12/2023 | CARE Biannual Newsletter

C A R E
CORONA ACCELERATED R&D IN EUROPE

Preparing for future pandemics

In this issue we share EC sponsored workshop recommendations about **pandemic preparedness** and ask how these have been taken forward into action. We also take a closer look at two of our partners: **Iktos** and **Leiden University Medical Center**

The CARE consortium is a public-private coalition uniting scientists from academia, research centres, SMEs, EFPIA members and IMI Associated Partners in the fight against coronavirus. This multidisciplinary organisation cuts across traditional silos by mixing expertise from 38 different organisations. Despite its size it was mobilised at unprecedented speed and continues to work at pace: delivering new ideas, new methods and new molecules all the time.

Read on to find out more about how the findings of a workshop held in November 2022 are shaping the future approach to pandemic preparedness; as well as learning more about three of our partner organisations.

While Covid-19 is no longer deemed to be a pandemic, the risk of future pandemics remains. Application of lessons learned during our collective recent experience is vital to being in a stronger position to handle this situation again.

European Commission

Members of the CARE consortium were among the participants of a workshop held a year ago, organised by the EC's Directorate-General for Research and Innovation (DG-RTD) and the European Health Emergency Preparedness and Response Authority (HERA) to explore the opportunities and challenges of providing globally available broad spectrum antiviral therapeutics as a tool for pandemic preparedness.

The future pandemic preparedness approach (Cont'd)

Given the evolving and unpredictable nature of the coronavirus, the delegates of the workshop recommended inclusion of broad-spectrum antiviral therapeutics as a key tool of pandemic preparedness. The workshop, which was set up with input from Dr. Ed Schmidt and Prof. Eric Snijder (LUMC), and Johan Neyts (KUL) from CARE, was also attended by Marnix Van Loock (Janssen).

Why broad-spectrum antiviral therapeutics?

Broad-spectrum antiviral therapeutics, in cocktail or combination formats to limit drug resistance, can potentially target broader viral families or groupings in an initial outbreak, crucially buying time for more targeted therapies to be developed and tested in parallel, by containing the spread of the (novel) virus in the early stages and limiting the impact of the pandemic on the health system. The reassurance of knowing there is a swift therapeutic response to an arising future epidemic is important for society, having experienced the impact Covid-19 had on so many lives and economies globally.

Key recommendations from the workshop

To make this a reality requires measures to support rapid global drug development including effective collaborations though global and harmonised research infrastructures, adequate and flexible manufacturing capacities, fast and efficient global clinical trials, clear regulatory frameworks for broad-spectrum antivirals (as current regulatory pathways only provide approval for a specific viral disease), and sufficient and flexible funding.

In this context, public-private partnerships such as CARE, are an important tool to mobilise the expertise needed in an emergency response and to enable sustainable funding. Moreover, the importance of basic research to understand pathogens was highlighted as it is the foundation for the research done in response to an epidemic or a pandemic.

Since the workshop took place, almost 12 months ago, a new series of calls for proposals was launched by HERA on broad-spectrum antivirals with various projects being approved in 2023. One of them is the Panviprep consortium, which will start on 1 January 2024 and in which all eight partners of the SCORE consortium (who are also all CARE partners) together with seven additional partners, will develop antiviral drugs against a range of pandemic viral threats.

The future pandemic preparedness approach (Cont'd)

How does this relate to CARE?

CARE is heavily involved in broad-spectrum antiviral development as part of its preparedness track. These recommendations lend weight to the ongoing antiviral discovery and preclinical work being undertaken today in CARE across numerous work packages.

For more information, please contact:

November 2022 meeting outputs: https://op.europa.eu/s/y449

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Introducing Iktos – a CARE SME organisation

IKTOS

Artificial Intelligence for new drug design

Iktos was founded in 2016 by Yann Gaston-Mathé, Quentin Perron and Nicolas Do Huu, to develop an innovative and user-friendly technology platform for deep learning-based de novo drug design, leveraging a proprietary algorithm developed by Quentin and Nicolas.

Iktos is an innovative company specialising in the development of artificial intelligence (AI) solutions applied to chemical research, more specifically medicinal chemistry and new drug design. These solutions foster productivity improvement in small molecule discovery, which in turn enables major productivity gains in upstream pharmaceutical R&D.

Yann Gaston Mathé, Founder and CEO, Iktos

Quentin Perron Co-Founder and CSO, Iktos

Iktos' de novo design algorithm is based on deep generative models with reinforcement learning. It designs novel and easy to make compounds, optimised to meet a given multi-objective blueprint, with unprecedented speed, performance, and diversity.

Introducing Iktos (cont'd)

Why did Iktos choose to get involved in CARE?

Iktos joined the CARE consortium in 2022 because it was a great opportunity to firstly be able to contribute to the research and development of effective therapies for Covid-19 patients, and secondly, to become part of a consortium of great companies and organisations known for their excellence in drug discovery and to collaborate with all of them.

What has Iktos delivered for CARE?

Iktos' CARE objective was to discover potent SARS-CoV-2 antivirals through target-based and phenotypic-based drug discovery approaches, within the scope of Work Package 3. Iktos successfully employed a target-based approach, harnessing their Structure-Based AI technology, to design diverse and novel chemical structures. Iktos' AI platform generated approximately 142 compounds with excellent synthetic accessibility. They further optimised the synthetic accessibility to expedite Drug Metabolism and Toxicology Assessment (DMTA) cycles, leading to the discovery of a compound with a remarkable pIC50 value of 5.47.

For more information about the different work packages, please click here.

In addition, through a phenotypic approach, they set target parameters and rewards (related to the reinforcement learning algorithm) for their AI-driven generation, enabling the proposal of novel scaffolds and the exploration of a broader chemical space. Iktos' AI retrosynthesis tool ensured the security of synthetic accessibility, thus contributing to efficient DMTA cycles.

In addition to Yann and Quentin, the Iktos team in WP3 includes

Krisztina Feher
Senior Scientist Computational Chemistry

Christopher Housseman
Head of Medicinal Chemistry

Sota Takahashi
Project Management Officer

Brice Hoffman
Head of Computational Chemistry

Ennys Gheyouche
Research Scientist - Computer Aided Drug Design

Benefits enjoyed by Iktos include experiencing valuable interactions with pharma, mid-pharma and biotech collaborators, along with cutting-edge science to identify promising drug candidates.

Want to know more about Iktos? https://iktos.ai/

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Introducing LUMC – a CARE Academic organisation

Leiden University Medical Center

The LUMC has a long history and has its origins in the 16th century when in 1575, following a year-long siege, William of Orange granted Leiden the right to have a university. The university started with 3 faculties: Law, Theology and Medicine.

In 1996, the Leiden University Medical Center (LUMC) emerged from the collaboration between the Leiden University Hospital and the Faculty of Medicine of Leiden University.

Today, it is a centre of medical innovation that aims to improve patient care through scientific research. It trains doctors and biomedical researchers to contribute to this. In addition to general patient care, the LUMC offers specialist treatments that may only be performed in a limited number of medical centres. The LUMC distinguishes itself in particular as a referral centre for complex medical questions for which there are no ready-made answers. As of 2024, all fundamental, translational and clinical research related to pathogens and infectious diseases will be integrated in the new Leiden University Center of Infectious Diseases (LUCID). This month, LUMC is opening a new Biosafety Level 3 (BSL-3) research facility, including two units to be used for studies on SARS-CoV-2 and other pathogenic coronaviruses.



Pictures from LUMC's BSL-3 research facilities

The LUMC has 3 social spearheads: oncology, regenerative medicine and population health. These spearheads relate to important issues in society and medicine. Approximately 7000 people work at LUMC today.

Why did LUMC choose to get involved in CARE?

The LUMC molecular virology team has a >30-year track record in studying the biology of coronaviruses, including previous projects in antiviral drug research. LUMC decided to get involved with CARE because of the need to establish an international response to the rapidly developing SARS-CoV-2 pandemic,

Introducing LUMC (Cont'd)

thus facilitating scientific collaboration and the sharing of expertise and toolboxes. Moreover, since February 2020, LUMC was coordinating the EU-funded SCORE project to target SARS-CoV-2, and its eight partners thus became a sub-network within CARE. This enabled the rapid exchange of knowledge, technologies, reagents, and candidate antiviral drugs between the two projects.

What has LUMC delivered for CARE?

The LUMC's achievements in CARE include many aspects in Work Packages (WP) 1, 2, 5, 6, 7 and 8. LUMC developed assays and reagents in WP1 and 2 to better define coronavirus drug targets, and characterise and select antiviral compounds developed by other partners. Such studies into the mechanism-of-action of CARE's drug candidates continue to constitute the bulk of LUMC's contribution.

For more information about the different work packages, please click here.

Furthermore, LUMC performed "omics" studies in WP5, established animal models and performed preclinical studies on candidate antivirals in WP6, performed dual-transcriptomics studies in WP5, and organised a European Medicines Agency (EMA) meeting to obtain advice on combinational treatments for immuno-compromised patients in WP8.

Dr. Eric Snijder (left), Professor of Molecular Virology & LUMC Principal Investigator for CARE and **Dr. Ed Schmidt** (right), LUMC Project Manager for CARE

What benefits has the LUMC enjoyed through participating in CARE?

Prof. Eric Snijder, LUMC team lead, and Dr. Ed Schmidt, Project Manager, explain: "we have really appreciated having access to an international network and resources to continue and expand our research into coronavirus drug targets; it remains crucial to collaborate on the development of antiviral drugs against SARS-CoV-2 and future emerging coronaviruses".

The LUMC CARE team currently includes:

Montse Bárcena, Nina de Beijer, Jonna Bloeme, Brenda Bontes, Jutte de Vries, Mirjam Groenewold, Sytze Jorritsma, Marjolein Kikkert, Marissa Linger, Kees Mourik, Sebe Myeni, Ana Roque, Anna Roukens, Ed Schmidt, Eric Snijder, Thijs Steijaert, Ali Tas, Emmely Treffers, Martijn van Hemert, Peter van Veelen, Patrick Wanningen, and Jessika Zevenhoven.

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All about CARE

CARE is one of 8 IMI EC funded consortia playing a role in supporting efforts targeting coronavirus. It was launched in April 2020 and is Europe's largest scientific research initiative committed to tackling COVID-19.

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Its dual goals were firstly to find solutions to address the arising emergency; and secondly for future pandemic preparedness, exploring small molecule and antibody options.

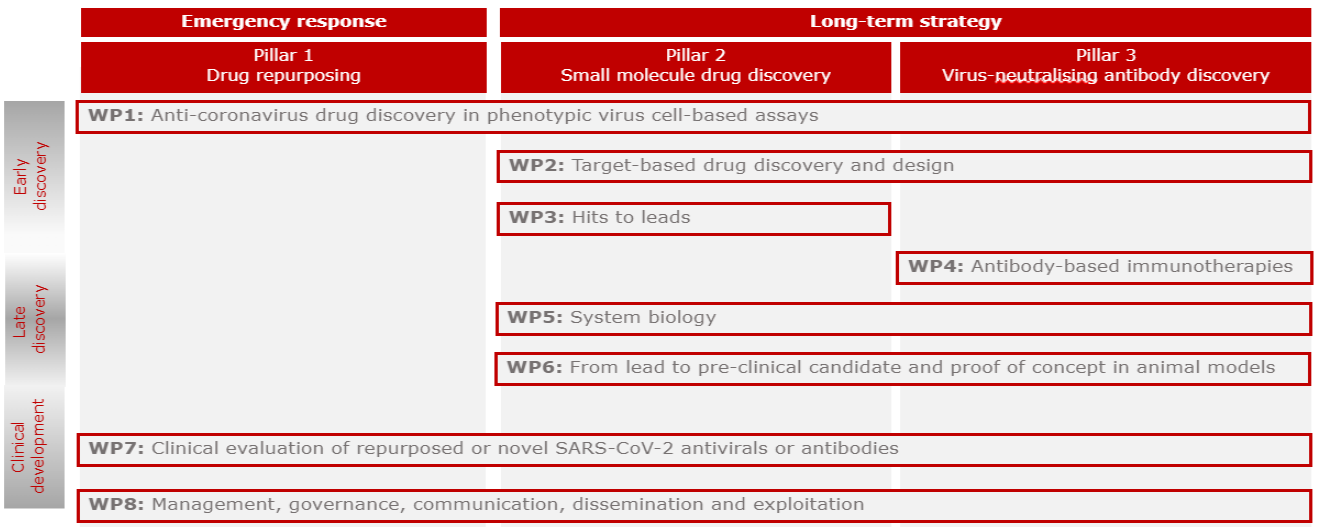
CARE comprises 38 highly respected partners from around the globe, bringing together the relevant academic and industry expertise, with a budget of 76 million euro split between contributing EFPIA partners and matched by the European Commission. It is led by Marnix Van Loock of Johnson & Johnson, with Kumar Singh Saikatendu of Takeda as co-lead, and Professor Yves Lévy of VRI-Inserm as the project co-ordinator.

Project Coordinator: Professor Yves Lévy, Professor of Clinical Immunology and Executive Director, VRI-Inserm

Project Lead: Marnix Van Loock, Senior Scientific Director and R&D Lead of Emerging Pathogens, Global Public Health, J&J

Project Co-lead: Kumar Singh Saikatendu, Senior Director Research Public-Private Partnerships, Takeda

The consortium comprises three research pillars, addressed by eight work packages working independently and collaboratively towards our goals.



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Initial efforts in the emergency space did not yield results, but progress has steadily been made in the preparedness space in both small molecules and antibodies, with teams continually taking account of the evolving context as the virus yielded new variants.

The consortium is steadily building a pipeline of potential small molecule assets to move forward, with promising signs of differentiation from current standard of care. On the antibody front, two very promising candidates were developed with good breadth and potency across all currently known variants of concern, which are now being developed in the clinic, outside of CARE.

CARE's ultimate objective is to run two phase 1 and one phase 2 clinical trials; with a bespoke clinical trial platform in readiness for this. The consortium will report on these trials before the project concludes in March 2025.

CARE is committed to serve society through science and collaboration. Its partners are dedicated to undertaking efforts to make potential new treatments accessible for broad populations including in low and lower-middle income countries at an affordable price. Naturally, the consortium is keen to focus its remaining resources towards the most promising candidates that will bring new benefit to patients.

More information: Go to the CARE website for more information about

The CARE project overview	The CARE consortium partners	The CARE Clinical Trial Platform
CARE news	CARE publications	CARE resources

About this Newsletter

Having passed the project half way point, with many new discoveries and achievements under our belt, we will be sharing our progress each June and December via the newsletter; as well as more frequent posts being shared on LinkedIn and now also X (formerly Twitter).

All CARE partners will automatically receive a link to this newsletter. If you would like to be added to the distribution list please e-mail the CARE Project Management Office.

Reminders

This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking (JU) under grant agreement No 101005077. The JU receives support from the European Union's Horizon 2020 research and innovation programme, EFPIA, BILL & MELINDA GATES FOUNDATION, GLOBAL HEALTH DRUG DISCOVERY INSTITUTE and UNIVERSITY OF DUNDEE.

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- Look for **#CAREvsCOVID**

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