EDISON

Cantargia

Company update

Useful insights from CANOPY-1 data

Pharma & biotech

Novartis presented full results from its CANOPY-1 trial with canakinumab (anti-IL1beta; Cantargia's CAN04 is an anti-IL1RAP with complete inhibition of IL-1) at the American Association for Cancer Research (AACR) Annual Meeting in April 2022. In our view one of the key findings was that patients with non-squamous non-small cell lung cancer (NSCLC) did better than those with squamous cancer types. This is beneficial for Cantargia, which already has a trial in non-squamous NSCLC underway. With regards to pancreatic cancer, the second lead indication, the company has now presented a plan for a registrational study. Multiple other catalysts are still due in the near term. Our valuation is SEK6.02bn or SEK60.1/share (from SEK68.9/share).

Year end	Revenue (SEKm)	PBT* (SEKm)	EPS* (SEK)	DPS (SEK)	P/E (x)	Yield (%)
12/20	0.0	(173.1)	(1.94)	0.0	N/A	N/A
12/21	0.0	(370.3)	(3.70)	0.0	N/A	N/A
12/22e	0.0	(368.5)	(3.68)	0.0	N/A	N/A
12/23e	0.0	(369.1)	(3.68)	0.0	N/A	N/A

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

Full CANOPY data provide insights for CAN04 strategy

Novartis had already reported that the CANOPY-1 trial had failed in October 2021, but the recently released subset analysis revealed several useful findings. In addition to differing outcomes depending on cancer histology, there were also some interesting data involving inflammatory markers. High sensitivity C reactive protein (hs-CRP) and interleukin-6 (IL-6) level reductions were more pronounced in those patients who received Novartis's canakinumab treatment. Those patients who had the largest reductions also had better outcomes. It appears that hs-CRP and IL-6 acted as prognostic factors, a finding that Cantargia can use in its trials.

Upcoming catalysts at ASCO

Following the R&D pipeline expansion, CAN04 is now being investigated in eight different cancers and different treatment lines and in a variety of combinations (Exhibit 2). This ensures plenty of catalysts to look forward to. The nearest significant event is the American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago on 3–7 June 2022. Cantargia will present three posters with a clinical data update from the lead Phase IIa CANFOUR trial (CAN04 plus chemotherapy in NSCLC and pancreatic cancer, which have been selected for discussion in a special session) and the first efficacy data from the Phase Ib CIRIFOUR trial (CAN04 plus pembrolizumab in solid tumours).

Valuation: SEK6.02bn or SEK60.1 per share

Our updated valuation of Cantargia is slightly lower at SEK6.02bn or SEK60.1 per share, versus SEK6.91bn or SEK68.9 per share previously (rolling our model forward was offset by a lower cash position). Cantargia's registrational study in pancreatic cancer will be longer than we had modelled, which led us to delay the assumed launch date and licensing deal. This was partially offset by an increased probability of success and rolling the model forward.

9 May 2022

Price	**SEK12.5**
Market cap	**SEK1.25bn**
Net cash and short-term investments (SEKm) at end-2021	559.4
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	(32.5)	(34.8)	(59.4)
Rel (local)	(24.4)	(24.0)	(53.8)
52-week high/low	SEK33.1	SEK12.5	

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 non-small cell lung cancer (NSCLC) and pancreatic cancer. The most advanced trial is in Phase II.

Next events

Updates from both Phase IIa CANFOUR trial arms (NSCLC and PDAC)	June 2022
Phase Ib CIRIFOUR first efficacy data	June 2022

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Edison profile page

Full Novartis Phase III CANOPY-1 results presented

As we have described several times before, canakinumab's development has a complicated history and the read-across to Cantargia's CAN04 is not straightforward. Canakinumab blocks only one of two cytokines that activate the IL-1 receptor, while Cantargia's CAN04 completely abrogates the IL-1 signalling pathway. In addition, CAN04's mechanism of action is not only inflammation modulation via IL1RAP, but also the antibody-dependent cellular cytotoxicity (ADCC), which directly causes cancer cell death. So, CANOPY studies provide valuable information of how to position CAN04, but do not invalidate the IL-1 axis theory in cancer, in our view.

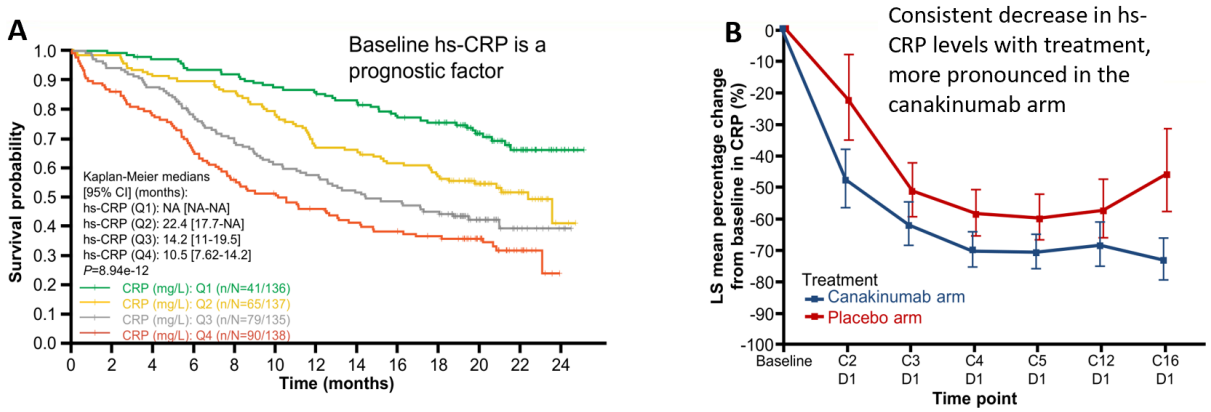
As a reminder, on 25 October 2021, Novartis reported that the CANOPY-1 trial did not meet primary co-endpoints of overall survival (OS) and progression-free survival (PFS). The trial investigated canakinumab plus standard of care checkpoint inhibitor (pembrolizumab) and chemotherapy (platinum doublet) in first-line NSCLC patients. However, back then Novartis pointed out that the data showed 'potentially clinically meaningful improvements' in both co-primary endpoints in pre-specified subgroups of patients based on the baseline inflammatory biomarker. This, it believed, justified the continuation of other CANOPY trials, which are enrolling patients with even earlier-stage disease.

The most recent development was Novartis's presentation of the full results from the CANOPY-1 trial at the AACR Annual Meeting in April 2022. The detailed results showed that the objective response rates were very similar in the canakinumab and placebo arms: 45.6% and 45.5%, respectively. The median PFS (co-primary endpoint) was 6.8 months for both treatment arms. The median OS (co-primary endpoint) was 20.8 months in the canakinumab arm and 20.2 months in the placebo arm.

The subset analysis revealed more interesting findings, which are relevant for Cantargia. In CANOPY-1 high sensitivity C reactive protein (hs-CRP) and interleukin-6 (IL-6) level reductions were more pronounced in those patients who received the canakinumab combination treatment (Exhibit 1B). Those patients who had the largest reductions also had better and clinically meaningful improvements in both PFS and OS (Exhibit 1A; hs-CRP ranges expressed as quartiles, Q). It appears that hs-CRP and IL-6 acted as prognostic factors, a finding that will be useful for Cantargia in its trials as well. Furthermore, subgroup analysis revealed that patients with non-squamous cancer did better than those with squamous cancer (Exhibit 1C).

The CRP test is the most common inflammatory biomarker to evaluate an active infection used in the clinic (the hsCRP test simply measures much smaller amounts of the same protein in seemingly healthy persons; one is used to estimate the risk of heart disease for example). Minimal signs of ongoing inflammation in the background could potentially be used as a biomarker to identify a more relevant subgroup of patients. This would make sense given the mechanism of action of canakinumab (anti-IL1β, which diminishes pro-inflammatory IL-1 signalling) or CAN04 (anti-IL1RAP, which abrogates signalling via IL-1).

Exhibit 1:Selected data from Novartis's CANOPY-1 trial



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OS subgroup analysis

		Favors canakinumab ← / → Favors placebo	HR (95% CI)	Canakinumab arm n/N (%)	Placebo arm n/N (%)
Overall			0.87 (0.70-1.10)	147/320 (45.9)	159/323 (49.2)
Age	<65 years		0.87 (0.63-1.18)	81/188 (43.1)	85/182 (46.7)
	≥65 years		0.95 (0.67-1.35)	66/132 (50.0)	74/141 (52.5)
Sex	Female		0.63 (0.39-1.01)	32/93 (34.4)	43/91 (47.3)
	Male		0.95 (0.73-1.24)	115/227 (50.7)	116/232 (50.0)
ECOG PS	0		0.95 (0.63-1.44)	46/127 (36.2)	47/121 (38.8)
	1		0.80 (0.61-1.06)	101/193 (52.3)	112/202 (55.4)
Smoking history	Former/current smoker		0.89 (0.69-1.14)	115/251 (45.8)	132/269 (49.1)
	Never smoked		0.96 (0.54-1.69)	32/69 (46.4)	27/54 (50.0)
Histology	Non-squamous		0.80 (0.61-1.04)	97/222 (43.7)	113/226 (50.0)
	Squamous		1.07 (0.71-1.60)	50/98 (51.0)	46/97 (47.4)
PD-L1	<1%		0.85 (0.62-1.16)	78/150 (52.0)	85/154 (55.2)
	1-49%		0.94 (0.55-1.60)	30/75 (40.0)	32/72 (44.4)
	≥50%		0.97 (0.61-1.54)	38/89 (42.7)	39/91 (42.9)
TMB	<10 mutations/megabase		0.84 (0.53-1.35)	39/66 (59.1)	46/68 (67.6)
	≥10 mutations/megabase		0.85 (0.38-1.90)	14/33 (42.4)	19/41 (46.3)

0.1 1 10

CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; OS, overall survival; PD-L1, programmed death-ligand 1; TMB, tumor mutational burden.

Source: Novartis

Cantargia's focus on non-squamous NSCLC

Cantargia's focus shifted to non-squamous NSCLC well before Novartis released its CANOPY-1 data. As we discussed in our last report, Cantargia presented the latest interim results from the NSCLC arm of the CANFOUR trial at the ESMO Congress in September 2021. It was not the first data update from this trial and the encouraging overall response rates (ORR) tracked those reported previously. The new and unexpected finding was that a subset of patients who had non-squamous NSCLC showed a more pronounced benefit compared to those with squamous histology. Based on this finding, Cantargia decided to focus on further development in non-squamous NSCLC, which is the largest subgroup of NSCLC and constitutes about 70–80% of all NSCLC cases. Cantargia initiated a new trial within the CANFOUR programme, which has started enrolling patients with non-squamous NSCLC for front-line treatment with CAN04 in combination with carboplatin/pemetrexed. In total, 40 new patients are planned to be recruited.

Other R&D developments

A detailed review of Cantargia's expanded R&D pipeline was presented in our last report. Since then, major developments include:

- Cantargia announced updated survival data from its CANFOUR trial with nadunolimab and chemotherapy in metastatic pancreatic cancer (n=36, of which 33 were evaluable). This is first-line treatment setting with patients receiving standard of care chemotherapy gemcitabine/nab-paclitaxel (around 50% of all pancreatic cancer patients receive it). Interim response data have been published on several occasions previously and compared very well with historical control data. The new update is in line with the previously published findings and strengthens the conviction in this indication, in our view, which is reassuring given Cantargia is currently preparing for a randomised and potentially pivotal trial in first-line pancreatic cancer. The next update from the pancreatic cancer arm of the CANFOUR study will be presented at ASCO in June 2022.
- Earlier this year, Cantargia initiated a collaboration with the Pancreatic Cancer Action Network (PanCAN), a US organisation. Nadunolimab will be included in PanCAN's ongoing Phase II/III clinical trial Precision Promise, which is a potentially registrational trial. The primary endpoint in this trial is OS. PanCAN plans to submit a pre-IND application to the FDA in H122 to include the nadunolimab treatment arm as an experimental arm in the Precision Promise trial, which also has other experimental arms. Each arm will enrol up to 175 patients. Nadunolimab will be combined with gemcitabine and nab-paclitaxel, or a standard of care chemotherapy regime alone. The study should start in late 2022 and the results for the nadunolimab arm are expected to be available in 2027 or earlier. Cantargia will fund the nadunolimab arm and will be responsible for supplying the drug, while PanCAN will fund the reminder of the trial, which makes it a cost-efficient strategy for Cantargia.

Exhibit 2: R&D pipeline

Study	Disease	Combination therapy	Estimated enrollment	Status	NCT number
CANFOUR	NSCLC	Cisplatin/gemcitabine	33	Recruitment completed	NCT03267316
	Non-squamous NSCLC	Carboplatin/pemetrexed	40	Recruiting	
	PDAC	Gemcitabine/nab-paclitaxel	76	Recruitment completed	
CIRIFOUR	NSCLC, bladder cancer, HNSCC, melanoma	Pembro	15	Recruitment completed	NCT04452214
	Non-squamous NSCLC	Pembro/carboplatin/ pemetrexed	24	Recruitment start in Q1 '22	
CAPAFOUR	PDAC	FOLFIRINOX	30	Recruiting	NCT04990037
CESTAFOUR	NSCLC	Docetaxel	55	Recruiting	NCT05116891
	Biliary tract cancer	Cisplatin/gemcitabine	55		
	Colon cancer	FOLFOX	55		
TRIFOUR	TNBC	Carboplatin/gemcitabine	113	Recruiting	NCT05181462
Precision Promise℠	PDAC	Gemcitabine/nab-paclitaxel	175	Pre-IND submission in Q2 '22	NCT04229004

NSCLC – non-small cell lung cancer; PDAC – pancreatic cancer; HNSCC – head and neck cancer; TNBC – triple negative breast cancer; Pembro – pembrolizumab

Source: Cantargia

Financials and valuation

In 2021, Cantargia reported an increased operating loss of SEK370m (FY20: SEK174m), driven by the growing R&D costs. We had already anticipated growing R&D costs. Following the latest results, we have extended our 2022 operating loss estimate somewhat, to SEK369m from SEK349m previously, and keep the spending similar in 2023. Existing cash and short-term investments (SEK559m at end-2021) are still sufficient well into 2023.

Our updated valuation of Cantargia is slightly lower at SEK6.02bn or SEK60.1 per share, versus SEK6.91bn or SEK68.9 per share previously, as rolling our model forward was offset by a lower cash position. This was a result of several changes to our model. We have delayed the assumed launch of CAN04 in pancreatic cancer to 2027 from 2024 now that Cantargia has communicated its registrational trial plans.

In our base case valuation we assume a licensing deal for both indications, which we delay now to 2024 from 2023. A full out-licensing deal, as explained in our initiation report, is a theoretical component of our model. In reality, there could be various arrangements from out-licensing to co-development or Cantargia could complete the development of CAN04 in pancreatic cancer on its own. We have also increased the success probability in the pancreatic cancer project to 40% from 25%, which is in line with historical success probabilities in Phase III, and we have rolled the model forward, which has partially offset the delays.

Exhibit 3: Sum-of-the-parts Cantargia valuation

Product	Launch	Peak sales ($m)	NPV (SEKm)	NPV/share (SEK)	Probability	rNPV (SEKm)	rNPV/share (SEK)
CAN04 – NSCLC	2026	3,100	9,240.2	92.2	25.0%	2,620.0	26.1
CAN04 – PDAC	2027	2,124	6,504.6	64.9	40.0%	2,845.1	28.4
Net cash* (last reported)			559.4	5.6	100%	559.4	5.6
Valuation			**16,304.2**	**162.7**		**6,024.5**	**60.1**

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

Exhibit 4: Financial summary

SEK'000s	2019	2020	2021	2022e	2023e
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	(97,477)	(158,396)	(352,709)	(350,000)	(350,000)
EBITDA	(111,577)	(170,697)	(366,821)	(365,101)	(365,657)
Operating Profit (before amort. and except.)	(111,589)	(173,945)	(370,267)	(368,547)	(369,103)
Intangible Amortisation	0	0	0	0	0
Exceptionals	0	0	0	0	0
Other	0	0	0	0	0
Operating Profit	(111,589)	(173,945)	(370,267)	(368,547)	(369,103)
Net Interest	780	860	0	0	0
Profit Before Tax (norm)	(110,809)	(173,085)	(370,267)	(368,547)	(369,103)
Profit Before Tax (reported)	(110,809)	(173,085)	(370,267)	(368,547)	(369,103)
Tax	0	0	0	0	0
Profit After Tax (norm)	(110,809)	(173,085)	(370,267)	(368,547)	(369,103)
Profit After Tax (reported)	(110,809)	(173,085)	(370,267)	(368,547)	(369,103)
Average Number of Shares Outstanding (m)	71.1	89.4	100.2	100.2	100.2
EPS - normalised (SEK)	(1.56)	(1.94)	(3.70)	(3.68)	(3.68)
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	6,868	12,622	9,556	9,556	9,556
Intangible Assets	0	7,360	6,459	6,459	6,459
Tangible Assets	6,868	5,262	3,097	3,097	3,097
Investments	0	0	0	0	0
Current Assets	159,189	912,892	590,687	230,679	31,301
Stocks	0	0	0	0	0
Debtors	0	0	0	0	0
Cash	39,870	693,354	247,322	199,378	0
Other*	119,319	219,538	343,365	31,301	31,301
Current Liabilities	(23,785)	(30,469)	(66,607)	(66,607)	(66,607)
Creditors	(23,785)	(30,469)	(66,607)	(66,607)	(66,607)
Short term borrowings	0	0	0	0	0
Long Term Liabilities	0	(3,111)	(892)	(892)	(162,076)
Long term borrowings	0	0	0	0	(161,184)
Other long term liabilities	0	(3,111)	(892)	(892)	(892)
Net Assets	142,272	891,934	532,744	172,736	(187,826)
CASH FLOW					
Operating Cash Flow	(111,852)	(156,887)	(347,370)	(360,006)	(360,562)
Net Interest	597	500	924	0	0
Tax	0	0	0	0	0
Capex	(6,880)	(890)	0	0	0
Acquisitions/disposals	0	0	0	0	0
Financing	98,037	917,545	0	(320)	(317)
Other (incl. change in short term investments)	(16,560)	(106,784)	(99,586)	312,381	317
Dividends	0	0	0	0	0
Net Cash Flow	(36,658)	653,484	(446,032)	(47,944)	(360,562)
Opening net debt/(cash)	(76,528)	(39,870)	(693,354)	(247,322)	(199,378)
HP finance leases initiated	0	0	0	0	0
Other	0	0	0	0	0
Closing net debt/(cash)	(39,870)	(693,354)	(247,322)	(199,378)	161,184

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

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