

Webinar | IMI2 - Call 15

Development and validation of translational platforms in support of synaptopathy drug discovery

04.07.2018

Agenda

- How to use GoToWebinar – Catherine Brett, IMI
- Introduction – Oussama Karroum, IMI
- The Call topic – Darrel Pemberton, JnJ
- Involvement of SMEs, patient groups, regulators – Oussama Karroum, IMI
- Questions & answers

How to use GoToWebinar

Expand / minimise control panel →

Microphone status →

Full screen →

Raise / lower your hand
e.g. if you want to ask a
question orally

Send a question in writing →

The screenshot shows the GoToWebinar interface with several key elements highlighted by a red border and green arrows:

- Expand / minimise control panel:** A red circle highlights the expand/collapse arrow icon in the top-left corner of the control panel.
- Microphone status:** A red circle highlights the microphone icon in the top-left corner of the control panel.
- Full screen:** A red circle highlights the full screen icon in the top-left corner of the control panel.
- Raise / lower your hand:** A red circle highlights the hand icon in the top-left corner of the control panel.
- Send a question in writing:** A red circle highlights the text input field and the "Send" button in the "Questions" section.

The interface includes the following components:

- Audio Control Panel:** Features a "Sound Check" indicator, "Computer audio" (selected) and "Phone call" options, a "MUTED" status, and dropdown menus for "Transmit (Plantronics Savi 7xx-M)" and "Receive (Plantronics Savi 7xx-M)".
- Questions Section:** A text input field with the placeholder "[Enter a question for staff]" and a "Send" button.
- Webinar Housekeeping:** Displays "Webinar ID: 608-865-371" and the "GoToWebinar" logo.

How to use GoToWebinar - audio

To listen via your computer, select **Computer audio**

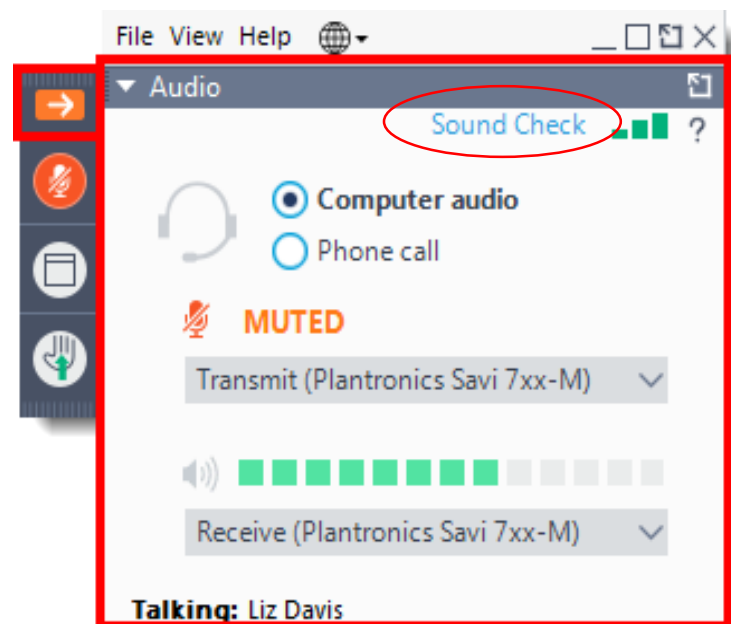
Can't hear us?

- Check your **speakers are switched on and not muted**
- Do a **Sound Check** to make sure GoToWebinar is picking up the right speakers
- Still not working? Select **Phone call** and dial the numbers given on your phone

To listen in via your phone, select **Phone call**, pick your country, and dial the numbers given

Can't hear us?

- Check you have selected **Phone call** in the audio panel
- Try **another country's** phone number
- Still not working? Select **Computer audio** and listen over your computer's speakers



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 after approval by the IMI Governing Board.



Webinar | IMI2 - Call 15

Development and validation of translational platforms in support of synaptopathy drug discovery

Karroum Oussama
IMI Scientific Officer
4th July 2018

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
Tuesday 10 July at 10:30

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.

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**.

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

receive no funding

contribute to projects 'in kind'

Associated Partners

e.g. charities, non-EFPIA companies

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

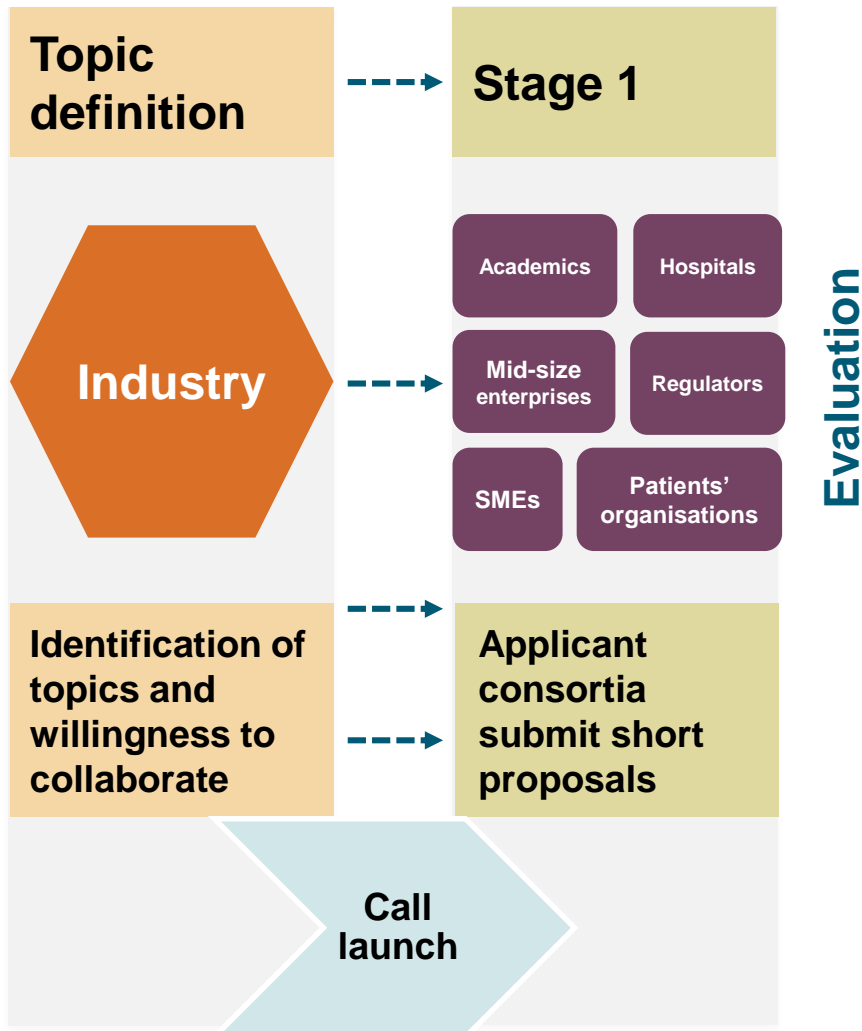
Scale is a key to success and is provided through IMI funding

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

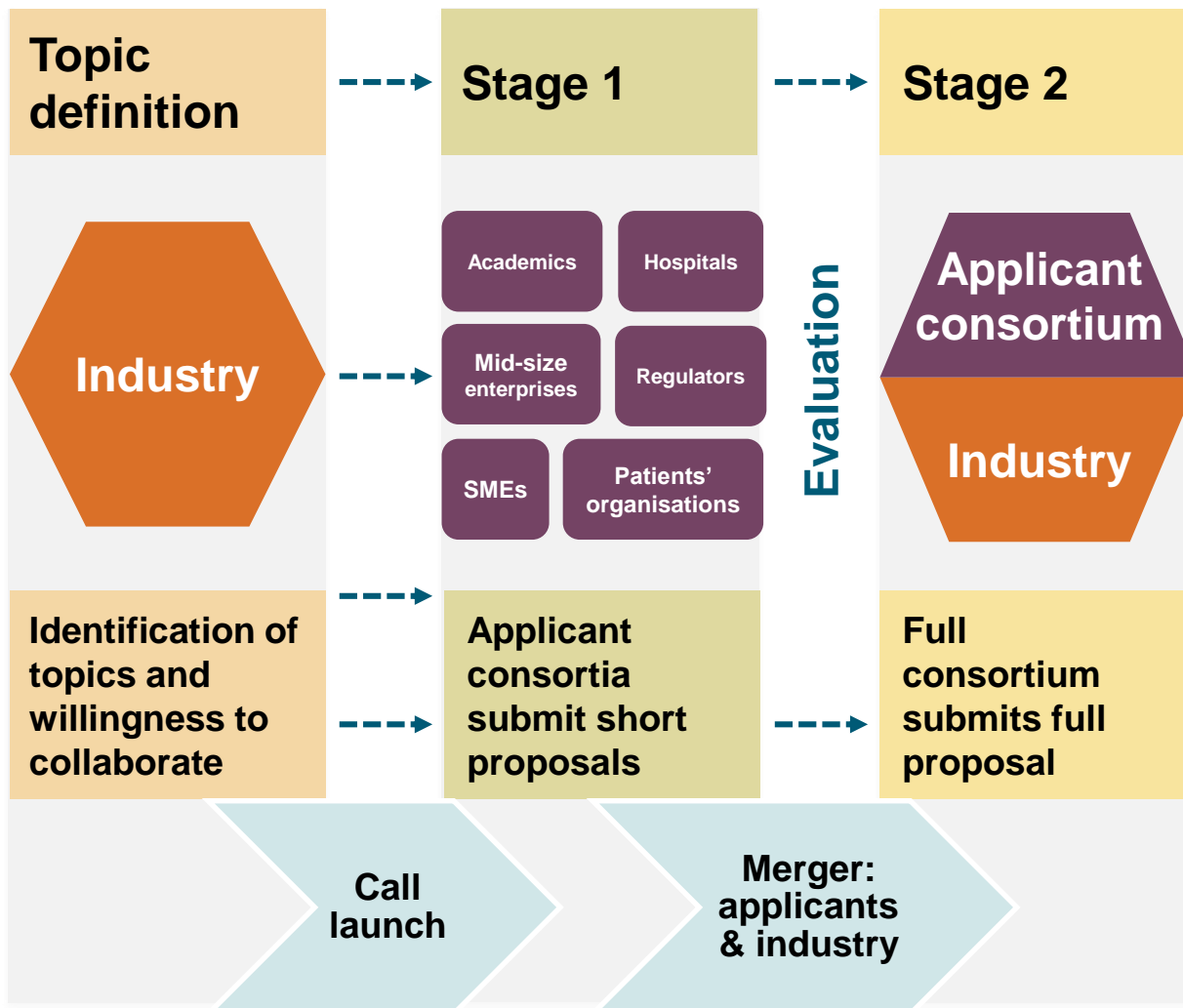
Typical IMI project life cycle



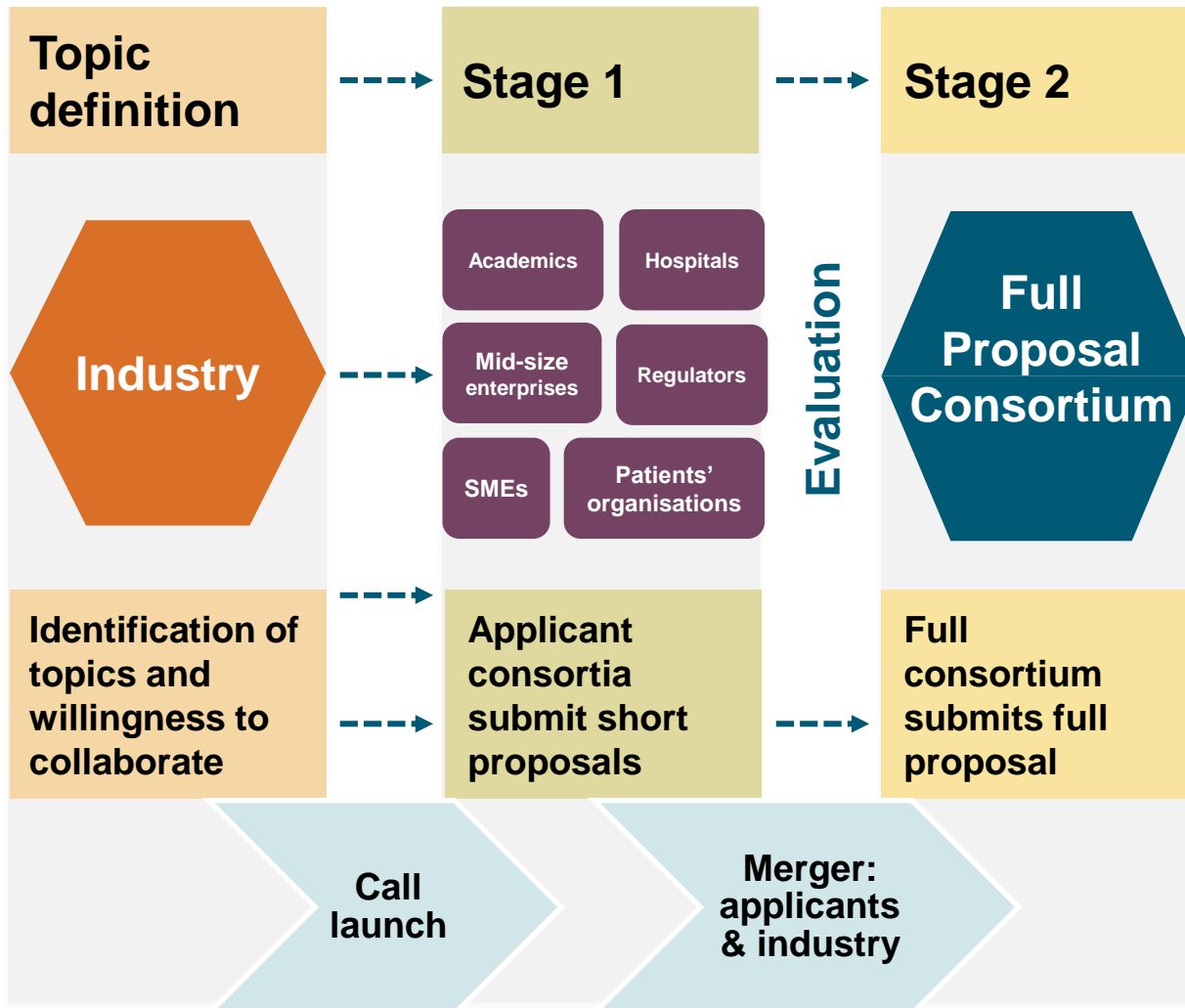
Typical IMI project life cycle



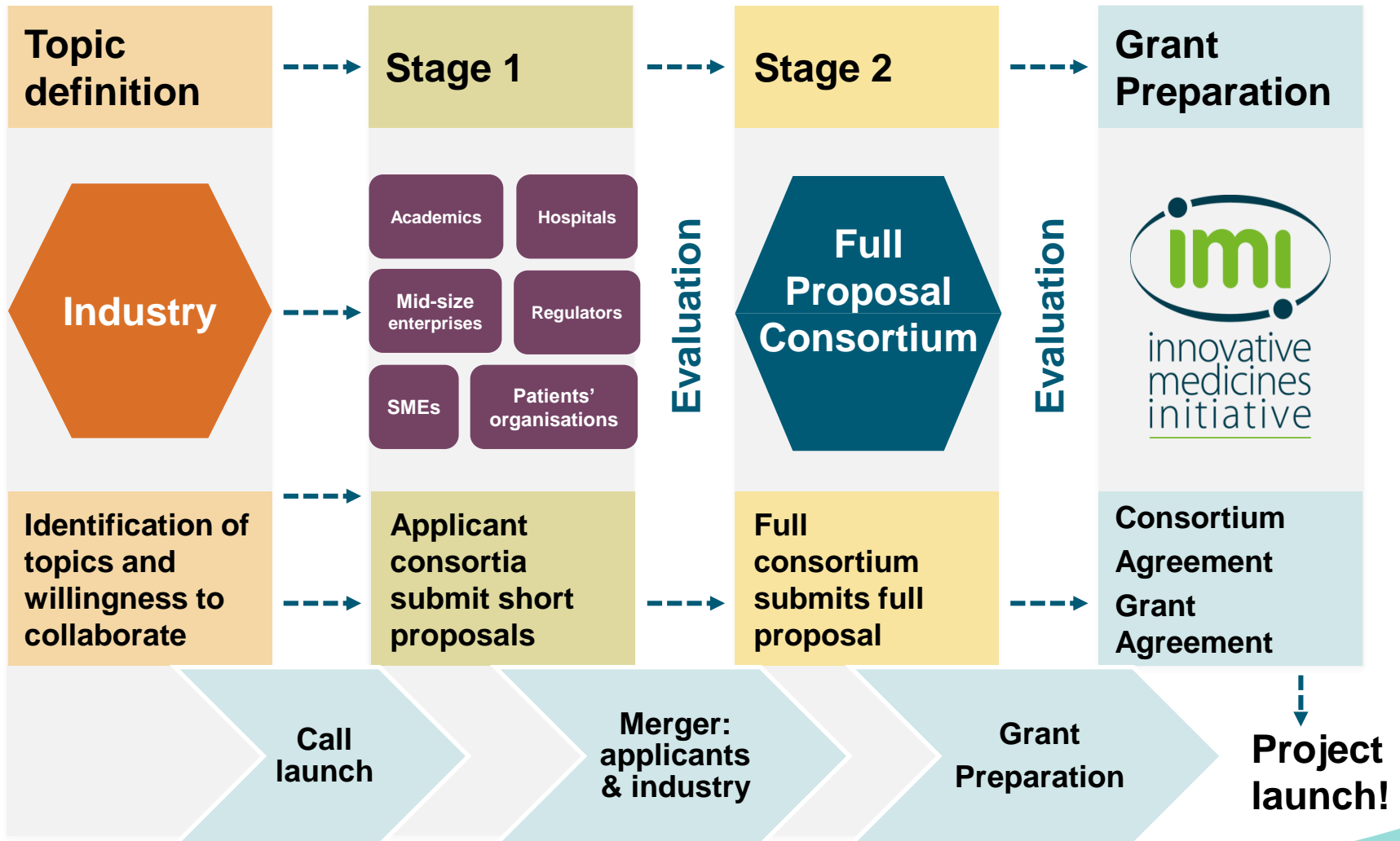
Typical IMI project life cycle



Typical IMI project life cycle



Typical IMI project life cycle



Submitting a proposal

- <https://ec.europa.eu/research/participants/portal/desktop/en/opportunities/h2020/index.html>

The screenshot displays the 'Participant Portal' for 'RESEARCH & INNOVATION' by the European Commission. The main navigation bar includes 'HOME', 'FUNDING OPPORTUNITIES', 'HOW TO PARTICIPATE', 'EXPERTS', and 'SUPPORT'. A search bar and 'LOGIN'/'REGISTER' buttons are also present. The left sidebar lists 'EU Programmes 2014-2020' with categories like 'Search Topics', 'Updates', and 'Calls', where 'H2020' is selected. The main content area is titled 'Calls for Proposals' and features a 'Horizon 2020' section with a list of topics: 'Excellent Science' (including ERC, FET, Marie-Sklodowska-Curie Actions, and Research Infrastructures) and 'Industrial Leadership' (including LEIT and ICT). Below this, there are filters for 'Status' (Calls with forthcoming topics, open topics, or closed topics) and 'Sort by' (Call title, Call identifier, or Publication date). A search filter 'IMI2' is entered in the search bar.

Proposal Template

- 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	3. IMPLEMENTATION
1.1 Objectives	3.1 Outline of project plan — Work packages, and major deliverables
1.2 Relation to the call topic text.	3.2 Management structure and procedures
1.3 Concept and approach	3.3 Consortium as a whole
1.4 Ambition	3.4 Table 3.1a: List of work packages
2. IMPACT	4. PARTICIPANTS
1 Expected impacts	4.1. Participants (applicants)

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 **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

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.

Find project partners

- Network with **your contacts**
- **Network** with fellow webinar participants
- Use **Partner Search Tools**:
 - EU participant portal:
https://ec.europa.eu/research/participants/portal/desktop/en/organisations/partner_search.html
 - 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)

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...)

Development and validation of translational platforms in support of synaptopathy drug discovery

Darrel Pemberton

04.07.2018 • IMI webinar

Need for public-private collaboration

- CNS disorders are a ticking time bomb due to the considerable societal costs and the fact that these expenses will increase exponentially due to an ever-growing aging population
- Major discrepancy between the impact of CNS disorders and the modest resources that are directed to brain research
- To improve efficiencies and ultimately drive success, it is imperative that intensive, collaborative research programs be implemented
- These should connect experts across sectors and disciplines, breaking silos and allowing pooling of resources and expertise from industry, academia and small and medium-sized enterprises (SMEs).
- The Innovative Medicines Initiative public-private partnership model is best placed to implement such collaborations to achieve a leap forward in scientific understanding and deliver a robust and highly validated platform of tools and technologies that can be exploited to deliver much needed novel CNS medicines.

Objectives of the full project

- Science linking alterations in synaptic function, genetics, and underlying pathways with CNS disorders is emerging.
- The aim is to construct a precompetitive research consortium focused on furthering our scientific understanding of how synaptopathies can elicit or contribute to brain disorders.
- Work streams can broadly be divided into:
 1. Deep clinical phenotyping of CNS disorder patients to enable the development of robust tools to measure disease and treatment effects on the synapse
 2. Characterisation of existing and development of novel preclinical synaptopathy disease models
- To achieve the overall aim of the topic, applicants should focus on at least one of the four major brain disorders namely Alzheimer's, Parkinson's disease, major depression and schizophrenia, and ideally at least two, one in the neurodegenerative and one in the psychiatric/neurodevelopmental field.

Pre-competitive nature

- Despite progress in translational research, we are still falling short in developing the innovative medicines required to address major public health challenges. Moreover, the high failure rate, time, and cost required for registration of a new drug are pushing the economics of the industry to the breaking point.
- Resources in industry, academia and SME's are also limited and thus replicating efforts tackling non-competitive scientific challenges can be perceived as wasteful and unnecessary.
- New consortia models have moved away from the vigorous pursuit of intellectual property towards exploration of pre-competitive cross-industry collaborations and engagement with public domains.
- The consortia whilst working in an open and truly collaborative manner will focus on areas that will deliver on the key scientific challenges impeding growth and delivery in CNS drug development.

Expected impact

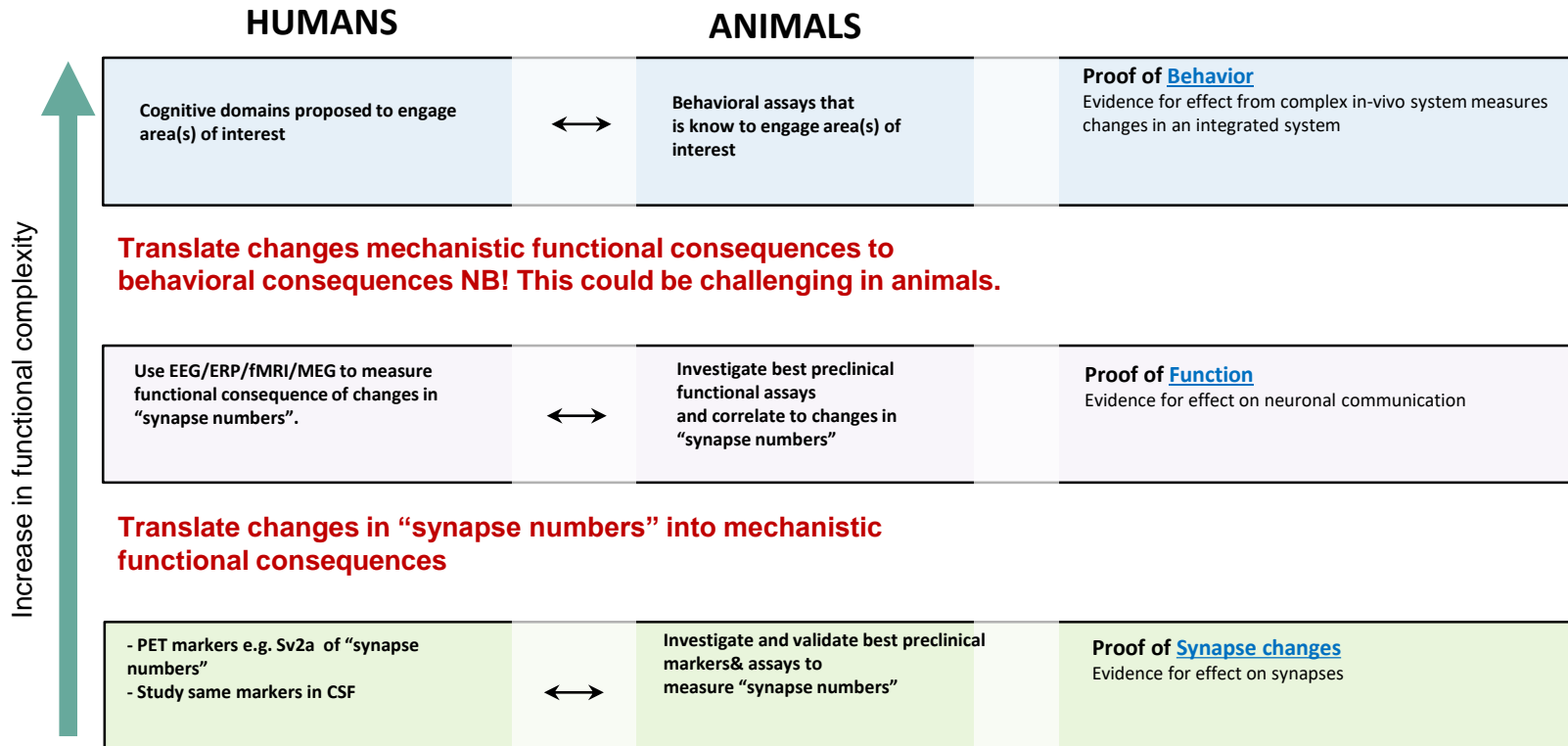
- The expanded knowledge base generated to define the contribution that synaptopathies play in neurodevelopmental, psychiatric and neurodegenerative disorders will lead to improved disease pathway understanding and thus better position academia, SMEs and pharmaceutical companies to identify and validate tractable drug targets.
- The concerted and aligned efforts will minimize duplication and redundancy. The tools, platforms and technologies will ultimately drive success in both the discovery and clinical arenas by providing robust translatable evidence of early clinical efficacy as compounds are evaluated in patient populations.
- These achievements will facilitate the delivery of much needed, highly effective medicines and treatments for CNS disorders.

Suggested architecture of the project

- 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 work plan should enable the construction of a precompetitive research platform focused on furthering our scientific understanding on how synaptopathies can elicit or contribute to brain disorders.
- It should focus on the development and validation of both existing and innovative translational tools and platforms to facilitate drug-discovery-targeted synaptic health.
- All deliverables should be achieved using scientifically robust experimental studies, agreed upon with the consortium partners, and conducted across multiple sites employing both existing and novel experimental models of synapse dysfunction together with deep clinical phenotyping of defined patient populations.

Suggested architecture of the project

Establish translation between multiple translational evidence levels



Expected contributions of the applicants

Clinical work streams

- Clinical and disease area experts with access to patient cohorts
- PET ligand development expertise
- Rodent PET capabilities
- Imaging experts
- Clinical trial operation and execution
- Expertise in clinical data management and clinical statistics
- Expertise in patient advocacy and engagement, privacy and ethical considerations
- Regulatory expertise and experience in development and qualification of novel end-points
- Data management

Expected contributions of the applicants

Preclinical work streams

- •Academics and SMEs with disease understanding of neurodevelopmental, psychiatric and neurodegenerative disorders
- •Expertise in disease model generations and characterisation
- •Preclinical imaging, electrophysiology and fluid biomarker experts.

Expected (in kind) contributions of industry consortium

Clinical work streams

- Clinical and disease area experts with access to patient cohorts
- Clinic ready PET ligands (synaptic vesicle glycoprotein 2A (SV2A) and α -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid transmembrane regulatory proteins (AMPA TARP) in addition to PET chemistry support for novel ligand development
- Clinical expertise in trial design, implementation and regulatory support

Expected (in kind) contributions of industry consortium

Preclinical work streams

- Disease models known to demonstrate synaptic dysfunction linked to neurodevelopmental, psychiatric and neurodegenerative disorders including, but not exclusive to, transgenic mouse strains expressing risk genes for neurodevelopmental, psychiatric and neurodegenerative disorders.
- Access to technologies, know-how and protocols including but not limited to:
 - Electrophysiological (MEA, LTP/LTD, EEG, ERPs);
 - Imaging (calcium, high content, immunohistochemical, autoradiography, 2-DG)
 - Synaptic fluid biomarkers measurements (SNAP-25, GAP-43, LAMP-2 for example)
 - Microdialysis, neurotransmitter sensors and optogenetics
 - Behavioural platforms (cognitive, motor and psychosis/mood related)
- Commercially available and development tool compounds.

What's in it for you?

- Opportunity to tackle critical scientific challenges in CNS drug discovery and development in partnership with eight leading EFPIA and associated partner companies
- Access to leading scientific expertise, models, technologies and clinic ready PET ligands and tool compounds
- Opportunity to generate robust and convincing evidence of translational value of specific technologies/platforms for measuring synaptic changes
- Opportunity for adoption of relevant project outputs into regulatory practices, and regulatory, clinical and healthcare practice
- Opportunity for gaining a heightened understanding of key remaining symptomology from patient advocacy groups that could be addressed with novel synaptopathy agents

Key deliverables of the full project

Initial phase (approx. 3 years)

- Prioritised list of robust disease models, preclinical and clinical platforms fit for purpose for synaptopathy drug discovery
- In vitro and vivo synaptopathy disease models that have been characterised and validated across sites using the predefined platforms and technologies to identify those disease models and platforms most optimal for drug discovery efforts
- Robust clinical assessment battery able to detect synaptic alterations in relevant patient cohorts
- Selected CNS disorder animal models that have been both behaviorally and deeply phenotyped to establish the translation between synaptic marker and behavioral endpoints
- Initial interactions with patient groups and regulatory bodies to discuss appropriate development paths forward for novel therapies targeting synaptopathies

Key deliverables of the full project

Late phase (approx. 2 years)

- Comprehensive cross-site profiling of existing and novel therapies believed to positively address synaptopathy in the defined in vivo disease models using the battery of preclinical platforms;
- Definitive clinical evaluation of novel positron-emission tomography (PET) ligands targeting pre- and post-synaptic proteins, for example synaptic density protein 95 (PSD-95), vesicular glutamate transporters (VGLUT1/2), excitatory amino acid transporter-2 (EAAT2) or others to be determined;
- Determination of the pharmacological sensitivity of the defined clinical assessment battery using existing chemical entities thought to modulate synaptic function, for example ketamine or others to be determined;
- Some conclusions, based on the discussions of the results achieved with regulatory bodies and patients, on the best development paths forward for novel therapies targeting synaptopathies.



Thank you

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Involvement of SMEs, patient groups, regulators

SME participation

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

The participation of SMEs with the following expertise is highly encouraged:

- PET ligand development;*
- imaging and image analysis technologies;*
- clinical trial operation and execution;*
- targeted mass spectrometry based proteome analysis;*
- data and knowledge management;*
- project management with expertise and experience relevant to IMI2 JU/H2020 projects.*

Patient participation

Interactions with patient groups and regulatory bodies will be initiated to discuss appropriate development paths forward for novel therapies targeting synaptopathies.

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](#)'



Thank you

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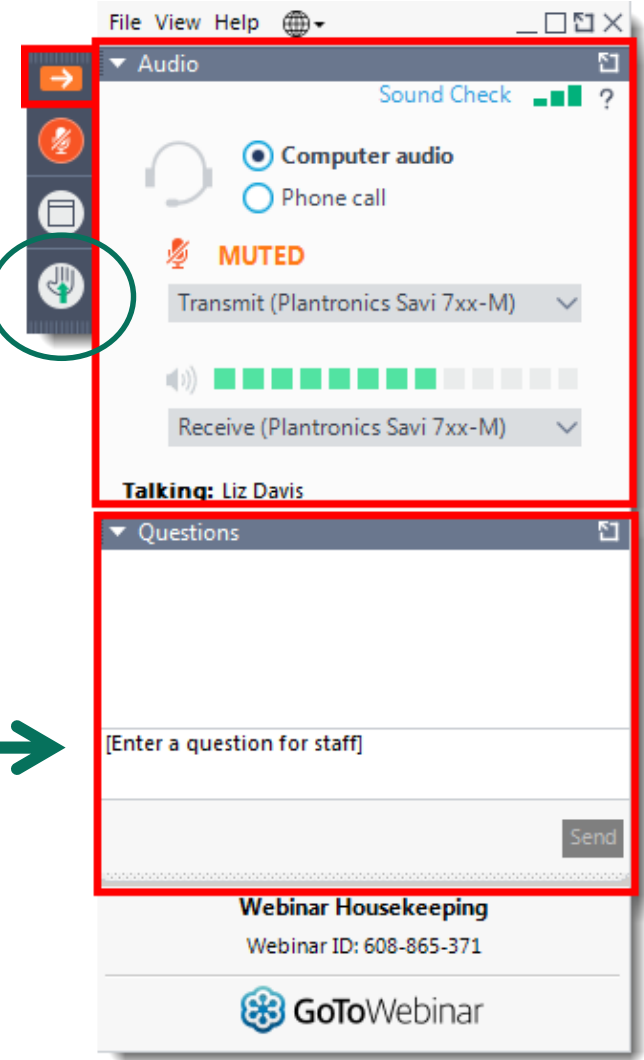
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Questions & answers

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



Thank you!