 1L NSCLC (+ pembrolizumab + chemo) (CANOPY-1, NCT03631199, n=673)	Fully enrolled (Jan 2020), interim efficacy analysis passed Q320. DSMB recommended that trial continue to final analysis (OS & PFS) in H221. Another interim analysis planned but timing has not been provided.
		Phase III in 2/3L NSCLC (+ docetaxel) (CANOPY-2, NCT03626545, n=245)	**Negative headline data reported 9 March 2021, with the study failing to meet its primary endpoint (OS). Analysis and presentation of the data can be expected at an upcoming conference.**
		Phase III in adjuvant NSCLC (CANOPY-A, NCT03447769, n=1,500)	Trial c 40% enrolled in June 2020, expected to be fully enrolled in 2022. Interim analysis expected in 2022 ahead of final analysis in 2023.
		Phase II in neoadjuvant NSCLC (+ pembrolizumab) (CANOPY-N NCT03968419, n=110)	Trial c 20% enrolled in June 2020.
Anti-IL1RAP Mab Cantargia	CAN04	Phase I/IIa in 1L NSCLC & PDAC (+ SoC chemo) (CANFOUR, NCT03267316, n=100)	Positive interim data reported in Sep/Oct 2020, final efficacy readouts (OS & PFS) expected during 2021.
		Phase Ib in NSCLC, HNSCC, urothelial cancer and melanoma (+ pembrolizumab) (NCT04452214, n=15)	Patient recruitment started in Oct 2020, headline data are expected to be reported in H221

Source: EvaluatePharma, company websites, clinicaltrials.gov. DSMB – drug safety monitoring board

Broadening CAN04's scope beyond NSCLC

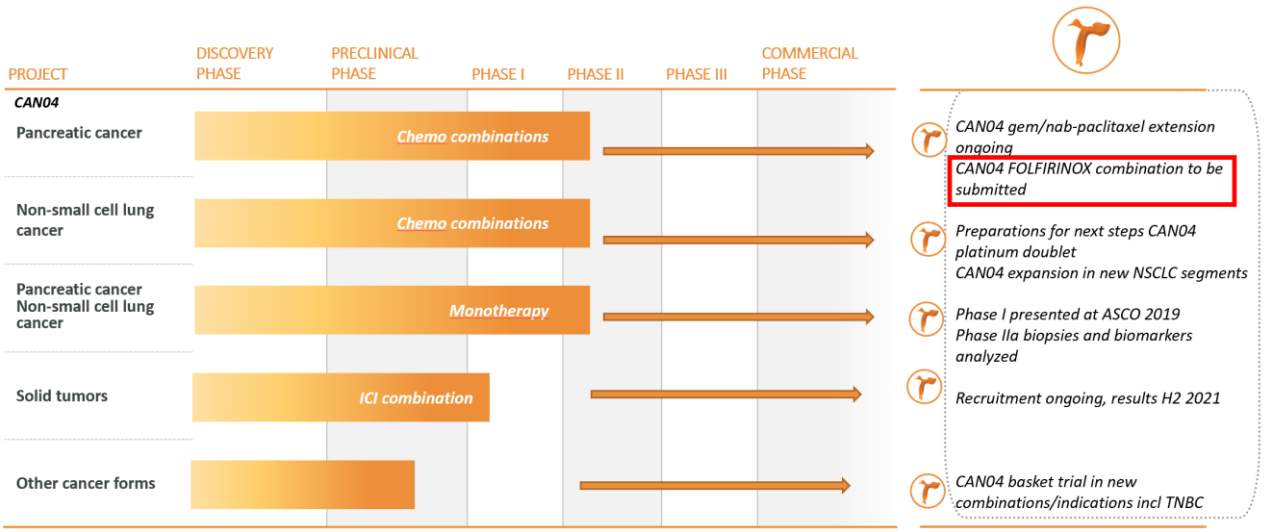
Currently, Cantargia is running a Phase IIa CANFOUR trial, with three arms: CAN04 in first-line NSCLC or metastatic pancreatic cancer (PDAC) and in combination with chemotherapy or monotherapy (Exhibit 2). Available interim data were presented in our last update report. The final analysis from the PDAC arm is expected **during H121** and will provide efficacy data including progression-free survival (PFS), duration of response (DoR) and some biomarker data. Cantargia also recently started enrolling PDAC patients into the extension phase of the CANFOUR study. Similarly, the NSCLC arm of the CANFOUR trial should also move into the next phase, as communicated before, but details are yet to be announced.

In March 2021, Cantargia announced it will initiate another Phase I/II trial (n=30) with CAN04 in combination with the FOLFIRINOX chemotherapy regimen as a first-line treatment for PDAC (highlighted in Exhibit 2). This is in addition to the PDAC arm in the same indication in the CANFOUR trial, but with a different combination (gemcitabine plus nab-paclitaxel chemotherapy). The two chemotherapies (FOLFIRINOX and gemcitabine/nab-paclitaxel) are standard of care and would cover most of the patients in this setting, so this new trial significantly expands the target patient population.

It is worth noting that recently Novartis also initiated a Phase Ib study in PDAC before receiving an orphan drug designation in pancreatic cancer from the FDA on 24 March 2021. These developments demonstrate a strong interest in this indication, in our view. The new trial will evaluate canakinumab in combination with nab-paclitaxel/gemcitabine (the same chemotherapy as in CAFOUR trial), but also spartalizumab, an anti-PD-1 antibody owned by Novartis. Cantargia has been exploring the idea of combining the IL-1 axis inhibition with checkpoint inhibitors for a while now and already has a US-based Phase Ib trial up and running. It investigates CAN04 in combination with pembrolizumab, with initial data **expected in H221**. These should provide an initial indication of CAN04 benefit across a range of solid tumours.

We also note that with proceeds from its December 2020 share issue, Cantargia has guided that it intends to start a basket trial investigating CAN04 with various chemotherapy regimens in a range of cancers, including triple-negative breast cancer (TNBC). So again, we expect Cantargia will deliver much more data for CAN04 beyond NSCLC.

Exhibit 2: R&D pipeline



Source: Cantargia

CAN10 expected to enter clinical development in early-2022

Cantargia's second drug candidate CAN10 is an antibody designed to block the signalling of the inflammatory cytokines (IL-1, IL-33 and IL-36) and is in preclinical development for inflammatory diseases, systemic sclerosis and myocarditis. In March, Cantargia reported that it successfully completed preclinical proof of concept studies in myocarditis for CAN10 and the IND-enabling safety studies are on track to finish **during H221**, which could enable progression into the clinic in **early-2022.** CAN10 will diversify the R&D pipeline with a second asset and in non-oncology indications.

Financials

During FY20, Cantargia reported an increased operating loss of SEK173.9m (FY19: SEK111.6m), driven primarily by the growing R&D costs of SEK158.4m (SEK97.5m in FY19) stemming from advancement of the Phase IIa CANFOUR study, initiation of the Phase Ib pembrolizumab combination study, higher spending on CAN04 production to support these trials and the maturing preclinical pipeline (CAN10 and CANxx). We anticipate a continued growth in R&D spend during 2021 and 2022 and have revised our forecasts. Our operating loss estimates for 2021 and 2022 increased to SEK276m and SEK297m from SEK138m and SEK139m, respectively.

The extensive revision of our estimates is underpinned by the fact that over 2020 Cantargia raised in total SEK974m. This will allow Cantargia to expand its clinical footprint for CAN04, including the additional Phase Ib trial for CAN04 in PDAC (FOLFINRINOX combo) and the expected CAN04 basket trial across new cancer indications. Likewise, progression of CAN10 into clinical development is expected early-2022, which will incrementally add cost. The balance sheet is robust and the reported cash position at end-2020 was SEK693m with short-term investments of SEK210m. This, according to the management, is sufficient for rapid advancement of the broader R&D programme over the next two years.

Valuation

Our updated valuation of Cantargia is marginally higher at SEK6.86bn or SEK68.5 per share, vs SEK5.93bn or SEK65.1/share previously. We have rolled our model forward, incorporated the December 2020 capital raise and increased the near-term R&D spend as described above. These changes had a slight net positive effect on the valuation. The capital raise was done at a share price close to the market price and to our per share valuation, therefore the dilutive effect to our current valuation per share was minimal.

Potential use of CAN04 in NSCLC contributes c 35% of our valuation and, while we acknowledge sentiment has been knocked and the share price declined significantly after the Novartis Phase III CANOPY-2 trial data, because of the differences described above we do not feel this currently necessitates a fundamental change to our assumptions.

Near-term catalysts include the readout from Novartis's Phase III CANOPY-1 trial (H221, first-line NSCLC) and results from Cantargia's Phase IIa CANFOUR trial (2021), either of which could re-instal confidence.

Exhibit 3: SOTP Cantargia valuation

Product	Launch	Peak sales ($m)	NPV (SEKm)	NPV/share (SEK)	Probability	rNPV (SEKm)	rNPV/share (SEK)
CAN04 – NSCLC	2026	3,100	8,495.1	84.8	25%	2,515.3	25.1
CAN04 – PDAC	2024	2,100	8,862.0	88.4	25%	3,440.6	34.3
Net cash* (end-2020)			903.3	9.0	100%	903.3	9.0
Valuation			**18,260.4**	**182.3**		**6.859.2**	**68.5**

Source: Edison Investment Research. Note: WACC = 12.5% for product valuations. *Including short-term investments.

Executive interview

Exhibit 4: Executive interview with Göran Forsberg, Cantargia's CEO

Source: Edison Investment Research

Exhibit 5: Financial summary

SEK'000s	2018	2019	2020	2021e	2022e
Year end 31 December	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS					
Revenue	0	0	0	0	0
Cost of Sales	0	0	0	0	0
Gross Profit	0	0	0	0	0
Research and development	(76,951)	(97,477)	(158,396)	(260,000)	(280,000)
EBITDA	(93,306)	(111,577)	(170,697)	(276,314)	(297,117)
Operating Profit (before amort. and except.)	(93,306)	(111,589)	(173,945)	(276,314)	(297,117)
Intangible Amortisation	0	0	0	0	0
Exceptionals	0	0	0	0	0
Other	0	0	0	0	0
Operating Profit	(93,306)	(111,589)	(173,945)	(276,314)	(297,117)
Net Interest	2,145	780	860	0	0
Profit Before Tax (norm)	(91,161)	(110,809)	(173,085)	(276,314)	(297,117)
Profit Before Tax (reported)	(91,161)	(110,809)	(173,085)	(276,314)	(297,117)
Tax	0	0	0	0	0
Profit After Tax (norm)	(91,161)	(110,809)	(173,085)	(276,314)	(297,117)
Profit After Tax (reported)	(91,161)	(110,809)	(173,085)	(276,314)	(297,117)
Average Number of Shares Outstanding (m)	66.2	71.1	89.4	100.2	100.2
EPS - normalised (SEK)	(1.38)	(1.56)	(1.94)	(2.76)	(2.97)
Dividend per share (SEK)	0.0	0.0	0.0	0.0	0.0
Gross Margin (%)	N/A	N/A	N/A	N/A	N/A
EBITDA Margin (%)	N/A	N/A	N/A	N/A	N/A
Operating Margin (before GW and except.) (%)	N/A	N/A	N/A	N/A	N/A
BALANCE SHEET					
Fixed Assets	2,957	6,868	12,622	12,622	12,622
Intangible Assets	0	0	7,360	7,360	7,360
Tangible Assets	0	6,868	5,262	5,262	5,262
Investments	2,957	0	0	0	0
Current Assets	168,486	159,189	912,892	644,783	355,871
Stocks	0	0	0	0	0
Debtors	0	0	0	0	0
Cash	76,528	39,870	693,354	425,245	136,333
Other*	91,958	119,319	219,538	219,538	219,538
Current Liabilities	(16,398)	(23,785)	(30,469)	(30,469)	(30,469)
Creditors	(16,398)	(23,785)	(30,469)	(30,469)	(30,469)
Short term borrowings	0	0	0	0	0
Long Term Liabilities	0	0	(3,111)	(3,111)	(3,111)
Long term borrowings	0	0	0	0	0
Other long term liabilities	0	0	(3,111)	(3,111)	(3,111)
Net Assets	155,045	142,272	891,934	623,825	334,913
CASH FLOW					
Operating Cash Flow	(105,165)	(111,852)	(156,887)	(268,970)	(289,773)
Net Interest	478	597	500	860	860
Tax	0	0	0	0	0
Capex	0	(6,880)	(890)	0	0
Acquisitions/disposals	0	0	0	0	0
Financing	0	98,037	917,545	0	0
Other	31,434	(16,560)	(106,784)	1	0
Dividends	0	0	0	0	0
Net Cash Flow	(73,253)	(36,658)	653,484	(268,109)	(288,913)
Opening net debt/(cash)	(149,781)	(76,528)	(39,870)	(693,354)	(425,245)
HP finance leases initiated	0	0	0	0	0
Other	0	0	0	0	0
Closing net debt/(cash)	(76,528)	(39,870)	(693,354)	(425,245)	(136,333)

Source: Cantargia accounts, Edison Investment Research. Note: *Mainly short-term investments.

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