EDISON

Ultimovacs

Clinical results preview

NIPU and INITIUM readouts incoming for UV1

Pharma and biotech

Ultimovacs is gearing up for top-line readouts from two of its five ongoing Phase II studies, marking potential major clinical milestones for its cancer vaccine candidate UV1 and, in our view, significant catalysts for investor attention. Results from the NIPU and INITIUM trials in second-line malignant pleural mesothelioma (MPM) and first-line unresectable metastatic melanoma are expected in Q223 and H223, respectively. Readouts from the INITIUM trial had initially been expected in H123; however, this has been pushed back to H223 due to patients in the study taking longer than expected to experience disease progression. In our view, positive results from NIPU and INITIUM would represent the most compelling evidence to date of UV1's clinical utility in treating solid tumours. We have rolled our model forward and updated our FX assumptions and value Ultimovacs at NOK8.0bn or NOK234/share (previously NOK7.4bn or NOK216/share). We expect to revise our valuation once the NIPU and INITIUM results are released.

Year end	Revenue (NOKm)	PBT* (NOKm)	EPS** (NOK)	DPS (NOK)	P/E (x)	Yield (%)
12/21	0.0	(164.7)	(5.09)	0.0	N/A	N/A
12/22	0.0	(167.8)	(4.89)	0.0	N/A	N/A
12/23e	0.0	(217.1)	(6.31)	0.0	N/A	N/A
12/24e	0.0	(279.3)	(8.12)	0.0	N/A	N/A

Note: *PBT is reported. **EPS is fully diluted.

The major catalysts of FY23 approach

In our view, the upcoming readouts from the NIPU and INITIUM studies represent the most significant catalysts for investor attention, to date, for UV1 and Ultimovacs. Positive results from either study could set UV1 up to be Phase III-ready within the assessed indication and may provide a material value uplift for the asset. Additionally, positive data are likely to create a halo effect across the company's pipeline where UV1 is also being investigated in the Phase II DOVACC (ovarian), LUNGVAC (non-small-cell lung) and FOCUS (head and neck) studies.

AACR puts melanoma vaccines firmly in the spotlight

Previously, we discussed the positive results Merck and Moderna reported from their Phase II study for their personalised mRNA cancer vaccine (mRNA-4157/V940) in advanced melanoma and how the results have helped enhance the clinical reputation of cancer vaccines. However, the study has only recently received widespread media attention following detailed presentation of the results at the American Association for Cancer Research (AACR) meeting. We believe UV1 has potential advantages over personalised therapies that include shorter production lead times and potentially wider access to patients.

Valuation: NOK8.0bn or NOK234/share

We value Ultimovacs at NOK802m or NOK234/share. We have rolled our model forward and updated our historic six-month average FX assumption to NOK10.18/$, which had a c 6% upside effect on our rNPV. We note that results of the upcoming NIPU and INITIUM studies are likely to have a material impact on our valuation and we will look to revise this after the readouts.

26 April 2023

Price	**NOK136**
Market cap	**NOK4678m**
	NOK10.59/US$
Net cash (NOKm) at end-December 2022 (excluding leases)	425.3
Shares in issue	34.4m
Free float	56%
Code	ULTI
Primary exchange	Oslo Stock Exchange
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	23.2	25.7	72.2
Rel (local)	16.8	23.9	80.7
52-week high/low	NOK136	NOK60	

Business description

Ultimovacs is developing novel immunotherapies against cancer. Its lead product candidate, UV1, is a peptide-based vaccine against the universal cancer antigen telomerase (hTERT), which is expressed in c 85% of all cancer types. UV1 therefore has a broad potential in a variety of different settings and combinations.

Next events

Phase II NIPU top-line data	Q223
Phase II INITIUM top-line data	H223
Phase I TENDU initial data	H223

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NIPU and INITIUM leading the UV1 clinical charge

The upcoming trial readouts expected from the NIPU and INITIUM studies, in our view, represent the most significant potential catalysts for investor attention in FY23 for Ultimovacs. We expect NIPU to be the first study to report top-line data in Q223 followed by INITIUM in H223. Management had previously communicated that it expected the results from INITIUM in H123; however, this has been delayed slightly due to patients taking longer than expected to experience disease progression (cancer progression must be verified in 70 patients). While this is a positive for patients enrolled in the study as the trial is blinded, we cannot ascertain, at this time, whether the extension in disease progression is due to the influence of UV1. Positive results from both studies would be the most compelling clinical evidence, to date, for the company's universal cancer vaccine candidate, UV1. As a reminder, UV1 is Ultimovacs' lead pipeline asset, a universal, peptide-based, cancer vaccine targeting antigens associated with the human telomerase reverse transcriptase (hTERT), a protein estimated to be overexpressed in up to 90% of human cancers but not in healthy tissues. The company's clinical strategy aims to leverage combinational synergies between cancer vaccines and ICIs, that is, UV1's ability to prime the immune system (stimulate a T-cell response) to specifically target cancer cells and the ability of ICIs to make cancer cells vulnerable to the stimulated T cells.

The primary endpoints for both NIPU and INITIUM is disease progression-free survival (PFS), the time between treatment initiation and metastatic tumour progression or death from any cause. The key secondary endpoints from the study include overall survival (OS), objective response rate (ORR), duration of response and safety.

The randomised, open-label Phase II NIPU (n=118) trial in MPM is split into two arms with 59 patients in each. In the experimental arm, the patients are treated with the same combination as INITIUM (UV1 plus ipilimumab plus nivolumab), while patients in the second arm are to receive ipilimumab plus nivolumab only. The NIPU trial is investigating the UV1 combination in second-line MPM following disease progression after first-line platinum-doublet chemotherapy. With no treatments specifically approved in second-line MPM and limited disease control provided by existing therapies, we believe only moderate improvements in mPFS of at least 20% (c 1–2 months) from the UV1 arm of the NIPU study would be required to be of clinical significance compared to previously reported mPFS data for ipilimumab plus nivolumab (mPFS: 5.6 months).

The Phase II INITIUM trial (n=156) in metastatic malignant melanoma, fully funded by Ultimovacs, is an open-label, randomised and statistically powered study. The trial is split into two arms with 78 patients receiving first-line treatment with nivolumab (anti-PD-1 ICI) and ipilimumab (anti-CTLA-4 ICI), and the other 78 patients receiving a combination of nivolumab, ipilimumab and UV1 plus sargramostim as a UV1 vaccine adjuvant (helps create a stronger immune response). While there are no standardised or regulatory set factors that define a clinically meaningful result from oncology studies, we note that the average improvement in median PFS (mPFS) for FDA-approved drugs is 4.6 months versus standard of care (SoC). In our view, with UV1 being at the Phase II stage of clinical studies in INITIUM, an improvement in mPFS by at least 30% (c 3–4 months), compared to ipilimumab plus nivolumab (mPFS: 11.5 months in ICI-naïve patients, those who have not have undergone previous treatment with ICIs), may potentially be interpreted as a clinically meaningful improvement on the ipilimumab/nivolumab combination. Although ipilimumab/nivolumab is indicated as a first-line therapy in advanced melanoma, we note it directly competes with pembrolizumab monotherapy within this treatment space, which has previously reported mPFS of 16.9 months in ICI-naïve patients. UV1 may therefore need to demonstrate improvements in mPFS by up to 17 months to gain a clinically competitive advantage in the market over pembrolizumab.

Mesothelioma: Rare cancer with cases on the rise

Mesothelioma is a highly aggressive, rare cancer that forms in the mesothelium, a thin layer of tissue that covers most internal organs in the body. It is estimated that in the United States, c 3,000 people will be diagnosed every year with the condition. The primary cause for the development of mesothelioma is through asbestos exposure, a product once widely used worldwide before its carcinogenic properties were fully understood. However, despite asbestos use now being widely banned, its latency period (time between exposure and diagnosis) is often greater than 30 years, an effect that has resulted in mesothelioma cases almost doubling between 1990 and 2019. Pleural mesothelioma specifically affects tissues lining the lungs and accounts for c 75% of mesothelioma cases with c 80–90% of these diagnosed as MPM. Today, MPM continues to carry a poor prognosis with a median OS of 9–12 months and five-year OS of c 10% and there remains a significant need for the development of novel treatments.

Second-line treatments remain underwhelming

The mainstay of first-line treatment for MPM is often a combination of pemetrexed (Alimta) and platinum-based cisplatin (Platinol) or carboplatin (Paraplatin) chemotherapy. The most recent development in the MPM treatment landscape came in 2020 with the FDA approval of the combination of ICIs nivolumab and ipilimumab for the first-line treatment of unresectable metastatic mesothelioma. However, as mesothelioma is incurable, virtually all patients will disease progress and there are currently no treatments specifically approved for patients with relapsed mesothelioma. There remains a divide in the clinical community over the most appropriate second-line therapy for MPM; however, the most widely used often include off-label platinum re-challenge or single-agent chemotherapy and immunotherapy. However, disease control in this patient population remains poor, with studies reporting mPFS rates of 3.0 months for nivolumab monotherapy, 3.1 months for pembrolizumab monotherapy, 3.6 months for chemotherapy and 5.6 months for nivolumab in combination with ipilimumab.

Scope to differentiate in a quieter pipeline

Ultimovacs' NIPU study is evaluating a triple combination of nivolumab, ipilimumab and UV1 in patients who have progressed after treatment with first-line platinum doublet chemotherapy. In our view, with the limitations of existing second-line treatment options in MPM, UV1 may only need to demonstrate modest improvements in mPFS (c 1–2 months) to differentiate with a competitive and clinically meaningful treatment profile.

To our knowledge, the NIPU trial represents one of the largest (n=118), active, Phase II studies focused on second-line MPM. An analysis of the pipeline highlights very few emerging therapeutic agents being investigated in this area, Exhibit 3. The most advanced clinical asset is Trizell's adenoviral gene therapy, TR002, which is being investigated in a Phase III study in combination with gemcitabine chemotherapy. However, as previously discussed in our cell and gene therapy (CGT) report, CGTs have limitations that include potential safety concerns around viral vector delivery technology, high cost, limited patient access and the requirement of specialised centres to deliver treatment. As an 'off-the-shelf' product, UV1 may facilitate broader access to patients and, compared to CGTs, is associated with lower production costs. Sellas Life Science's galinpepimut-S is another peptide-based cancer vaccine being investigated in second-line MPM; however, we note the drug is still in the very early stages of clinical development in smaller trial populations.

Exhibit 1: Relapsed MPM pipeline

Drug	Company	Phase	Technology	Description	Notes
TR002	Trizell	Phase III	Gene therapy	Adenovirus-delivered interferon alfa 2b gene (Ad.IFN) therapy. Mesothelioma cell transduction with Ad.IFN is designed to induce cell death triggering an immune response against cancer cells (immuno-gene therapy).	Results of Phase II study (n=40) in second-line MPM reported median OS of 17 months with two- and three-year survival rates of 25% and 20%, respectively. Phase III study aims to recruit up to 300 patients in combination with gemcitabine chemotherapy. There is detail on trial status or expected readouts.
Keytruda / Lenvatinib	Netherlands Cancer Institute / Merck	Phase II	Checkpoint inhibitor / VEGF inhibitor	Pan-tyrosine kinase inhibitor (Lenvatinib) with primarily vascular endothelial growth factor receptor (VEGFR) inhibiting properties combined with PD-1.	Preliminary results from investigator-sponsored Phase II study (n=38) reported that trial met its primary endpoint, achieving an ORR of 58% vs 25% from previous studies of pembrolizumab monotherapy.
Gavo-cell	TCR2	Phase I/II	Gene modified cell therapy	A form of autologous gene modified T-cell receptor therapy. Uses engineered T cells called TRuC-T cells, designed to target multiple patient antigenic peptide presenting human leukocyte antigen subtypes.	Phase I portion of the Phase I/II study in mesothelin expressing solid tumours reported mPFS of 5.6 months and mOS 11.2 months in MPM patients when treated with gavo-cell. Company has now prioritised Phase II portion of study in ovarian cancer but expects interim readouts from those MPM patients treated with gavo-cell and ICIs (ipilimumab and nivolumab) in H123.
Galinpepimut-S (Zeltherva)	Sellas Life Sciences	Phase I	Cancer vaccine	A Wilms tumor-1 (WT1) peptide cancer vaccine. WT1 is a protein highly overexpressed in MPM, making it a potential target for tumour selective cancer vaccines.	In an ongoing investigator sponsored Phase I study in combination with with nivolimuab. Results from a Phase II Investigator sponsored trial studied Galinpepimut-S in combination with immunologic adjuvants (Montanide and GM-CSF) in post-surgery patients reported mPFS of 10.1 months. Trial was not powered to show statistical significance.
MTG201	Momotaro Gene	Phase II	Gene therapy	Adenovirus-delivered Reduced Expression in Immortalized Cells/Dickkopf-3 gene (REIC/Dkk-3 gene). Increased REIC/Dkk-3 gene expression in cancer cells triggering cell death and cancer-cell specific immune response.	Study intends to recruit up to 12 patients investigating intratumoral injections of MTG201 in combination with nivolumab.

Source: EvaluatePharma, Edison Investment Research

While we acknowledge MPM may be a niche indication, limited competitive technologies in the pipeline combined with existing sub-optimal second-line treatments provides greater scope for UV1 to differentiate even if only marginal improvements in efficacy are exhibited, in our view. Additionally, combined sales of nivolumab/ipilimumab in MPM are estimated to reach c $130m by 2028 (according to EvaluatePharma) representing a reasonable market opportunity for Ultimovacs to capture with UV1.

UV1 positioning to disrupt SoC in melanoma

The existing SoC for the treatment of metastatic melanoma depends on whether a tumour contains a driver BRAF mutation (ICIs are more commonly used in metastatic melanoma when there is no BRAF mutation). Around 40–50% of all metastatic melanomas have the driver BRAF mutation, in which case BRAF inhibitors are used in combination with MEK inhibitors to decrease MAPK-driven acquired resistance (dabrafenib/trametinib or vemurafenib/cobimetinib). In patients with no BRAF mutation, the guidelines from the National Comprehensive Cancer Network recommend single-agent immunotherapy with pembrolizumab or nivolumab or combination therapy, with nivolumab plus ipilimumab as the first choice (Exhibit 2).

Exhibit 2: ICIs approved for first-line metastatic melanoma

Company	Drug	Target/s	2028 estimated sales according to EvaluatePharma	FDA approval basis
Bristol Myers Squibb	Nivolumab (Opdivo)	PD-1	$2.6bn	mPFS 5.1 months
Bristol Myers Squibb	Ipilimumab (Yervoy)	CTLA-4	$540m	Two-year survival rate 24%
Bristol Myers Squibb	Nivolumab plus ipilimumab	PD-1 / CTLA-4	See above	mPFS 11.5 months
Bristol Myers Squibb	Nivolumab plus relatlimab (combo brand name Opdualag)	PD-1/ LAG-3	$2.4bn	mPFS 10.1 months
Merck	Pembrolizumab (Keytruda)	PD-1	$2.5bn	ORR 34%

Source: EvaluatePharma, Edison Investment Research

With melanoma one of the most immunogenic tumour types, patients who are eligible to receive immunotherapy often respond well to ICI treatments. In contrast, historically, attempts to develop cancer vaccines as immunotherapies shown disappointing results. However, with the evolution of ICIs, there is potential for a synergistic relationship between ICIs and cancer vaccines such as UV1, with the former making tumour cells vulnerable to attack by the immune system cells and the latter designed to prime the body's immune cells to fight tumours. Although ICIs have had a major impact on the oncology treatment landscape, they still suffer from relatively low response rates and in 2018 it was estimated only 12% of eligible patients would respond to ICI monotherapy. However, we acknowledge that this number has likely increased since then. In our view, Ultimovacs' UV1/ICI combination, from a clinical perspective, makes strategic sense with the addition of UV1 to the current SoC treatment protocol providing scope for further efficacy enhancements.

Merck/Moderna combo further validates vaccines in melanoma

Merck and Moderna released highly encouraging results in December 2022 from a Phase II study (KEYNOTE-942, n=157) investigating the jointly developed, personalised mRNA vaccine (mRNA-4157/V940) in combination with Merck's ICI, pembrolizumab (Keytruda). The study investigated the combination as a post-surgery adjuvant treatment for patients with stage III/IV melanoma who have had complete resection of cutaneous melanoma (completely removed by surgery) but a high risk of disease recurrence. Initial results from the study reported a reduced risk of tumour recurrence, or death, in patients by 44% compared to pembrolizumab alone. Merck presented updated clinical data at the AACR Annual Meeting 2023, where it reported a disease RFS at 18 month follow-up of 78.6% in the combination arm and 62.2% in the pembrolizumab-only control arm. At two years of follow-up, recurrence or death was reported in 22.4% of patients (n=24/107) treated with the combination compared to 40% (n=20/50) treated with pembrolizumab monotherapy. Merck and Moderna intend to initiate a Phase III study for mRNA-4157/V940 in combination with pembrolizumab as an adjuvant treatment in high-risk melanoma patients following complete resection in 2023. In our view, the most recent results provide further clinical validation for the application of the cancer vaccine/ICI combinations in the treatment of advanced melanoma.

Notably, Ultimovacs' INITIUM study does not directly compete with KEYNOTE-942 as INITIUM is focused on patients with unresectable (not eligible for surgery) metastatic melanoma. Additionally, although comparisons between trial results may not be applicable, due to the differences in the melanoma populations being investigated, we note the similarity in trial designs (open-label, randomised, dual arm, multi-centre and statistically powered) and patient enrolment numbers (n=156 in INITIIUM and n=157 in KEYNOTE-942). With KEYNOTE-942 having recently received positive widespread media attention, following the data presented at AACR, and considering the robustness of both study designs, we believe positive readouts from INITIUM could be of equivalent significance that could, similarly, transform UV1 into a Phase III-ready asset.

…but off-the-shelf therapies such as UV1 may have an edge

While personalised therapy approaches may offer improved efficacies, with treatments tailored to an individual's specific disease profile, we believe it is highly likely that, from a cost and

manufacturing perspective, patient-specific vaccines are likely to encounter production issues similar to those faced by patient-specific cell therapies. Notably, the turnaround time from biopsy to treatment ('vein-to-vein' time) for Merck and Moderna's melanoma vaccine mRNA-4157/V940 has been reported to take 6–8 weeks, a potentially serious issue for patients with highly aggressive cancers, in our view. Additionally, personalised therapies may face pricing pressures associated with higher COGS, which may lead to concerns over the health economics of such treatments. Sipuleucel-T (Provenge), a personalised dendritic cell vaccine approved by the FDA in 2010 for the treatment of prostate cancer, was initially priced at $93,000. However, the treatment only extended OS by around four months, meaning the drug struggled to secure reimbursement and failed to achieve widespread commercial success. Although we acknowledge the costs of mRNA cancer vaccine production such as Merck/Moderna's mRNA-4157/V940 may not directly correlate with cell-based vaccines such as sipuleucel-T, personalised treatments are unlikely to benefit from the same economies of scale as 'off-the-shelf' products.

In our view, the operational infrastructure to support the commercialisation and mass production of personalised treatments is not yet in place and may not be for quite some time. In the case of cancer vaccines, which aim to target larger patient populations across a broad range of indications, we believe more universal approaches looking to provide timelier, upfront access to treatment for patients offer significant potential to differentiate in the market. With the advantages that 'off-the-shelf' therapies such as UV1 might possess with lower production costs, a shorter 'vein-to-vein' time and wider patient access, we believe this makes the upcoming readouts from the INITIUM study of even greater significance. Should UV1 demonstrate statistically significant improvements in PFS versus the nivolumab/ipilimumab combination, it not only may potentially disrupt existing first-line ICI treatment regimens, but, in our view, could provide UV1 with a distinct competitive advantage over personalised vaccine approaches such as mRNA. However, we note that UV1 is being investigated in a different melanoma patient population to Merck/Moderna's mRNA-4157/V940 avoiding potential direct competition and commercial overlap. Positive clinical data may also heighten the interest of BMS, whose ICI combination, nivolumab plus ipilimumab, is being used alongside UV1 in the INITIUM trial. BMS has publicly voiced support for the continued development of cancer vaccine technology and, if BMS looks to compete with Merck and Moderna's mRNA candidate in melanoma, UV1 may be viewed as an attractive asset, provided upcoming clinical study readouts are positive.

A cancer vaccine with a unique mechanism of action

To our knowledge, UV1 represents one of the most advanced cancer vaccines being investigated for the treatment of melanoma, Exhibit 1. The closest 'off-the-shelf' competitor to UV1 is IO-Biotech's peptide vaccine, IO102-IO103, in Phase III studies. However, IO102-IO103's mechanism of action (MoA) stimulates T cell responses that target indoleamine 2,3-dioxygenase (IDO) and PD-L1 associated antigens present on tumour cells and immune cells in the tumour microenvironment. UV1 therefore has a differentiating therapeutic MoA in targeting hTERT, primarily expressed in a subpopulation of cancer cells called cancer stem cells (CSCs). CSCs are often resistant to conventional cancer treatments, leading to metastasis and tumour resistance, making hTERT an attractive target for cancer vaccine development, in our view.

Although IO102-IO103 may be slightly further ahead in development, the most significant clinical results, to date, have come from a Phase I/II (n=50) investigator-sponsored study. Patients from cohort A of the study (n=30), who were PD-1 ICI naive and treated with IO102-IO103 in combination with nivolumab, reported a mPFS of 26 months. However, as this was an early-stage study, we caution interpretation of the clinical significance of this result compared to those to be reported from more rigorous trial designs such as INITIUM.

Exhibit 3: Selected cancer vaccine studies in first-line advanced melanoma

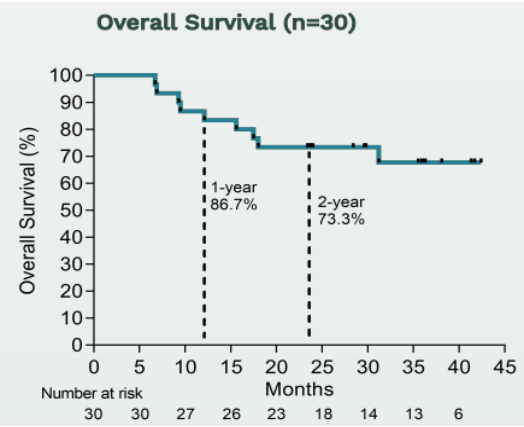
Drug	Company	Phase	Personalised	Technology	Notes
IO102-IO103	IO-Biotech	Phase III	No	Dual combination peptide vaccine stimulating production of IDO/PD-L1-specific CD4+ and CD8+ T cells. Thought to work synergistically with anti PD-1 therapy.	Pivotal Phase III study (n=300) recruiting patients, with enrolment expected to be completed by end 2023. Patients to be treated with IO102-IO103 in combination with pembrolizumab vs pembrolizumab monotherapy. Data corresponding to 30 patients treated with IO102-IO103 and nivolumab in investigator sponsored Phase I/II trial reported ORR of 80% and mPFS of 26 months.
mRNA-4157/V940	Merck/Moderna	Phase II	Yes	Personalised tumour neoantigen specific mRNA vaccine capable of coding for up to 34 neoantigens.	Phase II study met primary efficacy endpoint reducing risk of tumour recurrence, or death (RFS) in patients by 44% with mRNA-4157/V940 in combination with pembrolizumab compared to pembrolizumab alone. Combination was tested in melanoma patients with a high risk of recurrence after complete resection (post-surgery) of cutaneous melanoma. Expect initiation of Phase III study in 2023.
EVX-01	Evaxion	Phase II	Yes	Personalised tumour neoantigen specific peptide-based vaccine.	Data from Phase I/II trial (n=9) reported a 67% ORR, which included 22% complete response and 44% partial response in combination with anti-PD1 therapy. Interim readouts assessing EVX-01 in combination with pembrolizumab are expected in H223.
VB10.NEO	Nykode therapeutics	Phase I/II	Yes	Personalised tumour neoantigen specific DNA vaccine capable of coding for up to 20 antigenic epitopes (part of antigen recognised by immune cells) inducing CD4+ and CD8+ T cell responses.	Initial data from Phase I/II reported clinical responses to VB10.NEO treatment (lesion size reduction 10-100%) in 50% of patients assessed evaluated (seven out of 14) including one advanced melanoma patient. Patients are treated in combination with CD122 agonist bempegaldesleukin.

Source: Evaluate Pharma, Edison Investment Research

Long-term survival data provide glimpses of UV1 efficacy

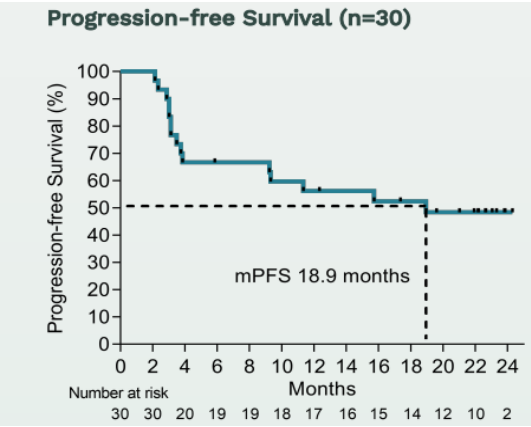
What we believe represents one the most significant clinical validations of Ultimovacs' technology shown to date, are the encouraging long-term survival data reported from the open-label Phase I study (UV1-103) in metastatic melanoma. The trial is investigating UV1 in combination with Merck's ICI, pembrolizumab (Keytruda), in a first-line setting with study split into two study cohorts (n=30) receiving different doses of UV1 adjuvant (37.5µg versus 75µg). The one- and two-year OS rates from the two cohorts combined were 87% (26/30) and 73% (22/30) respectively, Exhibit 4. Additionally, a three-year OS rate of 71% has been reported from patients in cohort one (12/17).

Exhibit 4: OS rates from the UV1-103 study



Source: Ultimovacs corporate presentation

Exhibit 5: mPFS rates from the UV1-103 study



Source: Ultimovacs corporate presentation

Of note, the three-year OS rate from the KEYNOTE-006 study investigating pembrolizumab as a monotherapy in first-line patients with metastatic melanoma was 51%. The UV1-103 study also reported a mPFS of 18.9 months (Exhibit 5), an improvement on the mPFS of 16.9 months in ICI-

naïve patients reported from a separate study for pembrolizumab, KEYNOTE-001. However, we caution there may be limitations in cross-trial comparisons given the differences in study designs, controls and trial populations.

It is worth highlighting that pembrolizumab appears to have a more beneficial clinical profile compared to the combination of ipilimumab/nivolumab in advanced melanoma (mPFS from KEYNOTE-001: 16.9 months vs mPFS from CheckMate-067: 11.5 months), which is being investigated in INITIUM. This means that, from a clinical perspective, the UV1/ ipilimumab/nivolumab combination would need to see an improvement in mPFS by at least 50% to be classified as best in class first line ICI treatment. However, we note that ipilimumab is currently a blockbuster drug in the melanoma market (2022 melanoma sales: $1.9bn, EvaluatePharma) with sales figures competing with that of pembrolizumab (2022 melanoma sales: $2.3bn, EvaluatePharma). Additionally, sales of ipilimumab in melanoma are estimated to surpass those of pembrolizumab by 2028 ($2.8bn vs $2.4bn, EvaluatePharma), which, in our view, provides evidence for the demand of ipilimumab and potential combinations in the melanoma treatment market.

Positive results may hook potential UV1 suitors

The re-emergence of cancer vaccine technology has seen the signing of some notable licensing deals in recent years, Exhibit 6. In our view, a comparable deal of note is the worldwide licensing agreement signed in 2020 between Roche and Nykode worth up to $715m for the Scandinavian biotech's personalised cancer vaccine, VB10.NEO. At the time of the agreement VB10.NEO was in the Phase I portion of a Phase I/II basket trial that included patients with advanced or metastatic melanoma, non-small-cell lung carcinoma, clear renal cell carcinoma urothelial cancer or squamous cell carcinoma of the head and neck. The study is ongoing and Roche will assume full development responsibilities after the conclusion of the Phase I portion of the trial. However, we acknowledge the upfront payment of $200m received by Nykode is at the upper end of the industry average.

In our view, positive readouts from both the INITIUM and NIPU studies would support the body of growing evidence demonstrating UV1's clinical utility while significantly enhancing the asset's value and potential deal value that could be commanded from future licensing opportunities. Additionally, UV1 is being investigated across five ongoing Phase II trials in advanced melanoma, MPM, head and neck cancer, ovarian cancer and non-small-cell lung cancer, and this broader application may add further value to UV1 in the eyes of potential licensing partners.

Exhibit 6: Comparison oncology vaccine and immunotherapy licensing deals

Phase	Date	Licensee/partner	Licensor	Product	Upfront milestone payments ($m)	Total potential deal value ($m)
Phase I	20/10/2022	Roche	Hookipa	HB-700	40	970
Phase III**	07/12/2020	3D Medicines	Sellas Life Sciences	Zeltherva	8	202
Phase I	01/10/2020	Roche	Nykode	VB10.NEO	200	715
Phase II	18/11/2019	Fosun	Mimivax	SurVaxM	10	148
Preclinical	02/08/2016	Amgen	Advaxis	ADXS-NEO	40	540
Phase II*	10/08/2015	AstraZeneca	Inovio Pharmaceuticals	INO-3112	28	728
Phase III*	03/04/2015	Bristol Myers Squibb	Bavarian Nordic	Prostvac	60	975
				Median	40	715

Source: EvaluatePharma, Edison Investment Research. Note: *Deal subsequently terminated; **deal includes Greater China only.

Financials and valuation

There are no significant changes to our operating expense forecasts (see our Q422 report for details) and adjustments in our valuation have been realised by rolling our model forward and updating our FX assumptions to NOK10.18/$. Our long-term assumptions remain unchanged and a

breakdown of our rNPV calculation can be seen Exhibit 7. We note that the top-line readouts from the upcoming INITIUM and NIPU studies are likely to have a material impact on our assumptions of Ultimovacs, which we will look to revise our valuation after the results.

Exhibit 7: Valuation of Ultimovacs

Product	Launch	Peak sales ($m)	NPV (NOKm)	NPV/share (NOK/share)	Probability	rNPV (NOKm)	rNPV/share (NOK/share)
UV1 – malignant melanoma	2028	1,270	5,961.9	173.3	25.0%	1,620.5	47.1
UV1 – mesothelioma	2028	570	2,789.6	81.1	25.0%	759.3	22.1
UV1 – ovarian cancer	2029	787	3,181.4	92.5	25.0%	893.3	26.0
UV1 – head and neck cancer	2029	1,370	5,772.7	167.8	25.0%	1,582.2	46.0
UV1 – NSCLC	2030	2,683	10,182.9	296.0	25.0%	2,757.4	80.2
Net cash, last reported			425.3	12.4	100.0%	425.3	12.4
Valuation			**28,313.8**	**823.2**		**8,038.0**	**233.7**

Source: Edison Investment Research

Because our model assumes an out-licensing deal by end-2024, we estimate that the company would be required to raise c NOK150m in funds in H224. We account for this raise as illustrative debt in our model. Alternatively, if the funding is realised through an equity issue instead (assuming at the current trading price of c NOK130/share), Ultimovacs would have to issue 1.15m shares, resulting in our per share valuation coming down to NOK226 from NOK234 (shares outstanding would increase from 34.4m to 35.7m). However, we do not expect Ultimovacs to be fully revenue generating and self-sustaining until the launch of UV1, which we forecast in 2028.

Exhibit 8: Financial summary

Accounts IFRS; year end 31 December; NOKm	2019	2020	2021	2022	2023e	2024e
Income statement						
Total revenues	0.00	0.00	0.00	0.00	0.00	0.00
Cost of sales	0.00	0.00	0.00	0.00	0.00	0.00
Gross profit	0.00	0.00	0.00	0.00	0.00	0.00
SG&A (expenses)	(20.16)	(50.99)	(61.92)	(71.47)	(85.76)	(102.91)
R&D costs	(35.53)	(64.66)	(96.74)	(95.18)	(109.52)	(136.90)
Other income/(expense)	(8.47)	(5.78)	(2.48)	(14.34)	(27.38)	(34.22)
Exceptionals and adjustments	0.00	0.00	0.00	0.00	0.00	0.00
Reported EBITDA	(64.15)	(121.43)	(161.13)	(180.98)	(222.65)	(274.03)
Depreciation and amortisation	(2.06)	(2.72)	(2.70)	(2.65)	(2.44)	(2.38)
Reported Operating Profit/(loss)	(66.22)	(124.15)	(163.83)	(183.63)	(225.09)	(276.41)
Finance income/(expense)	5.05	3.59	(0.89)	15.84	8.02	(2.93)
Other income/(expense)	0.00	0.00	0.00	0.00	0.00	0.00
Exceptionals and adjustments	0.00	0.00	0.00	0.00	0.00	0.00
Reported PBT	(61.17)	(120.55)	(164.72)	(167.79)	(217.08)	(279.34)
Income tax expense	0.00	0.00	0.00	0.00	0.00	0.00
Reported net income	(61.17)	(120.55)	(164.72)	(167.79)	(217.08)	(279.34)
Basic average number of shares, m	22.93	30.26	32.37	34.31	34.40	34.40
Basic EPS (NOK)	(2.67)	(3.98)	(5.09)	(4.89)	(6.31)	(8.12)
Diluted EPS (NOK)	(2.67)	(3.98)	(5.09)	(4.89)	(6.31)	(8.12)
Balance sheet						
Property, plant and equipment	0.536	0.377	0.212	0.220	0.125	0.007
Intangible assets	66.370	76.346	71.119	68.429	66.280	64.211
Other non-current assets	3.523	3.630	1.951	5.444	5.444	5.444
Total non-current assets	70.429	80.353	73.282	74.093	71.849	69.662
Cash and equivalents	399.607	440.925	574.168	425.309	212.206	87.189
Trade and other receivables	0.000	0.000	0.000	0.000	0.000	0.000
Other current assets	8.004	8.438	8.087	10.270	10.270	10.270
Total current assets	407.611	449.363	582.255	435.579	222.476	97.459
Non-current loans and borrowings	2.301	2.075	0.457	3.713	3.713	153.713
Deferred tax liabilities	10.851	11.795	11.031	10.701	10.701	10.701
Total non-current liabilities	13.152	13.870	11.488	14.414	14.414	164.414
Trade and other payables	11.768	8.611	22.555	7.655	9.383	11.523
Other current liabilities	8.489	18.856	28.342	38.252	38.252	38.252
Total current liabilities	20.257	27.467	50.897	45.907	47.635	49.775
Equity attributable to company	444.632	488.380	593.152	449.351	232.276	(47.067)
Cashflow statement						
Operating Profit/(loss)	(66.217)	(124.146)	(163.833)	(183.630)	(225.093)	(276.412)
Depreciation and amortisation	2.063	2.720	2.703	2.648	2.439	2.382
Other adjustments	(2.023)	3.215	12.331	4.437	(8.506)	(4.244)
Movements in working capital	(1.862)	6.395	23.860	(6.988)	1.728	2.139
Interest paid / received	0.000	0.000	0.000	0.000	0.000	0.000
Income taxes paid	0.000	0.000	0.000	0.000	0.000	0.000
Cash from operations (CFO)	(62.988)	(108.223)	(125.828)	(167.694)	(221.414)	(279.066)
Capex	(0.172)	(0.282)	(0.085)	(0.195)	(0.195)	(0.195)
Acquisitions & disposals net	0.000	0.000	0.000	0.000	0.000	0.000
Other investing activities	4.490	(0.455)	3.062	8.887	8.506	4.244
Cash used in investing activities (CFIA)	4.318	(0.737)	2.977	8.692	8.311	4.049
Net proceeds from issue of shares	344.582	152.933	261.852	5.484	0.000	0.000
Movements in debt	0.000	0.000	0.000	0.000	0.000	150.000
Other financing activities	(1.579)	(1.916)	(1.895)	(1.907)	0.000	0.000
Cash flow from financing activities	343.003	151.017	259.957	3.577	0.000	150.000
Increase/(decrease) in cash and equivalents	284.333	42.057	137.106	(155.425)	(213.103)	(125.017)
Cash and equivalents at beginning of period	115.540	399.608	440.925	574.168	425.310	212.206
Cash and equivalents at end of period	399.608	440.925	574.168	425.310	212.206	87.189
Net (debt) cash (including lease liabilities)	395.982	437.143	572.083	419.830	206.726	(68.291)

Source: Company reports, Edison Investment Research

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