EDISON

Targovax

Company update

FOLFIRINOX sets bar in pancreatic cancer high

Pharma & biotech

On 12 June, Targovax announced a strategic decision to move away from developing TG01, a neoantigen cancer vaccine for resected pancreatic cancer after new data with FOLFIRINOX set the bar for overall survival too high. With median overall survival of resected pancreatic cancer patients approaching five years, such a long clinical trial is beyond the capabilities of a relatively small biotech company, according to Targovax. We have removed pancreatic cancer from our valuation, which is now NOK1.31bn or NOK24.9/share (vs NOK33.8/share previously).

Year end	Revenue (NOKm)	PBT* (NOKm)	EPS* (NOK)	DPS (NOK)	P/E (x)	Yield (%)
12/16	0.0	(122.7)	(3.55)	0.0	N/A	N/A
12/17	0.0	(122.3)	(2.58)	0.0	N/A	N/A
12/18e	0.0	(147.5)	(2.80)	0.0	N/A	N/A
12/19e	0.0	(170.3)	(3.23)	0.0	N/A	N/A

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

New FOLFIRINOX data at ASCO

The FOLFIRINOX regimen has been shown to be effective before, but has also demonstrated increased toxicity. Adjuvant chemotherapy with gemcitabine (and with capecitabine more recently) was considered to be standard of care. The new Phase III data presented at ASCO suggest an almost two-year improvement in overall survival in the FOLFIRINOX arm compared to gemcitabine. Even though more patients receiving FOLFIRINOX experienced side effects, severe side effects were prevalent in both groups. During the Q&A call Targovax management shared its impression from the interactions with various stakeholders at the ASCO meeting last week that FOLFIRINOX is likely to become standard of care in this indication. Given that Targovax recently presented positive data with TG01 from the second pancreatic cancer cohort in the Phase I/II trial, we believe the decision was not an easy one to make. However, the company was about to start preparation for the next Phase II, hence the "go/no-go" decision had to be made swiftly.

Focus on ONCOS; detailed R&D update to follow

Other trials are running as planned and in the autumn Targovax will present an update on its R&D plans and how it will use the freed-up resources, which will warrant further revision of our valuation. Targovax emphasised increased focus on the ONCOS platform, for which recent industry news provided a tailwind as two large pharma companies, Merck & Co and Janssen (J&J) acquired oncolytic virus companies with assets in the early to mid-stages (described below).

Valuation: Revised to NOK1.31bn or NOK24.9/share

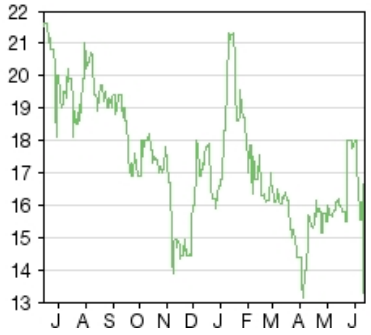
In line with the announcement, we have removed from our valuation the pancreatic cancer indication, which contributed 29% to our last published rNPV. This compares to a c 20% share price decline on the news. We believe the less pronounced market reaction is mainly due to the fact that the news reflects a strategic refocus away from pancreatic cancer rather than the failure of technology. We do not currently reflect the freed-up cash resources in our valuation. When Targovax presents more detail in the autumn, we will revise our SOTP model.

13 June 2018

Price	**NOK13.26**
Market cap	**NOK697m**

Net cash (NOKm) at end-Q118	180.5
Shares in issue	52.6m
Free float	55%
Code	TRVX
Primary exchange	Oslo Stock Exchange
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	(17.6)	(18.5)	(37.2)
Rel (local)	(18.9)	(24.3)	(49.1)
52-week high/low	NOK21.6	NOK13.1	

Business description

Targovax is an immuno-oncology company headquartered in Oslo, Norway, with two technology platforms that are being developed in a number of oncological indications. ONCOS-102 is an oncolytic virus technology. TG is a therapeutic cancer vaccine platform comprising peptides mimicking the most common RAS oncogenic mutations.

Next events

Interim data from Phase I trial with ONCOS-102 in melanoma	H218

Analysts

Jonas Peciulis +44 (0)20 3077 5728

Alice Nettleton +44 (0)20 3681 2527

healthcare@edisongroup.com

Edison profile page

FOLFORINOX data good news for patients

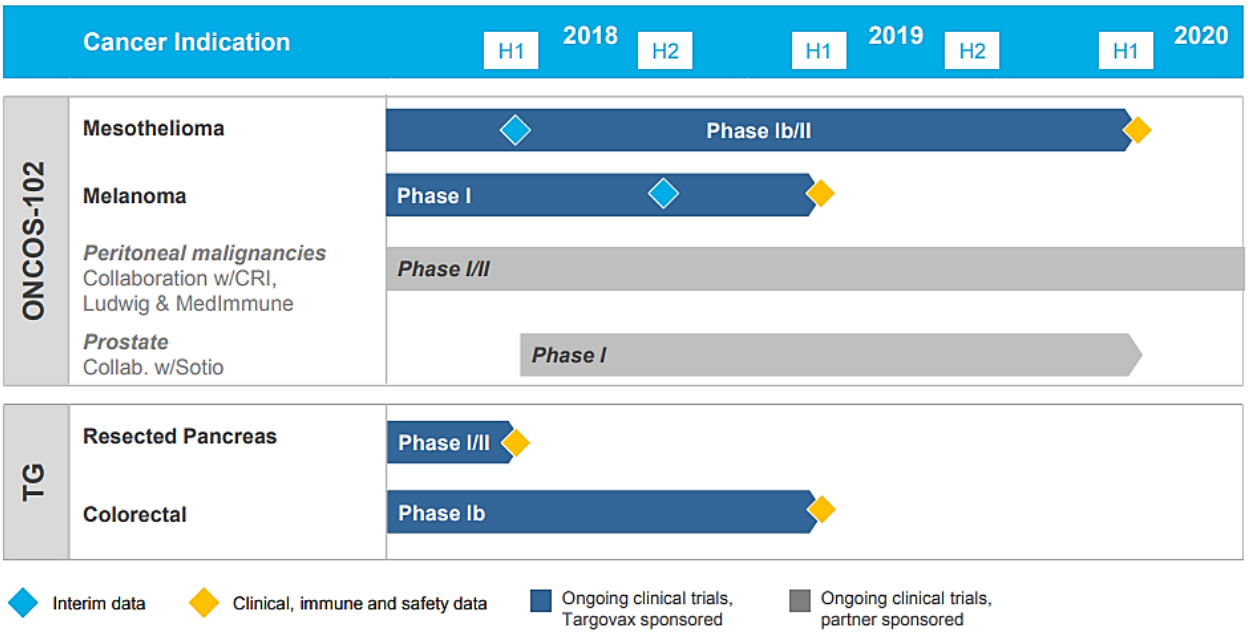
The FOLFIRINOX regimen (combination of generics fluorouracil, leucovorin, irinotecan and oxaliplatin) has been used in pancreatic cancer since 2010 and has been shown to be effective, but has also demonstrated increased toxicity. The Phase III trial (PRODIGE 24/CCTG PA.6), backed by a French and Canadian consortium, enrolled 493 pancreatic cancer patients with resected pancreatic cancer who were randomized to receive either an adjuvant (post-surgery) modified version of the FOLFORINOX regimen or gemcitabine. The median overall survival was 54.4 months with mFOLFIRINOX and 35.0 months with gemcitabine. The patients in the mFOLFIRINOX arm were also disease-free for about nine months longer than those taking gemcitabine (21.6 months with mFOLFIRINOX versus 12.8 months with gemcitabine). Patients treated with mFOLFIRINOX had more side effects such as diarrhoea, nausea, vomiting and fatigue, but these were manageable. Severe side effects were prevalent in both groups (grade 3-4 adverse events were reported in 51.1% vs 75.5% in gemcitabine vs mFOLFIRINOX arms). This was the first time such a large benefit was shown in the FOLFORINOX regimen compared to gemcitabine. So far, gemcitabine (lately with capecitabine) has been the standard adjuvant therapy.

Recent Phase I/II results with TG01 did not disappoint

The news came on the heels of positive data released on 24 May 2018, when Targovax announced that the overall two-year survival of pancreatic cancer patients in the second cohort of its Phase I/II trial with TG01 was sustained or even increased compared to the first cohort. The Phase I/II trial with TG01+gemcitabine was open label and included 32 pancreatic cancer patients, who were divided into two cohorts. The positive data from the first cohort (n=19) were presented at ASCO a year ago. The **overall survival rate** of these patients at two years was 68.4% (13/19), which compared favourably with historical survival rates of 30-53% of resected pancreatic cancer patients treated with gemcitabine alone. Three **serious adverse reactions** were linked to TG01 – two anaphylactic reactions and one hypersensitivity reaction, which resolved within 1-2 hours. These reactions were seen when TG01 was administered concomitantly with chemotherapy. While they were manageable, Targovax decided to initiate a modified second cohort where TG01 was given less frequently and not during chemotherapy. The data from this second cohort (n=13) was reported on 24 May 2018. The **two-year overall survival rate** in the second cohort was 77% (10/13 patients), higher than in the first cohort in 2017 (and the historical norm). Targovax also indicated that the modified dosing regimen used in the second cohort was **well tolerated**.

In summary, the second cohort received a less intensive TG01 administration schedule and no serious allergic reactions were reported. Therefore, Targovax decision to move away from the pancreatic cancer appears to be entirely related to increased evidence hurdle and not lack of trust in TG platform, in our view.

Exhibit 1: Targovax R&D pipeline



Source: Targovax

Increased focus on ONCOS platform

All remaining trials are continuing and while Targovax plans to provide more details about changes in R&D later this year, it noted that it plans to increase focus on its oncolytic virus platform with the mesothelioma indication currently in the lead. Mesothelioma is another tough indication, but unlike pancreatic cancer a five-year survival rate is still very low, only around 8%.

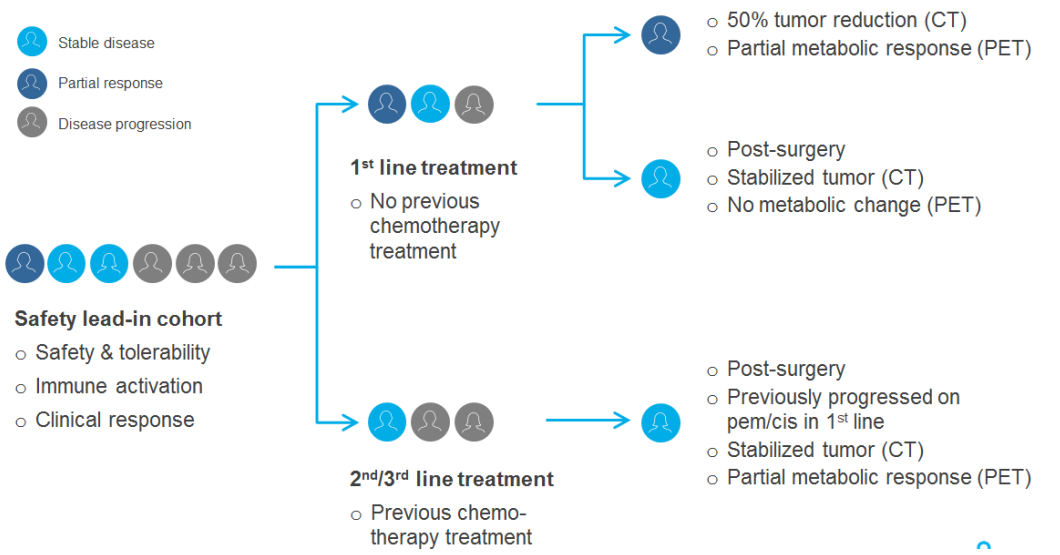
As described in our last update note, Targovax saw positive results from the safety lead-in of its ONCOS-102 open-label Phase I/II trial in patients with advanced malignant pleural mesothelioma (n=6). Based on the recommendation from the independent Data and Safety Monitoring Board, the company is moving to the randomised part of the trial and recruiting patients.

The first interim data readout has now been reached, which is an assessment of clinical response rate in the six patients from the safety lead-in cohort (n=6) that have continued to receive treatment (total of six months). As a reminder, these patients received ONCOS-102 in combination with standard-of-care pemetrexed/cisplatin, either as a 1L treatment (n=3) or 2L/3L (n=3). The findings include:

- Clinical activity (measured as disease control rate, using RECIST 1.1 guidelines) were seen in 50% (3/6) of these patients.
- Of the patients in the 1L treatment group, 2/3 patients achieved a clinical response, where one achieved partial response (tumour has shrunk) and one patient achieved stable disease (tumour growth has stopped). The third patient did not respond.
- Of the patients in the 2L/3L treatment group, 1/3 patients achieved stable disease. 2/3 patients did not respond.

In the experimental arm of the randomised part of the study, the patients will receive ONCOS-102 in combination with pemetrexed/cisplatin (n=20), and will be compared against a control arm where patients receive only pemetrexed/cisplatin standard of care (n=10). Final efficacy data will be available in 2020.

Exhibit 2: Efficacy signals seen in the safety cohort of the ONCOS-102 mesothelioma trial



Source: Targovax Q118 company presentation

Given the early stage of the data, no definitive conclusions can be made. However, we note that in general, mesothelioma is a very difficult condition to treat. It is a rare cancer with c 3,000 cases diagnosed in the US annually. Incidence of mesothelioma ranges from about seven to 40 per 1,000,000 in industrialised Western countries, depending on the amount of asbestos exposure in the past, which is a major risk factor.[1] Therefore, the main focus in managing mesothelioma is on prevention measures, as it is otherwise a hard-to-treat cancer with a five-year survival rate of only around 8%.[2] Surgery, radiation therapy and chemotherapy with cisplatin and pemetrexed are the main treatment options, as there are no novel drugs proven to be efficacious.

Mesothelioma is a rare cancer of the mesothelium, a sheet that covers most internal organs. Most often the location of mesothelioma is pleural mesothelium, a double layer sheet that covers the lungs and the inside of the pleural cavity, forming a pleural space. Breathing difficulty and pain are the hallmark symptoms of mesothelioma, with death occurring due to infection or respiratory failure.

Pemetrexed (Alimta, Eli Lilly; folate antimetabolite) was approved by the FDA for the treatment of malignant pleural mesothelioma in 2004, with patents starting to expire in 2016–17. In 2016, Alimta brought in $253m in sales in the mesothelioma indication (it is also approved for non-small cell lung cancer). There is a clear unmet need in this indication, given the aggressive nature of the cancer and lack of innovative treatment options.

M&A activity picks up in oncolytic virus space

There has been some recent deal activity in the field of oncolytic viruses involving large pharmaceutical players Merck and Janssen (subsidiary of Johnson & Johnson). In May 2018, Janssen agreed to pay $140m upfront to acquire private company BeneVir Biopharm, which is developing oncolytic viruses to treat solid tumours based on its T-Stealth platform, currently in pre-clinical stage. In February 2018, Merck & Co announced its acquisition of Viralytics with the lead product Cavatac, which previously we described as a peer to the ONCOS platform. Merck & Co

1 B W Robinson, R A Lake. Advances in malignant mesothelioma. *The New England Journal of Medicine. 353 (15): 1591–603, October 2005.*

2 Age-Adjusted SEER Incidence and U.S. Death Rates and 5-Year Relative Survival By Primary Cancer Site, Sex and Time Period. NCI. *Archive originally published on 6 September 2015. Accessed on 27 September 2016.*

agreed to pay A$502m, which was in line with our valuation of Viralytics of A$469m (published in December 2017) + A$29.6m placement by Viralytics (in January 2018). This represented a 178% premium to Viralytics' prior-day closing share price. In our view, these recent deals confirm interest in the technology field, and in the application to solid tumour therapy. Details of these deals, together with other deals we have identified, are summarised below:

Exhibit 3: Recent oncolytic virus deals

Date	Licensor/target	Licensee/acquirer	Deal type	Product	Stage	Upfront, $m	Deal value (excl. upfront), $m
02/05/2018	Janssen	BeneVir BioPharm	Company acquisition	T-Stealthoncolytic virus platform	Pre-clinical	140	
21/02/2018	Viralytics	Merck	Company acquisition	Cavatak	Phase Ib	-	394
28/09/2016	ViraTherapeutics	Boehringer Ingelheim	Licensing deal	VSV-GP	Pre-clinical		235
20/12/2016	PsiOxus	Bristol-Myers Squibb	Licensing deal	NG-348	Pre-clinical	50	886
07/09/2010	Jennerex Biotherapeutics	Transgene	Licensing deal	Pexa-Vec	Phase II		116

Source: EvaluatePharma, company press releases, Edison Investment Research

Q118 results and valuation update

Following the removal of the pancreatic cancer indication, our updated valuation is NOK1.31bn or NOK24.9/share compared to NOK1.78bn or NOK33.8/share previously. Our valuation is based on a risk-adjusted NPV analysis using a 12.5% discount rate, including NOK180.5m net cash at end-Q118 (cash of NOK229m, long-term debt of NOK48.8m in Finnish government grants – repayment needed only if the products are sold or launched). The assumptions relating to the remaining projects in our rNPV model are unchanged. An upcoming near-term catalyst is the interim data from the ONCOS-102 Phase I trial in melanoma (Exhibit 1) and an update on R&D plans, both in H218.

Exhibit 4: Sum-of-the-parts Targovax valuation

Product	Launch	Peak sales ($m)	Unrisked NPV (NOKm)	Unrisked NPV/share (NOK)	Probability (%)	rNPV (NOKm)	rNPV/share (NOK)
ONCOS-102 - Advanced melanoma	2025	604	2,178.7	41.4	10%	386.0	7.3
ONCOS-102 - Mesothelioma	2026	434	1,732.3	32.9	10%	293.9	5.6
TG02 - Colorectal cancer	2026	1,744	3,473.8	66.0	10%	451.9	8.6
Net cash at end-Q118			180.5	3.4	100%	180.5	3.4
Valuation			**7,565.2**	**143.8**		**1,312.3**	**24.9**

Source: Edison Investment Research. Note: WACC = 12.5% for product valuations.

With its Q118 results, Targovax reported immaterial revenues, while external R&D expenses were NOK11.2m, compared with NOK8.8m in Q117 and largely in line with our expectations. As of end-Q118, Targovax's cash position was NOK229m, compared with NOK262m in Q417. According to our model, cash reach should extend well into 2019, but this will be subject to revision when Targovax presents an update on its R&D strategy in H218. Given the removal of the pancreatic cancer indication, there is a downside risk to our R&D spend estimates, which we will review in due course.

Exhibit 5: Financial summary

NOK000s	2016	2017	2018e	2019e
December	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS				
Revenue	37	37	0	0
Cost of Sales	0	0	0	0
Gross Profit	37	37	0	0
Research and development	(45,001)	(45,571)	(72,948)	(91,368)
EBITDA	(119,226)	(119,630)	(149,276)	(169,994)
Operating profit (before amort. and except.)	(119,510)	(119,926)	(149,572)	(170,290)
Intangible Amortisation	0	0	0	0
Exceptionals	0	0	0	0
Other	0	0	0	0
Operating Profit	(119,510)	(119,926)	(149,572)	(170,290)
Net Interest	(3,203)	(2,347)	2,060	0
Profit Before Tax (norm)	(122,713)	(122,273)	(147,512)	(170,290)
Profit Before Tax (reported)	(122,713)	(122,273)	(147,512)	(170,290)
Tax	260	328	0	0
Profit After Tax (norm)	(122,453)	(121,945)	(147,512)	(170,290)
Profit After Tax (reported)	(122,453)	(121,945)	(147,512)	(170,290)
Average Number of Shares Outstanding (m)	34.5	47.3	52.7	52.8
EPS - normalised (ore)	(354.65)	(258.06)	(280.09)	(322.73)
EPS - normalised fully diluted (ore)	(354.65)	(258.06)	(280.09)	(322.73)
EPS - reported (NOK)	(3.55)	(2.58)	(2.80)	(3.23)
Dividend per share (ore)	0.0	0.0	0.0	0.0
Gross Margin (%)	100.0	100.0	N/A	N/A
EBITDA Margin (%)	N/A	N/A	N/A	N/A
Operating Margin (before GW and except.) (%)	N/A	N/A	N/A	N/A
BALANCE SHEET				
Fixed Assets	339,512	367,415	367,203	366,966
Intangible Assets	338,213	366,250	366,250	366,250
Tangible Assets	1,299	1,165	953	716
Investments	0	0	0	0
Current Assets	185,832	276,193	140,115	14,620
Stocks	0	0	0	0
Debtors	0	0	0	0
Cash	171,629	261,573	125,495	0
Other	14,203	14,620	14,620	14,620
Current Liabilities	(29,184)	(28,295)	(27,296)	(28,883)
Creditors	(29,184)	(28,295)	(27,296)	(28,883)
Short term borrowings	0	0	0	0
Long Term Liabilities	(94,992)	(108,156)	(108,156)	(138,906)
Long term borrowings	(39,714)	(48,806)	(48,806)	(79,556)
Other long term liabilities	(55,278)	(59,350)	(59,350)	(59,350)
Net Assets	401,168	507,157	371,866	213,796
CASH FLOW				
Operating Cash Flow	(112,892)	(111,093)	(138,055)	(156,186)
Net Interest	3,203	2,347	2,060	0
Tax	0	0	0	0
Capex	(37)	(56)	(84)	(59)
Acquisitions/disposals	0	0	0	0
Financing	114,593	194,407	0	0
Other	(8,738)	(4,753)	1	0
Dividends	0	0	0	0
Net Cash Flow	(3,871)	80,852	(136,078)	(156,245)
Opening net debt/(cash)	(135,786)	(131,915)	(212,767)	(76,689)
HP finance leases initiated	0	0	0	0
Other	(0)	0	0	0
Closing net debt/(cash)	(131,915)	(212,767)	(76,689)	79,556

Source: Targovax accounts, Edison Investment Research

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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
295 Madison Avenue, 18th Floor
10017, New York
US

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