# **2021** Fourth quarter report

Ultimovacs ASA







## Fourth Quarter 2021

Development of Ultimovacs' universal cancer vaccine UV1 is progressing, with one Phase I trial and five Phase II trials ongoing. The Company has shared the promising Phase I safety and efficacy data of UV1 in advanced melanoma with scientists, clinicians, potential partners, and investors. Ultimovacs' Phase I TENDU trial of its second technology approach, based on the Tetanus-Epitope Targeting (TET)-platform, is also advancing as planned.

#### Operational

- On December 2, 2021, Ultimovacs announced that UV1 received Orphan Drug designation from the U.S. FDA in the treatment of malignant melanoma.
- On October 26, 2021, Ultimovacs announced a new Phase II clinical trial (LUNGVAC) investigating UV1 in combination with pembrolizumab in non-small cell lung cancer (NSCLC). The LUNGVAC trial will be a multi-center, randomized, open-label trial sponsored by Drammen Hospital, a leading oncology research center in Norway. The trial will enroll approximately 138 patients and will be conducted at 8-10 clinical centers in Norway. (*also presented in the Q3-report*)
- On October 20, 2021, Ultimovacs announced that UV1 received Fast Track designation from the U.S. FDA in the treatment of unresectable or metastatic melanoma either as add-on therapy to pembrolizumab or as add-on therapy to ipilimumab. (*also presented in the Q3-report*)
- On October 13, 2021, Ultimovacs announced that the overall survival rate after two years of follow-up in the Phase I clinical trial of UV1 combined with pembrolizumab was 80% in this first cohort of 20 patients. As previously announced, median progression free survival for these patients was 18.9 months. (*also presented in the Q3-report*)

#### Clinical trial enrollment update

- INITIUM trial: 120 patients have been enrolled to date, up from 91 as of the previous quarterly report.
- NIPU trial: 66 patients have been enrolled to date, up from 45 as of the previous quarterly report.
- FOCUS trial: 10 patients have been enrolled to date, up from 5 as of the previous quarterly report.
- DOVACC trial: The first patient was enrolled on 15 December 2021, and 2 patients have been enrolled to date.
- TENDU trial: 6 patients have been enrolled to date in this dose escalation study compared to 4 patients in the previous quarterly report, completing treatment of the



second cohort. No safety concerns emerged in the first two dose level cohorts, allowing the enrollment of patients in the third, final dose cohort.

- COVID-19: Although Ultimovacs remain optimistic regarding progress in the Company's broad clinical program, the effect of the pandemic on the biotech industry and the conduct of clinical trials remains uncertain. Its lasting impact depends on the speed and extent of a return to a more normal situation. Ultimovacs will continue to provide enrollment updates in each quarterly report.
- Despite earlier and current pandemic-related challenges, the levels of patient enrollment have been increasing recently in both the INITIUM and NIPU studies. Ultimovacs' updated guidance is that both studies are estimated to have readouts during the **first half of 2023**, rather than during the second half of 2022 as indicated in the early guidance given in 2019 before either study started.
- The DOVACC and FOCUS trials are still in their early stages of hospitals/clinical site activation, and the start-up phase of both has taken somewhat longer than originally planned. Ultimovacs has guided that the readouts of topline results are expected to take place in 2023 and have done so since the trials began. In the LUNGVAC trial, Ultimovacs expects the first patient to be enrolled during the first half of 2022 with topline results expected by the end of 2024. Once each of these trials has progressed sufficiently to provide a reliable trajectory beyond initiation, Ultimovacs will review guidance and expect to give an update with the Q4 2022 report.



#### Financial

- Total operating expenses amounted to **MNOK 50.9** in Q4-21, and **MNOK 163.8** in FY21.
- Net negative cash flow from operations was **MNOK 33.9** in Q4-21, and **MNOK 125.8** in FY21. Total cash and cash equivalents increased by **MNOK 227.9** during Q4-21 and amounted to **MNOK 574.2** as per 31 December 2021.
- A private placement was successfully completed on October 26, 2021, raising gross proceeds of **MNOK 270** (net MNOK 259.0) and increasing the number of shares by 216,000 to a total of 34,221,761 shares. (*also presented in the Q3-report*)
- On October 12, 2021, 58,500 options, granted under Ultimovacs' option program, were exercised and subsequently the Company's share capital was increased by NOK 5,850 on 15 October by issuing 58,500 new shares, each share of par value NOK 0.10. (also presented in the Q3-report)

#### **Key financials**

NOK (000) Unaudited	Q4-21	Q4-20	FY21	FY20
Total revenues	-	-	-	-
Total operating expenses	50 930	25 588	163 832	124 146
Operating profit (loss)	(50 930)	(25 588)	(163 832)	(124 146)
Profit (loss) for the period	(51 152)	(24 582)	(164 722)	(120 552)
Diluted and undiluted earnings / (loss) per share (NOK)	(1.5)	(0.8)	(5.1)	(4.0)
Net increase / (decrease) in cash and cash equivalents	227 856	(12 524)	137 106	42 058
Cash and cash equivalents at end of period	574 168	440 925	574 16 <b>8</b>	440 925
	NOK/EUR - 9.9	888		
Cash and cash equivalents at end of period - EUR (000)	57 481			



## **CEO's Statement**

Ultimovacs continued to make strong clinical and financial progress in the fourth quarter of 2021, the culmination of a highly productive year. In the quarter, we reinforced our financial position with a private placement, part of which will fund a new Phase II clinical study with our universal cancer vaccine UV1 in a major indication, non-small cell lung cancer. We also advanced our ongoing Phase II clinical programs and received both US FDA Fast Track and Orphan Drug Designations in our lead indication, metastatic melanoma.

Our clinical program in malignant melanoma received two significant boosts during Q4 2021. The 24-month follow-up data from our Phase I trial



in malignant melanoma was released in October. The data indicated that UV1 in combination with pembrolizumab (KEYTRUDA<sup>®</sup>) provides an overall survival rate of 80% for treated patients while maintaining a balanced safety and tolerability profile. These are encouraging numbers compared to the historical overall survival rate of 58% for pembrolizumab alone in the KEYNOTE 006 trial.

That positive data was reinforced in the same month by the receipt of dual US FDA Fast Track designations for UV1 as add-on therapy to pembrolizumab or ipilimumab; a recognition of the encouraging data from the phase I studies and the unmet needs of patients with malignant melanoma. In December the FDA also granted UV1 orphan drug designation for the treatment of metastatic melanoma, which confers certain benefits to UV1, including potential seven-year market exclusivity if approved.

In October, Ultimovacs announced plans for a new Phase II trial of UV1 plus pembrolizumab (KEYTRUDA<sup>®</sup>) in one of the most common cancers, non-small cell lung cancer. This is the fifth Phase II trial testing the use of UV1 to improve the performance of checkpoint inhibitor antibodies.

At the end of October, the company raised NOK 270 million (gross) through a substantially oversubscribed private placement to new and existing shareholders. The net proceeds from the fundraising will help fund the new lung cancer trial, advance the UV1 platform towards Phase III studies, and further develop our second technology platform, Tetanus-Epitope-Targeting (TET). The total cash of MNOK 574 at the end of Q4, provides a solid financial foundation for the development of our programs to the first part of 2024 and across potentially large value inflection events.

Finally, in December, we announced the enrollment of the first patient in DOVACC, the randomized Phase II trial assessing the impact of UV1 in combination with durvalumab and olaparib in ovarian cancer.

Throughout 2021, we have been monitoring the progress of our Phase II clinical trials and the impact from the COVID-19 pandemic on our programs and timelines. During the early stages of the pandemic before vaccination was widely available, patients' reluctance to visit hospitals, together with restricted capacity at certain treatment facilities severely reduced the rate of recruitment across virtually all oncology trials. Our studies are enrolling patients in nearly 100 clinical centers across 15 countries. The impact of the pandemic has varied between regions. More recently recruitment rates have picked up in most countries, even though some hospitals are not yet fully operational.



Our own experience with the Ultimovacs-sponsored INITIUM trial has been relatively positive despite the challenges of the pandemic. More than 75% of the patients in INITIUM have now been enrolled. In addition, more than 55% of the patients in the NIPU trial of UV1 in mesothelioma have now been enrolled. Despite earlier and current pandemic-related challenges, the levels of patient enrollment have been increasing recently in both trials and the updated guidance reflects only minor delays.

I am very proud of the team's accomplishment this quarter and pleased with the significant progress that Ultimovacs has made in 2021. In 2022 we remain focused on advancing the clinical development of UV1 across our five Phase II programs, laying the foundation for pivotal trials. We also look forward to broadening our pipeline as we move our second technology platform, the Tetanus-Epitope Targeting (TET) platform, into the next stage of development.

Carlos de Sousa, Chief Executive Officer



## **Key Operational Highlights Q4 2021**

Clinical trial update (as per reporting date, unless otherwise specified)

#### Guidance on readout of Phase II topline results

All clinical pharmaceutical developers have experienced the consequences of the Covid-19 pandemic on initiation, execution, and finalization of clinical trials. Ultimovacs has shared such challenges across its portfolio of clinical trials. In our experience, the greatest impact has been on the time it takes to initiate new sites/hospitals in a trial. Once sites are up and running, the enrollment of patients in Ultimovacs' trials has progressed steadily, albeit somewhat more slowly than anticipated especially during the earlier stages of the pandemic. Ultimovacs has worked closely with participating hospitals, continuously providing relevant support and motivation to help hospitals identify and enroll patients. That Ultimovacs was able to communicate encouraging results from other relevant clinical studies of the company's UV1 cancer vaccine has also had a positive effect on patient enrollment in Phase II trials across the portfolio.

Ultimovacs is the sponsor of the INITIUM trial. This formal 'ownership' of the trial endows Ultimovacs with ultimate responsibility for the conduct of the trial and implies closer interactions with the clinical sites/hospitals and more frequent and more detailed access to information on progress in patient enrollment.

The four other UV1 phase II trials, NIPU, DOVACC, FOCUS and LUNGVAC, are 'investigator-initiated' trials, for which a medical institution or a specialized clinical trial research unit is the sponsor. In these trials, Ultimovacs seeks to support the sponsor throughout, but has less operational involvement and more limited access to information than in an Ultimovacs-sponsored trial such as INITIUM.

More than 75% of the patients in INITIUM and more than 55% of the patients in NIPU have now been enrolled. Despite earlier and current pandemic-related challenges, the levels of patient enrollment have been increasing recently in both trials. Based on statistical assumptions and expected patient recruitment, our updated guidance is that both **INITIUM** and **NIPU** are estimated to have readouts during the **first half of 2023**, rather than during the second half of 2022 as indicated in early guidance established in 2019 before either study started.

The DOVACC and FOCUS trials are still in their early stages of hospitals/clinical site activation, and the start-up phase of both has taken somewhat longer than originally planned. Ultimovacs has guided that the readouts of topline results are expected to take place in 2023 and have done so since the trials began. In the LUNGVAC trial, Ultimovacs expects the first patient to be enrolled during the first half of 2022 with topline results expected by the end of 2024. Once each of these trials has progressed sufficiently to provide a reliable trajectory beyond initiation, Ultimovacs will review guidance and expect to give an update with the Q4 2022 report.

In summary, Ultimovacs is pleased to report that, thanks to the efforts of our clinical collaborators and the positive news from earlier stage studies, the phase II trials of UV1 have been able to progress with only relatively limited departures from our original guidance.

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#### The INITIUM trial

The first INITIUM patient was treated at the Oslo University Hospital (OUS) in June 2020. A total of 120 patients have been enrolled, compared to 91 patients in the previous quarterly report.

INITIUM is an Ultimovacs-sponsored randomized Phase II trial for first-line treatment of patients with metastatic malignant melanoma. Patients will be administered UV1 in combination with ipilimumab (CTLA-4 checkpoint inhibitor) and nivolumab (PD-1 checkpoint inhibitor). A total of 39 sites/hospitals are participating in this trial being run in the US and Europe,

including Norway. In total, 154 patients will be enrolled, half receiving nivolumab and ipilimumab and the other half receiving nivolumab, ipilimumab and UV1. The readout of the primary endpoint of progression-free survival is expected in H1-2023. Dr. Karl Lewis, University of Colorado Hospital (U.S.), is the International Coordinating Investigator of the INITIUM trial.

#### The NIPU trial

The first patient in the NIPU trial was treated at the Oslo University Hospital in June 2020, and a total of 66 patients have been enrolled compared to 45 patients in the previous quarterly report. The study is being conducted in five countries (Norway, Sweden, Denmark, Spain, and Australia). The patient enrollment has increased significantly in Q4 2022 as more hospitals have been initiated.

NIPU is a randomized, multi-center Phase II trial in which the universal cancer vaccine, UV1, will be evaluated in combination with the checkpoint

inhibitors ipilimumab and nivolumab as second-line treatment in mesothelioma. Oslo University Hospital is the sponsor of the NIPU study. Bristol-Myers Squibb and Ultimovacs have entered into agreements with OUS to support the preparations and execution of the trial. NIPU will include 118 patients; half will be treated with the combination of UV1, ipilimumab and nivolumab and half will receive nivolumab and ipilimumab only.

The objective of the study is to achieve a clinically meaningful progression-free survival (PFS) benefit in patients with malignant pleural mesothelioma (MPM) after progression on first-line standard platinum doublet chemotherapy. The readout of the primary endpoint of progression-free survival is expected in H1-2023.

#### The DOVACC trial

Enrollment started in December 2021, and the main focus in the start-up phase is initiation of hospitals. So far, 2 patients have been enrolled. DOVACC (**D**urvalumab **O**laparib **VACC**ine) is a multi-center, multinational, randomized Phase II clinical collaboration trial with the Nordic Society of Gynaecological Oncology – Clinical Trial Unit (NSGO-CTU), the European Network of Gynaecological Oncological Trial Groups (ENGOT), AstraZeneca and Ultimovacs. The trial is sponsored by the NSGO, the leading









gynecological oncology research society in the Nordic and Baltic regions. Ultimovacs will provide the UV1 vaccine and AstraZeneca will provide durvalumab and olaparib for the study.

The trial is designed to evaluate UV1 in combination with AstraZeneca's durvalumab, a PD-L1 checkpoint inhibitor and its PARP inhibitor, olaparib, the maintenance therapy for BRCA-mutated, advanced ovarian cancer. The trial will be conducted at more than 40 hospitals in more than 10 European countries. Top line data on the primary endpoint has been expected in 2023. It is too early to discern a clear trend in the timeline of patient recruitment. Ultimovacs will review the guidance and expects to give an update with the Q4 2022 report.

The second-line maintenance study will enroll patients with high-grade BRCA-negative ovarian cancer after partial or complete response following the second round of chemotherapy. The study is enrolling a total of 184 patients divided (randomized) into three treatment groups: 46 patients will receive olaparib; another 46 will receive olaparib and durvalumab; 92 patients will receive Ultimovacs' UV1 vaccine in combination with both AstraZeneca drugs. The primary endpoint is to compare the preliminary efficacy of maintenance treatment (progression-free survival) with olaparib to that of the triple combination treatment arm (olaparib plus durvalumab and UV1).

#### The FOCUS trial

The first patient in the FOCUS trial was treated in August 2021 and 10 patients have been enrolled compared to 5 patients in the previous quarterly report. The FOCUS trial (First-line metastatic **O**r recurrent HNSCC/**C**heckpoint inhibitor **U**V1 **S**tudy) is an investigator-sponsored, randomized Phase II clinical trial. It will enroll patients with recurrent or metastatic PD-L1 positive head and neck squamous cell carcinoma at 10 sites across Germany. FOCUS is led by principal investigator Prof. Mascha Binder, Medical Director and Head of the Immunological Tumor Group at



University Medicine Halle, Germany, a renowned oncology clinician and researcher specializing in the analysis of immuno-oncology treatments and their interaction with tumor tissues.

The trial will evaluate the addition of UV1 to a standard of care treatment with PD-1 checkpoint inhibitor pembrolizumab as compared to pembrolizumab monotherapy. A total of 75 patients indicated for treatment with pembrolizumab will be enrolled in FOCUS, randomized 2-to-1 so that 50 patients will receive UV1 and pembrolizumab and 25 patients will receive pembrolizumab alone. The primary endpoint of the study is the progression-free survival rate at 6 months. Top line data on the primary endpoint has been expected in 2023. It is too early to discern a clear trend in the timeline of patient recruitment. Ultimovacs will review the guidance and expects to give an update with the Q4 2022 report.



#### The LUNGVAC trial

On October 26, 2021, Ultimovacs announced a new Phase II clinical trial, LUNGVAC, investigating the company's universal cancer vaccine, UV1, will be investigated in combination with pembrolizumab in the treatment of non-small cell lung cancer (NSCLC). The first patient is planned to be treated in H1-22, with topline readout expected by the end of 2024. Ultimovacs will review the guidance and expects to give an update with the Q4 2022 report.



The LUNGVAC trial will be a multi-center, randomized, open-label trial

assessing the safety and efficacy of UV1 in combination with pembrolizumab versus pembrolizumab alone in NSCLC patients with advanced or metastatic disease. The trial will treat patients with PD-L1expressing tumors classified within the adenocarcinoma or squamous subgroups of NSCLC, where at least half of their tumor cells express the PD-L1 antigen and who have not previously received pembrolizumab treatment. These subgroups represent approximately 30% of all advanced and metastatic NSCLC patients. The primary endpoint of the trial will be progression-free survival. Secondary endpoints will include response rate and overall survival.

Professor Odd Terje Brustugun will be the principal investigator for the trial, which will be sponsored by Drammen Hospital, a leading oncology research center in Norway. The trial will enroll 138 patients and will be conducted at 8-10 clinical centers in Norway.

Lung cancer is currently one of the most common cancers globally, and by far the biggest cause of cancer deaths in both men and women. NSCLC accounts for approximately 85% of all lung cancers. An estimated 850,000 new patients (in the US, EU5, Japan, China) are diagnosed with NSCLC each year. Most of these patients are metastatic, for which the 5-year survival rate is around 7%.

#### Ongoing Phase I trial in malignant melanoma

This US-based Phase I clinical trial is evaluating the Company's lead candidate, UV1, in combination with the PD-1 checkpoint inhibitor, pembrolizumab, as a first-line treatment in patients with metastatic malignant melanoma. 20 patients (first cohort) were enrolled by September 2019. Ten additional patients (second cohort) were enrolled by August 2020 to investigate an increased dosage of the adjuvant GM-CSF.



The combined response rates for the 30 patients in cohort 1 and cohort 2 are:

- Objective response rate (ORR): 57%
- Complete response rate (CR): 30%

Median Progression Free Survival (mPFS):

- Cohort 1: 18.9 months
- Cohort 2: not reached at 12 months
- Cohort 1+2 combined: not reached at 12 months



Overall Survival (OS):

- Cohort 1 after 12 months: 85%
- Cohort 2 after 12 months: 90%
- Cohort 1+2 combined after 12 months: 87%
- Cohort 1 after 24 months: 80%

UV1 has demonstrated a good safety profile. No unexpected safety issues related to UV1 have been observed in this trial. Two key data readouts from the ongoing Phase I malignant melanoma trial are expected in 2022: During Q3-22, 24-month survival data on the second cohort will be announced, and during Q4-22, 36-month survival data on the first cohort will be announced.

#### Follow-up trials

The three completed Phase I trials have been reviewed by the US Food and Drug Administration (FDA) and served as the basis for the opening of an IND (Investigational New Drug) application supporting the start of clinical research activity in the U.S. in malignant melanoma. Ultimovacs considers these trials a strong basis for the further development of UV1.

	Overall Survival (OS) <sup>1</sup>				Median OS	m PFS <sup>2</sup>	
Clinical trial⁴	Year 1	Year 2	Year 3	Year 4	Year 5	(months)	(months)
Prostate (n=22)	95 %	86 %	73 %	55 %	50 %	61.8	n.a.³
NSCLC (n=18)	72 %	50 %	44 %	39 %	33 %	28.2	10.7
Malignant Melanoma (n=12)	75 %	75 %	67 %	50 %	50 %	Will be>60 m onths	6.7

#### Completed Phase I trials in follow-up

1. Note that some patients have received other treatment supon progression and this is likely to affect survival

2. Median Progression-Free Survival

3.PFS (Progression-Free Survival) not possible to measure in the prostate cancertrial. 4.Prostate: (EudraCTNo. 2012-002411-26) NSCLC: (EudraCTNo. 2012-001852-20) MM: (EudraCTNo. 2013-005582-39)

#### The TET-platform and the TENDU clinical trial

In addition to its universal vaccine, UV1, Ultimovacs is planning to develop novel vaccine products based on the patent-protected Tetanus-Epitope Targeting (TET)-platform. The TET-platform combines antigens and the vaccine adjuvant in the same molecule. This allows a beneficial safety profile and simplifies administration, offering a promising approach to strengthen and increase T cell responses against cancer-specific peptides. The platform generates new, first-in-class cancer vaccine candidates that harness pre-existing antibody responses against tetanus induced by standard tetanus vaccination. TET vaccine candidates can be tailored to many types of cancer, and to infectious diseases.

In 2021, Ultimovacs started the **TENDU** trial, its first Phase I trial to test the TET technology in patients with the main objective to assess the safety of the TET technology. In TENDU, the TET technology incorporates prostate-cancer-specific antigens. The first patient was treated in February 2021. Enrollment of the first cohort (three patients dosed at 40 mcg) was completed during the second quarter in 2021, and of the second cohort (three patients dosed at 400 mcg) was completed in February 2022. The Drug Safety Monitoring Board (DSMB), a group of experts set up to monitor patient safety during a clinical trial, found no safety concerns related to the first two dose cohorts. The conclusion from the DSMB enables the dose escalation study to proceed with enrollment of patients in the third and last dose cohort (960 mcg).



The TENDU trial is being conducted at Oslo University Hospital and will enroll 9 patients in total. This Phase I trial will provide valuable safety and immune activation data that will support the further development of new vaccine solutions based on the TET technology.

#### **Regulatory designations**

#### Fast Track Designation

On October 21, 2021, Ultimovacs announced that its universal cancer vaccine, UV1, in combination with checkpoint inhibitors received Fast Track designation from the U.S. FDA in the treatment of unresectable or metastatic melanoma – either as add-on therapy to pembrolizumab or as add-on therapy to ipilimumab. Ultimovacs is currently evaluating UV1 as add-on therapy to ipilimumab and nivolumab as first-line treatment for unresectable or metastatic melanoma in the INITIUM trial.

The FDA Fast Track process is designed to facilitate the development and expedite the review of drugs that meet urgent needs in serious medical conditions. Fast Track designation enables early and frequent communication with the FDA to support the drug's development, as well as entitlement to a Rolling Review of the Biologic License Application. Drugs with Fast Track designation may also be considered for Accelerated Approval and Priority Review provided certain criteria are met. *(also presented in the Q3-report)* 

#### **Orphan Drug Designation**

On December 2, 2021, Ultimovacs announced that UV1 has received Orphan Drug designation from the U.S. FDA in the treatment of malignant melanoma. UV1, as add-on therapy to checkpoint inhibitors ipilimumab and nivolumab, is currently being studied as first-line treatment for metastatic melanoma in INITIUM.

The FDA Office of Orphan Products Development (OOPD) supports and advances the development and evaluation of new treatments for rare diseases that affect fewer than 200,000 people in the U.S. Orphan drug designation provides certain benefits, including seven-year market exclusivity upon regulatory approval, if received, exemption from FDA application fees and tax credits for qualified clinical trials.



#### **Publications and presentations**

Ultimovacs' presented data documenting the mechanistic effects of UV1 at the Society for Immunotherapy of Cancer's (SITC) 36th Annual Meeting in Washington, DC, USA on November 12, 2021. The data came from an early Ultimovacs' Phase I/IIa study of UV1 with the checkpoint inhibitor ipilimumab in twelve patients with melanoma (NCT02275416) and showed that the drug combination induces a T cell immune response in 91% of patients, and that the response can persist as long as 5 years (the end of the study period). The UV1-ipilimumab combination induces T cells that are polyfunctional and produce multiple effector cytokines such as interferon-gamma and TNF-alpha essential for a robust anti-tumor response. Tumor biopsies revealed an influx of tumor-infiltrating lymphocytes in patients who responded well to treatment. The data were shown in a poster entitled "The Synthetic Long Peptide Cancer Vaccine UV1 in Combination with Ipilimumab Induces a CD4+ Th1 Anti-hTERT Immune Response and an Inflammatory Tumor Microenvironment in Patients with Melanoma".

#### **Organization and board**

Ultimovacs has appointed two additional members to the management team: Orla Mc Callion as Head of Regulatory Affairs & QA and Anne Worsøe as Head of Investor Relations & Communication, both effective October 1, 2021.



## Background

Ultimovacs (the 'Company') is a pharmaceutical company developing novel immunotherapies against cancer. The Company was established in 2011 and is listed on the Oslo Stock Exchange. The Company's proprietary technology is based on preclinical and clinical research on immunotherapies conducted at Oslo University Hospital. Ultimovacs is advancing a broad clinical development program with clinical trials in Europe, Australia and the U.S.

The Company's lead product candidate is UV1, a next generation peptide-based vaccine inducing a specific T cell response against the universal cancer antigen telomerase (hTERT), expressed at a high level in 85-90% of human tumors. The vaccine's mode of action is to make the immune system produce CD4 T cells (i.e., T helper cells) that recognize cancer cells expressing telomerase. UV1 may potentially be applied universally across cancer types, in different stages of disease and in combination with different cancer treatments. The vaccine is easy to use and does not require sophisticated infrastructure in hospitals. UV1 is manufactured as an off-the-shelf product with a long shelf life. UV1 is being developed as a therapeutic cancer vaccine and a platform for other immuno-oncology drugs which require an ongoing T cell response for their mode of action. Longer-term, it would be attractive to investigate the use of a vaccine like UV1 in early-stage tumors.

Treatment with UV1 has been assessed in three Phase I studies (metastatic prostate cancer, metastatic non-small cell lung cancer and metastatic malignant melanoma) in 52 patients at the Oslo University Hospital. The observed clinical outcomes from the three completed trials served as a strong basis for the further clinical development of UV1, both with respect to safety, immune response and signals of clinical effect. In addition, Ultimovacs is the sponsor of the fully enrolled and ongoing Phase I clinical study in the U.S. evaluating the safety and tolerability of treatment with UV1 and pembrolizumab (PD-1 checkpoint inhibitor) in 30 patients with metastatic malignant melanoma.

Ultimovacs has an extensive development program with five phase II studies in five different indications that are expected to include more than 650 patients:

- **INITIUM (154 patients)**: Ultimovacs sponsored trial in malignant melanoma in which UV1 is combined with nivolumab and ipilimumab.
- **NIPU (118 patients)**: trial in mesothelioma, UV1 in combination with nivolumab and ipilimumab. Oslo University Hospital is the sponsor of the NIPU study. Bristol-Myers Squibb and Ultimovacs have entered into agreements with Oslo University Hospital to support the execution of the trial.
- **DOVACC (184 patients)**: trial in collaboration with the Nordic Society of Gynaecological Oncology Clinical Trial Unit, the European Network of Gynaecological Oncological Trial Groups and AstraZeneca. UV1 is tested in combination with AstraZeneca's durvalumab and olaparib (PARP inhibitor) in patients with relapsed ovarian cancer.
- **FOCUS (75 patients)**: trial in collaboration with the Immunological Tumor Group at University Medicine Halle, Germany, where UV1 will be given in combination with pembrolizumab in head and neck cancer patients.
- **LUNGVAC (138 patients)**: trial in non-small cell lung cancer where UV1 will be investigated in combination with pembrolizumab. Drammen Hospital is the sponsor of the study.

In addition, the Company is expanding its pipeline using its novel TET technology platform that can generate multiple vaccine candidates designed to achieve increased T cell responses to a broad range of target antigens.



## **Outlook**

Ultimovacs' UV1 vaccine technology is universal in the sense that it may have an effect across most types of cancer and could be used in combination with different types of cancer treatment. The cancer vaccine is expected to generate immune responses across the general population (i.e., independent of HLA type). The vaccine is easy to manufacture and does not require a sophisticated hospital infrastructure to be administered. If the ongoing clinical development and testing of Ultimovacs' cancer vaccine demonstrates that the vaccine gives clinical benefit to cancer patients, the potential clinical use of UV1 and related financial benefits could be highly attractive.

As of now, UV1 will be investigated in five randomized Phase II trials in five different cancer types, with Ultimovacs sponsoring one of the trials. The five Phase II clinical trials will enroll more than 650 patients in total, representing a strong potential platform for Ultimovacs to move toward a possible registration of the universal cancer vaccine, UV1. The main study objectives are efficacy and safety data on combination therapies.

Readouts of the primary endpoints of the INITIUM and NIPU trials are expected during the first half of 2023.

Ultimovacs has guided that the readouts of topline results in the DOVACC and FOCUS trials are expected to take place in 2023 and have done so since the trials began. In the LUNGVAC trial, Ultimovacs expects the first patient to be enrolled during the first half of 2022 with topline results expected by the end of 2024. Once each of these trials has progressed sufficiently to provide a reliable trajectory beyond initiation, Ultimovacs will review guidance and expects to give an update with the Q4 2022 report.

The Company will continue to actively monitor the impact of the COVID-19 pandemic on patient enrollment for its Phase II clinical trials and continues to implement activities to minimize the impact. With current funding, plans and expectations, Ultimovacs has a financial runway to the first part of 2024.

Ultimovacs continues to pursue strategic collaborations with cancer institutions and pharmaceutical companies to document the effect and safety of UV1 in a range of cancer types and in combination with different cancer treatments. Ultimovacs makes clinical development choices based on the universal nature of UV1 as a cancer vaccine. UV1 can potentially play a role across most cancer types, in most patients, in different stages of cancer and in combination with many cancer treatments. Positive results from ongoing randomized clinical trials reinforce the significant development potential of UV1.

Ultimovacs is also seeking to broaden its pipeline of drug candidates. Its R&D activities are currently focused on the development of new first-in-class cancer vaccine solutions building on Ultimovacs' base technology, the TET-platform, and on the development of new molecules and technologies based on biobank material from the ongoing and planned clinical studies conducted with UV1. Pending confirmation of the safety of the TET technology through the Phase I TENDU trial and further preclinical development, Ultimovacs' ambition is to apply the TET technology in identifying new cancer vaccine program candidates to move into clinical development.



## **Risks and uncertainties**

Ultimovacs is a research and development company. The Company has not generated revenues historically and is not expected to do so in the near term. Research and development up to approved registration is subject to considerable risk and is a capital-intensive process. The Company's candidates for cancer vaccines and technology platforms are dependent on research and development and may be delayed and/or incur higher costs than currently expected. Competing pharmaceuticals can capture market shares or reach the market faster than Ultimovacs. If competing projects have a better product profile (e.g., better efficacy and/or less side effects), the future value of Ultimovacs' product offerings may be lower than expected. The operations may also be impacted negatively by changes or decisions regarding laws and regulations. In addition, the Company is also dependent upon intellectual property rights.

The primary financial risks are foreign exchange risks and financing risks. The Company is affected by foreign exchange risk as the research and development costs for UV1 are mainly paid in USD and EUR. In addition, the Company has invested in foreign operations, the net assets of which are exposed to currency translation risk. Adequate sources of funding may not be available when needed or may not be available on favorable terms. The Company's ability to obtain such additional capital or financing will depend in part upon prevailing market conditions as well as conditions of its business and its operating results, and those factors may affect its efforts to arrange additional financing on satisfactory terms. The Board of Directors works continuously to secure the business operation's need for financing.

The coronavirus pandemic has a profound impact on the global economy and no industry is protected from operational and financial consequences. The ultimate impact of the pandemic is currently difficult to assess. For a biotech company like Ultimovacs, some of the possible implications of the COVID-19 pandemic may affect:

- The initiation, patient inclusion and conduct of clinical trials
- Disruption of the supply chain (manufacturing and/or logistics) for the investigational products
- Fluctuations in currency exchange rates, (NOK/EUR and NOK/USD), which may increase R&D costs

The effects of the pandemic on the biotech industry and the general ability to conduct clinical trials, and the specific potential effect on Ultimovacs, are still uncertain. Given the inherent uncertainties, it is difficult to ascertain the exact impact of COVID-19 on the Company's operations, or to provide a firm quantitative estimate of this impact.

Ultimovacs' financial risk exposures are described in more detail in the Annual Report 2020. No significant changes have occurred that affect these reported risks.



## **Financial review**

**Financial results** 

Ultimovacs does not yet generate revenues, as the Company is in a research and development phase. In FY21, the Company recognized government grants of **MNOK 14.6** compared to MNOK 8.9 in FY20, which have been deducted from payroll expenses and other operating expenses. The grants are primarily received during the year following the accounting year when the grants are booked in the P&L.

Payroll and payroll related expenses decreased in Q4-21 (**MNOK 11.9**) compared to the same period in FY20 (MNOK 14.7), mainly due to a reversal of the social security tax accrual related to share options, which fluctuates with the company share price. Disregarding costs related to the share-based compensation, the personal expenses in Q4-21 were MNOK 3.7 higher than in Q4-20, primarily due to five additional full-time employees in this period.

Total personnel expenses in FY21 were **MNOK 61.9** compared to MNOK 51.0 in FY20, primarily due to MNOK 9.3 higher expenses related to the share-based compensation option program. There were approximately 2.5 more FTEs employed in the company during FY21 compared to FY20, however the increase in costs for these were offset by the severance pay from the previous CEO and sign on fee from the new CEO in FY20, resulting in total personnel expenses, excluding costs related to the share-based compensation, being approximately the same these years.

Other operating expenses (**MNOK 38.4** in Q4-21 and MNOK 10.2 in Q4-20) primarily comprise R&D related expenses. These expenses, including IP and external R&D expenses, offset by government grants, amounted to **MNOK 35.5** in Q4-21, and MNOK 7.5 in Q4-20. The increase in R&D expenses was due to the initiation of two Phase II trials during FY21, and the R&D costs are expected to be at a higher level going forward than in prior periods as the DOVACC and FOCUS trials have just recently started, and the LUNGVAC trial is expected to commence during FY22. Total R&D expenditure, however, may vary significantly from quarter to quarter. Total other operating expenses in FY21 (**MNOK 99.2**, of which **MNOK 88.2** R&D related) were significantly higher compared to FY20 (MNOK 70.4 of which MNOK 60.9 R&D related) due to the increased R&D activity.

Net financial items amounted to negative **MNOK 0.2** in Q4-21, compared to MNOK 1.0 in Q4-20. Financial items primarily comprise currency fluctuations from EUR at bank and the value of EUR currency future contracts swapped on a monthly basis, in addition to interest gain from cash at bank accounts.

Total loss for the Q4-21 period amounted to **MNOK 51.2**, compared to MNOK 24.6 in Q4-20. Total loss in FY21 amounted to **MNOK 164.7** compared to a loss of MNOK 120.6 in FY20.

#### **Financial position**

Total assets per 31 December 2021 were **MNOK 655.5**, an increase of MNOK 125.8 from 31 December 2020 primarily as a result of the share issue in Q4-21 and partly offset by negative operational cashflow. MNOK 0.8 in 'receivables and prepayments' are related to the fair value of EUR future contracts.



Total liabilities as of 31 December 2021 amounted to **MNOK 62.4**, of which MNOK 11.5 non-current.

Total equity equaled **MNOK 593.2** as of 31 December 2021. A capital increase in March 2021 and another in October 2021 related to the exercise of stock options resulted in gross proceeds and equity of MNOK 0.9 and MNOK 1.9 respectively.

On October 26, Ultimovacs successfully carried out a private placement of 2,160,000 new shares at a subscription price of NOK 125 per share, raising gross proceeds of NOK 270 million. The net proceeds of the private placement will be used for (i) financing of the LUNGVAC Phase II trial evaluating UV1 in non-small cell lung cancer, (ii) bringing the UV1 platform into Phase III readiness, (iii) further development of the Tetanus-Epitope-Targeting ("TET") technology platform, and (iv) general corporate purposes. Following registration of the new share capital pertaining to the Private Placement, the Company will have a share capital of NOK 3,422,176.10 divided into 34,221,761 shares, each with a par value of NOK 0.10.

Further, total equity has since year-end 2020 been decreased by the period's operating loss and currency translation amounting to **MNOK 168.7**, and in addition been increased by the recognition of share-based payments/stock options of **MNOK 11.6**.

#### **Cash flow**

The total net increase in cash and cash equivalents in Q4-21 was **MNOK 227.9**, which is primarily related to net negative cash-flow from operations amounting to **MNOK 33.9** offset by the share issue raising net proceeds of **MNOK 259.0**. Total cash and cash equivalents was **MNOK 574.2** per 31 December 2021.

#### **Key financials**

NOK (000) Unaudited	Q4-21	Q4-20	FY21	FY20
Total revenues	-	-	-	-
Total operating expenses	50 930	25 588	163 832	124 146
Operating profit (loss)	(50 930)	(25 588)	(163 832)	(124 146)
Profit (loss) for the period	(51 152)	(24 582)	(164 722)	(120 552)
Diluted and undiluted earnings / (loss) per share (NOK)	(1.5)	(0.8)	(5.1)	(4.0)
Net increase / (decrease) in cash and cash equivalents	227 856	(12 524)	137 106	42 058
Cash and cash equivalents at end of period	574 168	440 925	574 168	440 925
	NOK/EUR - 9.9	888		
Cash and cash equivalents at end of period - EUR (000)	57 481			

#### The Board of Directors and CEO of Ultimovacs ASA

Oslo, 16 February 2022

Jónas Einarsson Chairman of the Board

(Sign.)

(Sign.)

Kari Grønås Board member

(Sign.)

Ketil Fjerdingen Board member

(Sign.)

Aitana Peire Board member

Henrik Schüssler

Board member

(Sign.)

Haakon Stenrød Board member

(Sign.)

Eva S. Dugstad Board member

(Sign.)

Leiv Askvig Board member

(Sign.)

(Sign.)

Carlos de Sousa CEO

Ultimovacs

#### Interim condensed consolidated statement of comprehensive income

NOK (000) Unaudited	Note	Q4-21	Q4-20	FY21	FY20
Other operating income		-	-	-	-
Total revenues		-	-	-	-
Payroll and payroll related expenses	3, 5	11 885	14 662	61 916	50 989
Depreciation and amortization		623	743	2 703	2 720
Other operating expenses	4, 5	38 422	10 184	99 213	70 438
Total operating expenses		50 930	25 588	163 832	124 146
Operating profit (loss)		(50 930)	(25 588)	(163 832)	(124 146)
Financial income		5 188	1 243	13 383	5 209
Financial expenses		5 410	236	14 272	1 616
Net financial items		(222)	1 007	(890)	3 594
Profit (loss) before tax		(51 152)	(24 582)	(164 722)	(120 552)
Income tax		-	-	-	-
Profit (loss) for the period		(51 152)	(24 582)	(164 722)	(120 552)
Other comprehensive income (loss) - Currency translation		(1 426)	491	(3 953)	4 590
Total comprehensive income (loss) for the period		(52 578)	(24 090)	(168 676)	(115 962)
Diluted and undiluted earnings/(loss) pr share (NOK)	6	(1.5)	(0.8)	(5.1)	(4.0)

#### Interim condensed consolidated statement of financial position

NOK (000) Unaudited	Note	31 Dec 2021	31 Dec 2020
ASSETS			
Goodwill		11 031	11 795
Licenses		53 549	57 258
Patents		6 539	7 293
Property, plant and equipment		212	377
Right to use asset	11	1 951	3 630
Total non-current assets		73 282	80 354
Receivables and prepayments	7	8 087	8 438
Bank deposits		574 168	440 925
Current assets		582 255	449 363
TOTAL ASSETS		655 537	529 717

EQUITY			
Share capital		3 422	3 197
Share premium		1 070 841	809 214
Total paid-in equity		1 074 264	812 411
Accumulated losses		(504 321)	(339 599)
Other equity		20 358	8 762
Translation differences		2 853	6 806
TOTAL EQUITY	6, 9	593 152	488 380
LIABILITIES			
Lease liability	11	457	2 075
Deferred tax		11 031	11 795
Non-current liabilities		11 488	13 870
Accounts payable		22 555	8 611
Lease liability	11	1 628	1 707
Other current liabilities		26 714	17 149
Current liabilities	8	50 897	27 467
TOTAL LIABILITIES		62 384	41 337
TOTAL EQUITY AND LIABILITIES		655 537	529 717

#### Interim condensed consolidated statement of changes in equity

NOK (000) Unaudited	Share Capital	Share Premium	Accum. Iosses	Other equity	Transl. differenc.	Total equity
Balance at 1 Jan 2020	2 786	656 692	(219 047)	1 985	2 216	444 633
Loss for the period	-	-	(120 552)	-	-	(120 552)
Issue of ordinary shares	411	159 589	-	-	-	160 000
Share issue costs	-	(7 067)	-	-	-	(7 067)
Recognition of share-based payments	-	-	-	6 777	-	6 777
Translation differences	-	-	-	-	4 590	4 590
Balance at 31 Dec 2020	3 197	809 214	(339 599)	8 762	6 806	488 380
Balance at 1 Jan 2021	3 197	809 214	(339 599)	8 762	6 806	488 380
Loss for the period	-	-	(164 722)	-	-	(164 722)
Issue of ordinary shares	225	272 640	-	-	-	272 864
Share issue costs	-	(11 012)	-	-	-	(11 012)
Recognition of share-based payments	-	-	-	11 595	-	11 595
Translation differences	-	-	-	-	(3 953)	(3 953)
Balance at 31 Dec 2021	3 422	1 070 841	(504 321)	20 358	2 853	593 152

#### Interim condensed consolidated statement of cash flow

NOK (000) Unaudited	Q4-21	Q4-20	FY21	FY20
Loss before tax	(51 152)	(24 582)	(164 722)	(120 552)
Non-cash adjustments				
Depreciation and amortization	623	743	2 703	2 720
Interest received incl. investing activities	(1 312)	(1 120)	(3 062)	(4 545)
Net foreign exchange differences	1 451	92	3 619	747
Other finance expense	35	57	179	236
Share option expenses	3 014	2 169	11 595	6 777
Working capital adjustments:				
Changes in prepayments and other receivables	(6 499)	1 362	351	(433)
Changes in payables and other current liabilities	19 980	8 187	23 509	6 828
Net cash flow from operating activities	(33 859)	(13 092)	(125 828)	(108 223)
Purchase of property, plant and equipment	(85)	(65)	(85)	(282)
Patent milestone payment	-	-	-	(5 000)
Interest received	1 312	1 120	3 062	4 545
Net cash flow used in investing activities	1 227	1 055	2 977	(736)
Proceeds from issuance of equity	271 935	-	272 864	160 000
Share issue cost	(11 012)	-	(11 012)	(7 067)
Interest paid	-	-	-	-
Payment of lease liability	(434)	(488)	(1 895)	(1 916)
Net cash flow from financing activities	260 489	(488)	259 957	151 017
Net change in cash and cash equivalents	227 856	(12 524)	137 106	42 058
Effect of change in exchange rate	(1 493)	(73)	(3 863)	(739)
Cash and cash equivalents at beginning of period	347 804	453 523	440 925	399 607
Cash and cash equivalents at end of period	574 168	440 925	574 168	440 925



## Notes

#### **1.** General information

Ultimovacs ASA (the Company or Ultimovacs) and its subsidiary (together the Group) is a pharmaceutical Group developing novel immunotherapies against cancer. The Company is a public limited liability company listed on the Oslo Stock Exchange in Norway.

Ultimovacs is headquartered at the Oslo Cancer Cluster Innovation Park in Oslo, Norway, and is an active member of Oslo Cancer Cluster.

#### 2. Basis for preparations and accounting principles

The Group's presentation currency is NOK (Norwegian kroner).

These interim condensed financial statements have been prepared in accordance with IAS 34 Interim Financial Reporting. The accounting policies applied in the preparation of these financial statements are consistent with those followed in connection with the Company's 2020 financial statements. These condensed interim financial statements should therefore be read in conjunction with the 2020 financial statements.

The Group uses derivative financial instruments to hedge its risks associated with foreign exchange rates. Derivatives are initially and subsequently measured at fair value. Derivatives are carried as assets when the fair value is positive and as liabilities when the fair value is negative. The gain/(loss) arising from changes in fair value of currency derivatives is presented as part of "Financial income/expenses" in the consolidated statement of comprehensive income.

The Group does not have any derivatives that are used for hedge accounting.

The consolidated financial statements comprise the financial statements of the Ultimovacs ASA and its 100% owned subsidiary Ultimovacs AB as at the reporting date.

These interim financial statements were approved for issue by the Board of Directors on 16 February 2022. The figures in the statements have not been audited.



#### 3. Personnel expenses

#### **Personnel expenses**

NOK (000)	Q4-21	Q4-20	FY21	FY20
Salaries	10 097	8 198	34 543	34 612
Social security tax	1 756	1 640	6 686	5 179
Social security tax related to options	(4 445)	2 901	8 557	4 121
Pension expenses	821	429	2 690	2 020
Share-based compensation	3 014	2 169	11 595	6 777
Other personnel expenses	196	131	318	430
Government grants	447	(807)	(2 472)	(2 150)
Total personnel expenses	11 885	14 662	61 916	50 989
Number of FTEs at end of period	24	19	24	19

Please refer to note 10 for additional information regarding the share-based payments.

#### 4. Operating expenses

The Group is in a development phase, and the majority of the Group's costs are related to R&D. These costs are expensed in the statement of comprehensive income.

#### **Operating expenses**

NOK (000)	Q4-21	Q4-20	FY21	FY20
External R&D expenses	40 533	12 312	96 735	64 660
Clinical studies	28 460	8 114	56 675	47 680
Manufacturing costs	7 218	(226)	21455	5710
Other R&D expenses	4 855	4 424	18 605	11270
IP expenses	1 027	1 359	3 540	2 949
Rent, office and infrastructure	903	837	3 645	2 786
Accounting, audit, legal, consulting	1 306	1 430	5 061	3 978
Other operating expenses	675	380	2 338	2 802
Government grants	(6 022)	(6 134)	(12 106)	(6 738)
Total other operating expenses	38 422	10 184	99 213	70 438



#### 5. Government grants

The following government grants have been received and recognized in the statement of profit and loss as a reduction of operating expenses and personnel costs.

#### **Government grants**

NOK (000)	Q4-21	Q4-20	FY21	FY20
Skattefunn from the Research Council of Norw ay (RCN)	4 750	4 750	4 750	4 750
Eurostars	262	450	786	2 015
Innovation Norw ay	-	-	3 000	-
Innovation Project grant from the RCN	296	-	5 241	1 383
Other grants	267	1 741	802	739
Total government grants	5 576	6 941	14 578	8 888

Please refer to note 3 and 4 for information on how the government grants have been attributed to (i.e., deducted from) personnel expenses and other operating expenses.

#### 6. Earnings per share

The basic earnings per share are calculated as the ratio of the profit for the year divided by the weighted average number of ordinary shares outstanding.

#### Earnings per share

NOK (000)	Q4-21	Q4-20	FY21	FY20
Loss for the period	(51 152)	(24 582)	(164 722)	(120 552)
Average number of shares during the period ('000)	33 502	31 974	32 373	30 260
Earnings/loss per share (NOK)	(1.5)	(0.8)	(5.1)	(4.0)

The share options issued to employees as a part of the employee incentive program have a potential dilutive effect on earnings per share. No dilutive effect has been recognized as potential ordinary shares only shall be treated as dilutive if their conversion to ordinary shares would decrease earnings per share or increase loss per share from continuing operations. As the Group is currently loss-making, an increase in the average number of shares would have anti-dilutive effects. Diluted and basic (undiluted) earnings per share is therefore the same.

Please see note 10 for more information regarding the option program.



#### 7. Current assets

#### **Receivables and prepayments**

	31 Dec	31 Dec
NOK (000)	2021	2020
Government grants	5 314	6 941
Prepayments	878	748
Financial instruments	759	-
Other receivables	1 135	749
Total receivables and prepayments	8 087	8 438

#### 8. Current liabilities

#### **Current liabilities**

	31 Dec	31 Dec
NOK (000)	2021	2020
Accounts payable	22 555	8 611
Public duties payable	2 506	2 922
Public duties payable related to options	12 888	4 332
Lease liability	1 628	1 707
Other current liabilities	11 320	9 896
Total current liabilities	50 897	27 467



#### 9. Shareholder information

The share capital as of 31 December 2021 was NOK 3,422,176.1, with 34,221,761 ordinary shares, all with equal voting rights and a nominal value of NOK 0.10 per share. Ultimovacs ASA has approximately 5,000 shareholders as of 31 December 2021 and the 20 largest shareholders as of this date are listed below:

#### Share register as per 31 Dec 2021

Sharahaldar		
Sharenoluer	# of shares	Share-%
Gjelsten Holding AS	6 495 866	19.0 %
Canica AS	2 705 957	7.9 %
Watrium AS	1 780 575	5.2 %
Inven2 AS	1 555 492	4.5 %
Radiumhospitalets Forskningsstiftelse	1 506 913	4.4 %
Folketrygdfondet	1 400 000	4.1 %
Langøya Invest AS	1 389 006	4.1 %
Helene Sundt AS	965 802	2.8 %
CGS Holding AS	882 132	2.6 %
Sundt AS	803 321	2.3 %
Danske Invest Norge Vekst	736 440	2.2 %
Stavanger Forvaltning AS	596 999	1.7 %
Prieta AS	533 988	1.6 %
Verdipapirfondet Nordea Avkastning	483 573	1.4 %
JPMorgan Chase Bank, N.A., London	402 495	1.2 %
Verdipapirfondet KLP Aksjenorge	348 416	1.0 %
SEB Prime Solutions Sissener Canopus	324 000	0.9 %
Verdipapirfondet Nordea Kapital	282 549	0.8 %
Avanza Bank AB	274 520	0.8 %
Swedbank AB	258 629	0.8 %
20 Largest shareholders	23 726 673	69.3%
Other shareholders	10 495 088	30.7%
Total	34 221 761	100.0%

#### 10. Share-based payments

#### Share option program

A share option program was introduced in June 2019 and the Board was at the ordinary General Assembly held on 15 April 2021 authorized to increase the Company's share capital in connection with the share incentive arrangement by up to NOK 320,032.60 until the next ordinary General Assembly in 2022.

The share option program is groupwide and includes all employees in the Group. After the distribution of 600,000 new options in 2021, a total of 1,833,585 share options are outstanding as per 31 December 2021 (net of exercised and lapsed options), corresponding to 5.36% of the outstanding number of shares in the Company.



Each option gives the right to acquire one share in the Company and is granted without consideration. Pursuant to the vesting schedule, 25% of the options will vest one year after the day of grant, 25% of the options will vest two years after the day of grant and the remaining 50% will vest three years after the day of grant. The options granted in 2020 to the CEO, Carlos de Sousa, will vest with 33.33% one year following the grant date, 33.33% after two years, and the remaining 33.34% on the third anniversary following the grant date. Vesting is dependent on the option holder still being employed in the Company.

The exercise price for all options granted in 2019 was NOK 31.25, NOK 39.15 for the options granted in 2020 and NOK 61.99 for the options granted in 2021.

Options that are not exercised within 5 years from the date of grant will lapse and become void.

#### Number of options outstanding to Management Team

Name	Position	Number of options
Carlos de Sousa	Chief Executive Officer	416 035
Hans Vassgård Eid	Chief Financial Officer	177 500
Jens Egil Torbjørn Bjørheim	Chief Medical Officer	168 000
Audun Tornes	Chief Technology Officer	107 500
Gudrun Trøite	Head of Project Coordination	107 500
Ingunn Hagen Westgaard	Head of Research	107 500
Øivind Foss	Head of Clinical Operations	107 500
Ton Berkien	Chief Business Officer	59 000

The Ultimovacs Employee Share Options' fair value is calculated according to the IFRS-2 regulations. As stated in IFRS-2 Appendix B §B5, the Black-Scholes-Merton Option Pricing Model ("B&S Model") may be used to estimate the fair value of employee share options, which is therefore used to estimate the fair value of the Ultimovacs Employee Share Options. The model uses the following parameters: the exercise price, the current price of the underlying shares, the life of the option, the expected volatility of the share price, the dividends expected on the shares, and the risk-free interest rate for the life of the option.

Equity-settled share-based payments are measured at the fair value of the equity instruments at the grant date. For equity-settled share-based payment transactions, the liability needs to be remeasured at the end of each reporting period up to the date of settlement, with any changes in fair value recognized in the profit or loss with a corresponding adjustment to equity. This requires a reassessment of the estimates used at the end of each reporting period.

#### Movement of share options

		Weighted
	Number of	average
	share options	strike price
Outstanding at closing balance 31 Dec 2020	1 330 435	36.16
Granted	600 000	61.99
Exercised	88 250	32.46
Forfeited	8 600	39.15
Outstanding at closing balance 31 Dec 2021	1 833 585	44.77
Vested at closing balance	419 328	35.42



On 5 March 2021, 29,750 options, granted under Ultimovacs' option program, were exercised at a strike price of NOK 31.25 per share, and 8,600 options were forfeited in May 2021.

On the basis of the approval by the General Meeting on 15 April 2021, the Board of Directors resolved to issue a total of 600,000 options distributed amongst the employees. The number of options granted corresponded to 1.87% of the outstanding number of shares in the Company.

On 12 October 2021, 58,500 options, granted under Ultimovacs' option program, were exercised at a strike price of NOK 31.25 per share for 45,000 shares, and a strike price of NOK 39.15 for 13,500 shares. Subsequently, the Company's share capital was increased by NOK 5,850 on 15 October by issuing 58,500 new shares, each share of par value NOK 0.10. Following this option exercise, the total number of outstanding options is 1,833,585.

The total IFRS cost recognized for the option program in Q4-21 is MNOK 3.0, and the social security accruals related to the options is MNOK -4.4. Total IFRS costs in FY21 is MNOK 11.6, and MNOK 8.6 in social security accruals.

#### **11.** IFRS 16 – rental contracts

The Group implemented IFRS 16 in 2019 with the modified retrospective approach. The most significant agreement classified as operating lease is the rental agreement for office premises in Oslo with 3 years left in the rental contract as of 1 January 2020. In addition, there are five car-leasing contracts also classified as operating leases. With the transition to IFRS 16, the Group has recognized these contracts as a right-of-use assets of MNOK 4.6, and lease liabilities of MNOK 4.6 as of 1 January 2019. The weighted average discount applied on 1 January 2019 was 6.0%. Please see the 2020 Annual report for more information.

#### **12.** Events after the balance sheet date

No other events with significant accounting effect have occurred after the balance sheet date.



# Glossary

Words/terms	Description
General/basic terms	
UV1	UV1 is Ultimovacs' synthetic peptide vaccine
Peptides	Peptides are short or long-chains of amino acids, and amino acids are the
	building blocks of protein.
Adjuvant	A medical substance used to enhance the effect of another medical
	substance.
GM-CSF	"Granulocyte-macrophage colony-stimulating factor". Ultimovacs uses GM-
	CSF as adjuvant together with UV1 to strengthen the ability of UV1 to
	stimulate the immune system.
Immune checkpoint	Medicines that "takes the brakes off the immune system". The immune
inhibitors	system has brakes necessary to balance a normal immune response. The
	downside to these brakes is that it makes it easier for a tumor to grow because
	the immune system becomes less able to fight the tumor. By "blocking the
	brakes", the immune system becomes more potent in killing tumor cells. PD-
	1 / PDL-1 inhibitors (e.g., pembrolizumab and nivolumab) and CTLA-4
	inhibitors (e.g. ipilimumab). There are many others in development.
Immune response	The activity of the immune system against foreign substances (antigens).
	The United States Feed and Drug Administration's Investigational New Drug
	(ND) program is the means by which a pharmacoutical company obtains
	(IND) program is the means by which a pharmaceutical company obtains
	across state lines (usually to clinical investigators) before a marketing
	application for the drug has been approved. Similar procedures are followed
	in the European Union, Japan, and Canada
CTLA-4	A protein found on T cells (a type of immune cell) that helps balancing a
	normal immune response. The balance is needed to avoid collateral damage
	of normal cells. When CTLA-4 is bound to another protein called B7, it helps
	keep T cells from multiplying and killing other cells, including cancer cells.
	Ipilimumab works by making it difficult for the CTLA-4 to bind to B7.
	Ipilimumab was the first checkpoint inhibitor to reach the market.
PARP Inhibitor	PARP inhibitors are a group of pharmacological inhibitors of the enzyme poly
	ADP ribose polymerase. They are developed for multiple indications, including
	the treatment of heritable cancers. Several forms of cancer are more
	dependent on PARP than regular cells, making PARP an attractive target for
	cancer therapy.
PD-1 / PD-L1	A protein found on T cells (a type of immune cell) that helps balancing a
	normal immune response. The balance is needed to avoid collateral damage
	of normal cells. When PD-1 is bound to another protein called PD-L1, it helps
	keep T cells from killing other cells, including cancer cells. Some anticancer
	drugs, called immune checkpoint inhibitors, are used to block PD-1 or PD-L1.
	When this checkpoint is blocked, the "brakes" on the immune system are
	released and the ability of T cells to kill cancer cells is increased.
Telomere	To prevent the loss of genes as chromosome ends wear down, the tips of
	eukaryotic chromosomes have specialized DNA "caps" called telomeres.

Telomerase	Some cells have the ability to reverse telomere shortening by expressing telomerase (hTERT), an enzyme that extends the telomeres of chromosomes. Telomerase is expressed at a high level in over 80% of human tumors. UV1 uses telomerase (hTERT) as an immune therapy target.
Tetanus	Tetanus (Norwegian: "Stivkrampe") is a serious illness contracted through exposure to the spores of the bacterium, Clostridium tetani, which live in soil, saliva, dust, and manure. The bacteria can enter the body through deep cuts, wounds or burns affecting the nervous system. The infection leads to painful muscle contractions, particularly of the jaw and neck muscle, and is commonly known as "lockjaw". Tetanus vaccination protects against the disease.
Checkpoint and PARP inhibitors	
Ipilimumab	CTLA-4 checkpoint inhibitor from BMS (Bristol-Myers Squibb)
Nivolumab	PD-1 checkpoint inhibitor from BMS (Bristol-Myers Squibb)
Pembrolizumab	PD-1 checkpoint inhibitor from Merck
Durvalumab	PD-L1 checkpoint inhibitor from AstraZeneca
Olaparib	PARP inhibitor from AstraZeneca
Clinical trial terms	
CR	Complete response (The disappearance of all signs of cancer in response to treatment. Also called complete remission.)
PR	Partial response (A decrease in the size of a tumor, or in the extent of cancer in the body, in response to treatment. Also called partial remission.)
SD	Stable disease (Cancer that is neither decreasing nor increasing in extent or severity.)
PD	Progressive disease (Cancer that is growing, spreading, or getting worse.)
ORR	Objective response rate = CR + PR
DOR	Duration of response (The length of time that a tumor continues to respond to treatment without the cancer growing or spreading.)
OS	Overall survival (The length of time from either the date of diagnosis or the start of treatment for a disease, such as cancer, that patients diagnosed with the disease are still alive. In a clinical trial, measuring the overall survival is one way to see how well a new treatment works.)
PFS	Progression-free survival (The length of time during and after the treatment of a disease, such as cancer, that a patient lives with the disease but it does not get worse. In a clinical trial, measuring the progression-free survival is one way to see how well a new treatment works.)
mPFS	Median overall survival means (The length of time during and after the treatment of a disease, such as cancer, that half of the patients in a group of patients diagnosed with the disease are still alive.)
Medical terms	
Intradermal	In order to initiate an immune response, a vaccine must be taken up by antigen presenting cells (dendritic cells). UV1 is administered via the intradermal route, i.e., injection in the dermis, one of the layers of the skin. This layer, underneath the epidermis, is highly vascularized and contains a large number of immune cells, mainly dermal dendritic cells.
Biopsy	A piece of tissue, normal or pathological removed from the body for the purpose of examination.



IgE	Immunoglobulin E (IgE) are antibodies produced by the immune system.
	With an allergy, the individual's immune system overreacts to an
	allergen (what they are allergic to) by producing IgE. These antibodies
	travel to cells that release chemicals, causing an allergic reaction when
	an allergen enters the body.
Metastasis /	The development of malignant growths at a distance from a primary site
Metastatic cancer	of cancer / Metastatic cancer is cancer that spreads from its site of origin
	to another part of the body.
SAE	A serious adverse event (SAE) in human drug trials is defined as any
	untoward medical occurrence that at any dose
	1. results in death,
	2. is life-threatening
	3. requires inpatient hospitalization or causes prolongation of
	existing nospitalization
	4. results in persistent or significant disability/incapacity
	5. Is a congenital anomaly/birth detect, or
	6. requires intervention to prevent permanent impairment or
	damage.
	The term "life-threatening" in the definition of "serious" refers to an
	event in which the patient was at risk of death at the time of the event:
	it does not refer to an event which hypothetically might have caused
	death if it were more severe. Adverse events are further defined as "Any
	untoward medical occurrence in a national or clinical investigation
	subject administered a pharmaceutical product and which does not
	necessarily have to have a causal relationship with this treatment "
DSA	Prostate-specific antigen (PSA) is an enzyme (protein) important for
	roproduction DCA is procept in small quantities in the sorum of man with
	healthy prostates but is often alguated in the presence of prestate
	nearing prostates but is often elevated in the presence of prostate
	cancer or other prostate disorders.



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## **About Ultimovacs**

Ultimovacs was established in 2011 and is a public limited liability company listed on the Oslo Stock Exchange in Norway. The Company and its proprietary technology is based on preclinical and clinical research on immunotherapies conducted at the Oslo University Hospital. Ultimovacs is headquartered at the Oslo Cancer Cluster Innovation Park in Oslo, Norway, and also has an office in Uppsala, Sweden. Ultimovacs is an active member of Oslo Cancer Cluster.

Ultimovacs is developing immune-stimulatory vaccines to treat a broad range of cancers. Ultimovacs' lead universal cancer vaccine candidate UV1 targets human telomerase (hTERT), present in 85-90% of cancers in all stages of tumor growth. By directing the immune system to hTERT antigens, UV1 drives CD4 helper T cells to the tumor to activate an immune system cascade and increase antitumor responses. With a broad Phase II program, Ultimovacs aims to clinically demonstrate UV1's impact in multiple cancer types in combination with other immunotherapies. Ultimovacs' second technology approach, based on the proprietary Tetanus-Epitope-Targeting (TET) platform, combines tumor-specific peptides and adjuvant in the same molecule and entered Phase I studies in 2021.

