Webinar | IMI2 – Call 18

Supporting the development of engineered T cells

25.06.2019

Agenda

- How to use GoToWebinar – Catherine Brett, IMI
- Introduction – Oussama Karroum, IMI
- The Call topic – Virginie Jacquemin and Sophie Amsellem-Bosq, Servier
- Involvement of SMEs, patient groups, regulators – Oussama Karroum, IMI
- Questions & answers

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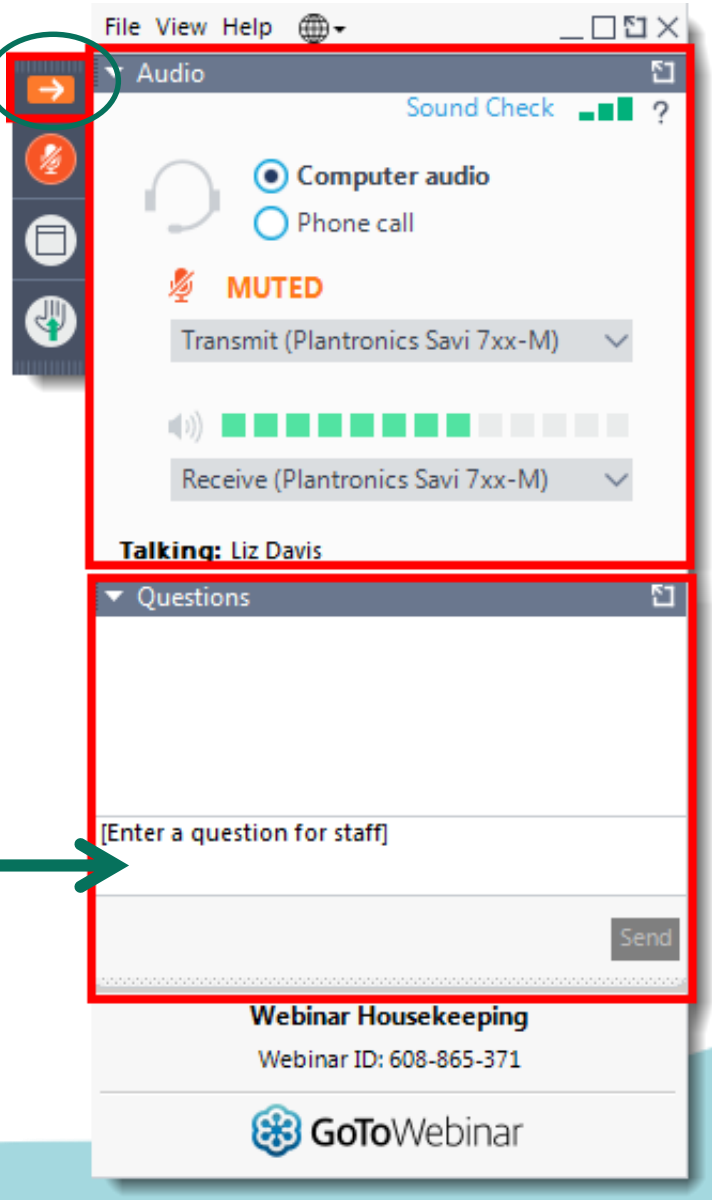

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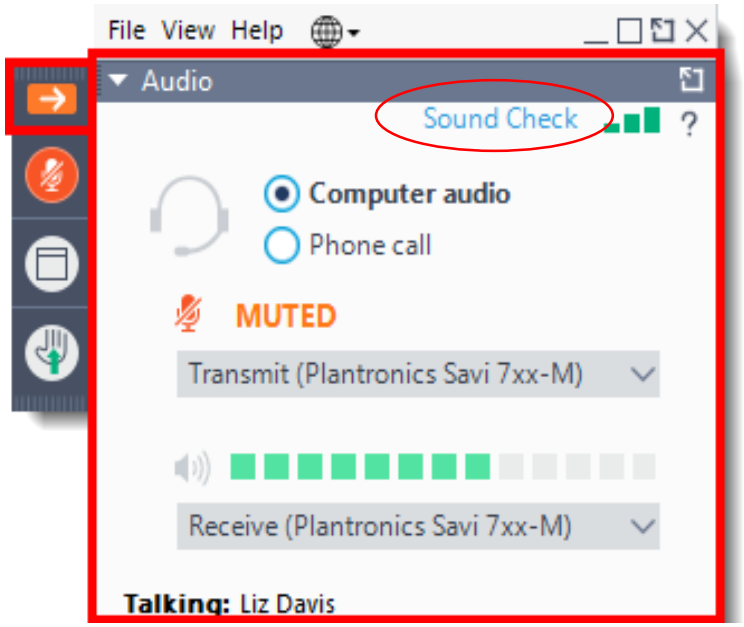

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Before we start…

- 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
- All information regarding future IMI Call topics is indicative and subject to change. Final information about future IMI Calls will be communicated when the Call is officially launched.

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Webinar | IMI2 - Call 18

Supporting the development of engineered T cells

Karroum Oussama

25 June 2019

Today's webinar

Will cover all aspects of the Call topic

- Introduction to IMI programme
- Proposed project
  - Objectives, need for public-private collaborative research
  - Key deliverables
  - Structure of the project
  - Expected contribution of the applicants
  - Contribution of industry consortium

Will not cover rules and procedures

- A webinar on rules and procedures will take place on

  18 June, 11:00 Brussels time

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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

efpia

€1.425 bn

EFPIA companies

receive no funding

contribute to projects ‘in kind’

Other €213 m

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

IMI 2 total budget €3.276 billion

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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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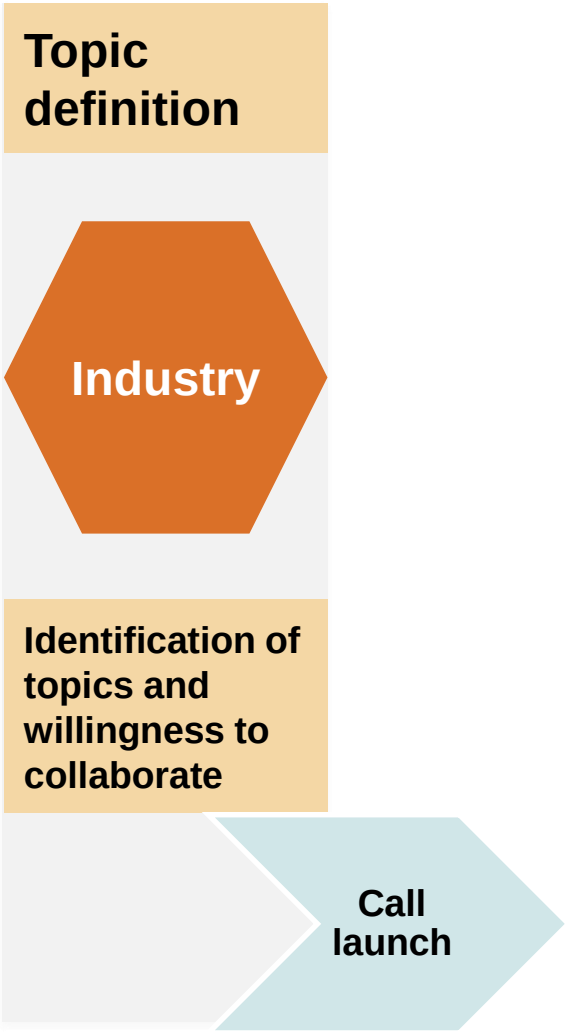
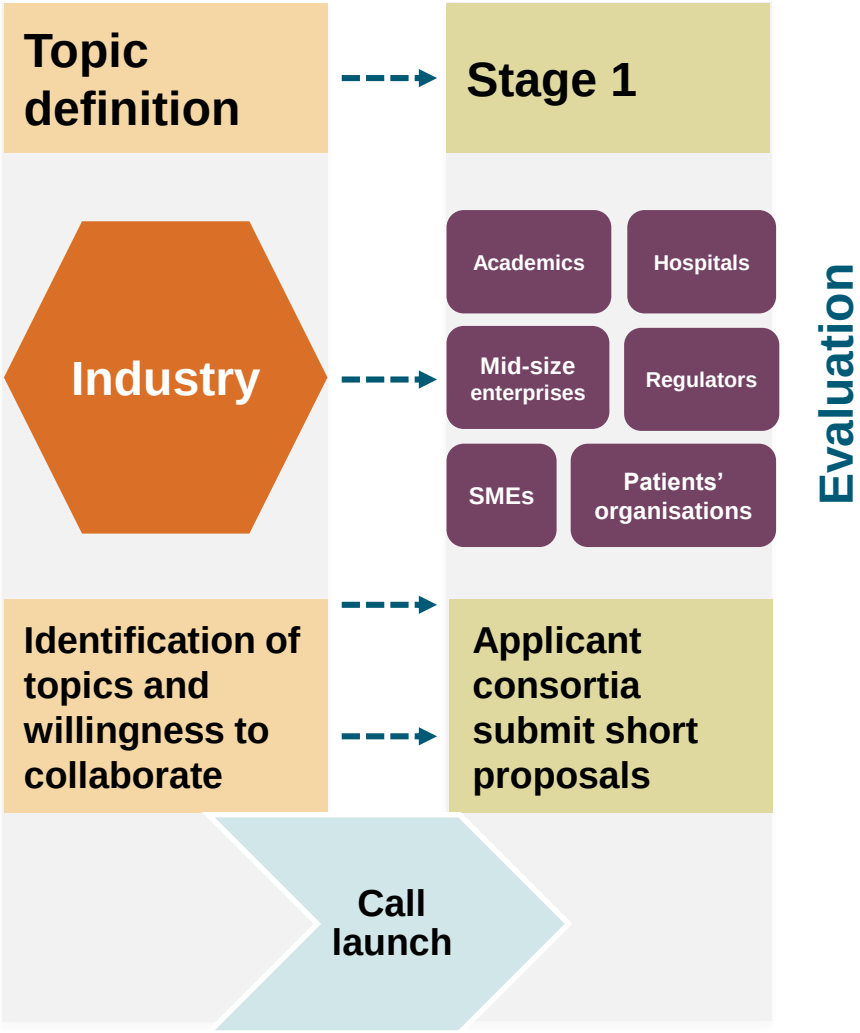
Typical IMI project life cycle



Typical IMI project life cycle



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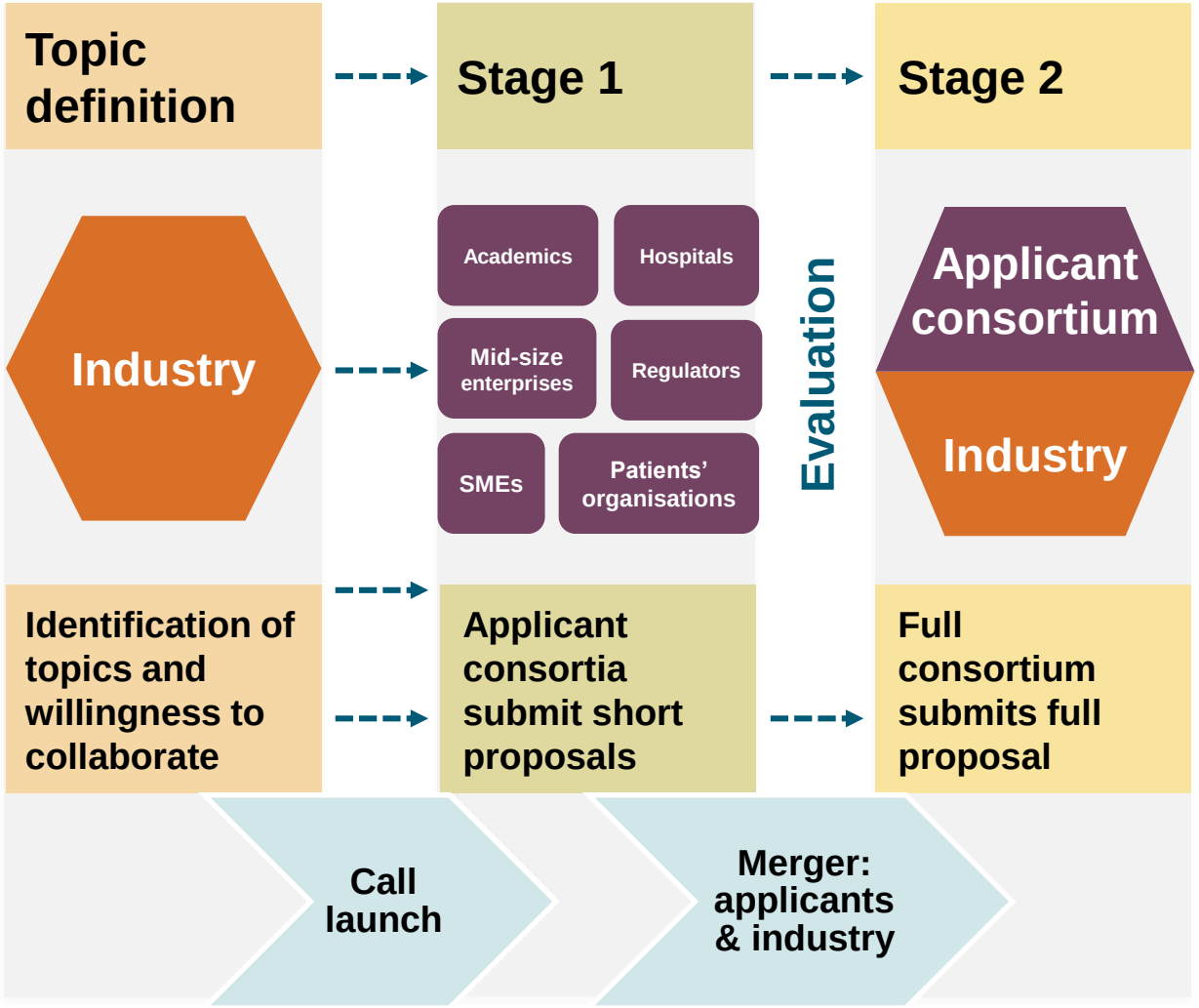
Typical IMI project life cycle



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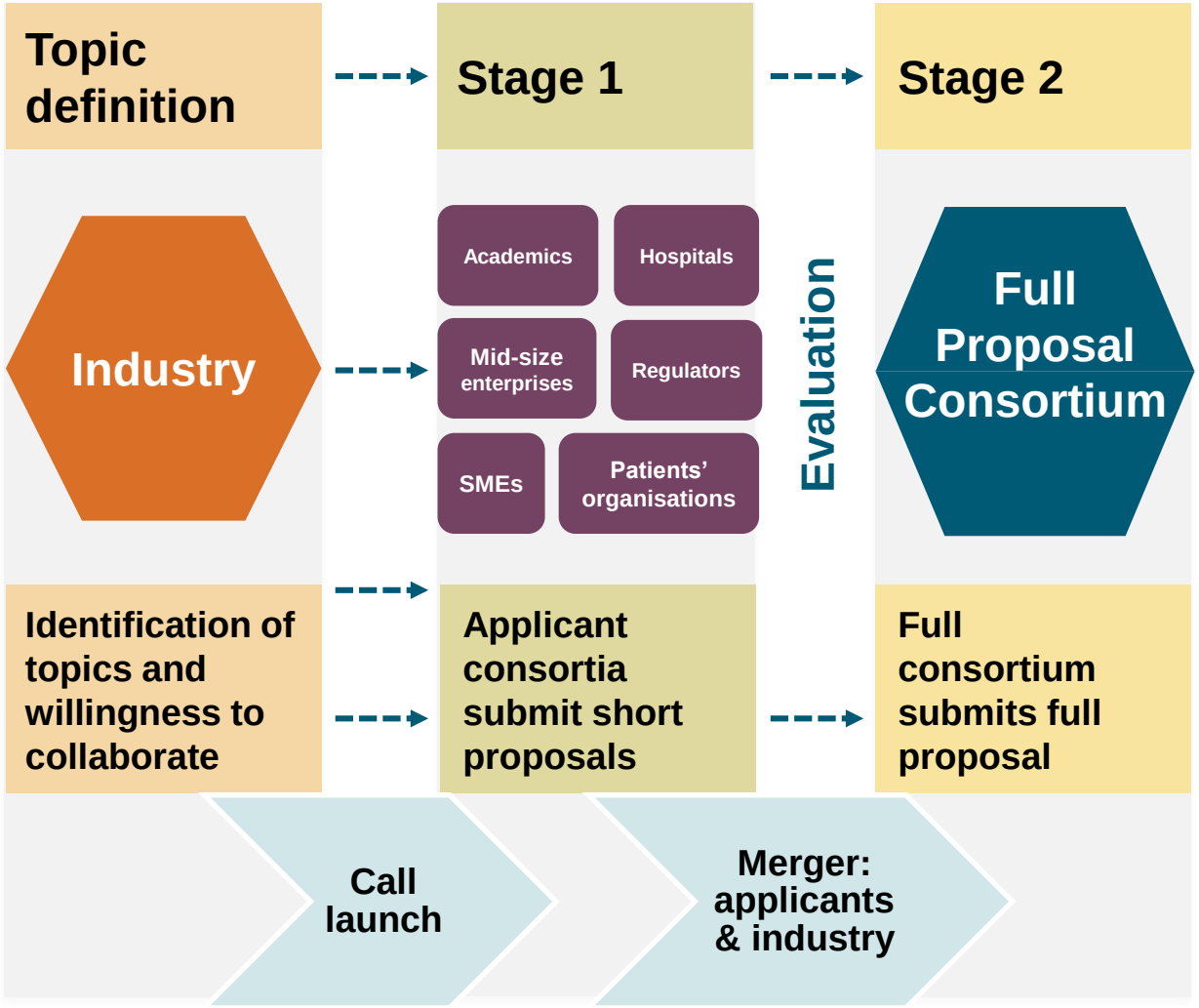
Typical IMI project life cycle



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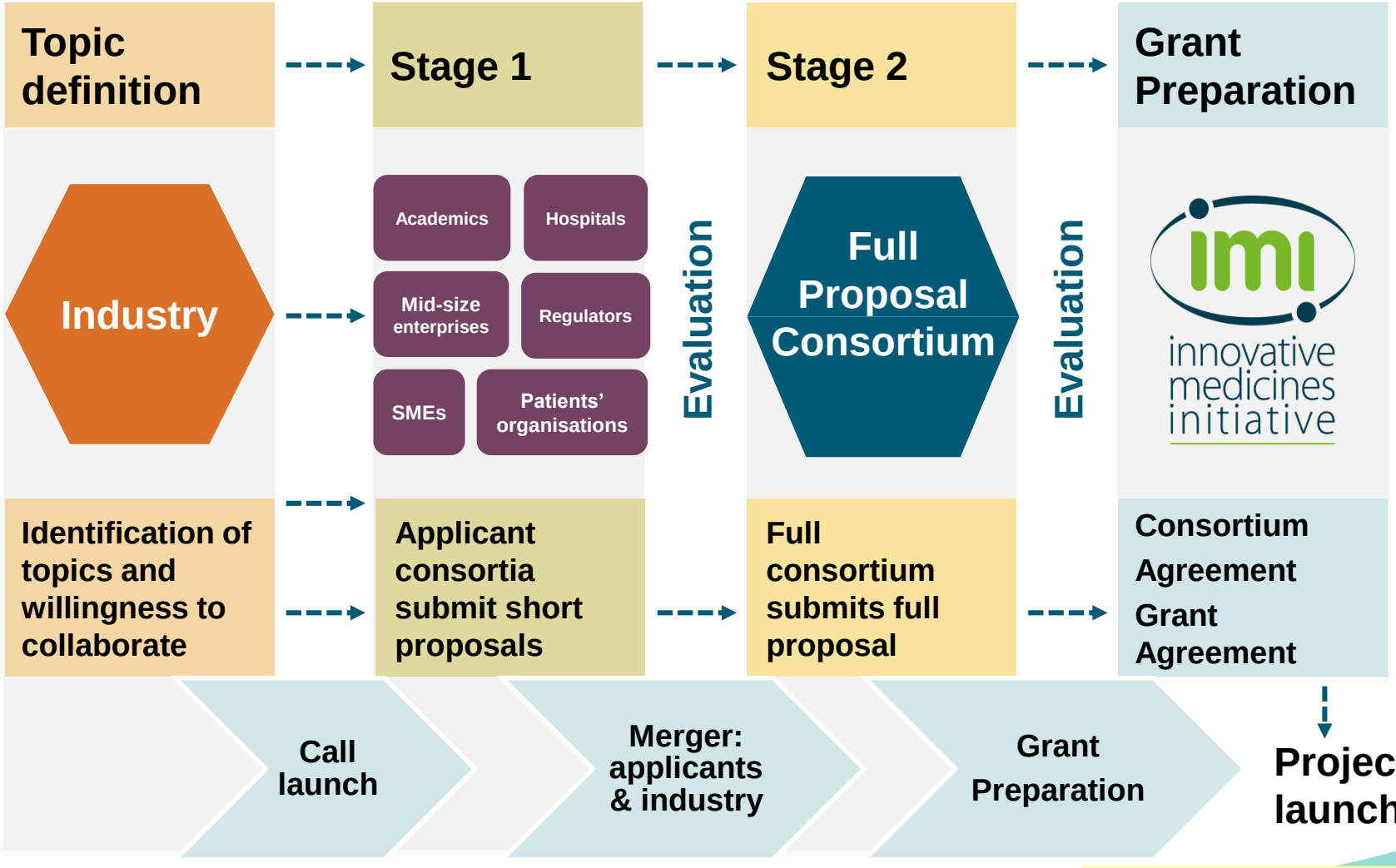
Typical IMI project life cycle



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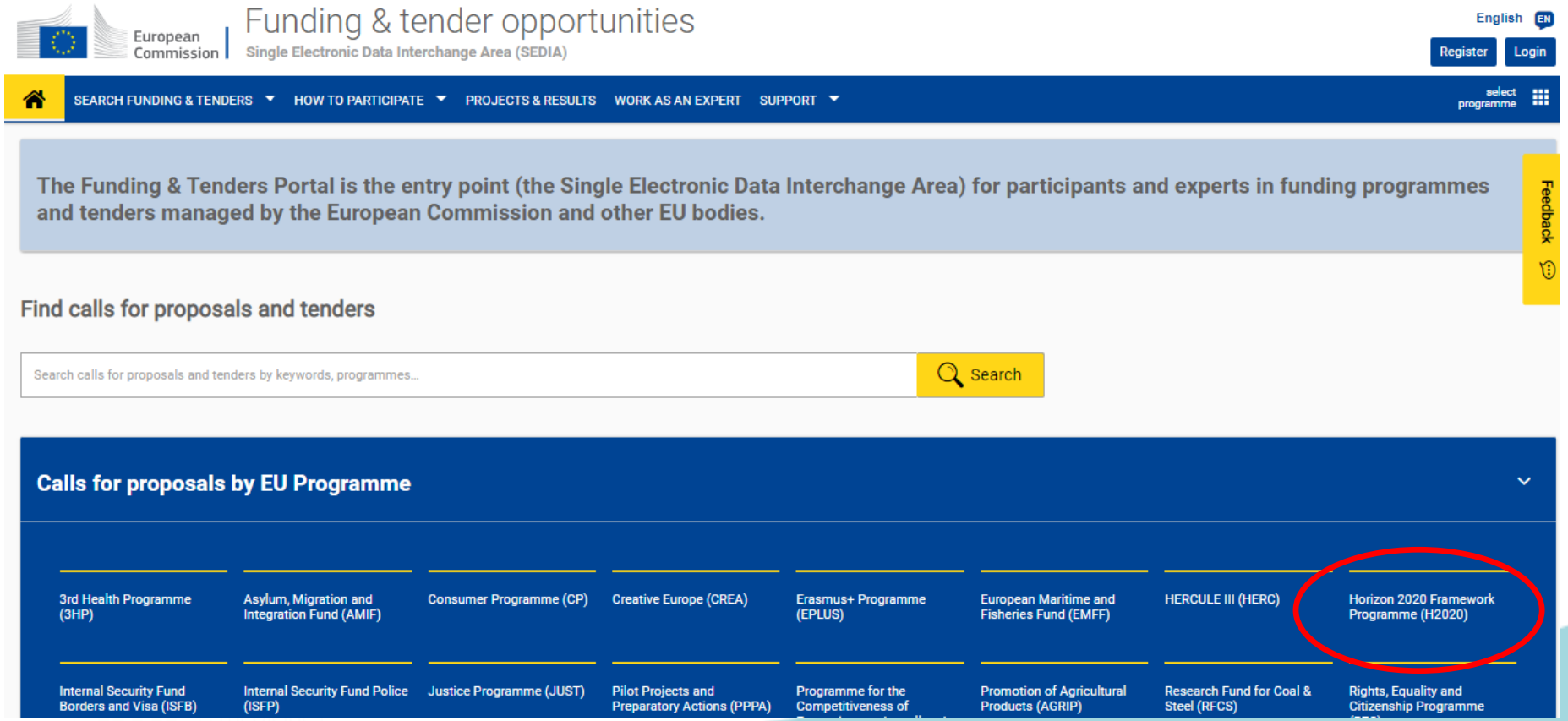
Expected GA signature – Sep/Oct 2020

Submitting a proposal

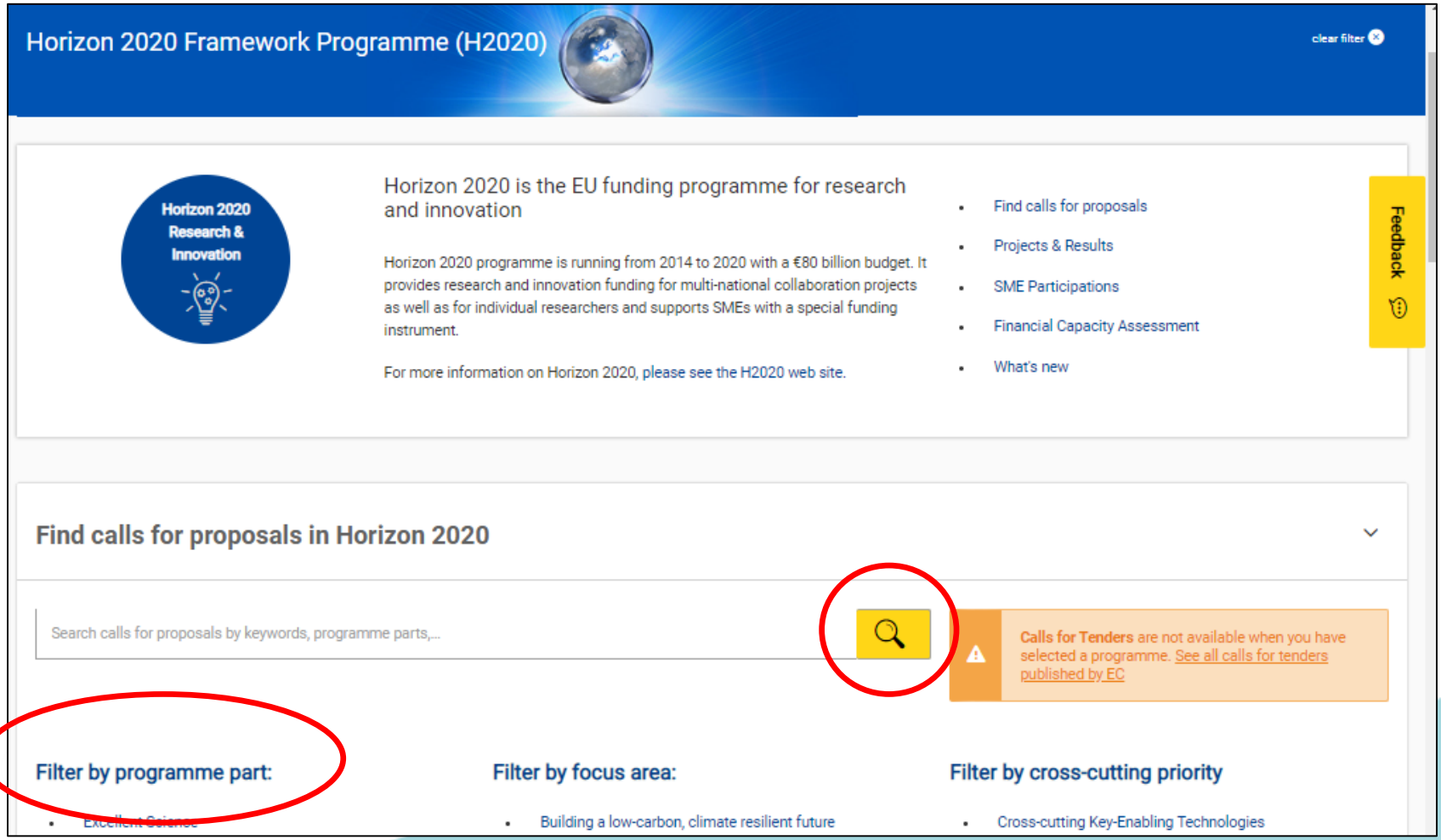
Via the **new** Funding and Tenders Portal

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



Proposal Template – Newly updated

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

Title of Proposal

List of participants

Table of Contents

1. EXCELLENCE

- **1.1 Objectives**
- **1.2 Concept and methodology**
- **1.3 Ambition**

2. IMPACT

- **2.1 Expected impacts**
- **2.2 Outline Measures to maximise impact**

3. IMPLEMENTATION

- **3.1 Outline of project work plan — Work packages, and major deliverables**
- **3.2 Management structure and procedures**
- **3.3 Consortium as a whole**
- **3.4 List of work packages**

4. PARTICIPANTS

- **4.1. Participants (applicants)**

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Evaluation Criteria (1/2) – Newly updated

- **Excellence**
  - Level to which all the objectives of the Call topic text are addressed;
  - Soundness of the concept and credibility of the proposed methodology;
  - Extent that the proposed work is beyond the state of the art and demonstrates innovation potential;
  - Appropriate consideration of interdisciplinary approaches and use of stakeholder knowledge.
- **Impact**
  - Demonstration of how the outputs of the project will contribute to each of the expected impacts mentioned in the relevant Call topic text;
  - Outline of how the project plans to leverage the public-private partnership model to achieve greater impact on innovation within research and development, regulatory, clinical and healthcare practices, as relevant ;
  - Impacts on competitiveness and growth of companies including SMEs;
  - Quality of the proposed outline to:
    - Disseminate, exploit and sustain the project results;
    - Manage research data;
    - Communicate the project activities to relevant target audiences.

Evaluation Criteria (2/2) – Newly updated

- **Quality and efficiency of the implementation**
  - Quality and effectiveness of the work plan outline, including extent to which the resources assigned to work packages are in line with their objectives and deliverables;
  - Appropriateness of the outline management structures and procedures;
  - Appropriateness of the allocation of tasks, ensuring that all participants have a valid role and adequate resources in the project to fulfil that role;
  - Complementarity of the participants and extent to which the consortium as whole brings together the necessary expertise;
  - Strategy to create a successful partnership with the industry consortium as mentioned in the Call topic text.

New thresholds:

- 3 for each of the evaluation criteria ‘excellence’, ‘impact’ and ‘quality and efficiency of the implementation’
- the overall threshold is 10

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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 **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.

- 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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Supporting the development of engineered T cells

Virginie JACQUEMIN

25.06.2019 • IMI webinar

Engineered T-cell immunotherapies

- The first two **autologous CD19 CAR-T cell therapies have recently approved** by FDA and EMA
  - Kymriah™ (Tisagenlecleucel, Novartis)
  - Yescarta™ (Axicabtagene Ciloleucel, Gilead/Kite)

- **Engineered T cells :**
  - T cells modified to express a **CAR** (Chimeric Antigen Receptor) or a **TCR** (T Cell Receptor)
  - Promising new treatment modality for a broad range of cancers
  - Have **not yet reached their full potential**, especially in solid tumors

Need for public-private collaboration

"CAR therapy is at the same time cell therapy, gene therapy, and immunotherapy. It represents a radical departure from all forms of medicine in existence until now" Michel Sadelain

Complex medicinal products
"A living drug"

Emerging therapies
Only 2 recently approved therapies

A wide **range of complex issues**

- Need for **strong cooperation** amongst different stakeholders **bringing their diverse expertise**
  - Industry & SMEs, academia, patients and patient organisations, policymakers, public health experts and regulators

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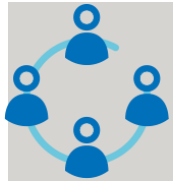
Challenges related to engineered T cells

Research and translational

Pre-clinical models, tools and PD markers, analytical methods

Industrial (Manufacturing and CoG)

Consistency, product characterization, regulatory, logistics, cost



Clinical challenges

Practices, monitoring, pre-conditioning regimen, long term follow-up

Patient access to therapies

Infrastructure, reimbursement, training of HCPs, patients viewpoint

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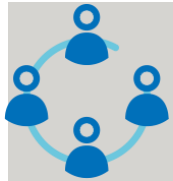

Clinical challenges

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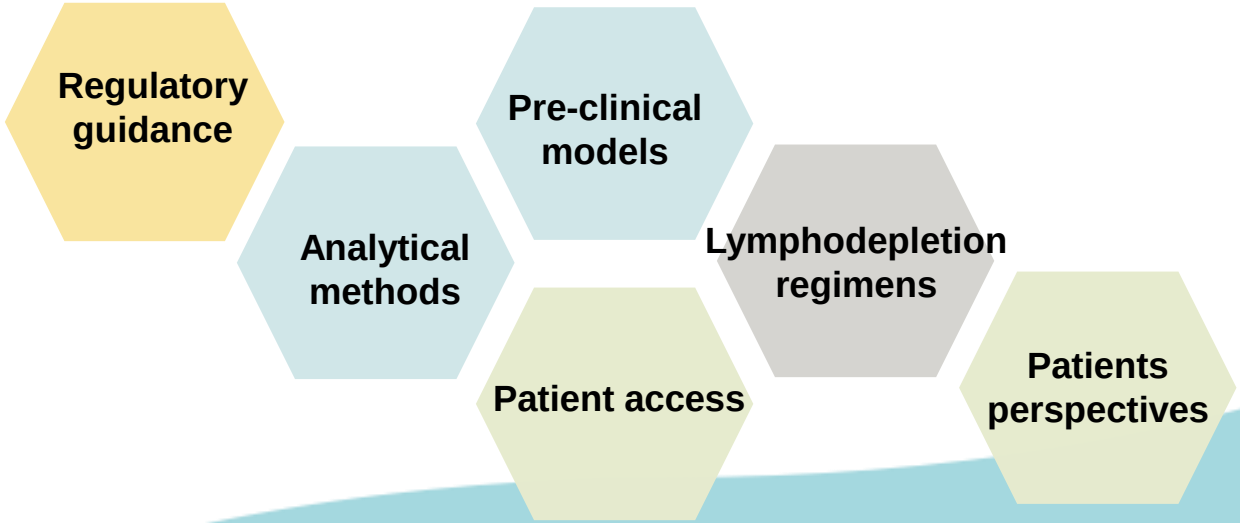
“Supporting the development of engineered T cells”

- **OBJECTIVE**
  - TO SUPPORT THE DEVELOPMENT OF ENGINEERED T-CELL THERAPIES
- **SCOPE**
  - AUTOLOGOUS AND ALLOGENEIC
  - CAR AND TCR ENGINEERED T CELLS
  - BOTH HAEMATOLOGICAL AND SOLID TUMOURS
- **CHALLENGES**



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Key deliverables of the full project

1. Pre-clinical models, pharmacodynamic markers or tools with high translational potential to predict safety of engineered T cells
2. Pre-clinical models, pharmacodynamic markers or tools with high translational potential to predict efficacy of engineered T cells
3. Gold standard analytical methods used both pre- and post-infusion
4. Optimised lymphodepletion regimens for engineered T cells
5. Customised European Pharmacopoeia and GMP for ATMPs for engineered T cells
6. Communication tools for patients and healthcare providers
7. White paper on patient access to engineered T cells

GMP: Good Manufacturing Practice
ATMP: Advanced Therapy Medicinal Products

Deliverables 1 & 2

Pre-clinical models, pharmacodynamic markers or tools with high translational potential to predict safety & efficacy of engineered T cells

- Mapping of existing pre-clinical models and identification of gaps
- Optimization of existing models, development of new models and tools, modelling

Safety

- Cytokine Release Syndromes
- Neurotoxicity
- Graft versus Host Disease
- Off-target toxicity of gene editing technologies
- Insertional mutagenesis linked to the use of viruses

Efficacy

- Anti-tumour activity
- Pharmacokinetics (expansion, trafficking, homing, infiltration, persistence)
- Impact of tumour heterogeneity
- Role of tumour microenvironment
- Epitope spreading

Industry contribution (in kind)

- Pre-clinical models (*in vitro* and *in vivo* models)
- Pharmacometrics (PK-PD) / modelling

Applicant contribution

- Development of pre-clinical models and tools (*in vitro and in vivo* models), imaging
- Cellular and molecular biology, immunology, imaging
- Pharmacometrics (PK-PD) / modelling

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Deliverable 3

Gold standard analytical methods used both pre- and post-infusion

- Optimization/development of analytical methods including but not limited to qPCR, flow cytometry, NGS, single cell analysis, RCL, omics

Pre-infusion

- Characterisation of the product
- Assessement of off-target toxicities of gene editing technologies and insertional mutagenesis linked to the used of viruses
- Rapid and less product consuming assays to assess microbiological safety

Post-infusion

- Assessment/quantification of engineered T cells
- Clinical fate of engineered T cells (homing, persistence, efficacy)
- Immune monitoring of patients (kinetics of reconstitution of immunity, profiling of engineered T cells, immune response against T cells)

Industry contribution (in kind)

- CMC
- Translational
- Analytics
- Bioinformatics
- Standardisation of monitoring tools/systems
- CAR-T characterization gene panels

Applicant contribution

- Cellular and molecular biology
- Immunology
- Imaging

Deliverable 4

Optimised lymphodepletion regimens for engineered T cells

- Better understand the impact of lymphodepletion on engineered T-cell safety, efficacy,
- Optimise or develop new conditioning regimen

- Collect existing biological and clinical data from patients who received lymphodepleting regimens
- Create a database
- Meta-analysis of the data
- Develop *in vivo* models to better understand the impact of lymphodepletion regimens on engineered T-cell safety, efficacy, and to optimise or develop new conditioning regimens

Industry contribution (in kind)

- Clinical expertise
- PK
- Bioinformatics
- IT

Applicant contribution

- Access to historical data/cohorts of patients treated with engineered T-cells and/or receiving lymphodepletion regimens
- Bioinformatics
- Clinicians with lymphodepletion experience
- Modelling,
- Pre-clinical models
- Immuno-biology

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Deliverable 5

Customised European Pharmacopoeia and GMP for ATMPs for engineered T cells

- Address some regulatory and quality aspects of manufacturing in order to achieve a standard product profile

- Biological and pharmaceutical characterisation of the products (i.e. potency activity, release assays, appearance)
- Critical Quality Attributes
- Quality control, including safety tests such as RCL
- Recommendations on the practical implementation of GMP for ATMPs and pharmaceutical requirements
- Some technologies from deliverable 3 could also be applicable for this deliverable.

Industry contribution (in kind)

- CMC
- Regulatory

Applicant contribution

- Regulatory / Health Technology Assessment/ Health economics
- Health authorities
- CMC/GMP
- Academic Centres, Contract Development and Manufacturing Organizations (CDMOs) or any other organisations that are interacting with regulatory health authorities

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Deliverables 6 & 7

Communication tools for patients and healthcare providers & White paper on patient access to engineered T cells

- Guarantee that the patient perspective is taken into account
- Ensure equitable patient access to engineered T cells

- Promote engagement of patients all along the R&D process
- Ensure adequate communication on engineered T-cell therapies to patients and their family/caregivers
- Ensure that HCPs are sensitised to patient needs
- Contribute to appropriate training for HCPs
- Propose solutions for broad and/or equitable patient access to engineered T cells

Industry contribution (in kind)

- Communication and dissemination
- Education and training
- Collaboration with patient advocacy groups
- Management of expert boards
- Knowledge of pharmaceutical life-cycle process
- Market access

Applicant contribution

- Patient expertise
- Patient organisations will be considered as key partners (collecting concerns from patients and caregivers, actively taking part in the R&D process and ensuring patient-friendly communication)
- Communication
- National health care authorities and societies
- Health economics
- IT support

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Suggested architecture of the project

Work Package architecture proposal	
1	Project management, coordination, communication and long-term sustainability
2	Patient involvement
3	Models and tools to assess safety of engineered T cells
4	Models and tools to assess efficacy of engineered T cells
5	Gold standard analytical methods used both pre- and post-infusion of engineered T cells
6	Development of optimal lymphodepletion /conditioning regimen
7	Data integration
8	Customised European Pharmacopoeia and GMP for ATMPs for engineered T cells

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GMP: Good Manufacturing Practice
ATMP: Advanced Therapy Medicinal Products

Pre-competitive nature

- Public-private partnership with **shared access to results** for research purpose for all partners
  - Creation of an **open-access set of pre-clinical models, tools and markers** that will better predict the safety, efficacy and PK of engineered T cells
  - **Analytical methods, assays** and **data** will be made publicly available without restriction for use and dissemination to facilitate global adoption
  - Creation of a **open-access platform** based on the collection of clinical and biological data from patients treated with **lymphodepetion regimens**
  - **Communication** and **training tools** will be made publicly available for use and dissemination

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Expected impact

- Development of **safer and more effective T-cell therapies** for a broader range of cancers
- Further generation of **comparable data** from standardised analytical methods
- Increased **industrial competitiveness** and improved **synergy** between industry, SMEs and academic organisations
- Broader **patient access** to T-cell therapies and increased awareness among HCPs of **patients' concerns**

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What's in it for you?

- **For academic researchers and SMEs**
  - The possibility to co-develop models and tools that will contribute to the development of next generation engineered T-cell therapies with better safety and efficacy
  - A better understanding of patients' needs

- **For patients and patients' organisations**
  - A better consideration of their perspectives by being a key actor of the whole R&D process
  - A better understanding of the mode of action and procedures of their treatment
  - Facilitated interactions with HCPs.

Thank you

www.imi.europa.eu

@IMI_JU

Involvement of SMEs, patient groups, regulators

Oussama Karroum
25 June 2019

SME participation

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

Contribution of SMEs would be considered especially beneficial in providing as example the following expertise and activities :

- Project Management
- IT expertise for data Integration activities or/and for training, education, communication & dissemination
- Development of new preclinical models or analytical methods

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Patient participation

Patient organisations will be considered as key partners of the funded action.

- To contribute by collecting concerns and needs from patients and caregivers
- Actively taking part in the R&D process
- Ensuring patient-friendly communication

"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?

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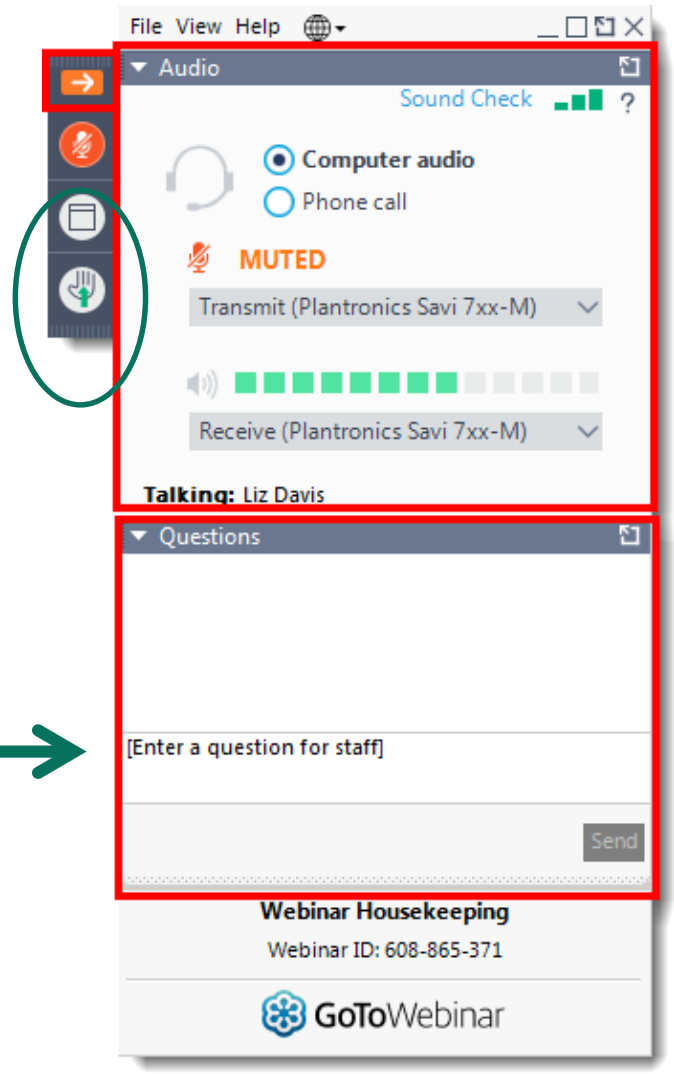
Questions?

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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