

Pilot programme on a Clinical Compound Bank for Repurposing

Topic: Cardiovascular diseases and diabetes

Topic: Respiratory diseases

Topic: Neurodegenerative diseases

Topic: Rare/orphan diseases

All information regarding future IMI Call topics is indicative and subject to change. Final information about future IMI Calls will be communicated after approval by the IMI Governing Board.

Topic details

Action type Research and Innovation Action (RIA)

Submission & evaluation process 2 Stages

Specific challenges to be addressed

On average it takes about 14 years for a new drug to travel from the research lab to market approval at an average cost of \geq €2 billion. Only 10% of compounds that enter preclinical testing ever make it into clinical trials, with only 20% of these achieving marketing approval [1][2].

A number of innovative programmes have been established over the last few years between research funding agencies and industry to provide academic researchers with access to high-quality pharmaceutical industry compounds that have stalled at some stage during research or development. Many of these compounds have already undergone preliminary testing in humans, but have not been progressed further because they were not found to be sufficiently effective in the indication for which they were originally developed.

These compounds represent valuable tools that researchers can use to test their novel hypotheses for alternative therapeutic indications, with the ultimate aim of identifying alternative uses for these compounds in other indications (“repurposing”, “repositioning”). Since partial preclinical and clinical documentation packages have been developed for these assets, any positive findings hold the opportunity to progress towards the

market more quickly and cost-effectively, with the ultimate goal of benefiting patients in diseases of high unmet need. Examples of ongoing open innovation schemes include the National Institute of Health/National Center for Advancing Translational Sciences (NIH/NCATS), the New Therapeutic Uses program in the US¹ and the Medical Research Council (MRC) industry asset sharing initiative in the UK² in which many EFPIA members already provide previously unprecedented access to a subset of their assets. Expanding this asset-sharing repurposing programme through IMI2 JU aims to provide researchers across the EU with the same opportunity to form hypothesis, to engage in collaborative research with industry and to access discontinued compounds that have already passed through several stages of the drug development process.

In this call, a number of compounds are made available for exploration in specific therapy areas: cardiovascular diseases and diabetes, respiratory diseases, neurodegenerative diseases and rare/orphan diseases.

The pharmaceutical small molecule compounds made available are listed in the [Appendix](#), together with key information on mechanism of action, pharmacology, safety, tolerability and exclusions relating to these compounds. The applicants will submit proposals to utilise these assets to test their hypotheses for alternative indications within the above-mentioned therapeutic areas, to generate clinical data and, if needed, prerequisite preclinical data, with the ultimate aim of taking these assets to the market in alternative indications to those that they were originally developed for.

If these pilot topics on drug repurposing are successful, the programme will be expanded in future calls.

Need and opportunity for public-private collaborative research

The European research organisations, including universities, hospitals and Small- and Medium-sized Enterprises (SMEs) are renowned for their cutting edge science and innovative spirit, yet often do not have the tools nor the expertise to develop their discoveries towards the clinic and regulatory approval. The pharmaceutical industry has built up significant experience, knowledge and research and development (R&D) information for a large number of deprioritised or disused compounds arising from terminated programmes. Public-private collaboration enables the investigation of scientific advances within research organisations using drugs and drug candidates from industry. Academic organisations benefit from access to clinic-ready assets and prior R&D information. This includes predefined preclinical and clinical dosing regimens, toxicological and pharmacokinetic/pharmacodynamic data packages which help to ensure their studies are designed with the best possible chance of success, alongside the industrial guidance on the data package needed to support development and transition towards the market.

By collaborating and bringing the strengths of European research communities and pharmaceutical companies together, it may be possible to accelerate the research in drug repurposing and potentially speed up the development of new treatments and giving patients access to these new therapies.

Parallel grant-funding schemes with the NIH/NCATS, MRC and selected institutions around the world, contain many examples of preclinical and clinical proof-of-concept studies in which the academic and industry collaboration has provided the opportunity for a rapid transition towards clinical development. This model has also previously provided the opportunity to spin out new SMEs based on positive repositioning data, enabling funds to be raised to progress to later stages of clinical development. All of these advantages have the long-term effect of getting drugs to the market quicker and more cost effectively for the benefit of patients.

A private-public partnership like IMI2 JU provides the opportunity to test interesting compounds in new indications that may not be otherwise tested. In addition, IMI2 JU provides an exciting possibility for translational research funding accessible to researchers across the EU and H2020 Associated Countries.

¹ https://ncats.nih.gov/ntu/about?_sm_au=iDVNkL6Rk8jPqH55

² <https://www.mrc.ac.uk/news/browse/world-s-largest-collection-of-deprioritised-pharma-compounds-opens-to-researchers/>

Scope

The overall objective of this pilot programme is to take one of the ten previously deprioritised clinical compounds listed in the [Appendix](#) – and investigate their therapeutic potential in new clinical indications in areas of high unmet need.

Under the Clinical Compound Bank for Repurposing pilot programme, there will be four separate topics, one for each disease area listed below:

- **Cardiovascular diseases and diabetes**
- **Respiratory diseases**
- **Neurodegenerative diseases**
- **Rare/orphan diseases**

Potential applicants must be aware that only the compounds identified in the [Appendix](#) are within the scope of these four topics. These compounds are listed therein together with key information including mechanism of action, original indication, route of administration pharmacology, safety, tolerability and links to previous clinical studies and publications, to facilitate idea generation by investigators with hypotheses for novel uses. The listed compounds have all been through clinical phase 1 studies.

All proposals submitted under one topic will be evaluated by a panel of independent experts and ranked together. For each topic, only one proposal will be eventually retained and a grant agreement will be signed.

- Proposals should cover clinical Phase 2A proof of concept studies, though larger Phase 2 studies are also in scope if these are within the budget. Clinical submissions should aim at moving towards the next stage of development and positive data should be a starting point for further investment into developing a drug towards clinic and regulatory approval;
- If preclinical work is deemed necessary to provide additional support and confidence before moving into a clinical study in an alternative indication, proof-of-concept/feasibility preclinical studies of up to a year in duration can be included in the proposal. These studies should have clear go/no-go criteria for progressing in to the clinical phase of the project.

Important note: This programme intends to support only innovative clinical development for the compounds listed in the [Appendix](#). This means that proposals for clinical development should not be considered in an indication which has been already tested (i.e. original primary indication or additional studies) or if there are already ongoing or planned clinical studies on identical or related disease indications with the compound or with a compound with overlapping mechanism of action that impacts the novelty of a given proposal.

Information on original primary indications, already tested indications, ongoing and/or planned clinical studies for each of these ten compounds can be found in the [Appendix](#).

Therefore, applicants must demonstrate in their stage 1 application (short proposal) that the proposed study is innovative for the chosen compound.

Expected key deliverables

Proposals should have the potential to identify a new indication for the compound chosen among those made available within this pilot programme. Each selected project must aim at making clear scientific advances within a given disease area.

Key deliverables for each selected project include:

- Initiation and completion of new Phase 2A clinical proof-of-concept study in the chosen indication which was not previously investigated with the specific compound;
- Preclinical data to support a go/no go decision for initiation of the clinical study in the new indication, if this is deemed necessary for the selected project;

- Dissemination of the results in high impact publications.

Expected impact

- Achieving early proof-of-concept for new mechanisms with the potential to rapidly bring novel drugs to patients in areas of high unmet need and/or those with greatest disease burden;
- Generation of ideas and/or data licensed from the research organisation, leading to further development of the compound in the new indication;
- Added value by repurposing pharmaceutical assets which have already passed through several stages of the R&D process. This can offer significant time, cost and risk savings over embarking on discovery programmes with novel targets;
- Supporting EU academic institutions to conduct well-designed and high standard translational and drug development research with quality compounds under GCP conditions, resulting in high impact publications and patents when possible;
- Pooling of resources and greater collaboration between the public and private sectors, with the potential for pharmaceutical involvement or establishment of SMEs following in/out-licencing;
- Boosting the discovery and development of therapeutics in the areas of cardiovascular diseases and diabetes, respiratory diseases, neurodegenerative diseases and rare/orphan diseases using a more cost-effective approach to drug development;
- Advancing science and knowledge of disease (patho)physiology through testing of new hypothesis;
- Boosting European competitiveness by contributing to the establishment of closer links between industry and academia across the EU, and ensuring Europe is competitive in line with initiatives already in place in other leading scientific regions around the world.

Potential synergies with existing consortia

Applicants should take into consideration, while preparing their short proposal, relevant national, European (both research projects as well as research infrastructure initiatives), and non-European initiatives. Synergies and complementarities should be considered in order to incorporate past achievements, available data and tools/models and lessons learned where possible, thus avoiding unnecessary overlap and duplication of effort.

The projects generated from this topic will be complementary to other ongoing similar initiatives in other parts of the world.

Industry consortium

The industry consortium will contribute the following expertise and assets:

Compounds for these pilot topics. The EFPIA companies will cover the costs associated with manufacturing, supply and delivery of Active Pharmaceutical Ingredient (API) required for a given study. Clinical studies costs associated with supply, packaging and distribution of drug product will also be covered by the EFPIA companies. The EFPIA companies will provide expert support for e.g. study design, protocol writing, study oversight, pharmacovigilance, as well as expert support throughout the duration of the funded studies with the aim of working with the consortium to move positive data towards the next stage of development. Under each topic, only one of the two contributing companies listed above will be involved in the full proposal and selected project. This will depend on the clinical compound which will be developed under a new indication.

Indicative duration of the action

The indicative duration of the action is 48 months.

Clinical studies are anticipated to have a maximum duration of 36 months per action. If preceded by a preclinical study, this study should have a maximum duration of 12 months, giving a maximum of total 48 months per action.

Applicant consortium

The applicant consortium will be selected on the basis of the submitted short proposals. Applicants are expected to form consortia with other investigators to bring in relevant expertise and ensure study recruitment targets are met in the clinical studies. All experimentation should be undertaken within the investigators' research institutions and/or their linked third parties.

The proposals should be based on a strong scientific rationale from prior preclinical and/or clinical data. The planned studies should have the potential for improvement of currently available treatments and it is also important that the proposed clinical studies in the projects have a clear feasibility for further clinical development and commercialisation of the compounds in the suggested indications, beyond the project duration.

The applicant consortium is expected to address all the research objectives and make key contributions to the defined deliverables in synergy with the relevant contributing company from the industry consortium which will join the selected applicant consortium for preparation of the full proposal in stage 2.

This may require mobilising, as appropriate, the following expertise and resources:

- experience and capability to conduct all aspects of a clinical trial using an investigational medicinal product (including data analysis and reporting) under Good Clinical Practice (GCP) in the proposed indication;
- clinical and preclinical expertise as necessary for the scope of a given study;
- expertise in the science of drug development including aspects of clinical pharmacology, study design and conduct;
- experience and capability to submit an application for clinical trial authorisation with the European Medicines Agency (EMA)/ national regulatory authorities in all member countries of a given consortium;
- strong project management and communication expertise.

Suggested architecture of the full proposal

The applicant consortium should submit a short proposal which includes their suggestions for creating a full proposal architecture, taking into consideration the contributing company participation including its contributions and expertise.

In the spirit of the partnership, and to reflect how IMI2 JU call topics are built on identified scientific priorities agreed together with EFPIA beneficiaries/large industrial beneficiaries, these beneficiaries intend to significantly contribute to the programme and project leadership as well as project financial management.

The final architecture of the full proposal will be defined by the participants in compliance with the IMI2 JU rules and with a view to the achievement of the project objectives. The allocation of a leading role within the consortium will be discussed in the course of the drafting of the full proposal to be submitted at stage 2. To facilitate the formation of the final consortium, until the roles are formally appointed through the consortium agreement, the proposed project leader from among EFPIA beneficiaries/large industrial beneficiaries shall

facilitate an efficient negotiation of project content and required agreements. All beneficiaries are encouraged to discuss the project architecture and governance and the weighting of responsibilities and priorities therein.

References

- [1] Frail DE, Brady M, Escott KJ, Holt A, Sanganee HJ, Pangalos MN, Watkins C, Wegner CD. Pioneering government-sponsored drug repositioning collaborations: progress and learning. 2015. *Nat Rev Drug Discov*:14(12):833-41.
- [2] Hughes JP, Rees S, Kalindjian SB, Philpott KL. Principles of early drug discovery. 2011. *Br J Pharmacol*: 162(6):1239-49

Indicative text

Appendix – Compound information template

	Compound name
Mechanism of action	
Overview	
Safety/Tolerability	
Additional information	
Suitable for and Exclusions	
<ul style="list-style-type: none"> - Clinical Trials - Previous, ongoing and planned 	Link to clinical trials.gov
Additional Characteristics: <ul style="list-style-type: none"> ▪ CNS penetrance ▪ Pediatric Diseases ▪ Other 	
Publications	