1. PUBLISHABLE SUMMARY

Summary of the context and overall objectives of the project (For the final period, include the conclusions of the action)

The COVID-19 pandemic is still at a rapidly evolving phase. COVID-19 is caused by SARS-COV2 infection and affects individuals with varied severity. Number of studies suggest that cardiovascular diseases predispose to the severity and poor clinical outcome of SARS-COV2 infection. Prediction of disease severity and clinical outcome could help the management of the patients at the clinics. In this study, we combine blood RNA quantification and artificial intelligence methodologies to predict the clinical outcome of the patients. The goal of COVIRNA study is to deliver an in-vitro diagnostic (IVD) test that can predict COVID-19 severity and mortality and that can be used for patient stratification, personalized healthcare and better management of patients at risk.

COVIRNA aims to develop and market a novel IVD test for COVID-19 severity. This will reduce the socio-economic burden of the current pandemic and help clinicians to stratify patients based on their risk and improve personalized healthcare.

In addition, COVIRNA will establish a strategic science-policy-business-society consultation to optimize the design of the IVD test complying with end user's needs, cost-efficiency analysis requirements, current EU regulation and highest quality standards to enable and accelerate its uptake into clinical practice.

Through a tailored dissemination programme, COVIRNA will also raise stakeholder's awareness on the advantages brought by the newly designed IVD test as a valuable decision-support tool for healthcare professionals to deliver the best health outcome for the most vulnerable COVID-19 patients.
COVIRNA will engage communities of stakeholders in sharing practical knowledge on the use of the novel medical technology.

Work performed from the beginning of the project to the end of the period covered by the report and main results achieved so far (For the final period please include an overview of the results and their exploitation and dissemination)

The COVIRNA project is an assembly of six scientific and dissemination work packages (WP) aiming at implementing a diagnostic test based on blood RNA biomarkers and artificial intelligence to predict the outcome of COVID-19 patients. We first conduct a multi-centre retrospective study in COVID-19 patients in which we measure blood RNA biomarkers (WP1). A centralized database is implemented (WP2) to receive patients' data and make it accessible for analysis based on artificial intelligence to identify predictive RNA biomarkers of clinical outcome (WP3). Functional links of the RNA biomarkers with disease progression are then investigated in laboratories (WP4). The IVD test based on these markers is being prepared for CE-marking and commercialization (WP5). WP6 is dedicated to dissemination and communication activities to relevant stakeholders, end-users (clinicians and patients) and more generally to the entire population.

For WP1, efforts were made to achieve the expected number of samples required. From COVIRNA partners, 930 COVID-19 positive and 583 control samples have been acquired so far. Collaborations have been setup with external partners to reach the expected number of 1500 COVID-19 positive

samples. The initially expected number of 500 control samples has been reached. The measurement of RNA biomarkers using the FIMICS panel of 3233 targets is partially complete and the data has been transferred to the centralized database.

In WP2, the necessary infrastructure allowing to centralize the data coming from the different partners of the COVIRNA consortium providing patient samples and clinical data has been set up. The clinical data from available cohorts was received and centralized in the database. Data curation of some of the cohorts was completed and COVIRNA glossary was prepared. Partial FIMICS data has been transferred to the centralized database. The data management plan was developed and ethically approved.

Data annotation of RNA biomarkers and generation of relevant metadata was generated by WP3 partners and shared with the consortium. These will be used to develop the statistical models and prediction tools based on machine learning.

Partners of WP4 have identified initial candidate RNAs that displayed significantly different levels in critical versus severe COVID19 patients. Functional analysis of this first set of candidate RNA biomarkers is being carried out to understand their role in COVID-19 pathology.

Work package 5 has just been initiated, with first drafting of data package that will be submitted to European Medicines Agency, in order to obtain its CE-marking.

WP6 have achieved a number of important results during the first year. Firstly, the project brand identity was developed and, consequently, the website and social media accounts (LinkedIn, Twitter and YouTube) have been set up. Dissemination materials such as press releases, news items, articles and interviews have been produced. The first issue of the project newsletter has been published and shared across networks. Additionally, a video has been produced for dissemination among a lay audience. In addition, COVIRNA has been presented at conferences.

Progress beyond the state of the art, expected results until the end of the project and potential impacts (including the socio-economic impact and the wider societal implications of the project so far)

COVIRNA WP1 partners contribute towards identification of best predictive biomarkers for complications after SARS-COV2 infection. This will improve the understanding of immune-cardiac pathology of COVID-19. The knowledge developed within WP1 may inform future epidemic-prone disease management strategies allowing newly emerging agents to be more promptly characterised, and thus control measures implemented sooner.

Centralized database combining clinical data and blood RNA markers of 2000 individuals (1500 COVID-19 positive patients and 500 controls) by WP2 partners is an important repository to identify most predictive RNA biomarkers of clinical outcome. In addition, this database constitutes an invaluable reservoir for future investigations aiming at a better understanding and prediction of the COVID-19 pathology.

The predictive model based on RNA biomarkers and artificial intelligence developed in WP3 will be the basis for the COVIRNA IVD test. The methodologies implemented for this test could also serve to develop predictive tools for other infectious and non-infectious diseases, as well as to prepare for future pandemics.

WP4 partners have identified a small set of candidate RNA biomarkers. Cell specificity of the RNA biomarkers as well as their functional association with disease severity are being investigated. We aim to characterize the functional role of the most predictive biomarkers included in the COVIRNA IVD test. This may lead to further investigations of their therapeutic potential, hence possibly impacting healthcare system and patient's outcomes, while at the same time advancing our scientific knowledge of the role of RNAs in the host antiviral response.

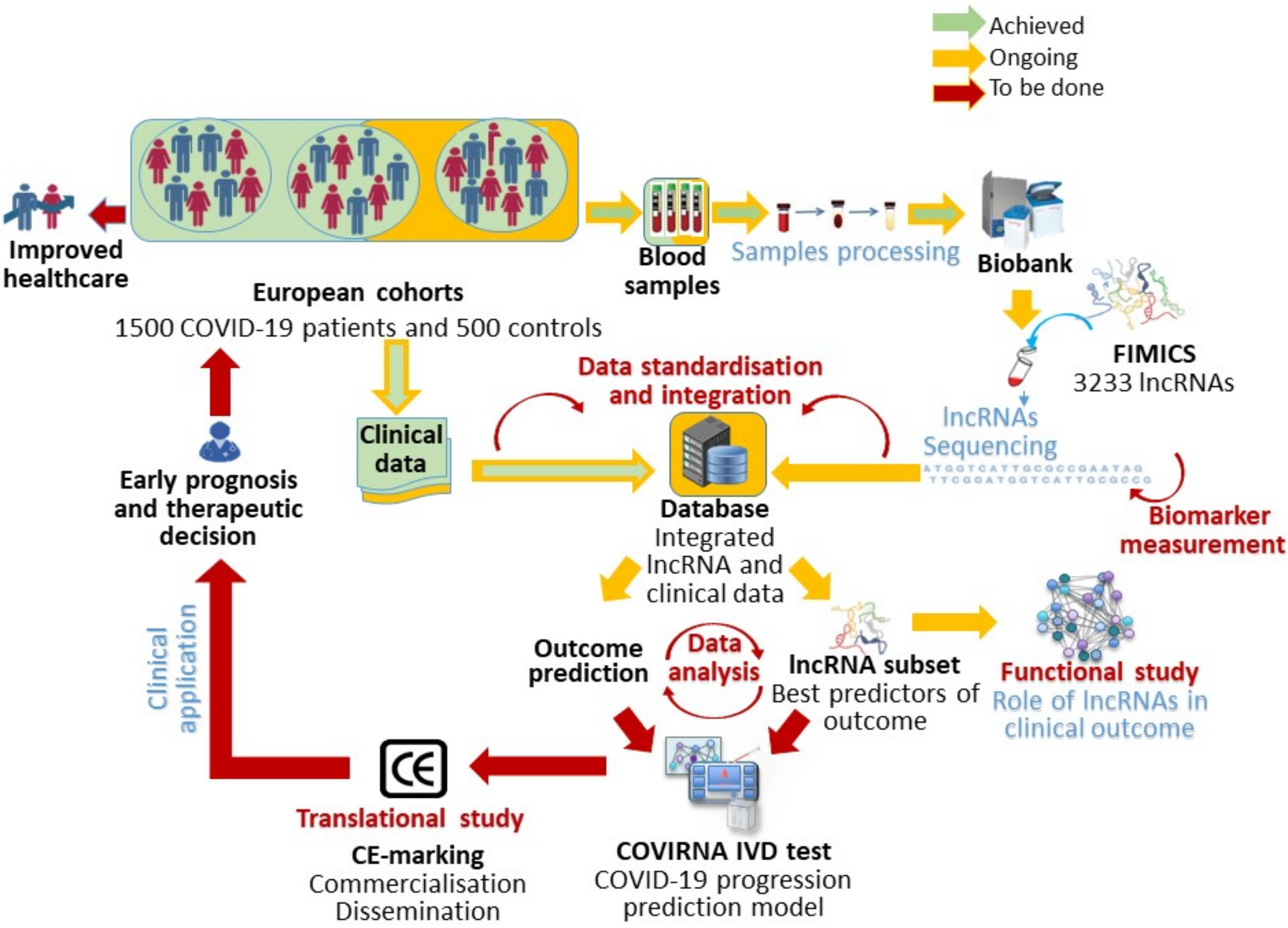
Partners of WP5 will deliver during the second year of the project the COVIRNA IVD test and complete its CE marking.

Through intense communication and dissemination activities, WP6 partners worked to make the general public aware of the COVIRNA novel scientific research, as well as the investment of resources made by the European Commission in such an innovative project that can benefit society at large.

Overall, the COVIRNA diagnostic test will help COVID-19 affected patients and will positively impact the management of the pandemic as it is critical in triaging COVID-19 patients, ensure they are properly monitored and receive the appropriate personalised care, thus improving healthcare outcomes, reducing length of stay in hospitals and the overall COVID-19 associated burden on health systems.

Address (URL) of the project's public website

https://covirna.eu/


Achieved
Ongoing
To be done
Improved healthcare
European cohorts
1500 COVID-19 patients and 500 controls
Blood samples
Samples processing
Biobank
FIMICS
3233 lncRNAs
lncRNAs Sequencing
Data standardisation and integration
Clinical data
Early prognosis and therapeutic decision
Database
Integrated
lncRNA and clinical data
Biomarker measurement
Clinical application
Outcome prediction
Data analysis
lncRNA subset
Best predictors of outcome
Functional study
Role of lncRNAs in clinical outcome
Translational study
CE-marking
Commercialisation
Dissemination
COVIRNA IVD test
COVID-19 progression prediction model