Development of therapeutics and diagnostics combatting coronavirus infections

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Specific challenges to be addressed by public-private collaborative research

Coronaviruses (CoV) are a large family of enveloped positive stranded RNA viruses that typically result in respiratory and enteric infections. CoV are zoonotic in origin, but they can evolve into a strain that can infect human beings leading to fatal illness. Typically, CoV infections were considered relatively benign to humans before the severe acute respiratory syndrome (SARS-CoV) outbreak in 2002/2003 in China and the Middle East respiratory syndrome coronavirus (MERS-CoV) outbreak in 2012 in the Middle Eastern countries.

On 31 December 2019, the local authorities of Wuhan, Hubei province, China, reported a cluster of pneumonia cases of unknown origin. On 9 January 2020, the China Centre for Disease Control reported a novel Coronavirus (as of February 11, 2020 named COVID-19) to be the causative agent.

As of 12 February 2020, 45,179 laboratory-confirmed cases of novel coronavirus (COVID-19) infection have been reported, including 1115 deaths. The disease has already spread to 28 countries outside China, with new cases continuing to emerge daily [1]. The COVID-19 outbreak has been declared by WHO as a Public Health Emergency of International Concern according to the International Health Regulation [2].

Recalling the SARS-CoV epidemic in 2003 with over 8000 cases reported (10% case fatality), it is crucial to rapidly gain a better understanding of the newly identified virus, especially in relation to potential clinical and public health measures that can be put to immediate use to improve patients’ health and/or contain the spread of COVID-19.

Considering the public health and humanitarian implications, there is a need for all stakeholders across the public and private sectors to collaborate in global efforts to care for those affected, contain the outbreak and develop the much-needed resources to prepare for the future. Collaboration of private companies, academia, international organisations, public bodies etc. has the potential to accelerate the development of therapeutics and diagnostics to tackle this current and future outbreaks. The actions resulting from this call will contribute to the pan-European efforts responding to this Public Health Emergency.

Scope

Proposals submitted under this topic are expected to advance the knowledge specifically on COVID-19 and more widely on the coronavirus family with the aim of contributing to an efficient patient management and/or public health preparedness and response to current and future outbreaks of coronavirus infection.
Considering that this is a newly identified virus, the scope of this topic remains broad and must address at least one of the following objectives:

- Development of therapeutics to address a rapid response towards the current COVID-19 outbreak: relevant "clinical ready"-assets include approved therapies or compounds in development, which could be repurposed for use in treating patients with the coronavirus. For example (but not limited to), angiotensin-converting-enzyme (ACE) inhibitors, protease inhibitors or immunotherapies (antibodies/antibody-like molecules) that could be relevant in the context of CoV. As relevant, evidence of regulatory and ethics approvals for the investigational products included in the study(ies) must be presented;

- Development of therapeutics to address the current and/or future coronaviruses outbreaks: identification of new potential assets and approaches that could be utilised including preventive strategies and combination approaches and could also address potential resistance. This may also include optimisation of promising treatments used in rapid response (e.g. reformulation);

- Development of diagnostics, ensuring rapid evaluation of candidates based on existing technologies, to allow for fast case detection and surveillance. Diagnostic tests will be essential in the frame of clinical trials for new or repurposed drugs, to help stratify patients and assess treatment efficiency (surrogate end point such as viral clearance);

- Development of fast and reliable detection of nCoV carriers and symptomatic individuals suspected of nCov infection. These are mandatory and of utmost importance to manage the outbreak, isolate patients at risks and treat people accordingly. It is crucial to differentiate and identify respiratory pathogens responsible of clinical sign (e.g. versus flu, RSV, other viruses or bacteria) and/or detect emerging pathogens such as COVID-19. This can be achieved through point of care (POC) testing or centralized testing;

Please note that vaccines are specifically excluded from the scope of the call.

For increased impact, proposals should consider building on promising avenues from previous or ongoing research.

Proposals covering investigation of therapeutic should consider engaging with the European Medical Agency (EMA) to ensure adequacy of the proposals from a regulatory point of view, i.e. via the innovation task force, scientific advice or consultation in the context of the health threats interactions [3].

Collaboration agreement(s)

To ensure the interactions between actions funded under this call, the selected consortia are expected to cooperate and share their learnings for the purpose of achieving the objectives of their respective actions, in order to maximise the impact. Therefore, all grants awarded under this call will be complementary grants. The respective options under Article 2, Article 31.6 and Article 41.4 of the IMI2 JU Model Grant Agreement\(^1\) will apply. Accordingly, the relevant consortia will conclude collaboration agreement(s) to ensure the exchange of relevant information, exploration of synergies, collaboration where appropriate.

Expected key deliverables

Each proposal must include at least one of the following key deliverables:

- Therapeutics to be used in the current outbreak, including preventive and symptomatic treatments;

- Novel therapeutics including combinations treatments to ensure appropriate treatment for current and/or future outbreaks and/or to prevent resistance;

- Diagnostics including associated enablers (for example antibodies, antigens etc).

In the context of achieving the above deliverables, i.e. development of therapeutics and diagnostics, it is recognised that studies related to the understanding of the mechanism of action will generate new knowledge on the virology, immunology and pathogenesis of the coronavirus, and that new analytical technologies and reagents may be developed.

When relevant, deliverables should include:

• Hit identification of suitable assets (e.g. existing libraries, approved drugs and assets passed phase 1 for repurposing; protease and (non)-nucleoside inhibitors) against COVID-19 and/or pan-coronavirus; implementation of High-Throughput Screening Assay in collaboration with Europe based centers of excellence;
• Lead optimization: Initiating Target-based Discovery Programs based for instance on literature for identification of promising approaches;
• Proof of Concept: Pre-Clinical animal studies and Clinical studies including at least first in human (FIH) and Phase 2A studies for both repurposed and new molecular entities;
• Diagnostics and associated enablers (e.g. production of antibodies and viral proteins); characterisation of nCoV strains; sustainability plans for data repositories, sample repositories etc., documentation supporting regulatory submission.

Expected impact

Proposals must be timely, with rapid activation, to enable early and valuable outcomes to be established.

On the basis of the proposed activities, applicants should describe how the outputs of the project will contribute to one or more of the following impacts and include wherever possible targets and metrics to measure them:

• Fast track development and availability of therapeutics and/or diagnostics to be used in the clinical management of patients infected by COVID-19 and/or future outbreaks of coronaviruses, and to ensure that a variety of drugs are available for patients, including tackling resistance, and combination therapy.
• Contribution to the public health preparedness and response in the context of the ongoing epidemic of COVID-19 and/or future outbreaks of pan-coronaviruses.
• Significant impact on global health, both at the individual and the public health level by leading to results that have a direct impact for persons at risk of exposure to coronavirus or for patients suffering from coronavirus disease.

To ensure maximum impact for patients, applicants should demonstrate the operational capacity to advance assets through clinical development and reach the market as rapidly as possible.

In addition, applicants must maximise the IMI2 JU public-private partnership value by harnessing support from different stakeholders, including the mobilisation of resources through the inclusion of contributing partners\(^2\), providing contributions (in kind and/or financial), to reflect the public-private character of IMI2 JU actions.

Beneficiaries in grants awarded under this topic must make available their research data, at the latest within 30 days after it has been generated, through open access or, if agreed by the IMI2 JU or the European Commission, by giving access rights to those third parties that need the research data to address the public health emergency. Therefore the relevant option of Article 29.3 will be applied.

Potential synergies with existing consortia

Synergies and complementarities are expected with relevant national, European and non-European initiatives (including suitable biological and medical sciences research infrastructures\(^5\)) in order to incorporate past achievements, available data and lessons learnt where possible, thus avoiding unnecessary overlap, and duplication of efforts and funding. In particular, applicants are expected to collaborate with any relevant project or initiative targeting the current COVID-19 outbreak supported by the European Commission, CEPI, Wellcome, BARDA, The Bill and Melinda Gates Foundation and others.

\(^2\) Contributing partners: EFPIA companies or organisations associated to EFPIA, and Associated Partners to IMI2 JU contributing resources to the action may report it as their in-kind or financial contribution to the IMI2 JU. If the contributing entity is not yet an affiliate or a constituent entity of an IMI2 Member other than the Union (i.e. EFPIA), or an Associated Partner at the time of the proposal submission, and the proposal is selected for funding, such a legal entity is invited to become an affiliate or a constituent entity of an IMI2 Member, other than the Union, or an Associated Partner in accordance with the IMI2 JU Statutes prior to the signature of the relevant Grant Agreement.
Where relevant, proposals should consider the close collaboration with leading European supercomputing centres to use high-end computing, data and simulation resources in order to accelerate the processes of diagnosis and vaccine research and development. In this respect, the Supercomputing facilities in Barcelona (BSC) and Bologna (Cineca) are open to collaborate with any interested proposer or successful proposal. Other leading European supercomputer centres, such as the organisations hosting the PRACE Tier-0 supercomputers, may also be interested in such collaborations.

**Indicative duration of the action**

Proposals should include a proposed duration for the action in relation to the activities and expected impact. Successful applicants may request a starting date prior the entry into force of the GA, up to the date of submission of the proposal.

**Indicative budget**

Applicant consortia will be competing for the maximum total financial contribution from IMI2 JU up to EUR 45 000 000.

Within this budgetary envelope, each proposal must include a sound justification of the budget requested, taking into account the proposed in-kind contributions from contributing partners, i.e. EFPIA constituents or affiliated entities and/or, when relevant, IMI2 JU Associated Partners.

All proposals submitted under this Call and evaluated above the threshold will be ranked in one single list. Proposals will be invited in order of ranking to prepare a Grant Agreement within the limits of the available overall budget.

**Applicant consortium**

Applicant consortia are expected to address at least one of the objectives of the topic and demonstrate the necessary expertise and access to facilities to meet the relevant key deliverables and ensure the expected impact.

The size and composition of each consortium should be adapted so as to respond to the objectives and the key deliverables of the Call while ensuring its manageability.

In accordance with the Horizon 2020 Rules for Participation in order to be eligible, a proposal must be made by a consortium of at least three independent legal entities, each established in a different Member State or associated country.

While preparing their proposals, applicant consortia should ensure that needs of patients are adequately addressed and, where appropriate, patient involvement is encouraged.

**Single stage proposal**

While preparing their proposal, applicants are requested to pay due attention to all the following points:

**Data management**

In their proposal, applicants should give due visibility to data management including use of the data standards. A full ‘data management plan’ (DMP) as a distinct deliverable must be delivered within the first 6
months of the action. The DMP needs to be kept up to date with the needs of the action and as such be updated as necessary during its lifetime.3

Applicants should be aware that data must be deposited in a relevant established international data platform, such as the one WHO, European Molecular Biology Laboratory (EMBL).

Dissemination, exploitation and communication
In their proposal, applicants must provide a draft plan for the exploitation and dissemination of results. A full plan as a distinct deliverable must be delivered within the first 6 months of the project.4 The proposed communication measures for promoting the action and its findings during the period of the grant should also be described and could include a possible public event to showcase the results of the action.

The principles established in the Statement on Data Sharing in Public Health Emergency will be applied.

Sustainability
In their proposal, applicants must describe a sustainability plan beyond the end of the Grant Agreement. This plan may be updated during the action lifetime and could include:

- identification of results that may need sustainability solutions;
- identification of potential end-users for these results;
- a proposed sustainability roadmap.

Sufficient resources should be set aside for activities related to the sustainability of the project results. This may involve engaging with suitable biological and medical sciences research infrastructures (RIs).5

Patient and healthcare provider engagement
Applicants are encouraged to include a strategy to engage with patients, learned societies and healthcare providers as relevant to ensure the project results impact on healthcare practices.

Regulatory strategy
Applicants are expected to have a strategy for the translation of the relevant outputs into the regulatory practice to promote the uptake of the results e.g. qualification advice, qualification opinion when relevant. A plan for interactions with regulatory agencies/health technology assessment bodies/payers, with relevant milestones and sufficient resources, should therefore, be proposed.

References

4 As an additional dissemination obligation under Article 29.1 of the IMI2 JU Grant Agreement will apply
5 http://www.corbel-project.eu/about-corbel/research-infrastructures.html