Webinar | IMI2 – Call 13 Mitochondrial dysfunction in neurodegeneration

4 December 2017 • 10:30 CET

Agenda

- How to use GoToWebinar – Catherine Brett, IMI
- Introduction – Elisabetta Vaudano, IMI
- The Call topic – Ian Reynolds & Neta Zach, Teva
- Involvement of SMEs & regulators – Elisabetta Vaudano, IMI
- Questions & answers

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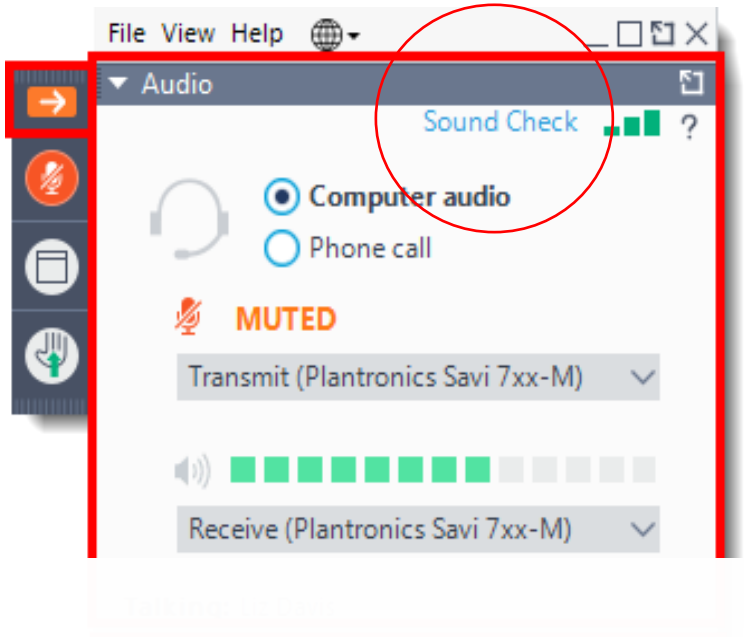

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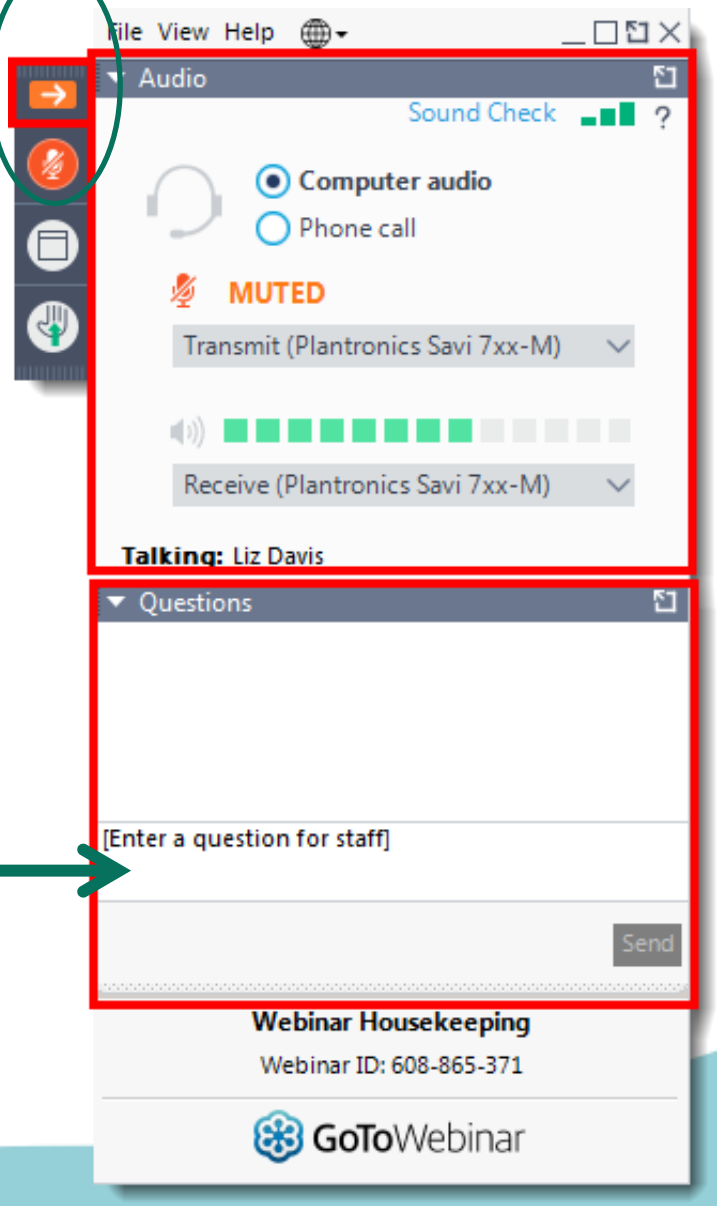

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Before we start…

- 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
- IMI2 – Call 13 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 13

Mitochondrial Dysfunction in Neurodegeneration

Elisabetta Vaudano

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 Thursday 7 December, 15:00-16:30

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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

receive no 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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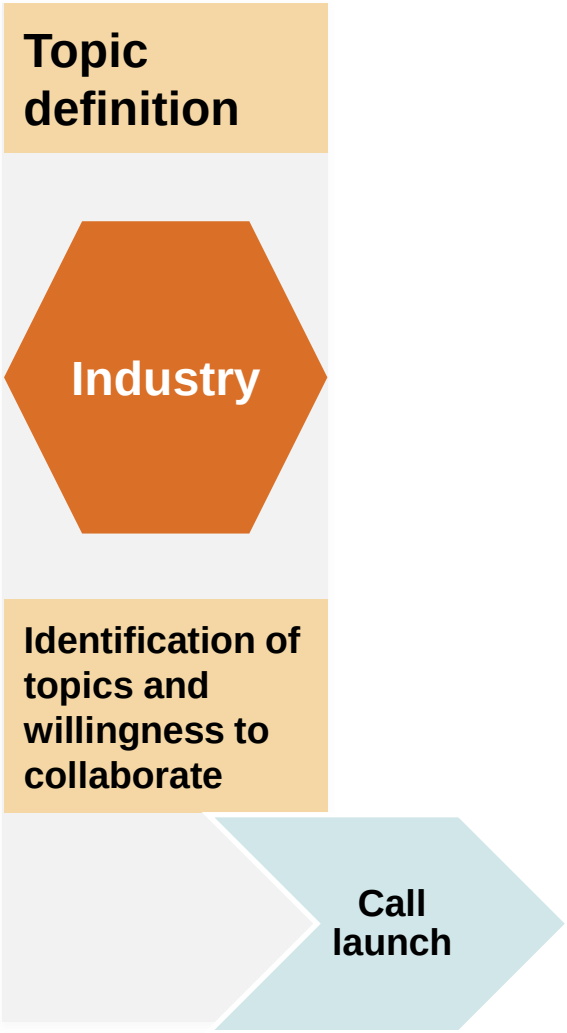
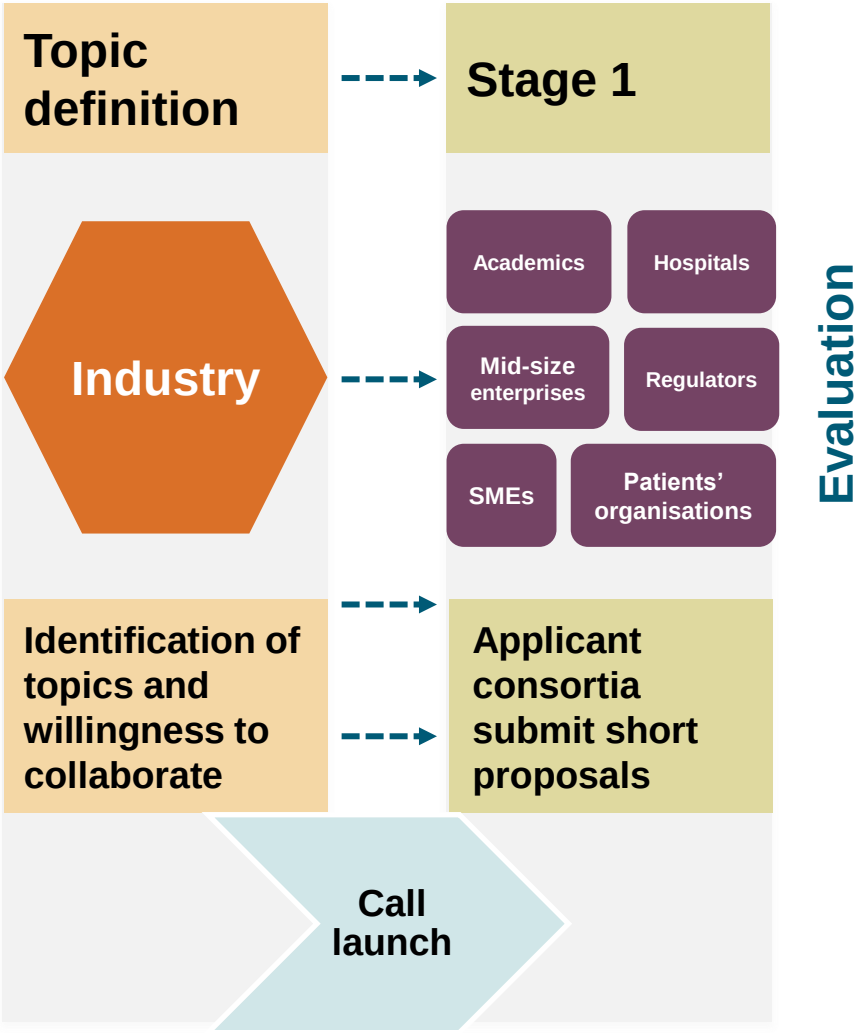
Typical IMI project life cycle



Typical IMI project life cycle



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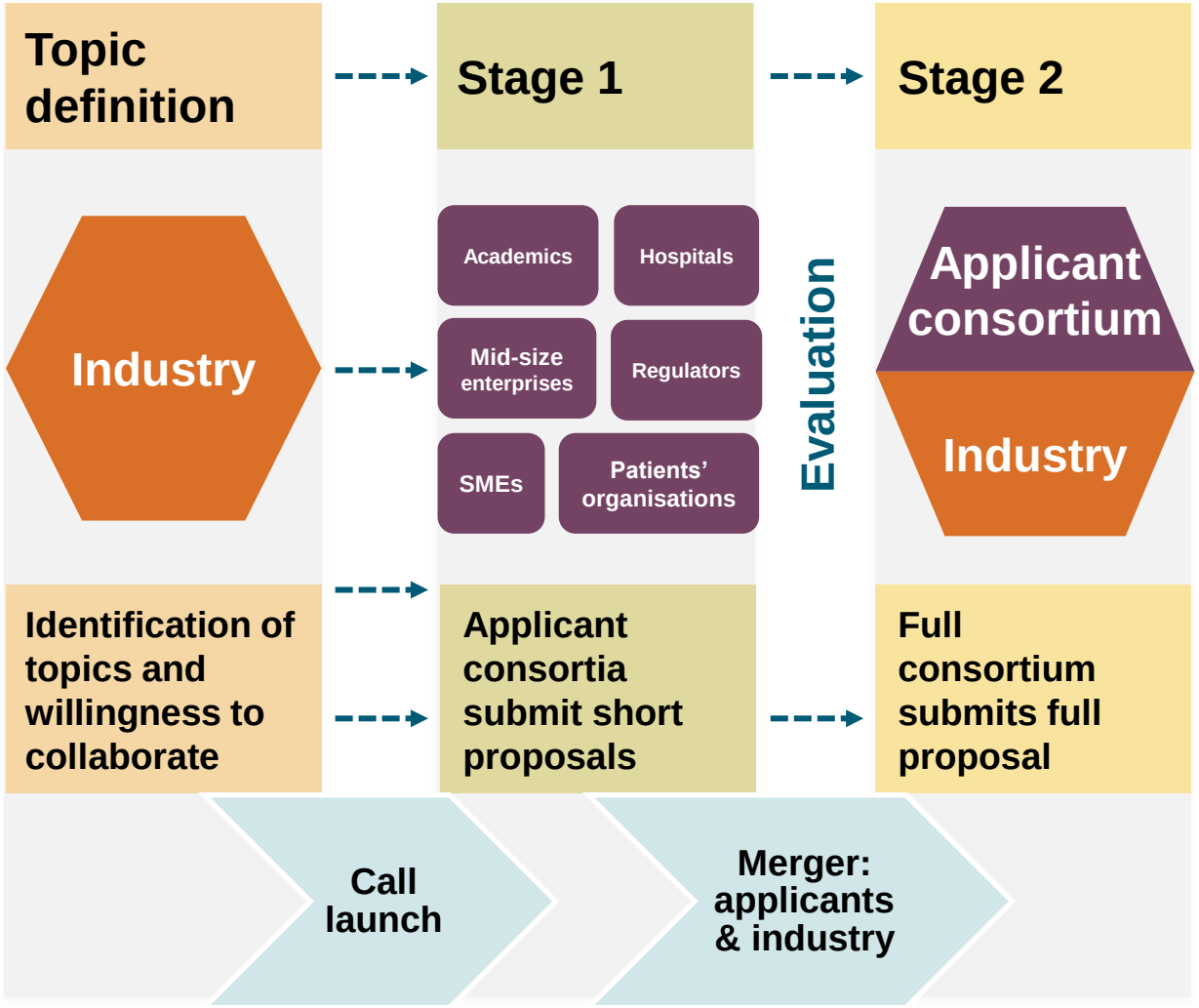
Typical IMI project life cycle



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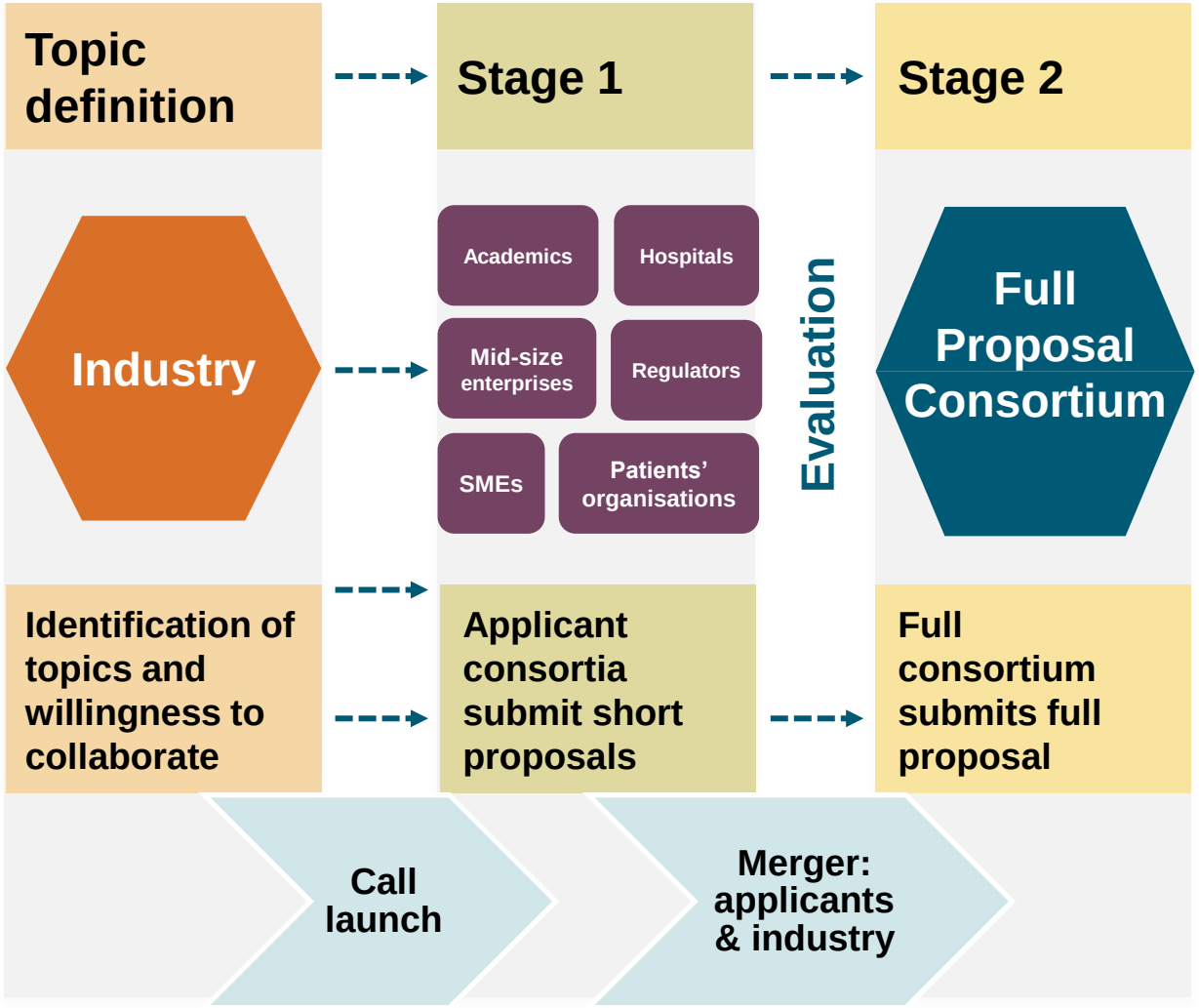
Typical IMI project life cycle



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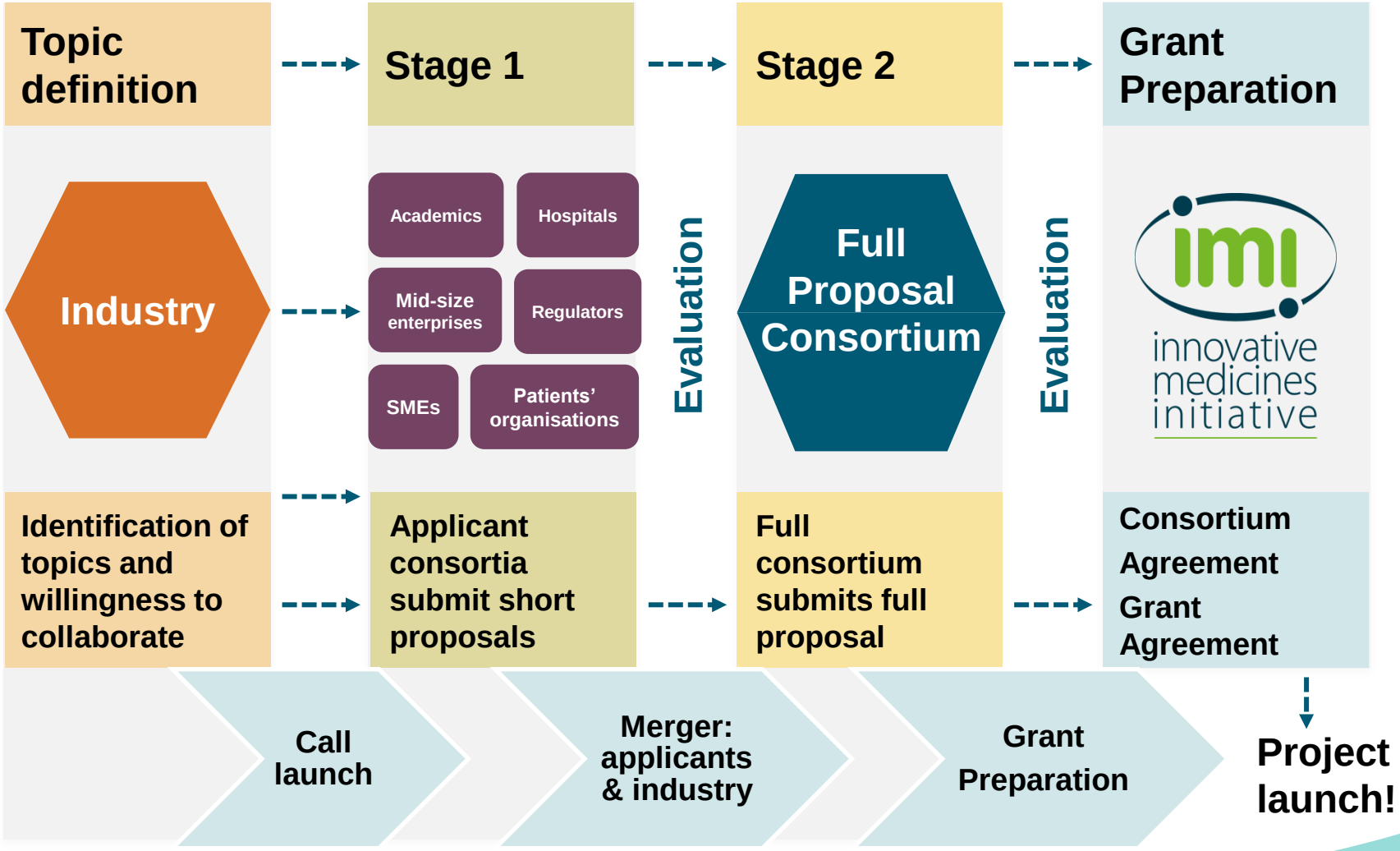
Typical IMI project life cycle



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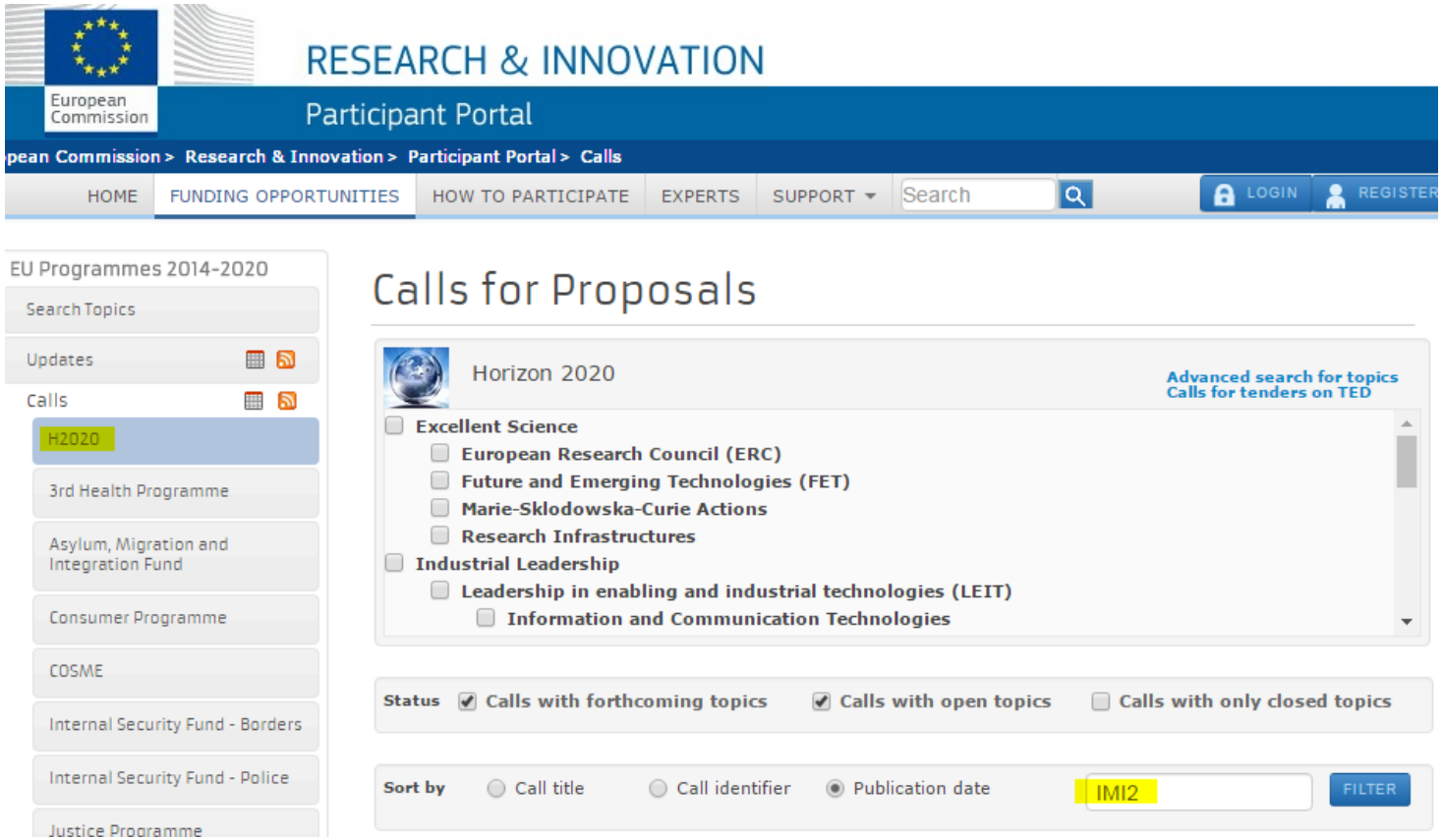
Submitting a proposal

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



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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)**

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Evaluation Criteria (1/2)

- **Excellence (threshold 3.0)**
  - 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 (threshold 3.0)**
  - 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

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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 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)

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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
  – *check the list of interested SMEs on the Call 13 web page*
- Companies / organisations from related fields (e.g. diagnostics, animal health, IT, imaging etc…)

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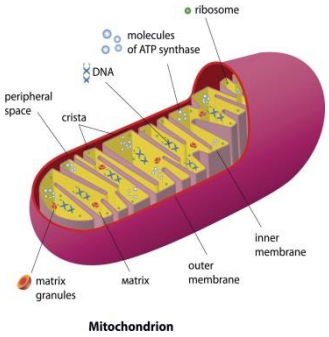
Mitochondrial Dysfunction in Neurodegeneration

Ian Reynolds, Neta Zach
Teva Pharmaceuticals

04.12.2017 • IMI webinar

Introduction



Mitochondrion

Mitochondrial dysfunction (such as respiratory function, biogenesis, trafficking, fission, fusion and mitophagy) is a common mechanism implicated in all neurodegenerative diseases. Yet, little is known about the precise role of mitochondrial dysfunction in disease etiology and severity. We are still lacking the tools and models to elucidate this question.

→**Our Goal**: To develop the understanding and tools to assess the evolution of mitochondrial dysfunction, preferably in human-derived cellular models and animal models of neurodegeneration, and to identify key molecular drivers of such processes.

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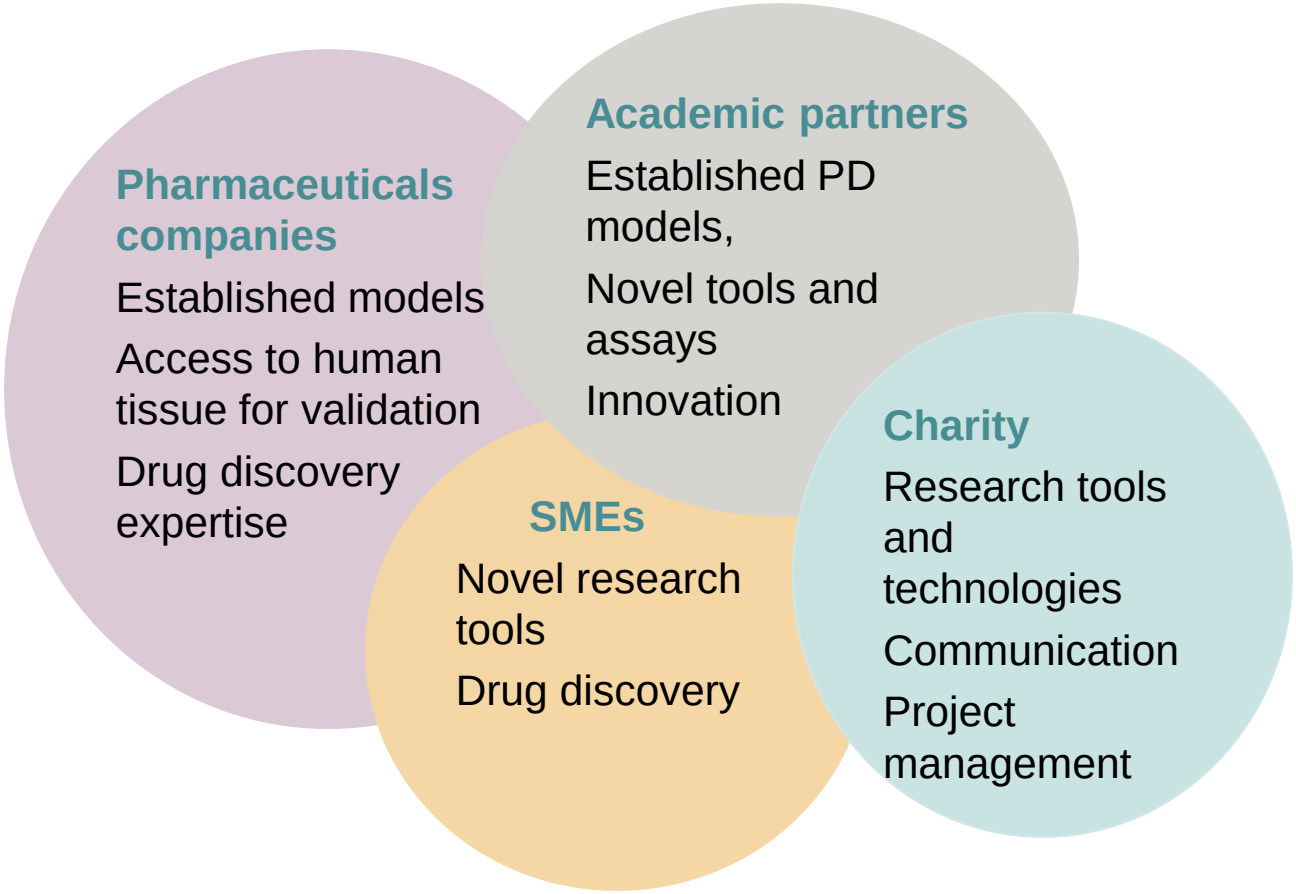
Objectives of the full project

- Exploring mitochondrial dynamics and dysfunction in models of neurodegenerative disease
- Connection between mitochondrial morphology and function
- Connection to protein misfolding
- Incorporating elements of mitochondrial ageing

Exemplary Indications: Parkinson’s disease

Need for public-private collaboration



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Expected impact

Better tools to understand mitochondrial dysfunction and its impact on neurodegenerative diseases

Identification of key molecular drivers and potential targets for treatments for PD, expandable to other neurodegenerative diseases

Biotech **SMEs** will be able to ‘stress-test’ their technologies in a non-competitive open innovation environment

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Scope of the project

In vitro

- Understand the impact of mitochondrial dysfunction on disease severity in established *in vitro* models of PD
- Demonstration of mitochondrial dysfunction induced by α-synuclein in a humanised model system such as inducible Pluripotent Stem cell (iPSC)-derived neurons
- Evaluate the impact of ageing on mitochondrial dysfunction using in vitro models

In vivo

- Assess the contribution of mitochonodrial dysfunction on disease severity, in a well characterised *in vivo* models of PD
- Focus on aged animals – transgenic or injected with fibrillary forms of disease associated proteins to trigger neurodegeneration
- Quantify the relative contribution of abnormal respiratory function, biogenesis, dynamics and mitophagy to mitochondrial dysfunction.

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Scope of the project- lower priorities

We would like to highlight that there are topics in the proposal that are of **lower priorities and are not mandated part of the submission**. These include:

- *In vitro* trauma and brain injury
- *In silico*: Reconstruct a mechanistic computational model of mitochondrial function to account for the gene products of each gene associated with mitochondria and closely associated organelles.

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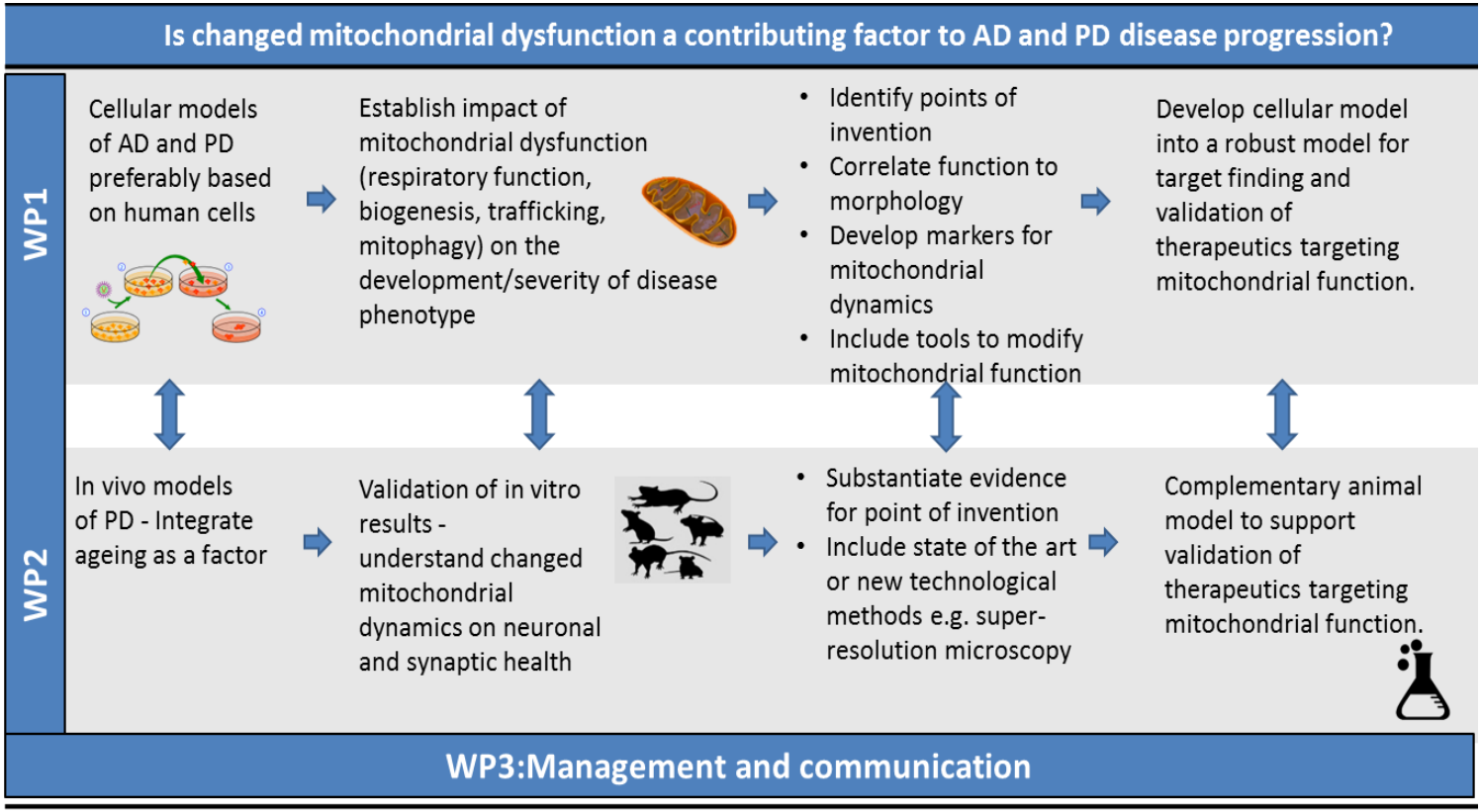
Suggested architecture of the project



Project duration: 36months

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Suggested architecture of the project

WP1- *In vitro*	**WP2- *In vivo***
Identification of specific mitochondrial dysfunctions in established PD models (*implementation of tools modulating mitochondrial functions*)	Identification of specific mitochondria dysfunctions in established PD models *(longitudinal assessment*)
Establishment of quantitative detection of mitochondrial dysfunction	Establishment of quantitative detection of mitochondrial dysfunction (*and genetic or pharmacological modification*)
Understanding the role of identified mitochondrial dysfunction on disease phenotype (*adding ageing model*)	Understanding the role of identified mitochondrial dysfunction on disease phenotype.
Identification and quantification of the relative contribution of key molecular drivers	Identification and quantification of the relative contribution of key molecular drivers
As necessary, development of new robust tools and assays	As necessary, development of new robust tools and assays. (*for example imaging*)

Work package 3- Project management and communication

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Expected contributions of the applicants

Models

- Expertise in **using *in vivo* and *in vitro* models of PD,** experience with **seeding models** an advantage
- **Access to *in vitro* models** which exhibit a robust and well characterised disease phenotype, i.e. protein aggregation in models such as **primary cultures or iPSCs.**

Tools

The budget is 4.5Mil

- Expertise in **evaluation of key elements of mitochondrial function in vitro,** including bioenergetics, ROS production, biogenesis, fission, fusion and mitophagy;
- Tool for ***in vitro/in vivo* imaging of mitochondrial morphology and trafficking**. For example, expression of mitochondrial-targeted fluorescent proteins in relevant cell populations;
- Knowhow and tools for **manipulation of mitochondrial function**. For example morphology changes through expression of DRP1, mitofusin 2, OPA1 or Miro.
- Development of **novel tools and assays to quantitatively assess mitochondrial dysfunction** in models of PD;
- Expertise in **approaches to model mitochondrial ageing in *in vitro* models**

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Expected (in kind) contributions of industry consortium

The indicative in-kind contribution is 3.27Mil Euro

- **Well established in vivo transgenic and seeding models** in rodents (SNCA-OVX Tg mice, F28 mice. Pre formed fibrils (PFF) mouse and rat model, α-synuclein rat model as well as assay protocols, seed material, and α-synuclein pathology endpoint analysis.
- Access to **iPSC lines**, iPSC neuronal progenitors and protocols for differentiation into neurons and glia. Protocols and tools for viral transduction and siRNA knockdown of proteins in iPSC neurons.
- Access **to human tissue samples for validation studies** (~1000 PD cases and 200 controls)
- Evaluation of consistency and robustness of mitochondrial dysfunction **key molecular endpoints** to ensure future application for target identification/validation.
- Support **communication and project management**.

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Key deliverables of the full project

- **Development, validation and application of robust tools and assays to study and quantitatively address mitochondrial dysfunction** in well characterised *in vitro* and *in vivo* models of neurodegenerative diseases with emphasis on PD;
- Understanding the impact mitochondrial dysfunction on **disease progression/severity**;
- Introduce **ageing** component to *in vitro* models;
- Understanding of the role of **misfolded proteins;**
- Identification of **key molecular drivers** of mitochondrial dysfunction promoting neurodegenerative diseases.

What's in it for you?

New insights and novel drug targets are our best way to

Develop drugs

Innovative tools

Cutting edge research

Bring hope to patients with Parkinson's disease and many more of the most disabling diseases of our times!

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Thank you

www.imi.europa.eu
@IMI_JU

Involvement of SMEs & regulators

Elisabetta Vaudano

SME participation

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

- SMEs can be of great benefit to IMI projects and, inter-alia strengthen the competitiveness and industrial leadership of Europe. Their involvement might offer a complementary perspective to industry and the academia, and help deliver the long-term impact of the project.
- For these reasons, applicants should consider engaging SMEs throughout the proposal. Thus participation of SMEs with relevant knowhow and standardised technologies and assays is strongly supported.

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Interactions with regulators

- Consider having a **plan for interaction** with relevant **milestones**, **resources** allocated
- You may need to go through a **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)
- If regulators are not project participants, consider including them in an **advisory board**
- Consider also 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: 'Raising awareness of regulatory requirements: A guidance tool for researchers'

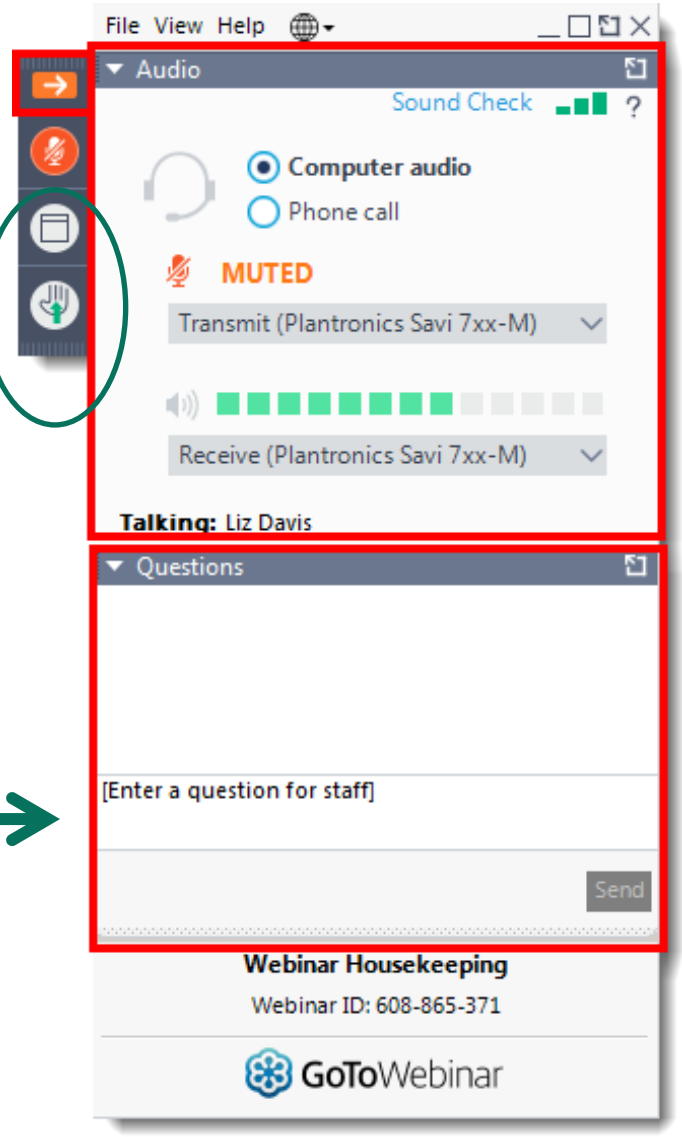
www.imi.europa.eu/sites/default/files/uploads/documents/apply-for-funding/call-documents/imi2/RegulatoryRequirementsGuide.pdf

Questions

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**

infodesk@imi.europa.eu

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