

IMI 2 – Call 10: Overview of Call topics

IMI Scientific Team

28.09.2016 • IMI Stakeholder Forum 2016 • Brussels, Belgium

Key information

Indicative Call launch date?

Late October

Webinars

Around the time of the Call launch

Where to find information

www.imi.europa.eu

Twitter: @IMI_JU

LinkedIn (Innovative Medicines Initiative group)

IMI newsletter (sign up via IMI website)

Unlocking the solute carrier gene-family for effective new therapies

Hugh Lavery

Objectives

- The main objective is to “unlock” as much of the SLC family as possible to enable drug discovery efforts to be conducted “at will” across the whole family of ~400 proteins.
- The first part of the project is broad and ambitious (aiming for >80% coverage of the gene family) in the areas of transporter deorphanization, generation of cell lines expressing SLC family members, and in the development of new screening methodologies. These are areas where more radical innovation from the public contributors will be required to achieve the goals of the project
- The second half project is more focused (on roughly 20% of the gene family) in areas where the proteins will be studied in more detail and resource intensive fashion. It is anticipated that knowledge, reagents and methods gained from this subset of the SLCs will provide an accelerator for other researchers.

Expected impact on the R&D process

- This IMI project is expected to deliver new open access research tools, techniques, reagents, and knowledge to the biomedical research community that will rapidly accelerate the pace of research in the field of SLCs. These advances are expected to impact both basic research and drug discovery alike

Expectations from applicant consortium (I)

Expertise, leadership and a proven track record in the following areas:

- Human genetic screens involving state of the art human cell culture technologies for high-throughput assessment
- Next-generation sequencing for high-throughput RNA and/or DNA sequencing, ChIP-sequencing
- Applying mass spectrometry to understand systems-wide cellular changes in proteins and metabolites Studies of physiologically and therapeutically relevant proteins.

Expectations from applicant consortium (II)

Expertise, leadership and a proven track record in the following areas:

- Expression of human full-length membrane proteins or membrane protein domains in multiple systems.
- Production and characterization of recombinant protein binding tools
- In vitro and in-cell target engagement assays.
- Expression, characterization and structure determination of integral membrane proteins in an integrated project at large scale
- Production and characterization of high quality chemical probes

Expectations from applicant consortium (III)

Expertise, leadership and a proven track record in the following areas:

- Having an established network of recognized thought leaders in all relevant sectors, with a track record of success, as evidenced by collaborative publications:
- Successfully collaborating in a network with industry:
- Capability to mobilise and access as appropriate, public databases:

Precision medicine approaches in autism spectrum disorders

Elisabetta Vaudano

Objectives

To create a European-wide strategy, in collaboration and in alignment with US-based efforts, to overcome key bottlenecks in the development and testing of treatments for ASD by building the necessary capacity within Europe for the conduct of future ASD trials, while contributing towards a more unified approach to clinical research in ASD within Europe.

- Create a European-wide clinical trials network trained to GCP standards to facilitate large-scale clinical trials.
- A fully aligned and integrated global framework for clinical trials in ASD and co-morbidities.
- Validate stratification biomarkers to enable identification of more homogeneous clinical and / or biological subgroups for clinical trials, including for co-morbidities.
- Enhance drug discovery efforts by testing translatability of drug effects (new and/or repurposed) between patients with ASD and preclinical models to enable and feed a sustainable pipeline of innovative treatments.

Expected impact on the R&D process

- Development of a unified approach to clinical research in ASD within Europe.
- Development of a Europe-wide infrastructure to accelerate and tailor patient recruitment to targeted (adaptive) clinical trials.
- Identify patient sub-populations for particular treatments through validation and qualification of stratification biomarkers
- A better understanding of common vs. distinct pathophysiological mechanisms underlying ASD subgroups, i.e. genetic, neurobiological and/or accounting for clinical variables such as comorbidities, developmental stage and sex.
- To set new standards for industry and allow potential identification of personalised medicines for patients in highly characterized patient groups.

Expectations from applicant consortium

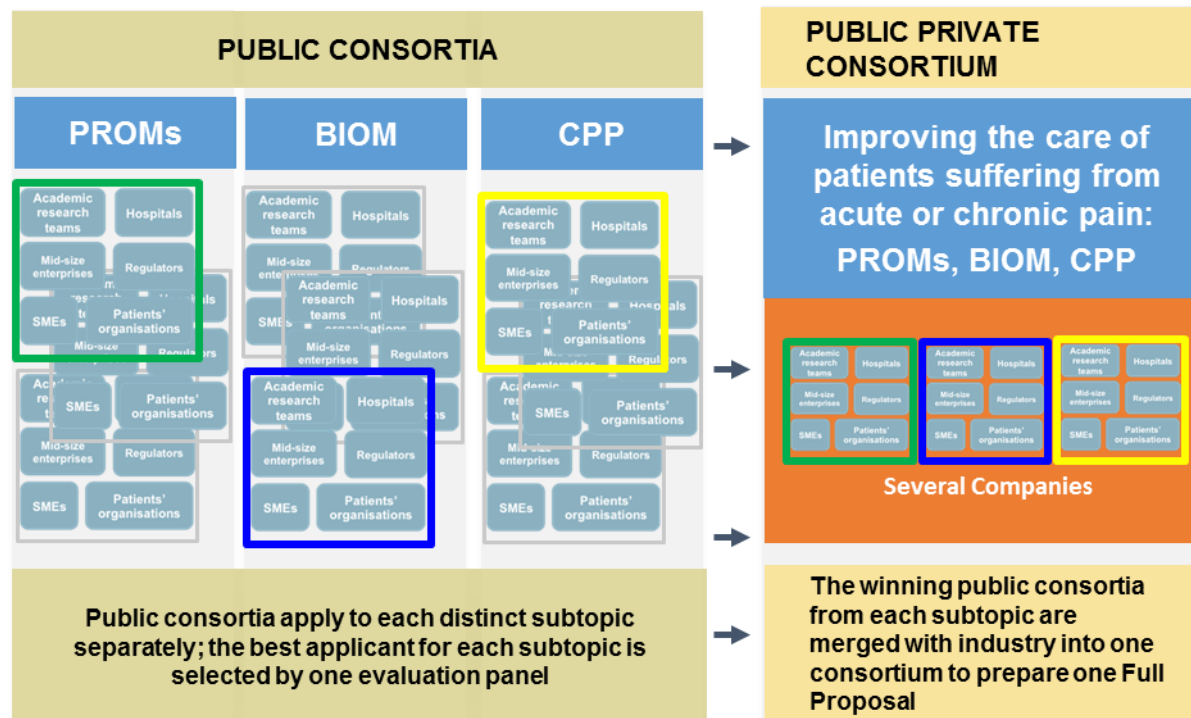
- Clinical expertise
- Biomarker expertise
- Regulatory and logistical (clinical network) expertise,
- Data and knowledge management,
- Project management and professional communication expertise
- Inclusion of patients and patient organizations;
- SME participation is encouraged.

Improving the care of patients suffering from acute or chronic pain

Objectives of the whole Topic

- The goal is to make advances in **three pain areas** in a complementary manner. These three Subtopics, each of which addresses a specific scientific challenge, together offer significant opportunities for cross-fertilisation:
- **Subtopic 3A:** using Patient Reported Outcome Measures to improve the management of acute and chronic pain (PROMs);
- **Subtopic 3B:** improving the translatability of pharmacodynamic biomarkers in pain pathways of healthy subjects and preclinical species (BIOM);
- **Subtopic 3C:** improving translation in chronic pelvic pain (CPP).

Structure of the Call



- Whilst contributions to each subtopic will require mobilization of specialist expertise, it is a key objective of this Topic to create a research platform for pain that will contribute significantly to reduce fragmentation and generate highest impact on the whole area.
- Thus at Stage 2, the full proposal will be submitted by the consortium created by the merger of the winning Applicant Consortia of each subtopic (3A+3B+3C) with the Industry consortium.

Subtopic A

Using Patient Reported Outcome Measures to improve the management of acute and chronic pain (PROMs)

Objectives

To foster the use and standardisation of Patient Reported Outcome Measures to improve the management of acute and chronic pain (PROMs)

- Standardize reporting of pain and treatment success by identifying and aligning on PROMs between clinicians/academic groups and companies
- Support usage of standardized PROMs for pain in real-world practice by Health Care Professionals (HCPs) to follow the experienced success of the treatment of individual patients
- Engage an existing network of hospital centers to set up an aligned approach and contribute to collection and analysis of the PROMs during pain treatment.
- Set up of a registry for storage and analysis of the data collected
- Aligned effort to identify chronification factors in pain

Expected impact on the R&D process

- More informed decisions on pain treatment for post-operative or other acute pain indications or chronic pain which lead to faster patient recovery and less resource consumption
- Improvement of pain relief (satisfied patients, faster recovery, less work loss)
- PROMs for clinical trials in pain pre-defined by patients and clinical experts
- Easier to identify suitable PROMs for clinical trial, information on expectable increments available, co-operation between clinical experts and companies will create trust in each other for future projects

Expectations from applicant consortium

- An existing network of hospital centres to set up an aligned approach in the use and documentation of PROMs in different surgeries;
- A functional technology platform enabling research studies using PROMs, and meta-analysis of the results;
- Expertise in data and knowledge management and building of databases and expertise and infrastructure required to collect, transmit, store, analyse, and visualize data;
- Smart-phone technology or other biosensors that may be particularly well suited for measuring functional changes in pain patients;
- Inclusion of patients and patient organizations
- Project management.
- SME participation is encouraged.

Subtopic B

Improving the translatability of pharmacodynamic biomarkers in pain pathways of healthy subjects and preclinical species (BIOM)

Nathalie Seigneuret

Objectives

Delivery of pharmacologically validated and standardised functional PD biomarkers in man, with accompanying back-translation to animals.

- Establish standardized protocols (EEG, ERPs, fMRI, etc) to measure neuronal activity in pain pathways in healthy subjects during baseline and acute experimental pain, in the presence of 3 standard analgesics.
- Develop methodological approaches translatable to preclinical in vivo models
- PK in relevant compartments during multiple time points in both clinical and pre-clinical studies to develop PK/PD models and assess statistically the translatability of these models (ie could these PD measures be used to predict dose)

Expected impact on the R&D process

- A better understanding of the successful translation (PK/PD) from preclinical into clinical studies, and of back-translation from the clinic into improved preclinical models
- A reduction in attrition rates in drug discovery
- An enhancement of the feasibility and speed of the development of novel drugs.
- Development of novel methodologies and advanced analysis techniques to identify specific target engagement in different compartments of pain pathways.

Expectations from applicant consortium

- Experience in the development and validation of clinical experimental pain models and neurophysiological measurements using fMRI, laser-evoked pain, EEG, and measures of peripheral nerve excitability;
- Experience in analytical and data management;
- Expertise in clinical pharmacology including a proven track record in delivering proof-of-concept clinical studies in healthy subjects;
- Competence in pharmacokinetic/pharmacodynamic modelling in healthy subjects and preclinical models;
- Data and knowledge management, building of databases;
- Project management.
- SMEs participation is encouraged

Subtopic C

Improving translation in chronic pelvic pain (CPP)

Objectives

Despite the high incidence of chronic pelvic pain (CPP), understanding of the pathological conditions leading to it is sparse, and diagnostic tools such as biomarkers are unspecific or do not exist at all.

- Provide deeper disease understanding in pathological conditions leading to CPP
- Thorough analysis of patient phenotype identify specific pain conditions, quality of life ratings, clinical, molecular markers etc. which could be used as biomarkers
- Patient stratification and consequently a specific, effective therapy might become possible
- Parallel identification of the clinically relevant biomarkers in preclinical models is planned
- Provide a back-translation from clinical to the preclinical situation and give insight into the validity of the respective models.

Expected impact on the R&D process

- To generate a new tool-box for research on CPP with the aim to satisfy medical need of the patients with new therapeutics
- Improvement of disease understanding will pave the way to new promising treatment options and foster further basic research
- Diagnostic biomarkers to confirm or exclude CPP indication as diagnosis would provide options to stratify patients and would lead to great efficiency gains for the health care system.
- Increasing feasibility for drug development and reducing attrition rates in projects addressing CPP with more predictive translational models

Expectations from applicant consortium

- Clinical expertise in the area and capability/interest in developing corresponding pre-clinical models
- Pre-clinical expertise in CPP models combined with expertise in assessment methodologies for allodynia and hyperalgesia, alternative behavioural endpoints, histology, and molecular biology
- Inclusion of patients and patient organizations
- Strong expertise in proteomics and/or metabolomics
- data and knowledge management, building of databases
- Project management
- SMEs participation is encouraged

**Understanding hypoglycaemia:
underlying mechanisms; addressing
clinical determinants and
consequences for people with
diabetes, by combining databases
from clinical trials**

Elisabetta Vaudano (on behalf of Magda Gunn)

Objectives

To reduce the risk and burden of hypoglycaemia and ultimately improve glycaemic control in people with diabetes, via:

- Better understanding the causes and impacts of hypoglycaemia
- Research into mechanisms of counter-regulation and hypoglycaemia unawareness to identify targets for intervention
- Establishment of clear, robust and consistent definitions of hypoglycaemia
- Creation of a standard guideline for measurement of hypoglycaemia episodes
- Standardised approach for the collection of clinical and laboratory data in clinical trials
- Shaping health economic outcomes research to determine the value of reducing hypoglycaemia risk
- Jointly with regulators defining clinically meaningful endpoints to document rates of hypoglycaemia and the potential to reduce these with pharmacological intervention

Expected impact on the R&D process

- Improved approaches for hypoglycemia management
- Improved design of diabetes trials for glucose lowering therapies
- Standard guideline on how to measure and manage hypoglycaemia
- Better understanding of factors and clinical consequences related to the development of hypoglycaemia
- Evidence for regulatory authorities on standardized approaches of measurement to be included in clinical trials.
- Enable development of therapeutic approaches that will help to:
 - Reduce the risk of hypoglycaemia
 - Improve glycaemic control
 - Reduce the risk of short and long-term diabetes related complications

Expectations from applicant consortium

- Expertise in medical diabetes research, clinical trials and research in hypoglycaemia detection;
- Access to clinical data from patients demonstrating hypoglycaemia unawareness
- Experience within analysis and filtering of glucose data, modelling of diabetes physiology including hypoglycaemia, and prediction of drug-glucose dynamics in humans;
- Capability to conduct non-clinical research in the areas of molecular, cellular and physiological mechanisms of hypoglycaemia, recurrent hypoglycaemia, hyperglycaemic unawareness and consequences of hypoglycaemia
- Experience with establishment of databases, data harmonization, database management and data security;
- Capability to analyse and link results across the project in support of the overall hypotheses, the regulatory framework and expertise provided by the industry.

Patient perspectives in medicines lifecycle

Nathalie Seigneuret (on behalf of Magda Gunn)

Objectives

- To enable patients to better reflect their perspectives in the medicines R&D processes of treatment development
- Provide a framework and guidance for all EU stakeholders about who, when and what information is needed, as well as how to engage patients to obtain beneficial and necessary input from patients and healthcare consumers.
- To create minimum expectations for effective engagement and metrics to support implementation within industry, healthcare authorities and other decision makers
- To define engagement capability
- To define rules of engagement

Expected impact on the R&D process

Enhanced and systematic engagement of patients and healthcare consumers in medicines lifecycle will ultimately contribute to:

- improved and sustainable innovation and meaningful outcomes for all stakeholders;
- successfully addressing objectives of IMI:
 - Reduce attrition in R&D;
 - Speed up patient access to medicines;
 - Improve patient outcomes and experiences.

Expectations from applicant consortium

- Various patient organisations (umbrella and disease specific), healthcare consumers groups and patient experts;
- The composition shall reflect the heterogeneity of patients (including unaffiliated patients) and carer populations and shall enable participation and input from the relevant groups and individuals;
- Regulators, HTA and payers from national or pan-European levels;
- Healthcare professionals, including general practitioners and clinicians;
- Academic experts in ethics, codes of conducts, performance evaluation;
- Experts in point of care know how and integration;
- Experts in communication and knowledge dissemination (including social media).

Creation of a pan-European paediatric clinical trials network

Nathalie Seigneuret

Objectives

Set up a large collaborative pan-European paediatric network that facilitates development & availability of new medicines by executing clinical trials for approval, and expansion of knowledge of medicines currently used for the entire paediatric population

- Create the network structure (with a lean central coordinating organisation, arranged around “national hub coordinating centres” cooperating with multiple sites within each member state)
- Set up network scientific advice and study design/feasibility groups
- Test the viability of the network by conducting clinical studies
- Develop a sustainable business model insuring viability of the network beyond the period of IMI2 funding

Expected impact on the R&D process

- Better access for paediatric patients to new experimental therapies, and improved labelling information for already marketed products
- Increased efficiency of executing trials
reduced timelines & cost through e.g standardised processes and procedures, one single point of contact
- Enhanced role of clinicians and patient/parent advocacy groups in planning and designing studies
- Opportunity for European clinical research personnel, sites and organisations to collaborate making Europe a more competitive place for delivering high quality paediatric clinical trials

Expectations from applicant consortium

- Large children's hospitals and medical centres, existing regional or national paediatric networks, transnational, pan-EU disease-specialty networks
 - Experience in conducting paediatric clinical trials
 - Expertise in the science of paediatric drug development
 - Access to a large paediatric population covering the entire spectrum of diseases and conditions across all age groups
 - Information technology / data management
 - Expertise in legal and clinical compliance
 - Strong project management and communication expertise
- SMEs with expertise in aspects of paediatric drug development.
- Patient advocacy organisations and youth advisory groups
- Regulators

How Big Data could support better diagnosis and treatment outcomes for Prostate Cancer

Part of the IMI Big Data for Better Outcomes programme

Objectives

To improve prostate cancer outcomes by broadening the relevant outcome measures across all stages of disease through collection and analysis of available data

- Identify data sources and a data strategy to characterize PCa patients' pathways across multiple geographies;
- Develop Pan- European, multi-country data sharing platform
- Identify and share best practices in collecting real world clinical outcomes data; data curation and analysis.
- Generate insights to support efforts to improve PCa patient access and the value of health care delivered;
- Develop a network of European Prostate Cancer stakeholders

Expected impact

- Improve Prostate Cancer patients' lives by optimising the way they are diagnosed and managed;
- Assemble data sets that will answer questions about the natural history, cost-effectiveness, and clinical utility of new and innovative diagnostics and treatments
- Enable initiation, maintenance, and evaluation of the right treatment to the right patient at the right time;
- Engagement with key stakeholders will ensure aligned future prospective data collection efforts.

Expectations from applicant consortium

- Expertise in
 - Regulatory, policy, observational/cohort study execution, economic modelling, informatics, statistics, data management and integration, healthcare privacy/ethics, health outcomes, age-related research, clinical research, and electronic health records.
- Caregiver and patient advocacy organisations
- A process for engaging Health Technology Assessment agencies, national payer organisations, providers, and regulatory agencies
- Access to real world datasets

**Biomanufacturing 2020:
Development of Innovative high
throughput analytical tools and
methods to characterize cell culture
fluid during development and
commercial cell culture processes**

Objectives

To develop/determine the best high throughput methods, novel analytical methods and feedback control methods to be used during the manufacturing of biopharmaceuticals, in particular the cell culture

- High-throughput methods
 - Miniaturisation & automatic sample prep to enable fast testing
- Novel methods
 - Novel technologies for online non-invasive testing, such as spectrophotometric methods to test cell culture conditions.
- Feedback control methods
 - Automated controls for the control of manufacturing operations.
- Data management tools
 - Development of data management tools to maximally explore datasets generated during the project.

Expected impact

- The validated innovative analytical tools developed in the project will:
 - Allow for more effective control and execution of the production phase of biopharmaceutical therapies.
 - Lead to consistent quality.
 - Increase supply chain reliability and reduce drug shortages.
- The developed analytical tools will be immediately 'fit for use' in the manufacture of Advanced Therapies Medicinal Products (ATMPs)

Expectations from applicant consortium

Specialists in:

- high-throughput screening assays
- 'omics' method development
- management, interpretation and modelling of complex data sets
- development and manufacturing of online probes and of devices for aseptic at-line sampling and rapid sample preparation.

Have the expertise to:

- develop automated highly-sensitive measurement tools & methods
- develop high throughput tools to measure product quality attributes
- develop innovative micro-Scale Fed-Batch Cultures
- develop rapid spectrophotometric methods for cell culture monitoring
- develop process analytical technology for biopharmaceutical products



Thank you

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