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GA 101003666 **Start date: 01/04/20** **End Date: 31/03/22**	
Project Title	OPENCORONA
WP number, deliverable number, and Title	WP8 D8.3 Interim Activity Report
Responsible partner name and contact	Partner number: 1 Organisation: Karolinska Institutet Name: Gustaf Ahlén Email: gustaf.ahlen@ki.se
Nature R-Report P-Prototype D-Demonstrator O=-Other	R: Report
Dissemination level **PU**-public **PP**-restricted to otherprogramme participants RE-restricted to a group of partners **CO**-only for consortium members	Public
Delivery Month Planned	M6 – 30 September 2020
Actual delivery date (dd/mm/yy)	11 December 2020

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Description of deliverable

- **COMPLETED**

- As part of the Interim Activity Report we have montored the status of tasks, deliverables, milestones, risks and financial status of the OPENCORONA project first 6 months.

- **ANNEXES**

- Interim Activity Report for the OPENCORONA project.

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Interim activity report OPENCORONA

Project Acronym:	OPENCORONA
Grant Agreement No:	101003666
Project Duration:	1 April 2020 – 31 March 2022
Responsible Partner:	Karolinska Institutet Name: Matti Sällberg E-mail: matti.sallberg@ki.se
Document version	
Version 1.4	Interim report (1 April 2020 – 30 September 2020)

Document History			
Version	Date	Author	Description
1.0	12 nov 2020	Gustaf Ahlén	WP2-7
1.1	13 nov 2020	Hanna Gador	WP8 and Annex 1
1.2	18 nov 2020	Matti Sällberg / Gustaf Ahlén	WP1
1.3	10 Dec 2020	Matti Sällberg/Hanna Gador	Cleaning and finalization of Annex 1-3.
1.4	11 Dec 2020	Matti Sällberg/ Hanna Gador/ Gustaf Ahlen	Final adjustments WP9

Contents

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Summary for publication

Out of a total of 12 different vaccine candidates, studies by KI, JLU, FoHM and Adlego have identified one construct as the most promising candidate with strong antibody and T cell responses as determined in mice, rabbits and ferrets and an optimized version of this gene, termed OC-007, has been forwarded for clinical evaluation. The selected candidate consists of the receptor binding domain (RBD) of Spike protein, the N and M proteins. This vaccine candidate induces a broad immune response with both potent neutralizing antibodies and T cell responses. In vitro data support a safety profile with no detrimental cytokines or suppression of beneficial innate immune responses. To evaluate the efficacy of the vaccine several different animal models are being established within the project and studies in these models are currently ongoing. IGEA has developed a new combined injection and electroporation handle device that has received CE approval. This device will be evaluated in pre-clinical studies including the toxicological evaluation. In October the selected vaccine candidate was delivered to Cobra that immediately started the HQ production of the vaccine to support the toxicological studies planned for Q1 2021. The consortium has had a scientific advisory meeting with the Swedish MPA with the purpose to establish the level of pre-clinical data required for providing a rationale for the chosen design of the DNA vaccine, and to provide data supporting safety. The OPENCORONA project expects to have completed all preclinical studies and file with the regulatory authorities during the first quarter of 2021, corresponding to the project month 10-12. This is actually well in line with the original proposal, but even a bit ahead of the plan.

Acronyms

OPENCORONA	Rapid therapy development through Open Coronavirus Vaccine Platform
GA	Grant Agreement No 101003666
WP	Work Package according to Grant agreement Annex 1
PSM	Project Steering Committee
PC	Project Coordinator
PMO	Project Management Office, the coordinators management team

Introduction

Delivery 8.3 Interim report for the OPENCORONA project activities during the first 6 months.
The Interim report is part of delivery 8.3 established according to the OPENCORONA project Grant Agreement no 101003666 in order to provide an update on the current status as well as highlighting the activities that have been started, completed, planned and evaluated for the first 6 months of the project. The report includes actions between the 1st of April to the last September 2020 and is to be considered as an interim report, not replacing the Period 1 reporting.

Explanation of the work and progress

Objectives and tasks

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WP1

Objectives:

The general objective of WP1 is to design vaccine DNA candidates and to test these in animal models to select the most immunogenic candidate to be forwarded to clinical development. The genes are also provided to WP2 for analysis of innate immune activation and WP3 for protection studies in the infectious mouse model.

Progress:

The vaccine candidates from Task (T) 1.1 have all been produced in house in quantities and of purity sufficient for immunization of rabbits and mice. Both two mouse strains have been used. The plasmids were also delivered to partner 2 JLU who in WP2 tested these for induction of innate responses. In T1.2 the candidates were found to induce strong T cell responses, in particular OC2 that contains the RBD, the M and the N protein. In T1.3 we found that no high levels neutralizing antibodies were induced by OC2 (or any other construct) whereby two modified genes were generated based on OC2, termed OC2.2 and OC2.3. Importantly, the OC2.3 construct was found to induce both T cells to the RBD, M and N proteins in the construct as well as high levels of antibodies to S and RBD that neutralized SARS-CoV-2 in vitro. The OC2.3 was therefore selected as the vaccine candidate and has been forwarded to Cobra Biologics for production according to GMP in WP5.

Challenge studies in animal models are ongoing or in the planning stage. Preliminary data from a first infection study show that the OC2 and OC12 (N) constructs induce T cell responses that can limit virus replication. This suggests that T cells alone can limit SARS-CoV-2 replication. This has not been shown before. We are now completing mouse and ferret studies for publication in a high impact journal. The final reports from the animal studies will be completed between January 2021 and the first week of February 2021.

Tasks; WP 1

WP leader: KI, Matti Sällberg

Duration from 1st April 2020 to 31st March 2022

Partners involved: FoHM, JLU, Adlego

Task 1.1: Vaccine design and synthesis of genes and reagents

Status: Completed

Work description and progress: Totally seventeen designed vaccine genes have now been synthetically generated by Genescript and delivered to us. All genes have been cloned into pVAX. In addition, several SARS-CoV-2 proteins RBD, Spike, M and N have been ordered and delivered. These reagents are being used in established methods including ELISA, ELISpot, Flow Cytometry, Western Blot and Transcription and translation assay.

Respective contribution of the partners: FoHM, JLU, Adlego – contribution in discussions related to design of vaccine candidates to induce immunogenicity perspectives for production.

Task 1.2: Evaluation of immunogenicity in wild-type and transgenic animals

Status: Ongoing

Work description and progress: The vaccine candidates from T1.1 have all been produced in house in quantities and of purity sufficient for immunization of rabbits and mice. Both C57BL/6 and BALB/c

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mice have been used. Of the original candidates, several were found to induce strong T cell response, in particular OC2 that contains the RBD, the M and the N protein. However, no detectable neutralizing antibodies were induced by OC2 whereby two modified genes were generated based on OC2, termed OC2.2 and OC2.3. The OC2.3 was found to induce both T cells to all proteins in the construct as well as high levels of antibodies to S and RBD that could neutralize SARS-CoV-2 in vitro. Challenge studies in animal models are ongoing or in the planning stage. Preliminary data from a first infection study show that the OC2 and OC12 (N) constructs induce T cell responses that can limit virus replication. This suggests that T cells alone can limit SARS-CoV-2 replication. This has not been shown before. The final reports from the animal studies will be completed between January 2021 and the first week of February 2021.

Respective contribution of the partners: FoHM – neutralization , JLU – innate immunity, IGEA – in vivo electroporation

Task 1.3: Evaluation of in vitro neutralization
Status: Ongoing
Work description and progress: Neutralizing assay for SARS-CoV2 established by FoHM. This assay has been validated and an S.O.P developed. The assay is used to measure neutralizing antibodies for samples produced in WP1.
Respective contribution of the partners: FoHM – established assay, KI & JLU – contribution to assay development

Task 1.4: Comparison of immunogenicity and selection criteria
Status: Ongoing and fulfilled
Work description and progress: The different vaccine candidates have been evaluated both in vitro and in vivo for expression and induction of immune responses.
The most promising vaccine candidate OC2.3 pass all selection criteria in mice i.e.
1) endpoint titers of specific antibodies (>1:10000).
2) high numbers of IFN-gamma producing specific T cells in ELISpot in mice (Cummulated >500 spot forming cells (SFCs)/million to one or more antigens).
3) induce neutralizing antibodies as determined by the 2019-nCoV micro titer in vitro neutralization assay (>1:10).
4) the candidate does not induce over activation of innate immunity.
Protection studies are still ongoing.
Respective contribution of the partners: JLU – evaluation of innate immunity, FoHM – neutralization assay, IGEA – in vivo electroporation technical support and electrodes

WP2

General objective:
The overarching objective of this WP is to ensure that the DNA vaccine candidates are not elicing detrimental cytokines or suppressing beneficial innate immune responses.

Specific objectives:
The specific objectives of this WP are to test the DNA vaccine candidates for their potential to:

- activate antiviral or pro-inflammatory innate immune responses
- inhibit innate immune responses

This has been completed for the first set of vaccine candidates

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In case the DNA vaccines encode any of these activities, we will identify and inactivate the responsible regions to optimize the DNA vaccines.
Potential IFN-suppressive activity on M (OC11 construct) detected, will attempt to identify and inactivate

- Primers, RT-qPCR assays, transfection protocols, control constructs, transfection protocols, and reporter assays were established and delivered (D 2.1)

Progress:
First set of vaccine candidates:

- RT-qPCR analyses of cytokine inductions (A549 cells) were performed
- Reporter assays for Toll-like receptors were performed

Results:

- slight activation of IFNs and ISGs
- very little cytokine activation
- inhibition of type I (but not type III) induction and signalling by OC-11 (M alone)
- Systems have been set up for TLRs 2,3,4,7,8,9
- No activation of any TLR, not even TLR4
    - ❖ No toxic cytokines or TLR activations detected
    - ❖ The IFN inhibitory action of M will be further investigated

Tasks; WP 2
WP leader: JLU, Friedemann Weber
Duration from 1st April 2020 to to 31st March 2022
Partners involved: JLU, KI, FoHM

Task 2.1: Activation of innate immune responses
Status: done for the first set of vaccine candidates
Work description and progress:

- Primers, RT-qPCR assays, transfection protocols, control constructs, transfection protocols, and reporter assays were established and delivered (D 2.1)
- RT-qPCR analyses of cytokine inductions (A549 cells) were performed
- Reporter assays for Toll-like receptors were performed

Respective contribution of the partners: Construction of plasmids, generation and delivery of tools, discussions: KI, FoHM, Assays: JLU

Task 2.2: Suppression of antiviral innate immune responses
Status: done for the first set of vaccine candidates, one such activity (though not very strong) detected on OC11 (M)
Work description and progress: included in assays of Task 2.1
Respective contribution of the partners: Construction of plasmids, generation and delivery of tools, discussions: KI, FoHM, Assays: JLU

WP3

Objectives:
To develop platform for screening of vaccine candidates

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Specific objectives:

1.Establish neutralization assay

2.Develop an infectious animal model

3.Investigate the protection of the vaccine candidate developed in WP1

Within the WP3, we have developed a neutralizing assay for SARS-CoV2. This assay has been validated and an S.O.P developed. We have used this assay to measure neutralizing antibodies for all samples produced in WP1. In addition, we have performed several animal experiments i) To set up an animal model for COVID-19 and ii) investigate the immune response for this animal model and also iii) develop a protocol for challenges studies after vaccination with different vaccine candidates.

Tasks; WP 3

WP leader: FoHM, Ali Mirazimi

Duration from 1st April 2020 to 31st March 2022

Partners involved: KI, JLU, IGEA and ALDEGO

Work description for whole WP 1st April 2020 to 30st September 2020:

We have mainly focused on developing and validating a neutralizing assay for measuring neutralizing Ab in vaccinated or infected animals within the OPENCORONA project. In addition, we have started to develop a reliable animal model for SARS-CoV2.

Task 3.1: Establish in vitro neutralization assay of 2019- nCoV

Status: On time

Work description and progress: We have developed an in vitro neutralization assay for determining and quantifying the neutralizing antibodies present in either vaccinated and/or infected animals. We have already developed a S.O.P for this assay. The assay has been validated by using SARS-CoV2 positive human samples. Furthermore, we are going to develop a state-of-the-art neutralizing antibodies assay by using human organoids, which will contribute to better understanding the protective immunity of SARS-CoV2

Respective contribution of the partners: FoHM and KI

Task 3.2: Establish an animal model for 2019-nCoV

Status: Ongoing, delayed

Work description and progress:

We have focused on three different animal models; i) Young and old immunocompetent BALB/C mice, ii) human ACE2 expressing mice, and iii) Ferret.

i) Young and old immunocompetent BALB/C mice: SARS CoV2 was propagated in VERO-E6 cells. Viral titers were determined using standard methods (Plaque assay). Young and Old BALC/Mice: 5 mice (10 weeks old) and 5 (7-8 months old) BALB/C mice were infected with SARS-COV2 i.n with 1000 or 100 000 infectious particles. The mice were sacrificed either at day 4 or day 14 post infection (see Below). Due to the procedure protocol for animal experiments at our biosafety level 4 (BSL-4) facility, we could not follow the surviving mice longer than 14 days post infection.

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All the samples from lungs were PCR negative. All there together demonstrated that we could not infect these mice. Most Probably either the volume used for intranasal infection were too low or these mice were not permissive to infection. We are planning to repeat this experiment with more volume of virus for i.n. infection

ii) hACE2 mice:
Due to the long delivery process of these mice, we have been delayed to perform this part of the tastk2.3, however, we have received these animals and started the experiments.

iii) Ferret (this model will be described later)

Respective contribution of the partners: FoHM, KI, Aldego

WP4

Objectives:

The main objective for WP4 is to establish a locked electroporation protocol for plasmid electrotransfer for the Cliniporator. To reach this goal, the pulse protocol effective in DNA delivery into the muscle tissue has to be tested. The pulse pattern locked into the software of the Cliniporator cannot be modified by the operator during the clinical trial.

Progress:

Currently, the effectiveness of EGT might be undermined by the low reproducibility of the procedure in use especially when injecting in deep tissue (such as muscle). The insertion of the electrode needles in the area of DNA injection might not be precisely centered thus limiting the efficiency of EGT.

IGEA has addressed this issue and identified a solution that can guarantee the positioning of the DNA in the centre of the electric field applied to the muscle tissue.

IGEA and KI considered which electric pulse protocols to be used for DNA vaccination. Based on literature review and on our previous experience, an electroporation (EP) pulse protocol composed of one short and intense electrical pulse (HV EP) and one long and less intense EP (LV EP) has been identified. Software upgrades to the Cliniporator have been investigated to be able to lock the pulse protocol. In collaboration with KI, the pulse protocol has been tested for efficacy in DNA vaccination settings and it is currently used in all the DNA vaccination experiments carried out within the OPENCORONA project.

IGEA has been working on the evaluation of a new one-step delivery procedure for DNA vaccination by means of electroporation. IGEA is designing a new device dedicated to DNA vaccination that will enable the injection of the DNA vaccine and the delivery of the electrical pulses within one simple and fast procedure. As today, several analyses aimed at identifying the technical solutions necessary for the realization of the new device have been performed and the first design of the one-step delivery device has been completed.

The expected results for WP4 are the following:

1. A Cliniporator device with the EP pulse protocol optimized for DNA vaccination locked in the software, so that it cannot be accidentally modified by the user during the clinical trial.
2. Documentation for EMA regarding both the Cliniporator and the electrodes to be included in the IB and IMPD.
3. Single step vaccination procedure: IGEA will develop a device dedicated to DNA vaccination that will enable the injection of the DNA vaccine and the delivery of the electrical pulses in one single step procedure. Based on the advancement of the CE certification, this device may or may not be

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used in the phase I clinical trial. To our knowledge, no such device for effective DNA vaccine delivery in humans has been CE marked.

The broader impact of WP4 is the development of an Electroporation technology that is extremely reliable and easy to adapt in different requirements:

1. The electroporation process induces a transient increase in cell membrane permeability, allowing the efficient delivery of nucleic acids, thus it can be successfully applied to deliver both DNA and RNA-based vaccines.
2. The device for the single step delivery procedure is currently designed for intramuscular injection, however with a simple revision of needle geometry, it can be easily converted to intradermal injection.
3. The Cliniporator with the locked EP pulse protocol will deliver the electric pulses optimized for the OC-007 vaccine, however the device is programmable and can be easily converted to deliver different electric pulse protocols optimized for other nucleic acid based-vaccines.

Tasks; WP 4

WP leader: IGEA, Matteo Cadossi

Duration from 1st April 2020 to to 31st March 2022

Partners involved: KI and Adlego

Task 4.1: Lock plasmid delivery pulse pattern for Cliniporator

Status: Ongoing

Work description and progress:

In order to choose the optimal combination of electrical pulses to achieve effective DNA transfer, extensive literature review has been performed. The application of electrical pulses to achieve ElectroGeneTransfer (EGT) has a dual role: in the first place, electrical pulses permeabilize transiently the cell membrane; then, they drive electrophoretically the DNA toward the electroporated cells. According to the literature, the combination of short (100 μs) and intense electrical pulses (HV EPs) and long (hundred(s) of milliseconds) and less intense EPs (LV EPs) constitutes a very safe procedure associated with a very good gene expression (Calvet CY. et al. Cancer Metastasis Rev 2016). Based on our previous experience on EGT in the human muscle tissue (Spanggaard I. et al. Human Gene Therapy Clin Dev 2013) and on DNA vaccination by prof. Matti Sallberg (Maravelia J. et al. Inf Disease 2020) an EP protocol composed of one HV and one LV pulse was chosen.

The electrical pulse protocol chosen is the following: 1 High-voltage pulse 600V/cm, 1ms length, 1s pause length, 1 Low-voltage pulse 60V/cm 400ms length. This pulse protocol has been tested for efficacy in DNA vaccination setting by KI and it is currently used in all the DNA vaccination experiments carried out by the partners of the OPENCORONA consortium. Cliniporator software upgrades allowing to lock the pulse protocol have been investigated.

Respective contribution of the partners:

KI tested the effectiveness of the EP protocol in DNA vaccination settings in different animal models.

Task 4.2: Writing documentation for regulatory authorities

Status: Ongoing

Work description and progress:

A Scientific Advice Meeting was held with EMA representatives to discuss the documentation to be included in the IB and IMPD.

Electro-gene-transfer (EGT) requires two medical devices: the electroporator (Cliniporator EPS02) to generate the electrical pulses and the electrodes to transfer the pulses to the target tissue.

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The electroporation device Cliniporator EPS02 that will be used in the clinical trial is a CE marked medical device with an intended use of electroporation of human tissue.
Regarding the electrode, IGEA foresees two different scenarios:

1) A two steps delivery with DNA injection by needle followed by insertion of electrodes and electroporation, using standard CE marked needle electrodes.
2) Evaluation of a new guide device optimized for DNA vaccination to allow the injection of the DNA vaccine and the delivery of the electrical pulse in one single step. The new device might not be CE marked by the time of the clinical study.
   Both scenarios have been discussed with the EMA representatives:

Scenario 1: CE certification and declaration of conformity for both the Cliniporator and the electrodes need to be provided. Also, technical and scientific explanation for the use of different electrodes between animal models and humans has to be submitted. Scientific rational based on electrical field distribution analysis and permeabilization threshold will be provided.
Scenario 2: a separate MPA application for the electrode is required. Preferably, the Medical Device application and the clinical trial application should be submitted in parallel, with a protocol compliant with both legislations. Also, the research person's information and informed consent shall be submitted and compliant with both legislations.
The information gathered during discussion with the EMA representative will allow us to thoroughly plan subsequent activities related to the development of the new device for the single step delivery procedures.

Respective contribution of the partners:
KI performed pre-clinical experiments to validate the effectiveness of the DNA delivery procedure by means of electroporation.

Task 4.3: Evaluation of single-step delivery of DNA and electroporation
Status: Ongoing
Work description and progress:
The activities of this task consist in the study and identification of the necessary technical solutions for the development of a device that enables injection of DNA and *in vivo* electroporation in a single step.
The single step delivery procedure has to be fast, intuitive and handful and must guarantee high reproducibility and reliability of vaccine delivery, regardless of the manual skills of the operator. The new device must integrate a system for the injection of the DNA and a system to deliver the electrical pulses into the target tissue. To allow effective DNA electrotransfer, the DNA injection has to be centered within the electrical field.
First of all, analysis and identification of design solutions and concepts for the realization of the new device have been performed. A technical analysis of the materials deemed most appropriate for the intended use (medical field) has been carried out. In particular, the material for the needles (AISI 304) and the materials in contact with the patient. The technical analysis is aimed at verifying biocompatibility, mechanical functionality and electrical performance.
Then number, diameter and length of the needle electrodes, geometry of the electrode and the electrode introduction system have been evaluated. In order to minimize pain related to needle insertion, electrodes with thin diameter have been selected (0.45 mm). Electrode length has been chosen based on the route of administration of the DNA vaccine (intramuscular): being the muscular

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tissue in the human forearm at least at 16 mm of depth from the skin, 30 mm electrode needles have been chosen. This needle length will cover for inter-individual variability.
The electrode geometry has been optimized to: 1) reduce the number of the needles (in order to minimize pain related to insertion); 2) guarantee a homogenous distribution of the electrical field; 3) provide a volume of electroporation sufficient to cover the volume of the injected DNA vaccine.
The number of needles has been reduced from the 8 needles configuration of the standard linear electrode produced by IGEA to either 2 or 4 needles. Modelling of the electric field distribution for different electrode configurations (2 or 4 needles) has been performed using COMSOL software (**Figure 1** and **2**). Figures 1 and 2 show the electrical field distribution of the 2 needles and 4 needles configuration, both geometries give rise to an homogenous distribution of the electrical field.

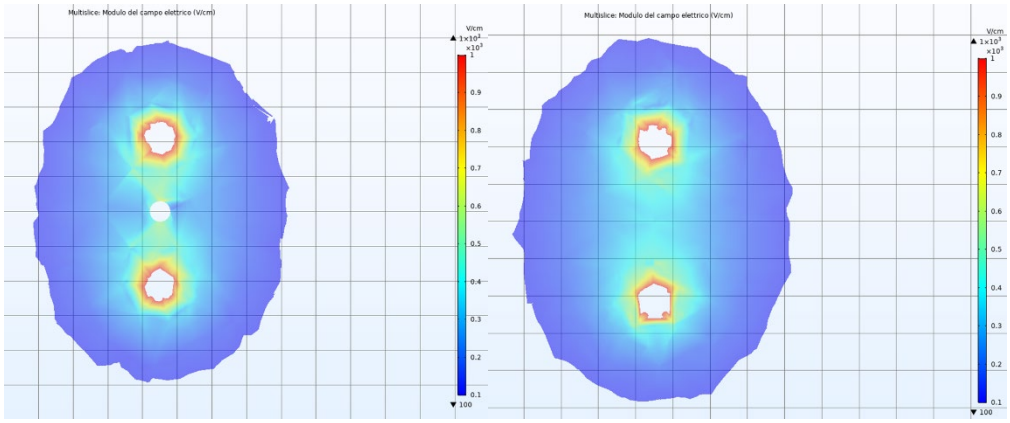

Figure 1. COMSOL modeling of the electric field distribution for the 2 needles electrode with (left panel) or without (right panel) the central needle for DNA electrotransfer.

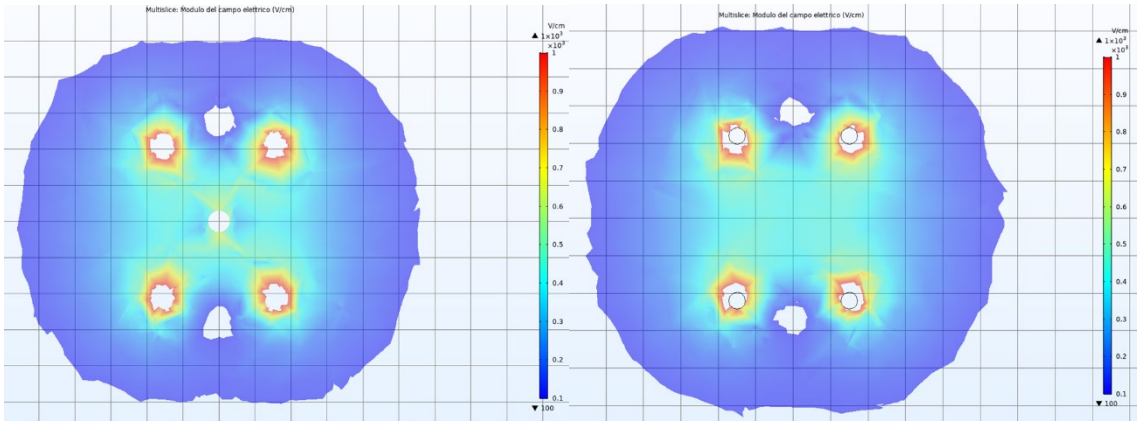

Figure 2. COMSOL modeling of the electric field distribution for the 4 needles electrode with (left panel) or without (right panel) the central needle for DNA electrotransfer.

The electroporation volume covered by the 4 needles configuration is sufficient to contain 1mL of DNA solution. The modeling results have been verified in the laboratory on experimental models (potatoes) for a qualitative and quantitative analysis of the electroporation volume.
As described above, the new guided device must also provide for the DNA injection system. The concept for the guided device foresees a site to accommodate the syringe containing the DNA vaccine. Based on the volume covered by the electroporation, a 1mL standard syringe was chosen. The needle characteristics for DNA injection has been set to 22G gauge based on standard needles characteristics for intramuscular vaccination.
The DNA needle length (40mm) was chosen based on the electroporation volume: to achieve effective DNA electrotransfer, the volume of the DNA solution needs to be confined within the

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volume covered by the electroporation. To this end, the tip of the DNA needle is foreseen to be position 5mm (± tolerance) backward from the tip of the electrodes.
To assess whether the DNA injection needle impacts on the distribution of the electrical field, COMSOL modeling has been performed. Results showed that the DNA injection needle significantly interferes with the electric field distribution (**Figure 2 and 3**), therefore a system to retract the DNA syringe after the injection and before the delivery of the electric pulses will be implemented in the design of the new guided device. Finally, conceptual usability analysis will be performed.

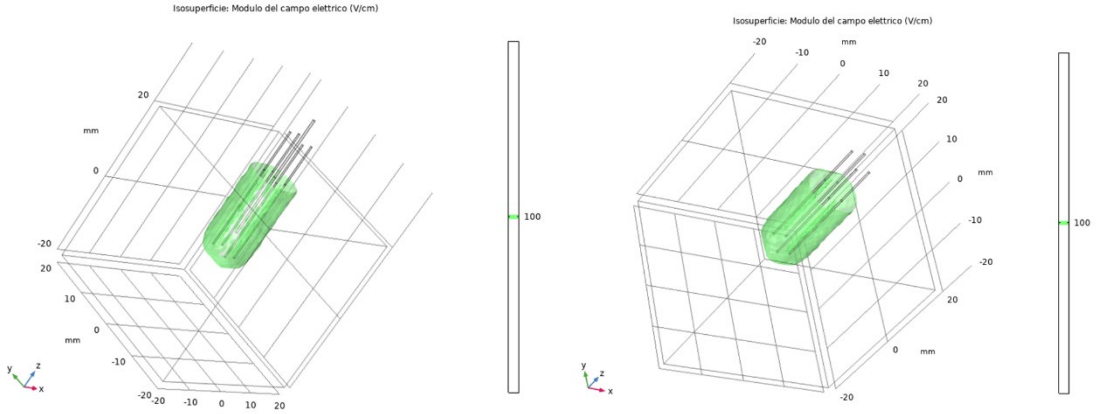

Figure 3. COMSOL 3D modeling of the electric field distribution in for the 4 needles electrode with (left panel) or without (right panel) the central needle for DNA electrotransfer.

So far, the activities of Task 4.3 led to the development of the first concept of the new guided device (**Figure 4**).

Figure 4. Concept of the new guided device for the single step delivery procedure.

Respective contribution of the partners:
KI will evaluate the effectiveness of new single step delivery procedures in experimental animal models.

WP5

Objectives:
The general objective of WP5 is to generate GMP material by performing activities such as pre-production evaluation, GMP Cell Bank generation, GMP plasmid bulk manufacture and QP certification. Prior to this a PCB and HQ DNA will be generated (during October-November) to support the upcoming toxicology studies, this work has been planned and managed as an internal project at Cobra during the time period reflected in this first report. No scientific results to report.

Tasks: WP 5
WP leader: Cobra, Ola Tuvesson

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Duration from 1st January 2021 to to 31st March 2022
Partners involved: KI

Task 5.1: Purchasing and reception of materials
Status: completed
Work description and progress:
152 items were purchased for the HQDNA production. The materials were registered and controlled against its specification according to Cobra's quality systems.
Respective contribution of the partners: Process Development and Purchasing/logistics resources were allocated for this task.

Task 5.2: Generate a Change Control for starting of activities
Status: completed
Work description and progress**:**
The project group has performed a risk assessment to justify the use of a HQDNA batch for stability and toxicology study. The risks were evaluated and accepted for the project. A report showing the main differences in the HQ and GMP- process is available in Cobra's quality system.
Respective contribution of the partners: QA group, Process Development (PD) and Safety, Health and Environmental (SHE) resources were involved in this task.

Task 5.3: Generate the Process Documents
Status: ongoing
Work description and progress:
The PD group has generated all documents necessary to perform the upcoming HQDNA production. These documentations include manufacturing specifications and batch records. These documents are used for the PCB, USP and DSP production. Approximately 70% of the work is completed.
Respective contribution of the partners: PD group was responsible for this task.

Task 5.4: Generate GMP-documents
Status: ongoing
Work description and progress:
The QC group at Cobra created the stability plan that will be used for the HQDNA batch. Additionally, the control directives and control reports for the analysis of the material were also written. A specified analytical package has been chosen and planned for the OpenCorona project and QC is currently preparing for this. Approximate 60% of the work is completed.
Respective contribution of the partners: QC group was designated for this task. QA performs the review of all documents since it is part of the GMP guideline.

WP6

Objectives:
The general objective of WP6 is to assess the immunogenicity and toxicity of the most immunogenic DNA vaccine, decided in WP2 and WP3, in an non-rodent animal model.

Progress:

A rabbit study has been performed and one challenge study in ferrets is being completed. The rabbit study was conducted with one of the first generated vaccine candidates to investigate

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immunogenicity of the SARS-CoV-2 N gene. This construct, OC12, was highly immunogenic as a DNA vaccine in mice and rabbits and strengthened the inclusion of the N gene in SARS-CoV-2 vaccine. This work was published in the Journal of Virology in July, 2020.

Tasks; WP 6
WP leader: Adlego, Urban Höglund
Duration from 1st April 2020 to 31st March 2022
Partners involved: Adlego, KI, JLU, FoHM, Karolinska

Task 6.1: Design of the GLP toxicity study
Status: Ongoing
Work description and progress:
An ongoing study in rabbits will determine the vaccine dose and injection volume. This study will be finalized in January and the results are needed to finalize the study plan for the toxicological study.

WP7

Objectives:
The purpose of WP 7 - Regulatory and Clinical Trial is to interact with regulatory authorities, compile all the documents required for the clinical trial, submit applications to relevant authorities and finally to conduct a phase I clinical trial with the OpenCorona DNA vaccine.

Karolinska has arranged a scientific advisory meeting with the Swedish MPA and received guidance related to the level of pre-clinical data required for a clinical trial with the OpenCorona DNA vaccine.

1. Interaction with regulatory authorities
2. Preparation of the IB and IMPD
3. Ethical application and application to EMA
4. Perform clinical trial
5. Data analysis and clinical study report writing – human study

Objective 1; Karolinska has arranged a scientific advisory meeting with the Swedish MPA with the purpose to establish the level of pre-clinical data required for providing a rationale for the chosen design of the DNA vaccine, and to provide data proving safety. The meeting also covered the production process and requirements for the specification of the OpenCorona DNA vaccine.

Tasks; WP 7
WP leader: Karolinska, Marie Westman
Duration from 1st January 2021 to 31st March 2022
Partners involved: All

Task 7.1: Regulatory and Clinical Trial
Status: Ongoing
1st Scientific advisory meeting regarding pre-clinical performed, 2nd scientific advisory meeting regarding clinical setup to be decided.

Work description and progress:

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Planning and executing a scientific advisory meeting including compilation of a briefing book and meeting minutes approved by the Swedish MPA. In general, the OpenCorona consortium's proposed pre-clinical setup was approved by the MPA. The production process was partly covered but further details remain to be elucidated at an additional meeting where also the clinical setup shall be proposed and discussed.

Respective contribution of the partners: Karolinska Institutet, IGEA SPA, Cobra Biopharma Matfors AB, ADLEGO BIOMEDICAL AB, STOCKHOLMS LÄNS LANDSTING contributed to the Briefing book and attended the scientific advisory meeting.

WP8

Objectives:

To manage all aspects of the OPENCORONA project, handle the ethical issues of the project, and handle dissemination.

To set up an effective management and governance framework for the OPENCORONA consortium, including the Independent Advisory Board (IAB) and the Ethics Board, ensuring the progress of the project towards its planned
objectives.

To act as the interface between the OPENCORONA consortium and the European Commission (EC).

To ensure that all actions are performed correctly and within the rules and regulations established by the EC and in the Consortium Agreement, including financial and legal management; and to ensure that the received funds are correctly distributed and accounted for.

To ensure the work and tasks are performed on time, within budget and to the highest quality standards.

To create an early warning and advisory system, also for Intellectual Property (IP), business and exploitation plans, as well as the sustainability strategy of the established cooperation.

To keep each partner, including the EC, fully informed about the project status, emerging issues, the work planning(adjustments) and all other aspects which are important and relevant in order to obtain maximum transparency and for achieving synergy in the cooperation.

Tasks; WP 8: Management ethics and dissemination
WP leader: Karolinska Institutet, Matti Sällberg
Duration from 1st April 2020 to 31st March 2022
Partners involved: All

Task 8.1 Contract and financial management

Status:

The Consortium Agreement has been signed by all partners. The management team has established contact with all partners' administrative focal persons. A “Management Handbook” has been distributed to all beneficiaries through the internal communication tool. The independent experts of the Independent Advisory Board have agreed to the assignments. The project Kick off took place between the 18-19th of April where the Management team took the opportunity to present on financial, administrative and legal matters. The presentations were attended to by both researchers and finance persons from the beneficiaries. In connection to the meeting the first Steering committee meeting was hosted. During this hecting start up face there has also been frequent Work package leader meetings

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to follow up tightly on the project development. As part of the Delivery 8.3 we have monitored the resources spent during the first 6 months of the project (Annex 1: Resources Monitoring Table)

Task 8.2 - Internal communication
Status:
Website, Consortium internal communication and sharing tool is up and running. Social media accounts have been established and are frequently used. During the first intense phase the communication has been intense and active between the partners. Data management plan has been established.

Task 8.3 - Periodic reporting
Status:
Templates have been proposed by KI for the collection and compilation of results and deliverables (activity reports), interim report and for monitoring.

Task 8.4 - Organisation of consortium meetings
Status:
We have organized the Kick off meeting that was held digitally due to the current situation . All partners presented on progress made and respective contributions, WP objectives, deliverables, milestones and possible hurdles/revised strategy for the forthcoming period was discussed. All participants were briefed by KI on the ethical, intellectual property and administrative aspects of the project. The meeting was hosted during 2 days where the media was invited to attend for half a day.

Task 8.5 - Project monitoring and risk management
Status:
Tools for risk management and a Risk Management handbook have been developed.

Task 8.6 - Project website, External communication and Dissemination
Status:
Website, and sharing tool is up and running. Social media accounts have been established and are frequently used. The first newsletter has been published on the website. Due to the big interest from the community as well as stakeholders we have had the opportunity to present the project and progress to a wide public. There has been medie interest at our kick off, for our daily laboratory work, interview's, news articles, tv shows. It took only two weeks before the project had a wikipedia page. Communication policy for external communication is being set up as a guideline for the project communication. The project, or project partners, have been presented almost on a weekly basis in Swedish media such as TV, newspapers, websites etc. In addition, the project has been presented also in Finnish, German, Russian, and Italian media.

The Opencorona project has so far generated one scientific publication.

Ahlén G, Frelin L, Nekoyan N, Weber F, Höglund U, Larsson O, Westman M, Tuvesson O, Gidlund EK, Cadossi M, Appelberg S, Mirazimi A, and Sallberg M. 2020. The SARS-CoV-2 N protein is a good component in a vaccine. J Virology 94(18):e01279-20.

Scientific Advisory Board

Two SAB members have been invited and accepted to join. Approved by the steering committee on November 2, 2020. Dr Heinz Feldmann at NIH, National Institute of Allergy and Infectious Diseases (NIAID) Hamilton, Montana USA and Professor Gregor Sersa at Institute of Oncology Ljubljana, Slovenia. Dr Feldmann is a world leading expert in developing vaccines for BSL-3 and BSL-4

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pathogens. He has helped in the animal testing of many of the COVID-19 vaccines in clinical development. Professor Sersa is a world leading expert in in vivo electroporation and has pioneered the use of in vivo electroporation for human therapy.

WP9

Objectives:
The objective of WP9 is to maintain an oversight on the preparations of the ethics requirement during animal studies, Phase 1 study, and laboratory work. The continued oversight and monitoring of the ethics will be performed in collaboration with an appointed ethics review board. An ethics review board is being organized.

Animals
Ethical approvals have been obtained for studies in mice, rabbits, and for challenge studies in immunized ferrets. These were approved by the local animal ethics committee prior to any experiment being initiated. The applications always consider the 3Rs.

Humans
The clinical trial has been planned and the ethical application will be prepared in early 2021.

Deliverables

A complete list of deliverables status is annexed.

Critical risks and mitigations

A complete list of critical risks and mitigation status is annexed.

Deviations

There have been delays in task 3.2, due to the long delivery process of hACE2 mice. The animals have now been received and the experiments are ongoing.

For Work Package 5 tasks planned for January 2021 has partly already been initiated

Annexes

1 Resources Monitoring Table M6

2 Deliverables Status Table M6

3 Critical risks and mitigations Table M6

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Annex 1

Resources Monitoring Table

PARTICIPANTS	UNIT (*PERSON MONTHS or EUROS*)	TYPE of EXPENDITURE	PLANNED	ACTUAL EXPENDITURE		Pct. Spent	REMAINING RESOURCES	SHORT DESCRIPTION and RELATED WP - Personnel, Travel, Equipment, Other goods and services
				Interim	Total	TOTAL		
			e	a1	e1	a1+b1+c1+ d1/e	e-e1	
Beneficiary 1	*PM*	Work Package 1	**12,00**	7,57	**7,57**	**63%**	**4,43**	M.S 0,78 PM, G.A 2,17 PM, J.Y, 2,26 PM, C.B 2,36 PM
KI	*PM*	Work Package 2	**2,00**		**0,00**	**0%**	**2,00**	
	PM	Work Package 3	**6,00**		**0,00**	**0%**	**6,00**	
	PM	Work Package 4	**2,00**		**0,00**	**0%**	**2,00**	
	PM	Work Package 5	**2,00**		**0,00**	**0%**	**2,00**	
	PM	Work Package 6	**2,00**		**0,00**	**0%**	**2,00**	
	PM	Work Package 7	**12,00**		**0,00**	**0%**		
	PM	Work Package 8	**12,00**	1,08	**1,08**	**9%**	**10,92**	M.S 0,17 PM and H.G 0,91 PM.
	PM	***Total***	**50,00**	**8,65**	**8,65**	**17%**	**41,35**	
	EUR	Personnel costs	**281 792,00**	44 584,23	**44 584,23**	**16%**	**237 207,77**	
	EUR	Subcontracting			**0,00**	**0%**	**0,00**	
		Other direct costs	**38 208,00**	99 926,38	**99 926,38**	**262%**		Laboratotory reagents, shipping costs and purchase of animals; Mice 5 621,55, Ferrets 67 561,93 and Macaques 26 063,75. WP1
	EUR	Travel			**0,00**	**0%**	**0,00**	
	EUR	Equipment			**0,00**	**0%**	**0,00**	
	EUR	Other goods and Services			**0,00**	**0%**	**0,00**	
	EUR	Indirect Costs	**80 000,00**	36 127,65	**36 127,65**	**45%**	**43 872,35**	
	EUR	**Total Costs**	**400 000,00**	**180 638,26**	**180 638,26**	**45%**	**219 361,74**	
	EUR	**Requested EU funding**	**400 000,00**		**0,00**	**0%**	**400 000,00**	
Beneficiary 2	*PM*	Work Package 1	**6,00**	1,00	**1,00**	**17%**	**5,00**	DNA vaccine design
JLU	*PM*	Work Package 2	**12,00**	1,00	**1,00**	**8%**	**11,00**	Innate immune responses to first set of DNA vaccines
	PM	Work Package 3	**2,00**		**0,00**	**0%**	**2,00**	
	PM	Work Package 4			**0,00**	**0%**	**0,00**	
	PM	Work Package 5			**0,00**	**0%**	**0,00**	
	PM	Work Package 6	**2,00**		**0,00**	**0%**	**2,00**	
	PM	Work Package 7	**2,00**		**0,00**	**0%**		
	PM	Work Package 8	**2,00**		**0,00**	**0%**	**2,00**	
	PM	***Total***	**26,00**	**2,00**	**2,00**	**8%**	**24,00**	
	EUR	Personnel costs	**156 000,00**	14 190,40	**14 190,40**	**9%**	**141 809,60**	R.S.G
	EUR	Subcontracting			**0,00**	**0%**	**0,00**	
		Other Direct costs	**4 000,00**	**7 987,69**	**7 987,69**	**200%**		
	EUR	Travel		0,00	**0,00**	**0%**	**0,00**	
	EUR	Equipment		0,00	**0,00**	**0%**	**0,00**	Laboratory supplies, € 6378,84
	EUR	Other goods and Services		0,00	**0,00**	**0%**	**0,00**	Publications, charges € 1608,85
	EUR	Indirect Costs	**40 000,00**	5 544,52	**5 544,52**	**14%**	**34 455,48**	
	EUR	**Total Costs**	**200 000,00**	**27 722,61**	**27 722,61**	**14%**	**172 277,39**	
	EUR	**Requested EU funding**	**200 000,00**		**0,00**	**0%**	**200 000,00**	

PARTICIPANTS	UNIT (*PERSON MONTHS or EUROS*)	TYPE of EXPENDITURE	PLANNED	ACTUAL EXPENDITURE		Pct. Spent	REMAINING RESOURCES	SHORT DESCRIPTION and RELATED WP - Personnel, Travel, Equipment, Other goods and services
				Interim	Total	TOTAL		
			e	a1	e1	a1+b1+c1+ d1/e	e-e1	
Beneficiary 3	*PM*	Work Package 1	**2,00**		**0,00**	**0%**	**2,00**	
FOHM	*PM*	Work Package 2	**2,00**		**0,00**	**0%**	**2,00**	
	PM	Work Package 3	**24,00**	11,29	**11,29**	**47%**	**12,71**	A.M, S.A, E.E, M.H.S.A
	PM	Work Package 4			**0,00**	**0%**	**0,00**	
	PM	Work Package 5			**0,00**	**0%**	**0,00**	
	PM	Work Package 6	**2,00**		**0,00**	**0%**	**2,00**	
	PM	Work Package 7	**6,00**		**0,00**	**0%**		
	PM	Work Package 8	**2,00**		**0,00**	**0%**	**2,00**	
	PM	***Total***	**38,00**	**11,29**	**11,29**	**30%**	**26,71**	
	EUR	Personnel costs	**228 445,00**	67 979,75	**67 979,75**	**30%**	**160 465,25**	
	EUR	Subcontracting			**0,00**	**0%**	**0,00**	
		Other direct costs			**0,00**	**0%**		
	EUR	Travel	**3 000,00**		**0,00**	**0%**	**3 000,00**	
	EUR	Equipment			**0,00**	**0%**	**0,00**	
	EUR	Other goods and Services	**88 555,00**	51 485,54	**51 485,54**	**58%**	**37 069,46**	WP3: Reagents 32235 EUR, Animals 5776 EUR, Freight 4326 EUR, Others 9149 EUR
	EUR	Indirect Costs	**80 000,00**	29 866,32	**29 866,32**	**37%**	**50 133,68**	
	EUR	**Total Costs**	**400 000,00**	**149 331,61**	**149 331,61**	**37%**	**250 668,39**	
	EUR	**Requested EU funding**	**400 000,00**		**0,00**	**0%**	**400 000,00**	
Beneficiary 4	*PM*	Work Package 1	**2,00**	1,17	**1,17**	**59%**	**0,83**	Vaccination
IGEA	*PM*	Work Package 2			**0,00**	**0%**	**0,00**	
	PM	Work Package 3	**2,00**	1,10	**1,10**	**55%**	**0,90**	Analysis of EP protocol performance
	PM	Work Package 4	**20,00**	4,61	**4,61**	**23%**	**15,39**	Electrical pulse protocol to be used for clinical trial. Concept for one- step EGT. Regulatory activities.
	PM	Work Package 5			**0,00**	**0%**	**0,00**	
	PM	Work Package 6			**0,00**	**0%**	**0,00**	
	PM	Work Package 7	**10,00**		**0,00**	**0%**		
	PM	Work Package 8	**2,00**		**0,00**	**0%**	**2,00**	
	PM	***Total***	**36,00**	**6,88**	**6,88**	**19%**	**29,12**	
	EUR	Personnel costs	**144 610,00**	31 718,00	**31 718,00**	**22%**	**112 892,00**	
	EUR	Subcontracting			**0,00**	**0%**	**0,00**	
		Other direct costs	**15 390,00**		**0,00**	**0%**		
	EUR	Travel			**0,00**	**0%**	**0,00**	
	EUR	Equipment			**0,00**	**0%**	**0,00**	
	EUR	Other goods and Services			**0,00**	**0%**	**0,00**	
	EUR	Indirect Costs	**40 000,00**	7 929,50	**7 929,50**	**20%**	**32 070,50**	
	EUR	**Total Costs**	**200 000,00**	**39 647,50**	**39 647,50**	**20%**	**160 352,50**	
	EUR	**Requested EU funding**	**200 000,00**		**0,00**	**0%**	**200 000,00**	

PARTICIPANTS	UNIT (*PERSON MONTHS or EUROS*)	TYPE of EXPENDITURE	PLANNED	ACTUAL EXPENDITURE		Pct. Spent	REMAINING RESOURCES	SHORT DESCRIPTION and RELATED WP - Personnel, Travel, Equipment, Other goods and services
				Interim	Total	TOTAL		
			e	a1	e1	a1+b1+c1+d1/e	e-e1	
Beneficiary 5	*PM*	Work Package 1			**0,00**	**0%**	**0,00**	
COBRA	*PM*	Work Package 2			**0,00**	**0%**	**0,00**	
	PM	Work Package 3			**0,00**	**0%**	**0,00**	
	PM	Work Package 4			**0,00**	**0%**	**0,00**	
	PM	Work Package 5	**24,00**	5,31	**5,31**	**22%**	**18,69**	
	PM	Work Package 6			**0,00**	**0%**	**0,00**	
	PM	Work Package 7			**0,00**	**0%**		
	PM	Work Package 8	**2,00**		**0,00**	**0%**	**2,00**	
	PM	***Total***	**26,00**	**5,31**	**5,31**	**20%**	**20,69**	
	EUR	Personnel costs	**660 000,00**	21 366,00	**21 366,00**	**3%**	**638 634,00**	Change request, GMP procurement, process documentation and GMP document (stability study) all started
	EUR	Subcontracting			**0,00**	**0%**	**0,00**	
		Other direct costs			**0,00**	**0%**		
	EUR	Travel	**3 000,00**		**0,00**	**0%**	**3 000,00**	
	EUR	Equipment			**0,00**	**0%**	**0,00**	
	EUR	Other goods and Services	**297 000,00**	3 969,00	**3 969,00**	**1%**	**293 031,00**	smaller pieces of material and equipment needed for set-up and production, freight for CB etc
	EUR	Indirect Costs	**240 000,00**	6 333,75	**6 333,75**	**3%**	**233 666,25**	
	EUR	**Total Costs**	**1 200 000,00**	**31 668,75**	**31 668,75**	**3%**	**1 168 331,25**	
	EUR	**Requested EU funding**	**1 200 000,00**		**0,00**	**0%**	**1 200 000,00**	
Beneficiary 6	*PM*	Work Package 1			**0,00**	**0%**	**0,00**	
ADLEGO	*PM*	Work Package 2			**0,00**	**0%**	**0,00**	
	PM	Work Package 3	**2,00**		**0,00**	**0%**	**2,00**	
	PM	Work Package 4			**0,00**	**0%**	**0,00**	
	PM	Work Package 5			**0,00**	**0%**	**0,00**	
	PM	Work Package 6	**12,00**	0,14	**0,14**	**1%**	**11,86**	TCs
	PM	Work Package 7	**2,00**		**0,00**	**0%**		
	PM	Work Package 8	**2,00**		**0,00**	**0%**	**2,00**	
	PM	***Total***	**18,00**	**0,14**	**0,14**	**1%**	**17,86**	
	EUR	Personnel costs	**140 000,00**	955,00	**955,00**	**1%**	**139 045,00**	TCs
	EUR	Subcontracting			**0,00**	**0%**	**0,00**	
		Other direct costs	**20 000,00**		**0,00**	**0%**		
	EUR	Travel			**0,00**	**0%**	**0,00**	
	EUR	Equipment			**0,00**	**0%**	**0,00**	
	EUR	Other goods and Services			**0,00**	**0%**	**0,00**	
	EUR	Indirect Costs	**40 000,00**	238,75	**238,75**	**1%**	**39 761,25**	
	EUR	**Total Costs**	**200 000,00**	**1 193,75**	**1 193,75**	**1%**	**198 806,25**	
	EUR	**Requested EU funding**	**200 000,00**		**0,00**	**0%**	**200 000,00**	

PARTICIPANTS	UNIT (*PERSON MONTHS or EUROS*)	TYPE of EXPENDITURE	PLANNED	ACTUAL EXPENDITURE		Pct. Spent	REMAINING RESOURCES	SHORT DESCRIPTION and RELATED WP - Personnel, Travel, Equipment, Other goods and services
				Interim	Total	TOTAL		
			e	a1	e1	a1+b1+c1+ d1/e	e-e1	
Beneficiary 7	*PM*	Work Package 1			**0,00**	**0%**	**0,00**	
KAROLINSKA	*PM*	Work Package 2			**0,00**	**0%**	**0,00**	
	PM	Work Package 3			**0,00**	**0%**	**0,00**	
	PM	Work Package 4			**0,00**	**0%**	**0,00**	
	PM	Work Package 5	**2,00**		**0,00**	**0%**	**2,00**	
	PM	Work Package 6	**2,00**		**0,00**	**0%**	**2,00**	
	PM	Work Package 7	**12,00**	1,00	**1,00**	**8%**		
	PM	Work Package 8	**2,00**		**0,00**	**0%**	**2,00**	
	PM	***Total***	**18,00**	**1,00**	**1,00**	**6%**	**17,00**	
	EUR	Personnel costs	**288 000,00**	6 600,00	**6 600,00**	**2%**	**281 400,00**	
	EUR	Subcontracting			**0,00**	**0%**	**0,00**	
		Other Direct costs	**32 000,00**		**0,00**	**0%**		
	EUR	Travel			**0,00**	**0%**	**0,00**	
	EUR	Equipment			**0,00**	**0%**	**0,00**	
	EUR	Other goods and Services			**0,00**	**0%**	**0,00**	
	EUR	Indirect Costs	**80 000,00**	1 650,00	**1 650,00**	**2%**	**78 350,00**	
	EUR	**Total Costs**	**400 000,00**	**8 250,00**	**8 250,00**	**2%**	**391 750,00**	
	EUR	**Requested EU funding**	**400 000,00**		**0,00**	**0%**	**400 000,00**	

EUR	**Total Costs**	**3 000 000,00**	**438 452,49**	**438 452,49**	**15%**	**2 561 547,51**	
EUR	**Requested EU funding**	**3 000 000,00**		**0,00**	**0%**	**3 000 000,00**	

Annex 2

Deliverables, Ethics, DMP, Other Reports for Project 101003666

Deliverables, Ethics, DMP, Other Reports												
WP No	Del Rel. No	Del No	Title	Description	Lead Beneficiary	Nature	Dissemination Level	Est. Del. Date (red = month 1-6)	Rev. Due Date	Receipt Date (green = submitted)	Approval Date	Status
WP1	D1.1	D1	Synthesis of vaccine candidates, proteins and peptides	All vaccine candidates, proteins and produced and delivered to KI	KI	Report	Public	30 Jun 2020		04 Sep 2020		Submitted
WP1	D1.2	D2	Evaluation of immunogenicity of all candidates	All vaccine candidates have been evaluated and if working, also tested for immunogenicity in mouse and rabbit studies. The samples have been analyzed.	KI	Report	Public	30 Sep 2020		13 Nov 2020		Submitted
WP1	D1.3	D3	Selection of the best vaccine candidate for GMP and tox studies	One vaccine candidate has been selected based on safety and immunogenicity for production according to GMP and GLP toxicology testing.	KI	Report	Public	31 Dec 2020				Pending
WP2	D2.1	D4	Assays to measure cytokine induction and IFN supression	Primers, RT-qPCR assays, transfection protocols, control constructs, transfection protocols, reporter assays	JLU	Report	Public	30 Jun 2020		04 Sep 2020		Submitted
WP2	D2.2	D5	Assessment of cytokine induction and IFN suppression by first set of vaccine candidates	Statistically robust data on upregulation of IFN-beta, IFN-lambda 1 and 2, IL-6, IL-8, TNF-alpha, CCL4, CCL5, CXCL10. Statistically robust data on dysregulation of IFN-beta induction or IFN signaling	JLU	Report	Public	30 Sep 2020		11 Nov 2020		Submitted
WP2	D2.3	D6	Optimization selected vaccine candidates to further avoid of suppression of IFN induction	ORF mutants of vaccine candidates that lost the ability to suppress IFN induction	JLU	Report	Public	31 Dec 2020				Pending
WP2	D2.4	D7	Optimization of selected vaccine candidates to further avoid a cytokine storm	ORF mutants of vaccine candidates that lost the ability to activate pro-inflammatory responses	JLU	Report	Public	31 Mar 2022				Pending
WP3	D3.1	D8	Protocol for neutralization assay	Established assay for determination of neutralizing antibodies to SARS-COV-2 that can be used to test mouse and rabbit sera	FoHM	Report	Public	30 Jun 2020		04 Sep 2020		Submitted
WP3	D3.2	D9	Challenge protocol	Established protocol for infecting mice with SARS-COV-2 before or completed vaccinations	FoHM	Report	Public	30 Sep 2020		25 nov 2020		Submitted
WP3	D3.3	D10	Results from vaccine and challenge study	Completed analysis of protection studies in mice were immunized mice have been challenged with SARS-COV-2. This assists in the selection of the vaccine candidate.	FoHM	Report	Public	31 Dec 2020				Pending
WP3	D3.4	D11	Screening of sera from human vacinees by in vitro neutralization	Completed analysis of human sera obtained from the vaccinated healthy volunteers in the phase I clinical trial to neutralize SARS-COV-2 in cell culture.	FoHM	Report	Public	31 Mar 2022				Pending
WP4	D4.1	D12	A locked Cliniporator with pulse pattern for plasmid DNA delivery	Establishment of a pulse pattern for in vivo electroporation that is optimized for delivery of plasmid DNA	IGEA	Report	Public	31 Mar 2021				Pending
WP4	D4.2	D13	Documentation for EMA	Provide complete documentation of the Cliniporator to the EMA/MPA for use in delivery of plasmid DNA vaccines in humans	IGEA	Report	Public	30 Jun 2021				Pending
WP4	D4.3	D14	A single step delivery procedure	Develop a device that is added to the Cliniporation electrode handle that enables injection of DNA and in vivo electroporation in a single step. This may or may not be used in the clinical trial depending on requirements from the EMA/MPA.	IGEA	Report	Public	30 Jun 2021				Pending
WP5	D5.1	D15	Pre-Production Evaluation and plasmid production for toxicology studies	Complete study report on the manufacturing system performance and plasmid production for toxicological evaluation.	Cobra	Report	Public	31 Jan 2021				Pending
WP5	D5.2	D16	Manufactured and QP released Master Cell Bank	Generation of a Master cell bank for the vaccine and QP release	Cobra	Report	Public	30 Jun 2021				Pending
WP5	D5.3	D17	Manufactured GMP grade bulk drug substance pDNA	Production of a GMP grade bulk drug substance of the vaccine candidate	Cobra	Report	Public	30 Jun 2021				Pending
WP5	D5.4	D18	QC tested and QP released GMP drug substance	Release of a GMP produced vaccine candidate	Cobra	Report	Public	30 Sep 2021				Pending
WP5	D5.5	D19	Summarizing stability data report(s) for BDS	Report that describes the long term stability of the vaccine candidate	Cobra	Report	Public	30 Sep 2021				Pending
WP5	D5.6	D20	GMP manufactured aseptically filled plasmid drug product	Dispensing of the vaccine candidate	Cobra	Report	Public	30 Sep 2021				Pending
WP5	D5.7	D21	QC tested and QP released GMP plasmid drug product	QC tested and QP released GMP produced vaccine candidate	Cobra	Report	Public	30 Sep 2021				Pending
WP5	D5.8	D22	Summarizing stability data report(s) for plasmid drug product	Written reports on the stability of the GMP produced vaccine candidate	Cobra	Report	Public	31 Mar 2022				Pending
WP6	D6.1	D23	Study plan for the GLP toxicity study	Written plan with the design of the toxocological study of the vaccine candidate	Adlego	Report	Public	30 Sep 2020	31 Jan 2021			Comment below
WP6	D6.2	D24	Completion of the GLP toxicity study, month	Completed toxicological evaluation according to GLP of the vaccine candidate	Adlego	Report	Public	31 Mar 2021				Pending
WP6	D6.3	D25	Report writing for the IMPD, month	A written report of the toxicological evaluation of the vaccine candidate according to GLPto be submitted to EMA/MPA	Adlego	Report	Public	30 Jun 2021				Pending
WP7	D7.1	D26	Approvals from ethics committee and EMA/MPA for phase I clinical trial	Approvals from ethics committee and EMA/MPA for phase I clinical trial	Karolinska	Report	Public	30 Sep 2021				Pending
WP7	D7.2	D27	Midterm recruitment report	Midterm recruitment report	Karolinska	Report	Public	30 Nov 2021				Pending
WP7	D7.3	D28	Completed clinical trial in humans and writing of report	Completed clinical trial in humans and writing of report	Karolinska	Report	Public	31 Mar 2022				Pending
WP8	D8.1	D29	Consortium secured intranet and Management handbook	These tools will facilitate communication and establish the principles of work within the consortium. The Management Handbook will contain all internal consortium agreement related rules (for publication, etc.), key contact and info to use the intranet, plus a "digest" of H2020 rules easier to understand for SMEs and advices adapted to the consortium.	KI	Report	Public	31 May 2020		04 Sep 2020		Submitted
WP8	D8.2	D30	Project risk management plan	This deliverable will outline the procedures for risk monitoring and evaluation throughout the project and include a risk register.	KI	Report	Public	30 Sep 2020		13 Nov 2020		Submitted
WP8	D8.3	D31	Interim Activity Report	Delivery of Interim Activity report for Month 1-6	KI	Report	Public	30 Sep 2020				Pending
WP8	D8.4	D32	Evaluation of the management tools and procedure	This document will outline the outcomes of the internal evaluation of the management tools and procedures put in place in OPENCORONA including recommendations for future improvements.	KI	Report	Public	31 Mar 2022				Pending
WP8	D8.5	D33	Update DMP	Update of the Data Management Plan.	KI	ORDP: Open Research Data Pilot	Confidential, only for members of the consortium (including the Commission Services)	30 Sep 2020		13 Nov 2020		Submitted
WP8	D8.6	D34	Website	External Project Website launch.	KI	Websites, patents filling, etc.	Public	30 Jun 2020		13 Nov 2020		Submitted

WP8	D8.7	D35	Communication and Dissemination Plan	Establish a Communication and Dissemination Plan	KI	Report	Public	30 Sep 2020		18 Nov 2020		Submitted
WP9	D9.1	D36	HCT - Requirement No. 2	1/ For the human cells obtained within the project, details on cell types must be kept on file and made available to the EC upon request. 2/ Copies of relevant documents for using or collecting human cells (i.e. ethics approval, accreditation /designation /authorisation /licensing) must be kept on file and made available to the EC upon request.	KI	Ethics	Confidential, only for members of the consortium (including the Commission Services)	31 Mar 2021				Pending
WP9	D9.2	D37	POPD - Requirement No. 3	1/ The beneficiary must check if special derogations pertaining to the rights of data subjects or the processing of health data have been established under the national legislation of the country where the research takes place and submit a declaration of compliance with respective national legal framework(s).	KI	Ethics	Confidential, only for members of the consortium (including the Commission Services)	30 Jun 2020				Pending
WP9	D9.3	D38	A - Requirement No. 4	1/ Copies of relevant authorizations for animal experiments (covering also the work with genetically modified animals, if applicable) must be submitted as deliverable.	KI	Ethics	Confidential, only for members of the consortium (including the Commission Services)	31 Mar 2021				Pending
WP9	D9.4	D39	EPQ - Requirement No. 5	1/ The applicant must demonstrate that appropriate health and safety procedures conforming to relevant local/national guidelines/legislation are followed for staff involved in this project. This must be confirmed in the grant agreement before signature.	KI	Ethics	Confidential, only for members of the consortium (including the Commission Services)	30 Sep 2020				Pending
WP9	D9.5	D40	GEN - Requirement No. 6	1/ The beneficiary must clarify that Swedish patient data and any human biological samples are fully anonymized. This must be submitted as deliverable.	KI	Ethics	Confidential, only for members of the consortium (including the Commission Services)	30 Jun 2020				Pending
WP9	D9.6	D41	H - Requirement No. 7	1/ For the Phase I clinical study, the following documents/information must be submitted as a deliverable (in one package) prior to enrolment of first study subject: (i) Final version of study protocol as submitted to regulators/ethics committee(s), (ii) Registration number of clinical study in a WHO-or ICMJE-approved registry (with the possibility to post results), (iii) Approvals (ethics committees and national competent authority if applicable) required for invitation/enrolment of first subject in at least one clinical centre.	KI	Ethics	Confidential, only for members of the consortium (including the Commission Services)	30 Sep 2020				Pending
WP9	D9.7	D42	H - Requirement No. 8	1/ The procedures and criteria that will be used to identify/recruit research participants must be kept on file and made available to the EC upon request. 2/ The informed consent procedures that will be implemented for the participation of humans must be kept on file and made available to the EC upon request . 3/ Templates of the informed consent/assent forms and information sheets (in language and terms intelligible to the participannts) must be kept on file and submitted to the EC upon request. 4/ Copies of opinions/approvals by ethics committees and/or competent authorities for the research with humans must be kept on file and made available to the EC upon request.	KI	Ethics	Confidential, only for members of the consortium (including the Commission Services)	31 Mar 2021				Pending
WP9	D9.8	D43	POPD - Requirement No. 9	1/ The host institution must confirm that it has appointed a Data Protection Officer (DPO) and the contact details of the DPO are made available to all data subjects involved in the research. For host institutions not required to appoint a DPO under the GDPR a detailed data protection policy for the project must be submitted as a deliverable. 2/ The beneficiary must explain how all of the data they intend to process is relevant and limited to the purposes of the research project (in accordance with the 'data minimisation 'principle). This must be submitted as a deliverable. 3/ A description of the technical and organisational measures that will be implemented to safeguard the rights and freedoms of research participants must be submitted as a deliverable. 4/ A description of the security measures that will be implemented to prevent unauthorised access to personal data or the equipment used for processing must be submitted as a deliverable.	KI	Ethics	Confidential, only for members of the consortium (including the Commission Services)	30 Sep 2020				Pending
WP9	D9.9	D44	POPD - Requirement No. 10	1/ Detailed information on the informed consent procedures in regard to data processing must be kept on file and made available to the EC upon request. 2/ Templates of the informed consent forms and information sheets (in language and terms intelligible to the participants) must be kept on file and made available to the EC upon request.	KI	Ethics	Confidential, only for members of the consortium (including the Commission Services)	30 Sep 2020				Pending
WP9	D9.10	D45	EPQ - Requirement No. 11	1/ Copies of authorisations for relevant facilities (e.g., security classification of laboratory, GMO authorisation) must be kept on file and made available to the EC upon request.	KI	Ethics	Confidential, only for members of the consortium (including the Commission Services)	30 Nov 2021				Pending

WP9	D9.11	D46	GEN - Requirement No. 12	1/ Before the beginning of any experimental activity involving humans or animals, ethics committee opinion/authorisation must be obtained and submitted as a deliverable.	KI	Ethics	Confidential, only for members of the consortium (including the Commission Services)	30 Jun 2020	15 Dec 2020			Comment below
WP9	D9.12	D47	A - Requirement No. 13	1/ Copies of training certificates/personal licenses of the staff involved in animal experiments must be kept on file and made available to the EC upon request.	KI	Ethics	Confidential, only for members of the consortium (including the Commission Services)	31 Mar 2021				Pending
WP9	D9.13	D48	GEN - Requirement No. 14	1/ Reports from the Independent Advisory Board including the ethics aspects of the research must be submitted as a deliverable, at the end of each reporting period together with the financial reports.	KI	Ethics	Confidential, only for members of the consortium (including the Commission Services)	31 Mar 2021				Pending
WP9	D9.14	D49	H - Requirement No. 15	1/ For the Phase I clinical study, a report on the status of posting results in the study registry(s) must be submitted as a deliverable, including timelines if/when final posting of results is scheduled after end of funding period.	KI	Ethics	Confidential, only for members of the consortium (including the Commission Services)	30 Sep 2021				Pending

WP6	D6.1	D23	Study plan for the GLP toxicity study	We (WP1, WP4, WP5 & WP6) are currently performing a study in rabbits to determine vaccine dose and injection volume. This study will be finalized in January and the results are needed to finalize the study plan for the toxicological study. We estimate submission of the deliverable D6.1 to January 31, 2021.

WP9	D9.11	D46	GEN - Requirement No. 12	The project currently has three animal ethics applications submitted for review by November 19, 2020. The final approval normally takes additionally one to two weeks. We would like to include these permits in the submission of deliverable D9.11 estimated to December 15, 2020.

Annex 3

Risk no	Description (low/medium/high)	WP involved	Proposed risk-mitigation measures	Reference reporting period	mitigation measures applied	Risk materialised	Comment
R1	Vaccine candidate not immunogenic (Low)	1-8	Several vaccine candidates generated and tested, delivery optimisation	Estimated M9	Design of modified versions of oroginal vaccine candidates.	New vaccine candidates was designed M6.	Selected vaccine candidate show broad immunogenicity. Studies still ongoing.
R2	Vaccine candidate causes cytokine storm (Medium)	2-8	Several vaccine candidates generated and tested	Estimated M9			Characterization ongoing, no pro-inflammatory responses or inhibition of innate immune responses detected.
R3	The vaccine candidate does not protect the challange mice (Low)	3-8	Several parallel vaccine concept will be developed by WP1				Studies ongoing.
R4	In vivo EP not tolerable (Low)	4-8	Cliniporator has been used extensively in clinical practice, extensive experience, adjust pulse patterns				Will be evaluated in toxicological study.
R5	Plasmid can not grow (Low)	5-8	Several vaccine candidates generated and tested				HQ production ongoing.
R6	Plasmid toxic (Low)	6-8	Several vaccine candidates generated and tested				Will be evaluated in toxicological study.
R7	Study not approved by ethics committy or MPA/EMA (Low)	7	Early contacts and Scientific advice with MPA/EMA				
R8	Clinical trial fails to show safety (Low)	7	Stop trial, analyze why this was missed in the preclinical development				
R9	Clinical trial fails to show immunogenicity (Medium)	7	Analyze why this was missed in the preclinical development				