Webinar | IMI2 – Call 17
Open access chemogenomics library and chemical probes for the druggable genome

30.01.2019

Agenda

- How to use GoToWebinar – Catherine Brett, IMI
- Introduction – Iwona Jablonska, IMI
- The Call topic – Adrian Carter, Boehringer Ingelheim & Anke Mueller, Bayer
- Involvement of SMEs, patient groups, regulators – Iwona Jablonska, IMI
- Questions & answers

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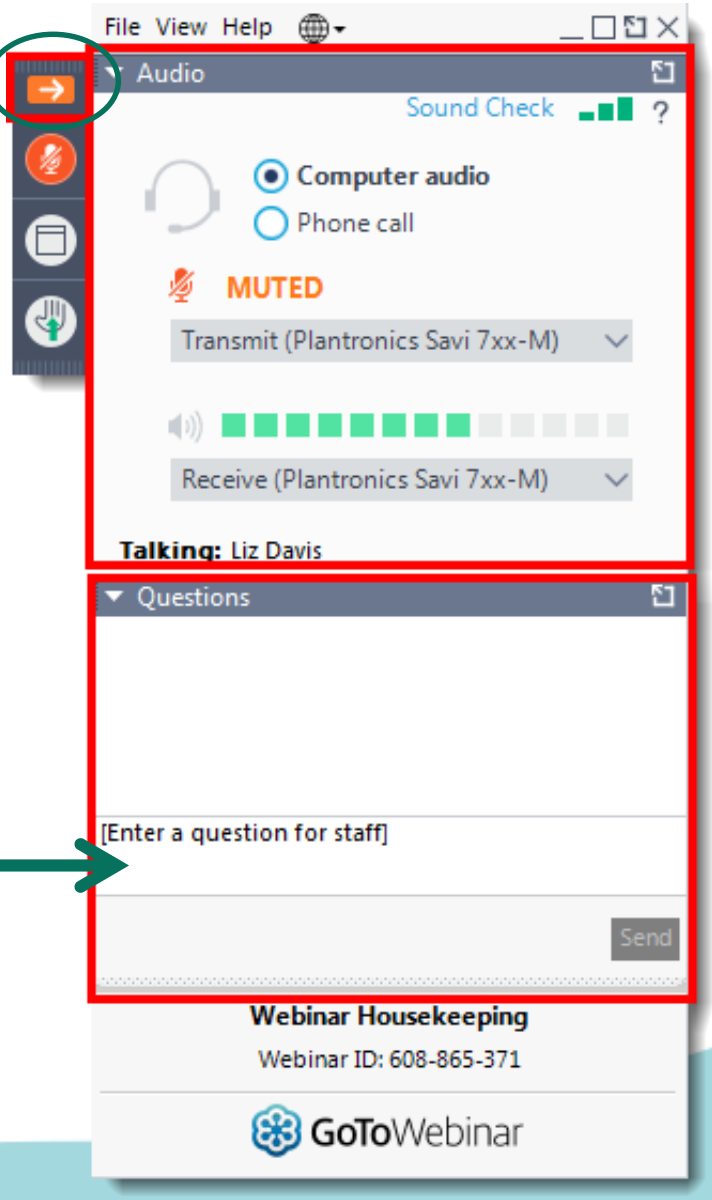

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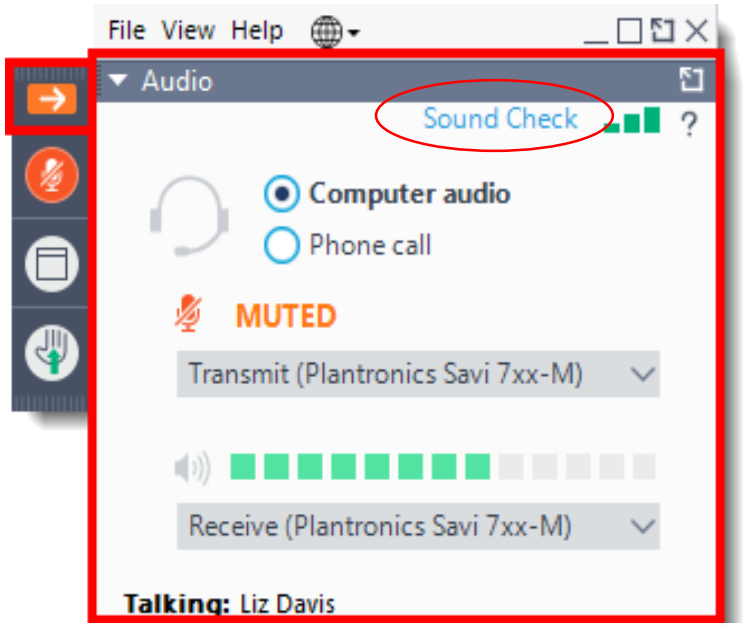

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Before we start…

- This webinar is being recorded and will be published on the IMI website and / or IMI YouTube channel
- Presentation slides will be published on the webinar web page
- A participant list will be circulated and published on the website
- IMI2 – Call 17 has been launched and all Call documents & details of how to apply can be found on the IMI website

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Webinar | IMI2 - Call 17

Open access chemogenomics library and chemical probes for the druggable genome

Iwona Jablonska

Today's webinar

Will cover all aspects of the Call topic, including:

- Introduction to the specificities of the IMI programme
- Expected content of the proposal:
  - Objectives,
  - Need for public-private collaborative research,
  - Key deliverables,
  - Structure,
  - Contributions of the academic/public applicants and from industry consortium

Will not cover rules and procedures

- A webinar on rules and procedures will take place on Thursday 31 January, 10:30 – 12:00

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IMI – Europe's partnership for health

IMI mission

IMI facilitates open collaboration in research to advance the development of, and accelerate patient access to, personalised medicines for the health and wellbeing of all, especially in areas of unmet medical need.

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IMI – Ecosystem for innovative collaborations

- Allow engagement in a cross-sector, multi-disciplinary consortium at the forefront of cutting-edge research
- Provide the necessary scale by combining funding, expertise, knowledge, skills and resources
- Build a collaboration based on trust, creativity and innovative and critical thinking
- Learn from each other - new knowledge, skills, ways of working
- Take part in transformative research that will make a difference in drug development and ultimately patients' lives

IMI is a **neutral platform** where **all involved** in drug development can engage in **open collaboration** on **shared challenges**.

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IMI 2 budget (2014 – 2024)

EU funding goes to:

Universities

SMEs

Mid-sized companies

Patient groups

etc…

€1.638 bn

€1.425 bn

Other €213 m

IMI 2 total budget €3.276 billion

EFPIA companies

Do not receive any funding

contribute to projects ‘in kind’

Associated Partners e.g. charities, non-EFPIA companies

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How a topic is generated

Industrial partners align themselves around a real challenge for industry and agree to work together **and commit resources**

New ideas from public sector, universities, SMEs etc. are needed to address the challenge

Scale is a key to success and is provided through IMI funding

Outcomes should be transformative for the industry as well as having a clear “public” value

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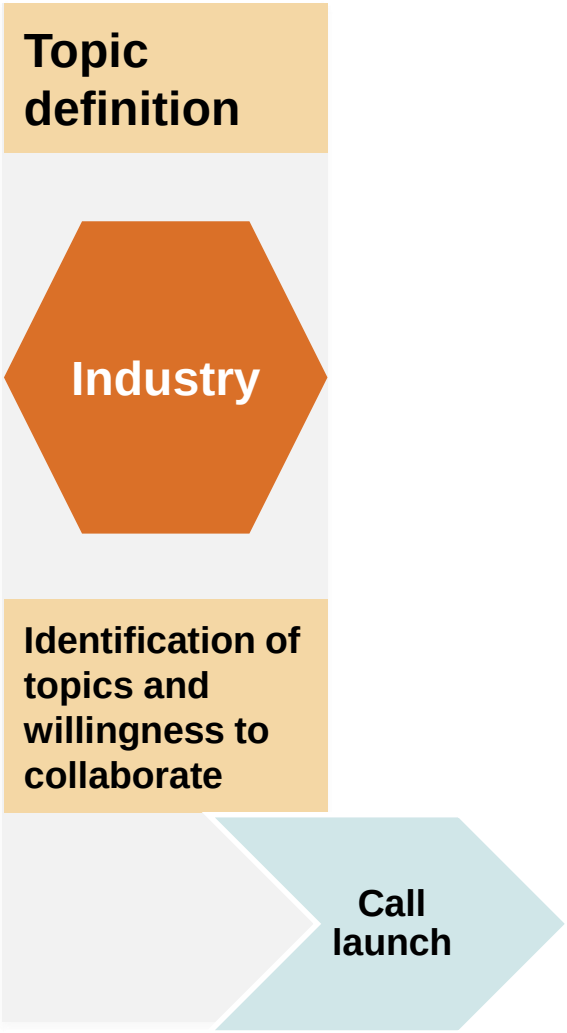
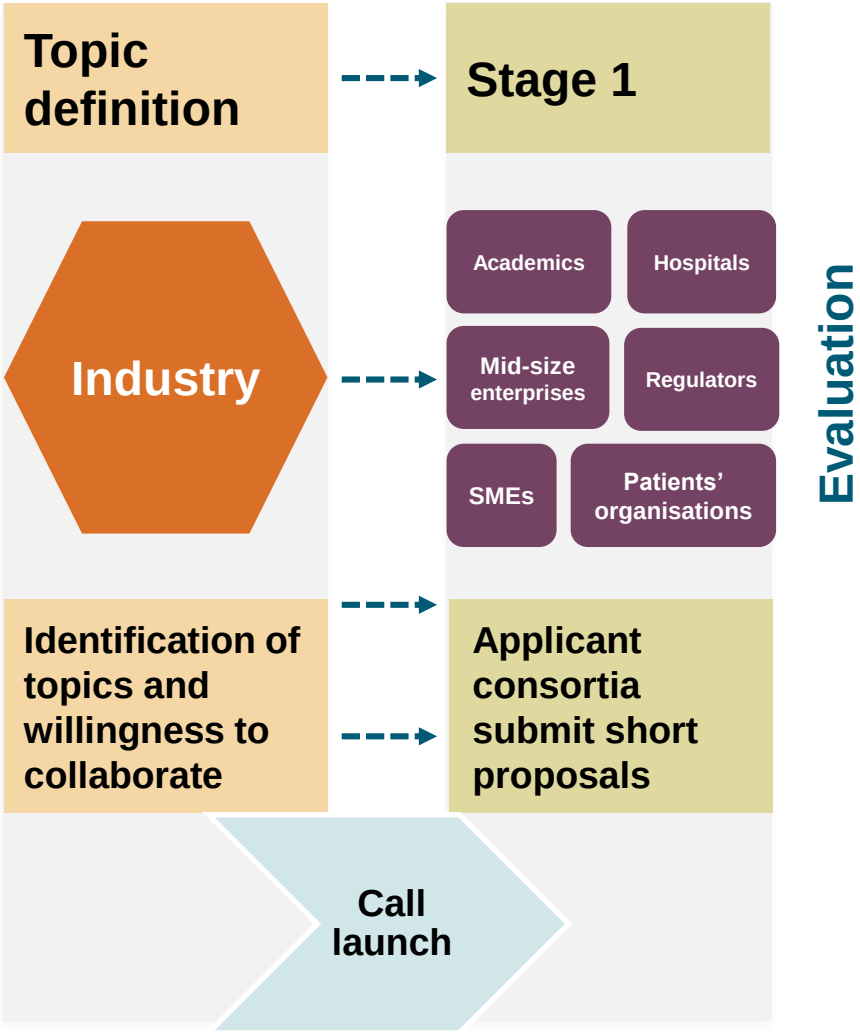
Typical IMI project life cycle



Typical IMI project life cycle



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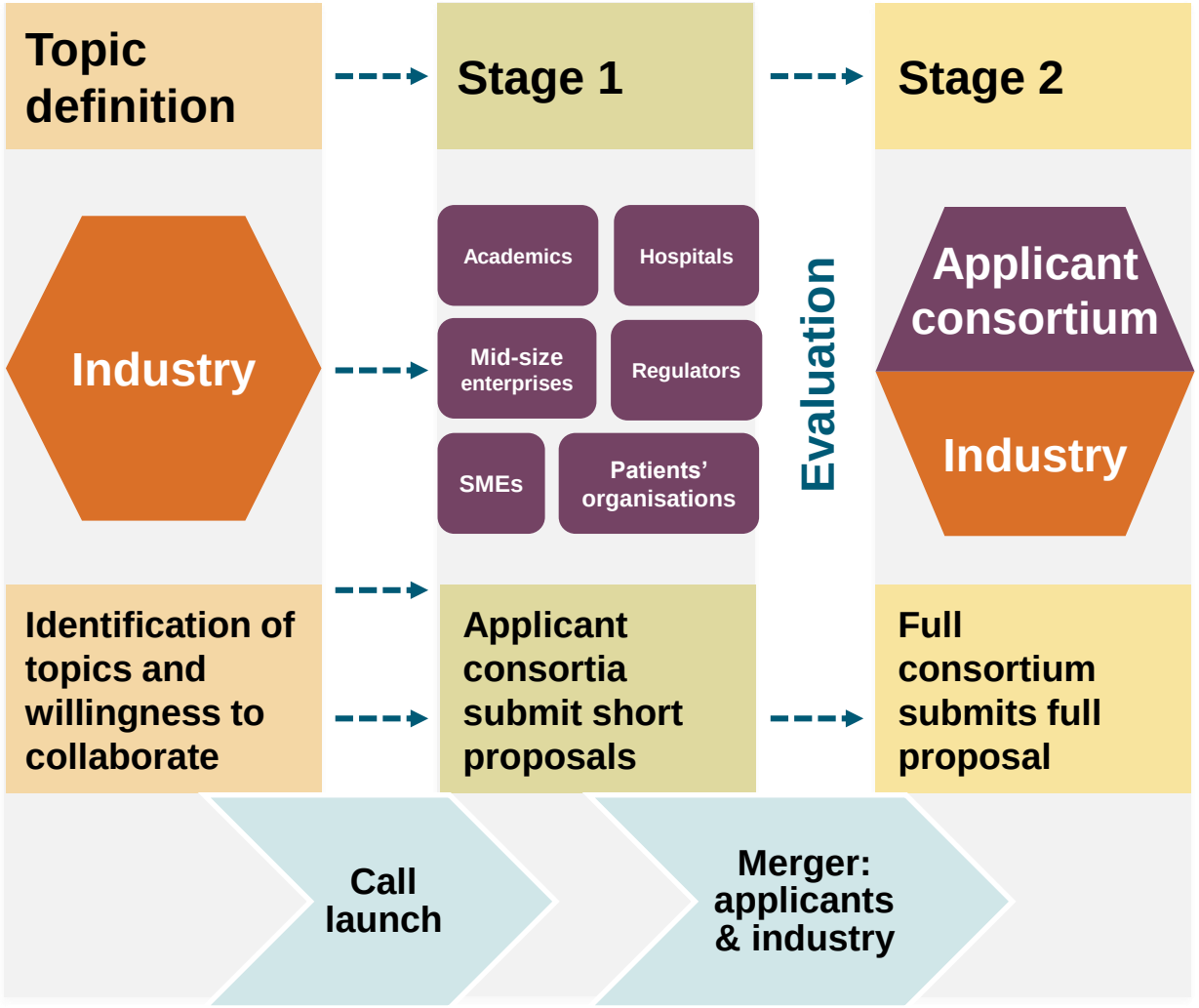
Typical IMI project life cycle



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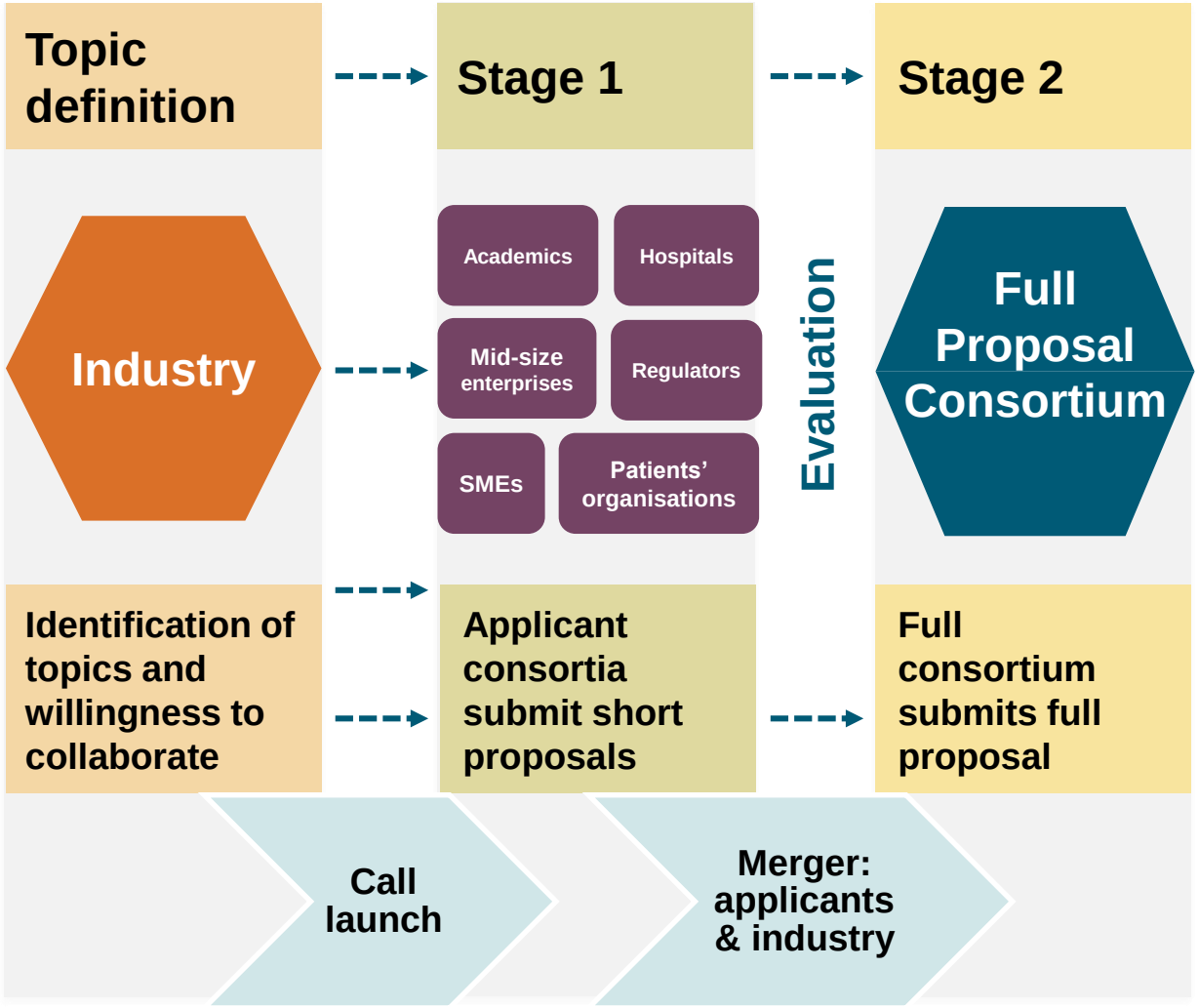
Typical IMI project life cycle



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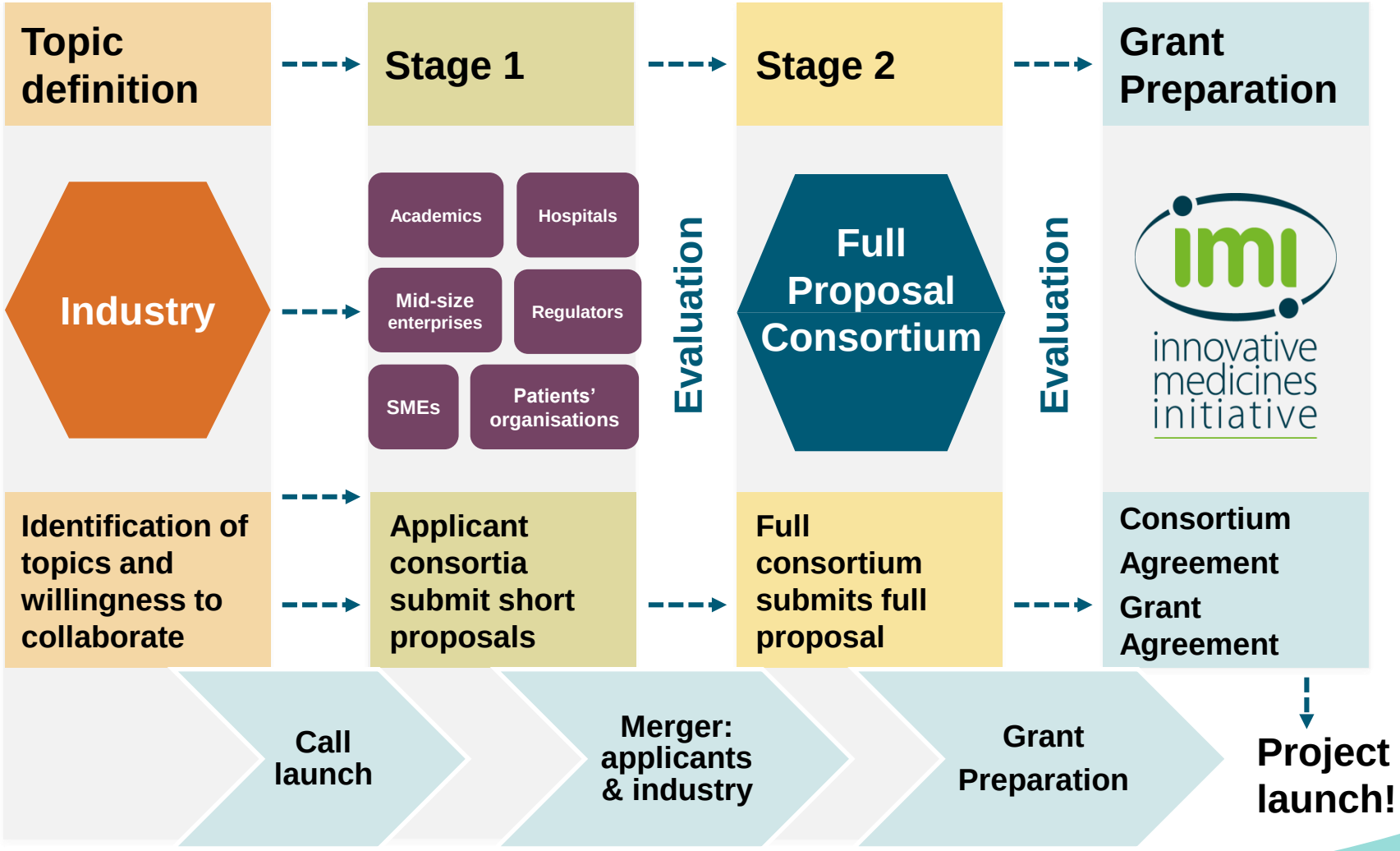
Typical IMI project life cycle



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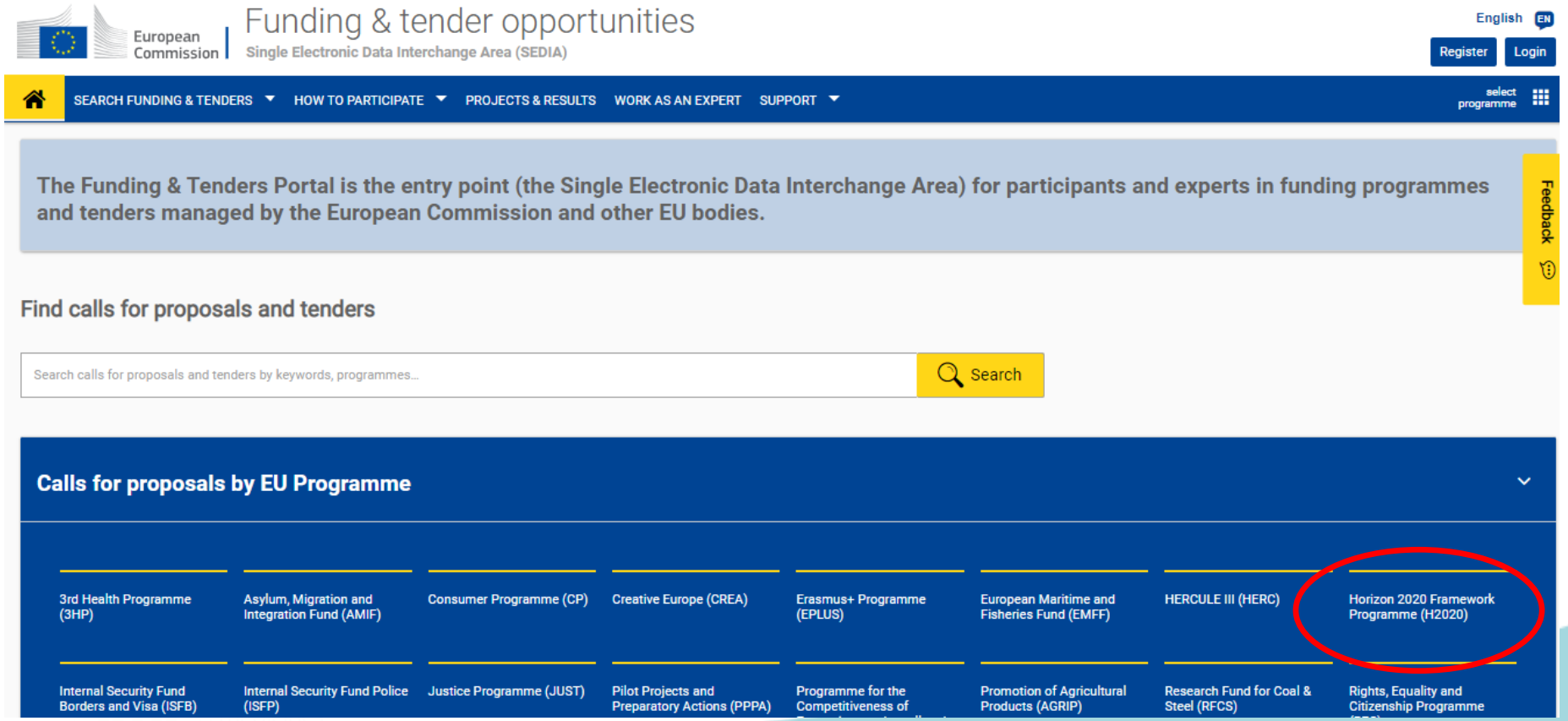
Submitting a proposal

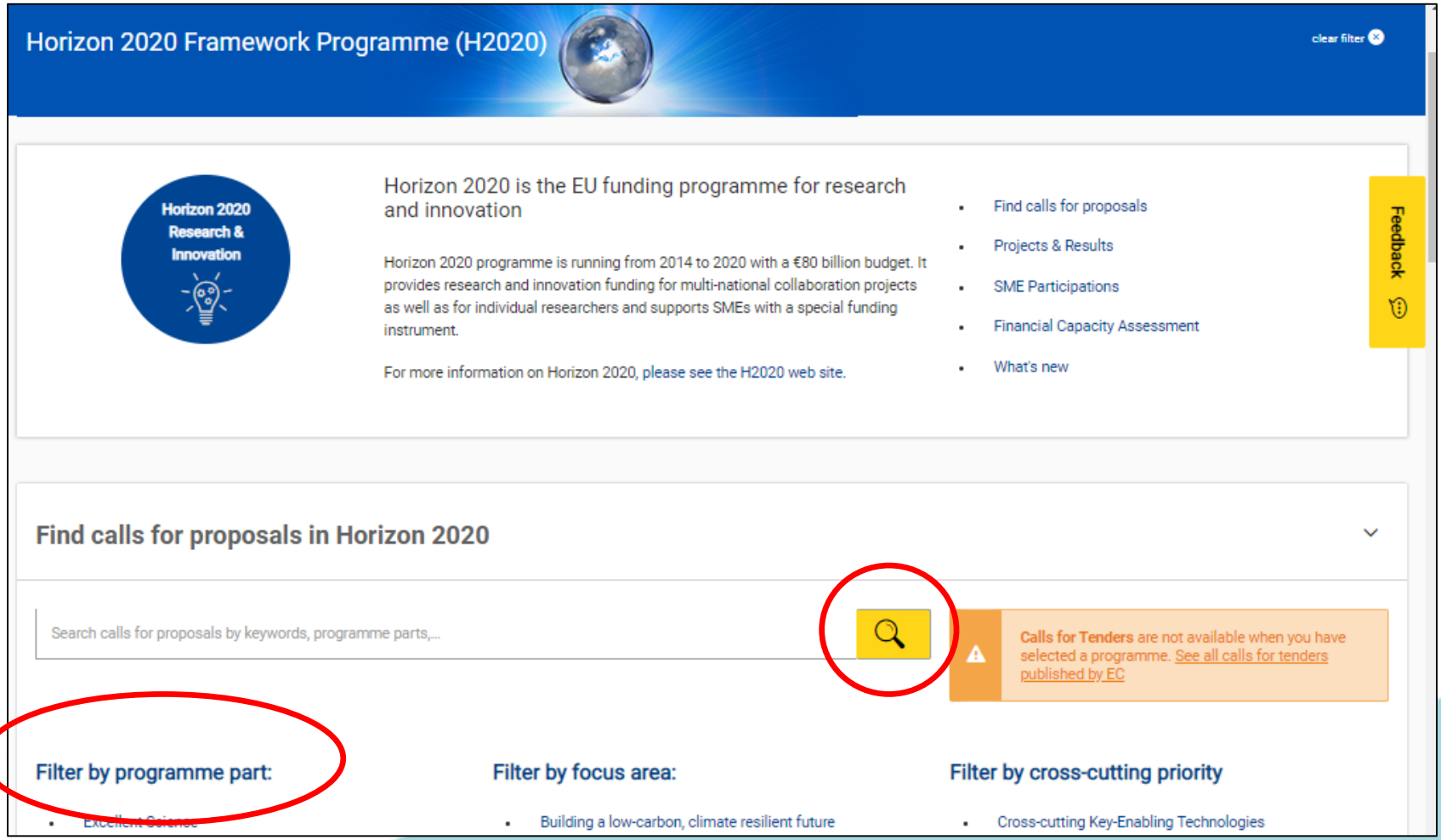
Via the **new** Funding and Tenders Portal

https://ec.europa.eu/info/funding-tenders/opportunities/portal/screen/home

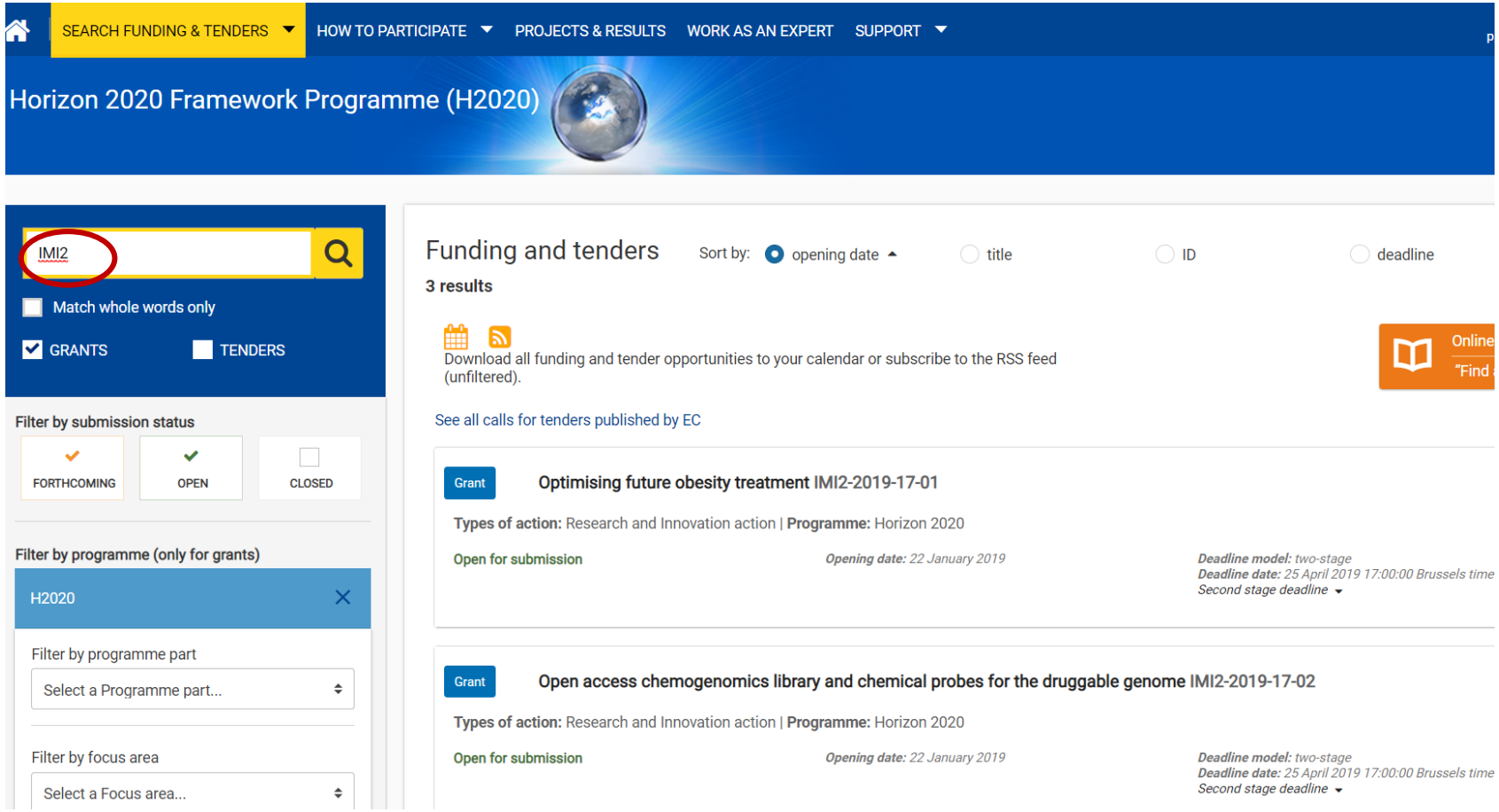


New Funding and Tenders Portal Horizon 2020 section

https://ec.europa.eu/info/funding-tenders/opportunities/portal/screen/programmes/h2020



New Funding and Tenders Portal IMI2 interface



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Proposal Template

- Available on IMI website & H2020 submission tool
- For first stage short proposals, the limit of **30 pages**.

Title of Proposal

List of participants

Table of Contents

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Evaluation Criteria (1/2)

- **Excellence**
  - Clarity and pertinence of the proposal to meet all key objectives of the topic;
  - Credibility of the proposed approach;
  - Soundness of the concept, including trans-disciplinary considerations, where relevant;
  - Extent that proposed work is ambitious, has innovation potential, and is beyond the state of the art;
  - Mobilisation of the necessary expertise to achieve the objectives of the topic, ensure engagement of all relevant key stakeholders.
- **Impact**
  - The expected impacts of the proposed approach as mentioned in the Call for proposals;
  - Added value from the public private partnership approach on R&D, regulatory, clinical and healthcare practice as relevant;
  - Strengthening the competitiveness and industrial leadership and/or addressing specific societal challenges;
  - Improving European citizens' health and wellbeing and contribute to the IMI2 objectives.

Evaluation Criteria (2/2)

- **Quality and efficiency of the implementation**
  - Coherence and effectiveness of the outline of the project work plan, including appropriateness of the roles and allocation of tasks, resources, timelines and approximate budget;
  - Complementarity of the participants within the consortium (where relevant) and strategy to create a successful partnership with the industry consortium as mentioned in the topic description in the Call for proposal;
  - Appropriateness of the proposed management structures and procedures, including manageability of the consortium.

Tips for writing a successful proposal

- Read **all the call-relevant material:**
  www.imi.europa.eu
- Begin forming your consortium **early**
  Partner search tools & networking events
- Provide **independent experts reviewers** with all the information requested to allow them to evaluate your proposal
- **Finalise and submit your proposal early**
- Contact the **IMI Office** (**NOT** industry topic writers):
  infodesk@imi.europa.eu

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Common mistakes

- Admissibility/Eligibility criteria not met**:**
  - submission **deadline** missed
  - minimum of **3 legal entities** from **3 member states & H2020 associated countries** not met
- The proposal does **not address all the objectives** of the topic
- A proposal is **scientifically excellent** but will have **limited impact**
- **Complementarity** with Industry consortium not well described.

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Find project partners

- Network with **your contacts**
- **Network** with fellow webinar participants
- Use **Partner Search Tools:**
  - EU Funding & Tenders portal: https://ec.europa.eu/info/funding-tenders/opportunities/portal/screen/how-to-participate/partner-search
  - German NCP partner search tool: www.imi-partnering.eu
- Get in touch with your **local IMI contact point**: www.imi.europa.eu/about-imi/governance/states-representatives-group
- Talk to your **Health National Contact Point** (NCP)
- Network on **social media** (e.g. IMI LinkedIn group)

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Participation of SMEs, patient groups, regulators

We encourage the participation of a wide range of health research and drug development stakeholders in our projects, e.g.:

- SMEs and mid-sized companies
- Patient organisations
- Regulatory bodies
- Companies / organisations from related fields (e.g. diagnostics, animal health, IT, imaging etc…)

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Call 17, topic #2

Open Access Chemogenomic Libraries and Chemical Probes for the Druggable Genome

Dr. Adrian J. Carter and Dr. Anke Müller-Fahrnow
30.01.2019 • IMI webinar

Discovering New Medicines is Difficult and Expensive

The true cost of discovering and developing new medicines may be much higher because of the cost of failure

$2.6 billion

DiMasi *et al.* (2016) J Health Econ. **47**, 20-33

Estimated average, discounted out-of-pocket costs per new drug approval

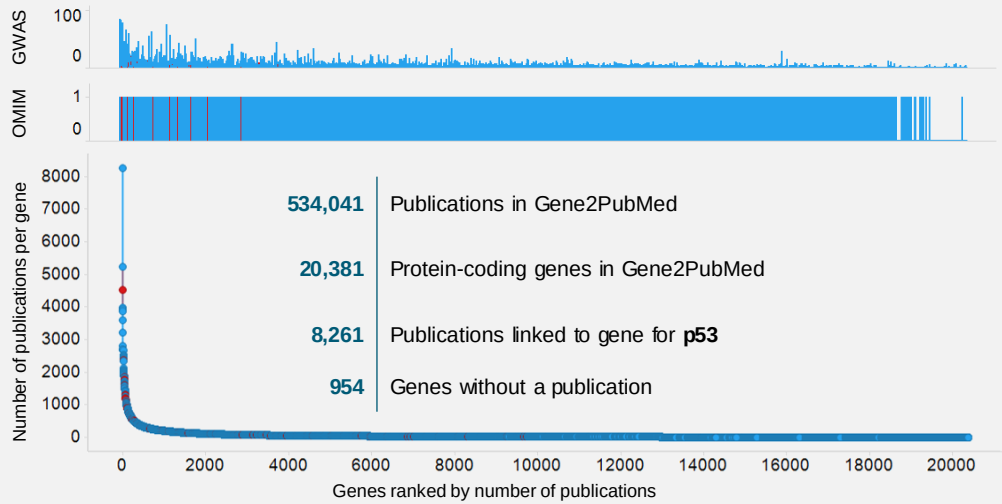
1 in 10 development candidates are approved | Clinical development takes 10 years

Research **Development** **Treatment**

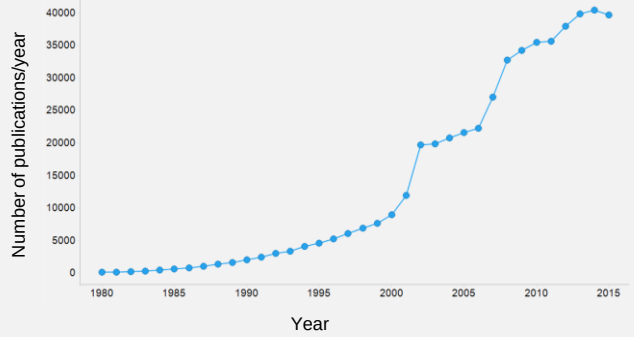
Natural Tendency for Scientists to Focus on Previously Studied Genes

We have used the NCBI and Gene2PubMed databases to evaluate the frequency patterns of publications annotated to human protein-coding genes, and compared this to the online catalogue of human genes and genetic disorders in OMIM and published GWAS (2017)

Gene2PubMed database



Great need for enabling access to exciting new biology



New Drug Concept

Three aspects must be aligned for a successful new medicine: Desired and meaningful clinical improvement, clear role of target or gene in disease pathway and the planned molecular or therapeutic approach for achieving this goal

Core Target Product Profile

Goal is to make a meaningful clinical improvement for any given disease or disease aspect that has been difficult to achieve previously

Target Gene or Protein

Target gene or protein and its role in a disease or pathological pathway, preferably with a clear genetic link

New Molecular Entity (NME)

Molecular approach to the target gene or protein that allows pharma to make a medicine

Need for a Precompetitive, Public-private Collaboration

Discovering new medicines relies on ability to identify and prioritize new drug targets

Biomedical science tends to focus on only a small fraction of the human genome

High-quality chemical probes and chemogenomic libraries encourage the biological interrogation of new drug targets and complement genetic approaches

Industry applies medicinal chemistry and screening facilities to support biological validation in academia

Academic physician-scientists provide access to patient samples that are genotyped and annotated

Associated Partners and SMEs develop new technologies for speeding up the creation of tool compounds

Pre-competitive partnership will provide the wider scientific community with access to reagents quickly and with no strings attached, thereby amplifying their impact

Open science assures adherence to high standards of quality and reproducibility

Generation of openly accessible, high-quality data lays the foundation for AI applications

Choosing the Right Tool

Chemogenomic tools support the identification of potential target proteins and chemical probes help interrogate biological systems selectively and specifically

Chemogenomic Libraries

Support the identification of possible target protein family members

- **Broad annotation**
- Defined mode of action
- Good specificity
- Reasonable selectivity
- Freely available
- If possible use 2 or more chemogenomic compounds with different selectivity and/or different chemotype

Chemical Probes

Interrogate biological systems selectively and specifically

- **Well defined mode of action**
- Highly selective and specific
- Broad annotation
- Physicochemical properties in line with intended use
- Freely available
- Wherever possible with inactive controls

Therapeutic Agent or Drug

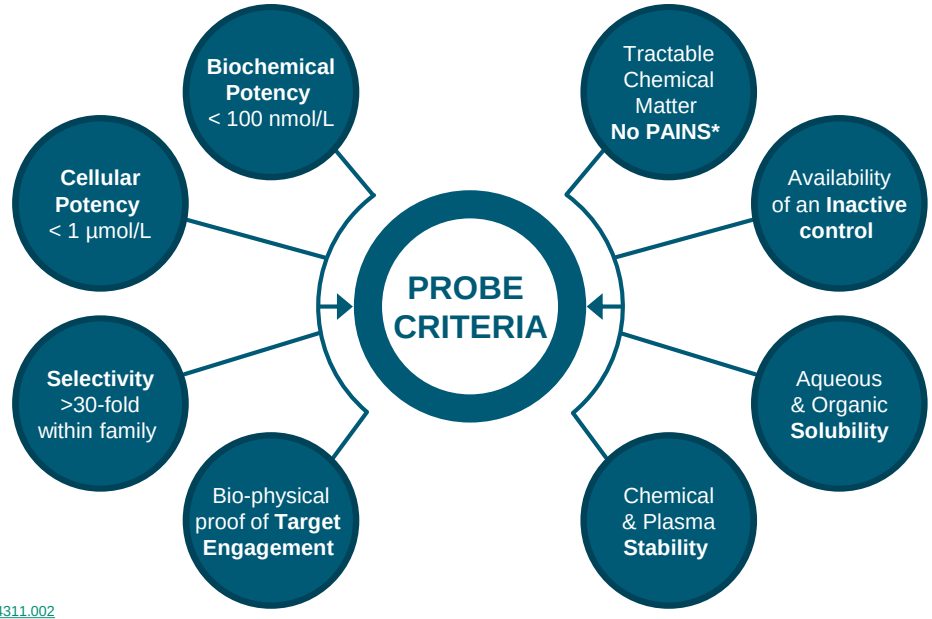
Used to treat human beings

- **Safe and efficacious**
- Adequate human bioavailability
- Safe and well tolerated in human beings
- Efficacy demonstrated in pivotal Phase III trials
- Favorable physicochemical and pharmaceutical properties

Chemical Probes must Fulfill Stringent Criteria to Qualify as Research Tools

A chemical probe is a small molecule that modulates the function of a protein in a specific and selective way

Target-Related Criteria



Chemical-Matter Criteria

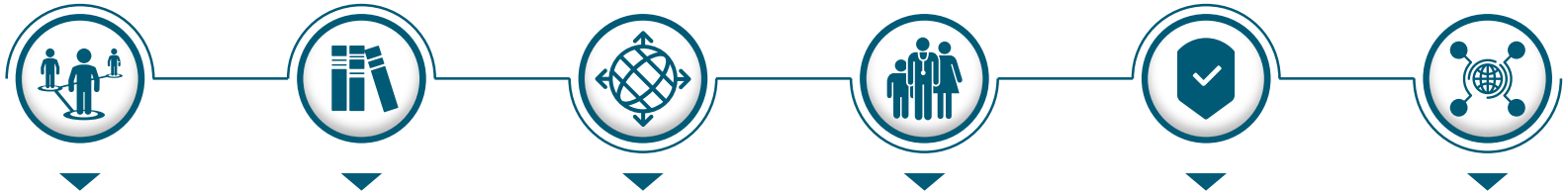
Müller et al. eLife 2018; 7 https://doi.org/10.7554/eLife.34311.002

* Pan-assay interference compounds (PAINS)

Objectives of the Full Project

- **Establish a framework** to assemble an open-access chemogenomic libraries for the druggable genome
- **Enrich the open access library** by creating new, deeply characterized chemical probes to selected specific protein families
- **Develop open-access assays** from well characterized human disease tissue with a special emphasis on immunology, oncology and neuroscience to profile the chemical tools and chemical probes
- **Establish sustainable infrastructure**, on accessible platforms and with appropriate governance, for discovery and dissemination of tool compounds, assays, and associated data, beyond the lifetime of this project
- **Develop a communication plan** to facilitate the dissemination of the compound sets and data to ensure their appropriate use

Pre-competitive Nature



The creation of an open access set of tools to interrogate the entire druggable genome is a challenge that cannot be solved by a single institution

The chemogenomic libraries, chemical probes, and accompanying meta-data are intended to be open access, i.e. use of the compounds will be made available unencumbered, in a pre-publication state and free from restrictions on use

Participants will provide non-exclusive access to the synthetic routes of these compounds to vendors willing to distribute the chemogenomic libraries and/or chemical probes and their controls worldwide

Assays and data generated will also be made publicly available without restrictions

Technologies developed throughout the project will be non-exclusive, ready for application, and openly and freely available for use and dissemination

Need a foundation on which to build and organize a worldwide network of laboratories to generate chemical tools for the entire druggable genome

Expected Impact

- Provide the wider academic community with unencumbered access to the highest quality tool compounds for a large number of novel targets
- Seed a massive community target prioritization and target deconvolution effort by making a high-quality, broader compound sets and the data available
- By providing chemical tools without restriction the consortium will enable new assays and unencumbered starting points for probe development or drug discovery
- Centralized, cell-based and biochemical assay panels and new technologies will serve as a resource for the chemical biology community and provide significant incentives for external scientists to contribute innovative compounds to the network
- High-quality, patient-derived cell assays will provide the opportunity for clinical scientists to undertake translational medical research and biomarker discovery

Suggested Architecture of the Project

01

Open-access chemogenomic libraries for the druggable genome

- Collection of available compounds from academia and industry
- Annotation of library compounds
- Develop new methods for chemogenomic compound generation and profiling

02

Chemical probes for 2 – 3 emerging target families (incl. E3 ligases and solute carriers)

- Protein purification and production
- Assay development for target engagement
- Structure determination and chemical starting matter
- Generation of chemical probes
- Technology development

03

Human tissue assays

- Develop novel human tissue-derived assays
- Validate assays with established tool compounds
- Create renewable resource with stem cells and organoids
- Phenotypic characterization

04

Infrastructure, platforms and governance for global effort on entire druggable genome

- Compound logistics
- Collate assays
- Establish database
- Global network of partners
- Project management

Expectations of Applicant Consortium

Adherence to open-access principles and expertise in developing and managing open-access projects

Expertise in expression, characterization and structure determination of soluble proteins, integral membrane proteins, and protein complexes, assay development, screening, generation of chemogenomic libraries and chemical probes and technology development for speeding up these efforts

Excellence and a proven record of accomplishment (evidenced by collaborative publications) in establishing networks of recognized thought leaders in all relevant sectors indicated in the topic

Previous successful examples of catalyzing research in pioneer target areas of drug discovery with a network of scientific researchers especially with industry

Track record of scientific success in partnerships with clinical research centres using patient-derived assays, and part of a global network of medicinal chemistry, biological assays, human biology, and clinical research centres

Expected Contributions of the Applicants

01	02	03	04
Open-access chemogenomic libraries for the druggable genome	**Chemical probes for 2 – 3 emerging target families**	**Human tissue assays**	**Infrastructure and governance for a global effort on the whole druggable genome**
Develop tools to identify chemogenomic compounds, synthesize solid material of chemogenomic compounds for testing, provide compound profiling to confirm that they meet the-agreed criteria, high-throughput, fragment-based screening, covalent-ligand chemoproteomic approaches, assemble the remaining 2,000 to 3,000 chemogenomics compounds, characterize compounds by determining 3D protein-small molecule complex structures, manage independent peer-review mechanism to assess suitability of compounds	Access chemical libraries from leading academic chemists, small-scale screening of chemical libraries, secondary biochemical screens to validate and prioritize hits, off-target biochemical and cell-based screens, crystallographic fragment screening and protein-ligand structure determination, design and synthesis of chemical probes, selectivity screening panels and 3D-structure determination to support probe development, high-throughput cloning, expression, purification, and novel 3D structure solution, technology development to improve quality and speed up the development and dissemination of chemogenomics compounds and chemical probes	Network of target and disease experts to profile each probe in disease-relevant assays, access to patient-derived human material (fluids, blood, tissue, other), ethical and legal frameworks to engage in such collaborations, strategies to include genotyping and deep phenotyping of patient-derived cells and tissue, mechanism to characterize probes in other consortia with panels of cell-based assays, engage additional collaborators who are leading the field in functional cell assays and disease models for particular targets, mechanism to access additional, relevant phenotypic assay panels in priority areas	Experienced managers to ensure that the key consortium deliverables are completed, senior scientists to manage project deliverables, to disseminate the project outputs and to engage in collaborations to maximize impact, database, loader and visualization tools to enable open access use of all data generated in this project and within related initiatives (e.g. ChEMBL), compound logistics for this project and for related initiatives to enable easy access to the chemogenomic compounds and the chemical probes, management of finance, valuation of deliverables, communications, create international alliance of screening, probe generation and compound profiling initiatives and align toward consortium objectives, dissemination of results in the form of publications, meeting presentations, and via the consortium's website, screening assays for broad profiling, e.g. broad panels for kinases, G-protein-coupled receptors (GPCRs); assays for cell permeability and unspecific toxicity, plan for sustainability of infrastructure after the end of this project, e.g. partnering with contract research organizations (CROs), national facilities and vendors

Expected (In-kind) Contributions of Industry Consortium

Provide at least 50 chemogenomic compounds and 10 chemical probes from EFPIA partner from proprietary compound collections as open access chemogenomic compounds	Compound profiling in established assay panels available within the companies
Free access to Diamond technology platforms for project deliverables	Design and access to fragment or other bespoke chemical libraries
Crystal-based fragment screening	Expertise in triaging and validating screening hits, design and synthesis of new chemical probes
Assays (e.g. selectivity screening panels)	Provide scientific expertise to support setup and develop human tissue assays

What's in it For You?

Academic researchers will have the ability to work collaboratively with industry to generate new chemical tools to explore exciting, unprecedented areas of biology

SMEs as vendors will have access to novel chemogenomic libraries and chemical probes with their synthetic routes for dissemination

Patient organizations and Associated Partners will be able to co-create meaningful human tissue-derived assays for their areas of disease interest and test new chemical tools

Other Associated Partners can use the consortium to accelerate the adoption of their cutting-edge technologies to speed up the creation of chemical tools

Patients and payers will ultimately benefit from access to a broader array of better medicines

Key Deliverables of the Full Project

- Establish new chemogenomic libraries consisting of at least 2,000 to 3,000 compounds meeting predefined target-specific criteria together with 2,000 collated from literature
- Generate at least 100 chemical probes for proteins from a minimum of 2-3 priority target families of high therapeutic interest. The initial priority will be on E3 ligases and solute carriers (SLCs), although we will not limit the scope to these
- Develop transferrable technologies for broadly applicable methods to speed up probe development and characterization
- Chemical probes and selected chemical tools will be subjected to unbiased phenotypic screening in existing and more than 500 patient cell-derived assays
- Align with similar efforts globally to reduce duplication of effort and to leverage the IMI investment. The consortium will work with global efforts to adopt common standards to characterize chemogenomic libraries and chemical probes

Thank You

Dr. Adrian J. Carter and Dr. Anke Müller-Fahrnow

www.imi.europa.eu

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Involvement of SMEs, patient groups, regulators

Iwona Jablonska

SME participation

IMI encourages the participation of SMEs in applicant consortia as they can offer a complementary perspective to other organisations.

Please read carefully the topic text and the section dedicated to the "**Applicant Consortium**" as well as "**Suggested architecture of the full proposal**" (e.g. Pillar 4).

In general, "*Applicants should consider engaging SMEs throughout the proposal. For example, under this topic,* ***the contribution of SMEs would be considered beneficial for broad profiling of chemogenomics compounds and chemical probes****.* "

Moreover, the applicant consortium must also demonstrate *the ability and history of leveraging additional funds together with other partners including* ***SMEs****, and also previous success in collaborations among networks of academics and* ***SMEs.***

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Patient participation

- Ultimate objective: improving patients' lives and treatments

- One of the topic's aims: *develop open-access assays from well characterised human disease tissue with a special emphasis on immunology, oncology (including immune-oncology) and neuroscience to profile the chemical tools and chemical probes*

- Members of the applicant consortium are expected to demonstrate the *ability and history of leveraging additional funds with diverse and international organisations, including patient groups, foundations, philanthropy and SMEs*

"The patient, doctor and researcher – each is a different kind of expert."

Interactions with regulators

- **Have a plan for interaction** with relevant **milestones** and **resources** allocated, as needed
- Consider the **formal regulatory process** to ensure **regulatory acceptance of project results** (e.g. qualification procedure for biomarkers)
- Get familiar with **services offered for dialogue** (e.g. at EMA through qualification advice, Innovation Task Force, briefing meetings)
- Consider involving regulators as project participants or in the **advisory board**
- Have a plan for dialogue with **HTA bodies / payers**, if relevant

To maximise impact of science generated by projects

Engage in dialogue with regulatory authorities

More info:

- Webinar & presentations 'How to engage with regulators EMA / FDA'
- 'Raising awareness of regulatory requirements: A guidance tool for researchers'

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Thank you

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Questions & answers

Questions?

Raise your hand if you want to ask a question orally

Send a question in writing

After the webinar, send any questions to the **IMI Programme Office**

applicants@imi.europa.eu

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Thank you!