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Finding a treatment for COVID-19 –the EU is contributing

COVID-19 is a disease caused by infection with a novel coronavirus called SRAS-CoV-2. This virus is entirely new to humans, meaning that there are **no approved medicines** to protect us from or treat COVID-19.

The current high and increasing number of patients makes it very clear that we **urgently need to improve our ability to cure COVID-19**. However, the development of treatments can be a lengthy process, depending on the treatment type. While efforts can be made to speed up, there are a number of mandatory steps that determine whether and how fast we can move forward through the process, while making sure that the safety of these treatments is assessed.

We can take different routes to find a good treatment. The fastest is to start with a treatment based on a medicinal product that is already approved (and therefore deemed safe) and available, even though it has not been developed for treatment of COVID-19. This is called **repurposing**; such products can be tested for their capacity to treat COVID-19 without the need to reassess their safety. Basing the treatment on the use of **anti-body rich blood plasma** or components thereof, collected from donors who have recovered from the virus, is another potentially beneficial treatment for COVID-19 patients. A third possibility is a **treatment based on monoclonal antibodies** that inactivate the virus by binding to it. A fourth possibility is screening for compounds that can be used to start developing **a completely novel treatment,** but it should be noted that this is a lengthy process that likely requires several years. In addition to this, it is important to assess any **detrimental effects of currently used medicines** since some of them could potentially increase sensitivity to infection with SARS-CoV-2, or negatively affect treatment and recovery. In addition to this all, **non-pharmaceutical interventions** can improve treatment/standard of care. Such interventions can cover a very broad area, including e.g. protective equipment, telemedicine and digital technologies that allow close monitoring while at home.

Clinical trials are crucial for developing effective and safe treatments. In order to have enough evidence about what works and what does not, it is essential to avoid fragmentation of study initiatives. Trials need to enrol a sufficient number of patients, and use standardised and agreed upon protocols to reach conclusive results on efficacy. For these reasons, the **European Medicines Agency** (EMA) has asked to **prioritise large randomised controlled trials**, as the best avenue to generate the conclusive evidence needed to enable rapid

[1] https://www.ema.europa.eu/en/news/call-pool-research-resources-large-multi-centre-multi-arm-clinical-trials-

development and approval of potential treatments of COVID-19.1 It also emphasises the need to include all EU countries in these trials.

Two multi-centre and multi-arm clinical trials have started in Europe, investigating different treatment options for the treatment of COVID-19. The **DisCoVery** trial, for all COVID19 patients entering hospital, and the **REMAP-CAP**[2] trial for patients in intensive care units. The DisCoVery trial and the REMAP-CAP trial are complementary and can co-exist in the same sites.

In the absence of short-term alternatives it is worthwhile to test the safety and efficacy of a **treatment based on using blood plasma** obtained from recovered patients.

The Commission funded actions so far include:

- The funding of eight projects that will use a **variety of research approaches to develop antibody-based therapies, antivirals, or focus on drug repurposing** (see Annex 1). The funding of the REMAP-CAP trial is one example, another is the project "**Exscalate4CoV**", which involves a coalition between scientists and three of the most powerful supercomputing centres in the EU to use this massive computing power to find potentially effective drugs against COVID-19.
- March 31, the Horizon 2020-supported **Innovative Medicines Initiative (IMI)**, a public-private partnership between the EU and the pharmaceutical industry, received 144 proposals for research on diagnostics or therapeutics under its fast track call. The evaluation of these proposals is ongoing. Horizon 2020 will contribute up to €45 million to this call and a commitment of a similar scale is expected from the pharmaceutical industry so that total investment could reach €90 million.
- March 18, 2020 the Horizon 2020 **European Innovation Council (EIC)** Accelerator pilot received 4000 applications for its bottom-up call for proposals, out of which 1000 COVID19 related. Assessment of these proposals is ongoing. A fast-track procedure for the signature of contracts with the selected companies working on COVID-19 related topics will be ensured.
- On 3 April the Horizon 2020-supported **European and Developing Countries Clinical Trials Partnership (EDCTP)**, a public-public partnership focusing on infectious diseases research in sub-Saharan Africa, launched an emergency call for expressions of interest for research projects to provide novel, critical and timely insights into the COVID-19 outbreak in sub-Saharan Africa and/or potential avenues for its management or prevention.

The Commission's ongoing actions and proposed actions to the Member States aim to strengthen and **speed up the development process**, making the EU contribution impactful,

generate-sound-evidence

[2] https://www.remapcap.org/coronavirus

and, importantly, **ensuring Europe's future autonomy and capacity** (beyond COVID) so that treatments can be **developed, produced and distributed according to the EU principles and values of ethics, fairness and solidarity.**

Proposed coordinated actions with Member States

i) To speed up the development process

In addition to funding the EU wide extension of clinical trials (as referred to in point three of the Action Plan for R&I coordinated action), the aim should be to set up and further develop an **EU wide COVID-19 clinical trials network.** Such a network would include a 'EU coordination hub' that would keep the overview of all ongoing trials, help select the most promising approaches and swiftly move those through advanced development phases, saving vital time and resources. Work would be closely coordinated with WHO. The network should help build capacity at European level to rapidly conduct clinical trials in relation to any serious future pandemic threat. As the work programme 2020 already dedicates EUR 30 million to the "Creation of a European wide sustainable network for harmonised large-scale clinical research studies for infectious diseases", this could provide the platform to further develop the network.

ii) To ensure autonomy in manufacturing and distribution

Many medicines are produced outside Europe, this is especially true for generics and even more so for precursors of medicines. Several Member States have proposed to work toward a joint, coordinated and collaborative development of treatments, also ensuring autonomy in their manufacturing and distribution. In this context, the Commission could explore the possibility of an **EU joint procurement mechanism**, possibly using advance purchase agreements, to ensure that effective and safe new treatments are produced and distributed at scale and in a fair, equitable and transparent matter.

The proposed actions at EU level should be deployed in synergy with initiatives at **international level** such the **'treatment accelerator'** launched by the Wellcome Trust, the Bill and Melinda Gates Foundation and Mastercard. Managed by Gates and Wellcome staff, the accelerator is intended to enhance coordination between the various groups working on COVID-19 compound identification and development, including those funded by governments, and focus on the last parts of the R&I chain (from drug pipeline development through to manufacturing and scale-up) and of course in close cooperation with **WHO.**

Annex

Eight COVID-19 research projects that have been shortlisted for EU funding

- **Drug repurposing**

EXCALATE4CoV - aims to exploit **the most powerful computing resources currently based in Europe** to empower smart *in-silico* drug design. Advanced Computer-Aided Drug Design (CADD) in combination with the high throughput biochemical and phenotypic screening will allow the rapid evaluation of the simulations results and the reduction of time for the discovery of new drugs. - Antiviral drugs and repurposing

RiPCoN – aims to identify approved drugs that can be repurposed for the treatment of 2019-nCoV using interactome profiling and deep-learning. The project will deploy rapid high-throughput protein-protein interaction mapping and computational protein-RNA interaction predictions to chart the coronavirus host interactome network (CoHIN).

SOLNATIDE – will use a peptide-based drug Solnatide IMP that has already been approved for the therapeutic treatment of Pulmonary Permeability Oedema and target the respiratory system

- **Antibody based therapy**

ATAC - aims at developing passive immunotherapy against COVID-2019. Human antibodies will be obtained from blood of CoV-recovered donors from China and Italy Those will be characterized by rapid experimental and computational work, optimized, produced and tested in consultation with the **EMA** to ensure prompt embedding of regulatory aspects.

MANCO – will perform preclinical and clinical evaluation of monoclonal antibodies against 2019-nCoV. It will build on and leverage outstanding results from the ongoing **IMI-funded project ZAPI**, including recently-discovered broadly cross-reactive monoclonal antibodies against beta-coronaviruses and an established pipeline for rapid identification of specific monoclonal antibodies against 2019-nCoV; antibodies that will be selected are to proceed to GMP manufacturing.

CoroNAb – aims to rapidly identify, validate, and disseminate pre-clinical protein therapeutic candidates with neutralizing activity against 2019-nCoV, and to recommend where their use would be maximally effective. The project intends to design and synthesize recombinant variants of nCoV glycoproteins to generate and characterize multiple nCoV-neutralizing antibodies and nanobodies.

- **Antivirals**

SCORE -will target the virus using five independent approaches: (i) using (combinations of) FDA-approved drugs, (ii) targeting viral RNA synthesis, (iii) inhibiting coronavirus proteases, (iv) blocking virus entry, (v) discovery and development of new antivirals. This program will be supplemented with 2019-nCoV toolbox and animal model development.

Fight-nCoV - will accelerate preclinical development of new broad-spectrum antivirals for inhalation. It will determine and characterize the antiviral activity and safety of three viral entry inhibitors against SARS-CoV-2 in vitro and in vivo. To enable this, the project will build capacity for evaluation

of antiviral efficacy against SARS-CoV-2 in vitro using viral pseudotypes and wild-type SARS-CoV-2 as well as in vivo in non-human primates.