NATO OTAN

Science for Peace and Security (SPS) Programme

Emerging Security Challenges Division

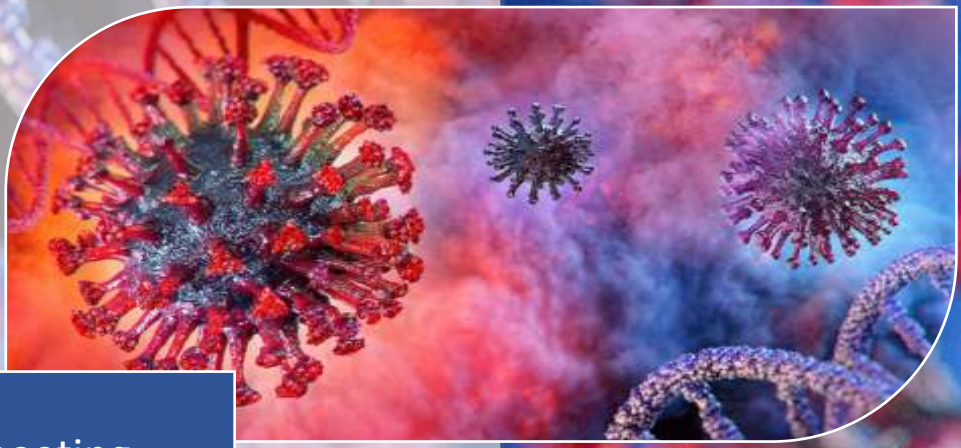
NATO SPS Multi-Year project

Learning a lesson: fighting SARS-CoV-2 Infection and get ready for other future PandEmic scenaRios

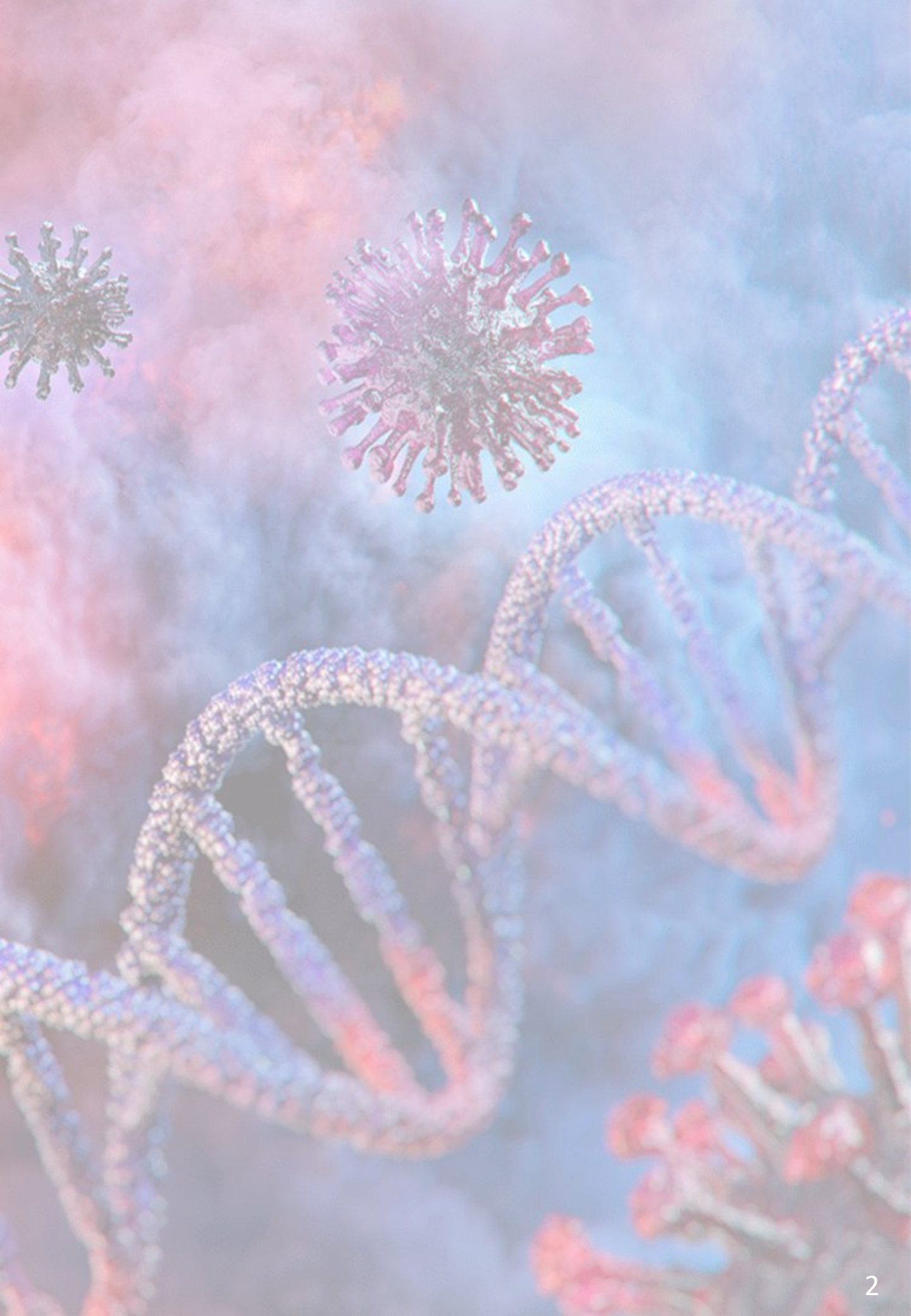
VIPER

Learning a lesson: fighting SARS-CoV-2 Infection and get ready for other future PandEmic scenaRios

NATO OTAN



Kick Off meeting
June 30th, 2022
11-13 CEO



Project Overview

Content

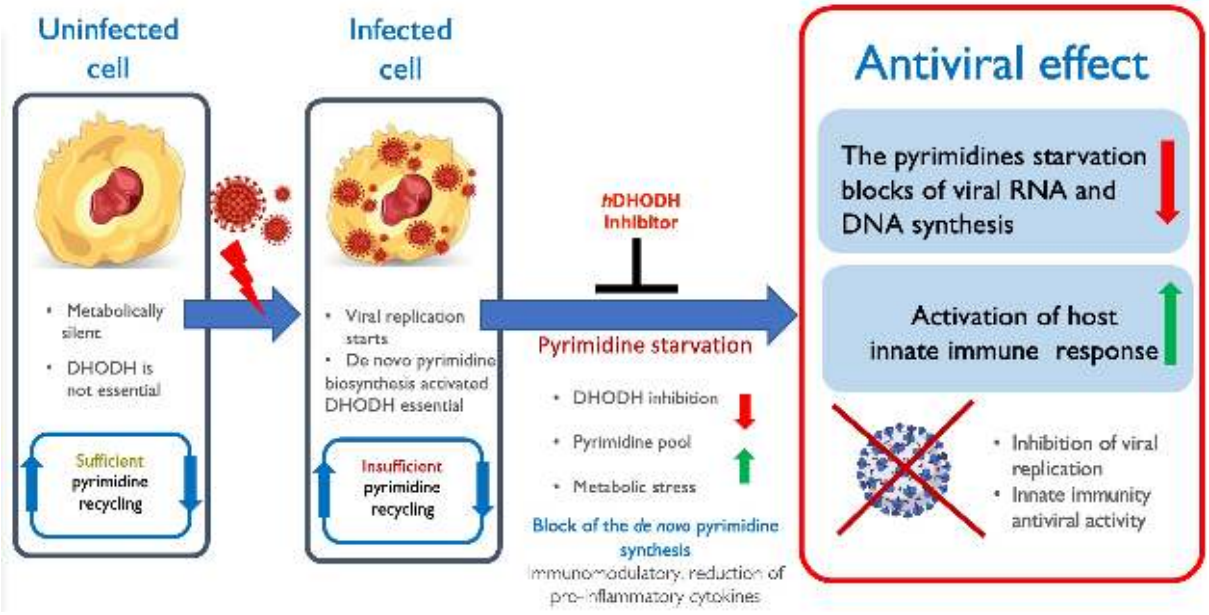
The SARS-CoV-2 pandemic has caused a devastating global health crisis, which created and revealed many challenges in our current societies, including the need to deploy effective antiviral drugs. One therapeutic option that has been considered is *de novo* pyrimidines biosynthesis inhibitors which are Host Targeting Antivirals (HTA). These small molecules target host factors exploited by SARS-CoV-2 and are responsible for virus replication in infected cells. MEDS433, an *in house* dihydroorotate dehydrogenase (*h*DHODH) inhibitor, acts as Broad Spectrum Antiviral Agent (BSAA), able to potently reduce the replication of a large virus panel, including SARS-CoV-2.

Goal

This project aims to obtain the proof-of-concept of its *in vivo* antiviral activity against SARS-CoV-2, as a dual acting HTA able to reduce both virus replication and pathogenic inflammation. Preliminary data suggests that MEDS433 has the potential to inhibit the *in vitro* SARS-CoV-2 replication safely in contrast to two potent *h*DHODH inhibitors that have already entered in Phase II of clinical trials (brequinar and PTC299) but have suffered from toxicity issues.

How does it work?

By targeting *h*DHODH, MEDS433 is able to lead the infected cell in a condition named "*pyrimidine starvation*". In such condition, the virus became unable to replicate and became prey of the immune defensive system. Such mechanism could be applied potentially to target any virus and will be effective also when the virus will start to mutate (variants) during the pandemic event.



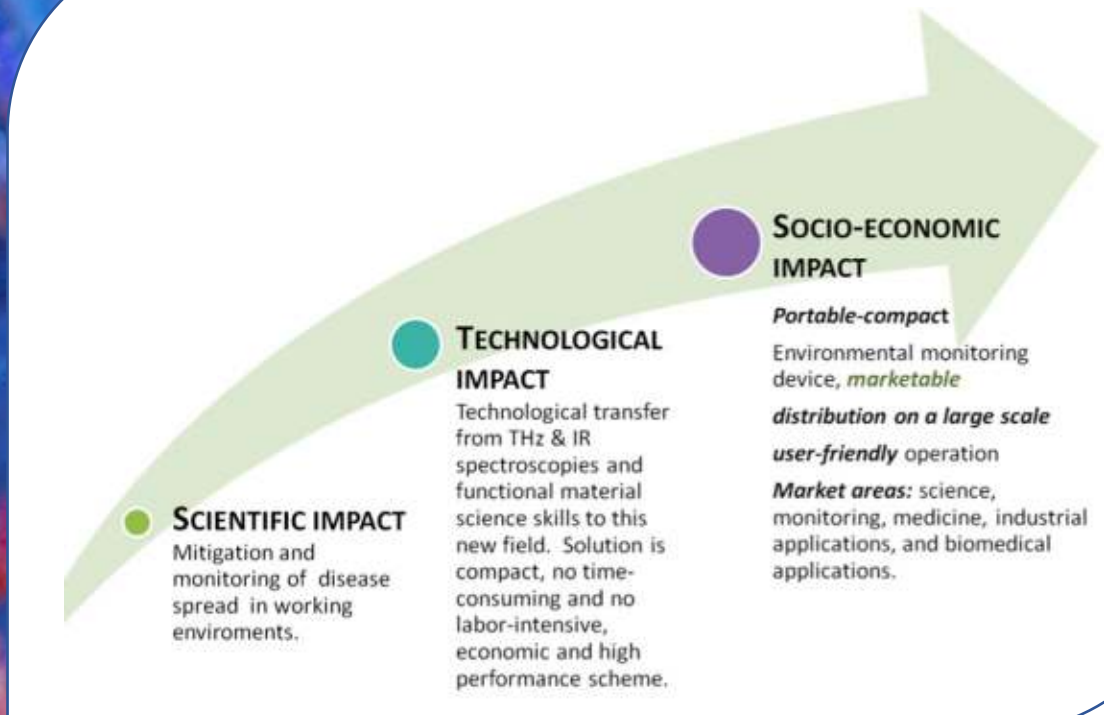
Deliverables

- Preparation of a Pharmaceutical Grade Purity MEDS433 batch in multi gram scale (5 g).
- Formulation of MEDS433 suitable for the *in vivo* tests and streamlining its delivery for oral and parenteral administration.
- Comparison of the *in vitro* antiviral activity of non-formulated and formulated MEDS433 against SARS-CoV-2, alone and in combination.
- Performing an *in vivo* pre-clinical study to accomplish the proof-of-concept of formulated MEDS433 as novel anti-SARS-CoV-2 therapeutic, alone or in combination with other anti-pyrimidines (inhibitors of salvage pathway).

Impact

This project will advance science through research on unique and valuable mechanism that seems to cause molecular vulnerabilities in both RNA and DNA viruses. Strong evidences indicate how drug-like *h*DHODH inhibitors could be effectively used in pandemic events as BSAAs.

If the project succeeds in proving the concept of MEDS433 as an *in vivo* agent in SARS-CoV-2 and several respiratory viruses, a new therapeutic option will be opened and the whole pandemic scenario will be reinforced. BSAAs could be very valuable in the control of emerging and re-emerging viral diseases since the repositioning of existing safe-in-man BSAAs from a pandemic event to another is certainly faster and cheaper than the development of virus-specific drugs and vaccines.



Meeting programme

11:15-11:45

Programme Opening Session

Moderator: **Marco L. Lolli**

- **Dr. Eyup Turmus,** SPS Advisor and Programme Manager, NATO(project management and implementation)
- **Ettore Marchesoni**, Programme Officer, ESCD, NATO (communication and public diplomacy)

11:50-12:50

Presentation of 'VIPER' project.

The project's co-directors will present the project, its objectives, scope and deliverables, including the roles and responsibilities, timelines, communication and meeting plans, and discuss the next steps.

Speakers:

Marco L. Lolli *"Human Dihydroorotate Dehydrogenase (hDHODH) drug target landscape: the discovery of MEDS433"*

Giorgio Gribaudo *"Targeting hDHODH activity to develop Broad-Spectrum Antivirals (HTA)"*

Question & Answers

13:00

Final remarks & Meeting closure

Meeting participants

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Participating institutions

University of Turin (UniTo), Turin, Italy.

UniTO is one of the largest Italian Universities and is deeply involved in scientific research encompassing all disciplines. The University has a longstanding tradition of biomedical and clinical research, with clinical activities being developed in the two University Research Hospitals. The Medicinal Chemistry Research Group is based at the Department of Drug Science and Technology and possesses all technologies necessary for developing early stage drug candidates. The University's Laboratory of Microbiology and Virology studies the molecular mechanisms of virus replication and pathogenesis and identifies and validates targets for designing new antivirals against different human DNA and RNA viruses.

Karolinska Institute, Stockholm, Sweden.

The Karolinska Institute is Sweden's largest centre of medical academic research and offers the country's widest range of medical courses and programmes. The Department of Laboratory Medicine conducts translational research, including in clinical pharmacology, clinical physiology, clinical chemistry, clinical microbiology, pathology, clinical immunology and transfusion medicine. The Department has access to the most advanced equipment and technologies for clinical studies and is equipped with advanced biosafety levels with access to animal houses.

Participating institutions

University of Messina (UniMe), Messina, Italy.

UniME is one of Italy's oldest universities with a strong international network. The Department of Chemical, Biological Pharmaceutical and Environmental Sciences coordinates the research activities of several laboratories in the chemical, biological and pharmaceutical areas. The Department collaborates with pharmaceutical industries for the fulfillment of projects in the field of the drug delivery and drug discovery.

University of Padua (UniPd), Padova, Italy.

The University of Padua was established in 1222 and is one of Europe's oldest and most prestigious seats of learning; it is a multi-disciplinary university that aims to provide its students with both professional training and a solid cultural background. The Department of Molecular Medicine is characterized by the presence of diversified skills from basic science to translational application in medicine that integrate in an interdisciplinary way.

Participating institutions

Uppsala University, Uppsala, Sweden.

Uppsala University (https://www.uu.se), which was founded in 1477 as the first university in Scandinavia, is a comprehensive research-intensive university with strong international standing. The university has over 54,000 students, more than 7,500 employees and a turnover of around SEK 8 billion. At the Uppsala University, the Department of Chemistry – Ångström conducts research and education in the field of chemistry within the very well-equipped Ångström laboratory, with leading research position at high international standard.

VIPER *end users*:

Drug Discovery and Clinic is a Biotech, Spin off of the University of Torino, focused in the development of innovative treatment to Acute Myeloid Leukemia and COVID-19.

Health department – Sicilian Region (Italy). The "*Assessorato della Salute*" of the Sicilian Region is a governmental agency with responsibilities of public health. Moreover, the Institution promotes and supports the collaboration among researchers, regional authorities, and end-users. In order to raise public awareness of new challenges emerged from the pandemic scenario, it will support (conferences, workshop, social media, ..) the dissemination and communication actions of VIPER in all its phases. In the final phases of the project, specific activities will be organized to capitalize the obtained results and to seek new funds for clinical studies of MEDS433.

The Science for Peace & Security programme

THE SCIENCE FOR PEACE AND SECURITY (SPS) PROGRAMME

The Science for Peace and Security (SPS) Programme is an established brand for NATO based on four pillars: science, partnership, security, and unconventional issues (hybrid threats). It has been contributing to the core goals of the Alliance for more than six decades. Today, the SPS Programme continues to be one of the largest and most important partnership programmes addressing 21st century security challenges, particularly cyber defence, counter-terrorism, CBRN defence, energy security and advanced technologies.

The NATO Science for Peace and Security (SPS) Programme enhances security-related civil science and technology to address emerging security challenges and their impacts on international security. It connects scientists, experts and officials from NATO and Partner countries to work together to address these challenges. The SPS Programme provides funding and expert advice for security-relevant activities in the form of Multi-Year Projects (MYP), Advanced Research Workshops (ARW), Advanced Training Courses (ATC), and Advanced Study Institutes (ASI). SPS activities are always demand-driven, modular, and designed to meet the requirements of the nation(s) and end user(s). The relevance of SPS activities in response to NATO Strategic Objectives and political priorities is reinforced also via special calls, which are issued on an ad hoc basis to draw the attention of the scientific community towards current topics of interest for Allies.

The Science for Peace & Security programme

The SPS Programme also has a high public diplomacy value for NATO, providing the Alliance with separate, non-military communication channels by bringing together experts from NATO and Partner countries, often in situations or regions where other forms of dialogue more directly focused on defence and security are difficult to establish. Accordingly, the Programme enables NATO to become actively involved in such regions, often serving as the first concrete link between NATO and a new partner.

Every year, approximatively 2000 experts participate in SPS activities and help to build capacity in partner nations, and support NATO's security efforts.

More than 20 Nobel Laureates have been involved in the SPS Programme, a testament to the scientific excellence supported by the SPS Programme.

Young scientists are also actively supported through SPS activities, which contribute to broaden their professional network and scientific expertise.

Emerging Security Challenges Division
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You can find further information on our website:
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