Introduction to the IMI2 Antimicrobial Resistance (AMR) Accelerator programme

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.

Background and problem statement

The discovery and development of new preventions and treatments to address antimicrobial resistance (AMR) is an undisputed European and global challenge that is compounded by a low return on investment (RoI) for the pharmaceutical sector driven largely by the lack of established reimbursement models and standard methods to express the true societal value for new technologies addressing AMR. This has subsequently led to a reduction in resources applied across the pharmaceutical industry and a decline in scientific discoveries. Overall this situation has compromised the delivery of new options to treat and prevent resistant infections. This was highlighted in the European One Health Action Plan against Antimicrobial Resistance (for more info please visit the following link: https://ec.europa.eu/health/amr/sites/amr/files/amr_action_plan_2017_en.pdf). Beyond Europe, it is of note that AMR is one of four public health concerns that has been raised to the level of discussion at the UN General Assembly (September 2016), putting it on par with subjects such as HIV and Ebola. Additionally, drug resistant tuberculosis (TB), the largest single contributor to AMR health, mortality, and economic impact, is scheduled to be discussed by heads of state at the UN General Assembly (September 2018).

There are significant scientific challenges to the discovery and development of new agents to treat and prevent AMR infections, including those caused by Gram-positive and Gram-negative bacteria, *Mycobacterium tuberculosis*, and non-tubercular mycobacteria (NTM). As an example, despite there being an extensive number of essential bacterial targets, no novel mechanism antibiotics for Gram-negative infections have been approved in 40 years.

Furthermore, despite some recent progress, we have a poor understanding of how to rationally design potent small molecules that are optimised to treat life threatening multi-drug resistant (MDR) Gram-negative pathogens. Models, approaches, and tools developed by large pharma or public entities to support antibiotic drug development need to be validated and shared more widely to serve the AMR community at large. At the same time, alternative approaches to treating infections require robust validation. The same is true for platforms that enhance the success of vaccines and monoclonal antibodies, or new imaging platforms to measure pharmacodynamic responses at the site of action.

In TB, the world's leading infectious disease killer with 1.7 million deaths in 2016, (from WHO TB report 2017 Executive Summary at the following link, http://www.who.int/tb/publications/global_report/Exec_Summary_13Nov2017.pdf) there is an acute need for the development of a novel combination regimen with an indication for the treatment of any form of TB ('pan-TB regimen') that will be more effective, shorter, and safer than current existing options. This applies to all types of TB (drug-sensitive (DS), multi-drug resistant (MDR) and extensively-drug resistant (XDR-TB)). A pan-TB regimen would encompass at least three new chemical entities, with properties better suited to protect against emerging resistance both individually as well as in combination. Many scientific hurdles must be overcome to understand how multiple chemical entities can be combined most successfully, keeping synergistic drug activity, drug-drug interactions, and translational aspects in mind. Regimen development in TB has provided and will continue to lead to learnings that will help to develop new treatments, including combination regimens, for other infections that have relied on mono-therapy thus far.

Overall objectives of the AMR Accelerator

The aim of the AMR Accelerator is to progress a pipeline of potential medicines, including but not limited to new antibiotics, to treat patients with resistant bacterial infections in Europe and across the globe or to prevent them. Specifically, if successful, projects in the Accelerator are expected to deliver up to >10 new preclinical candidates and >5 'phase 2-ready' assets over a roughly six-year period.

The AMR Accelerator will provide, under one operational structure, a wide-ranging series of projects that will address many of the scientific challenges in AMR. The scientific scope will be broad, including prevention (vaccines, mAbs, immunoprophylaxis, other means) and treatment (new antibiotics, non-antibiotic alternatives, and combinations). For clarity, the term 'AMR' should be interpreted to include Gram-positive and Gram-negative bacteria, tuberculosis (TB) and non-tubercular mycobacteria (NTM). Within this broad scope, projects in the Accelerator will develop new pre-clinical tools and methods, validate alternative or 'non-traditional' approaches, progress potential new treatments through phase 1-3 clinical trials, and analyse data from EFPIA-funded clinical trials to assist in the translation of preclinical data to clinical results of novel anti-infective agents and vaccines. The Accelerator will also potentially generate new clinical/regulatory phase 2-3 pathways. Over the past years, IMI's New Drugs for Bad Bugs (ND4BB) programme has created a vibrant drug discovery and development network in AMR, and met important milestones. The AMR Accelerator will complement and augment the capabilities of the IMI ND4BB programme.

Progression of successful assets beyond the scope of the Accelerator (pillar-dependent, see below) may occur, as appropriate, by other mechanisms such as EU funding programmes within Horizon 2020 (including SME instruments) or future framework programmes, InnovFin instruments, Structural Funds, venture capitals, other internal R&D funding mechanisms, etc. In addition, the applicable principles from the Davos Declaration on Antimicrobial Resistance– January 2016 or the Industry Roadmap for Progress on Combatting Antimicrobial Resistance – September 2016 (https://www.ifpma.org/wp-content/uploads/2016/09/Roadmap-for-Progress-on-AMR-FINAL.pdf[1]) should be taken into account.

The Accelerator will contribute to one of the three pillars of the European One Health Action Plan against Antimicrobial Resistance 'Boosting research and development and innovation in AMR' (June 2017: https://ec.europa.eu/health/amr/sites/amr/files/amr_action_plan_2017_en.pdf). The Accelerator will also directly address the IMI2 JU objective of 'develop new therapies for diseases for which there is a high unmet need, such as Alzheimer's disease and limited market incentives, such as antimicrobial resistance' (Article 2(b)(iii) of the Council Regulation establishing IMI2 JU: http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex%3A32014R0557)

AMR Accelerator programme structure

The AMR Accelerator programme consist of three pillars under which multiple actions are expected:

- **Pillar A:** Capability Building Network (CBN)
- **Pillar B:** Tuberculosis Drug Development Network (TBDDN)
- **Pillar C:** Company-specific Portfolio Building Networks (PBNs)

The two-stage IMI2 JU Call 15 includes two topics (topic 7 and topic 8) to launch Pillar A and Pillar B of the AMR Accelerator, respectively. The single-stage IMI2 JU Call 16 includes seven topics under Pillar C.

Applicants may submit a proposal to any of the topics under the different pillars and are not obliged to apply for all. If applicants wish to submit for more than one topic under the same or different pillars, separate proposals should be submitted.

[1] For example, points 3 and 4 from the 'Roadmap for Progress'.

For the two topics for Pillars A and B, launched as part of IMI2 JU Call 15:

- the indicative EFPIA in-kind contribution will be EUR 71 200 000
- the indicative Associated Partner in-kind contribution will be EUR 67 000 000.

The EFPIA and Associated Partner in-kind contribution will be matched by IMI2 JU funding across the whole of the Accelerator and not necessarily 1:1 on an individual project or pillar basis.

The overall IMI2 JU financial contribution to the AMR Accelerator topics under Pillars A, B and C of IMI2 JU Call 15 and IMI2 JU Call 16 will be a maximum of EUR 144 730 000.

Future call for proposals could be launched at a later stage to select under each pillar additional research projects or networks depending on developing scientific needs and objectives in AMR research.

Pillar A: Capability Building Network (CBN) to accelerate and validate scientific discoveries.

The CBN will: 1) create a coordination and support group to assist in the effective management of projects across the Accelerator and; 2) deliver pre-competitive science to accelerate scientific discoveries in AMR, the results of which will be disseminated widely. The CBN will include projects to further basic science and discoveries to enable future drug discovery and development in the prevention (vaccines, mAbs, immunoprophylaxis, and others) and treatment of MDR bacterial infections including tuberculosis (TB), and non-tubercular mycobacteria (NTM). Although most research in the Accelerator related to TB will be conducted in the TBDDN (below), TB projects could occur in the CBN if the scientific concepts are of broader applicability (e.g. immunoprophylaxis).

The initial action in the CBN resulting from topic 7 in IMI2 JU Call 15 will implement a coordination and support group that will support operations of all projects in the AMR Accelerator with effective management, communication, and data capture capabilities. The initial CBN action also will focus on the collection, sharing, and analysis of vaccine and/or antibacterial clinical trial data and the optimisation of animal infection models for bacterial infections.

Pillar B: Tuberculosis Drug Development Network (TBDDN) to accelerate and validate scientific discoveries and advance the R&D pipeline of new and innovative agents to address the global TB epidemic.

The TBDDN will work to address the innovation gap in the discovery and development of a pan-TB regimen by combining access to novel drug candidates with innovative tools and incorporation of clinical trial data to accelerate the discovery of new combination regimens for the treatment of TB.

The platform will be self-sustained and independent from other similar activities (Integrated Research Platform (IRP), TB Drug Accelerator (TBDA)). It is anticipated that there will be linkages with the TBDA (for more info on TBDA please visit: http://partnerships.ifpma.org/partnership/tb-drug-accelerator-program). It will provide ready-to-use services for rapid progression of available (1st line) new and innovative candidates. The platform will be partly supported by the coordination and support group from Pillar A but will include management resources to self-sustain its scientific and financial reporting as well as innovation management procedures.

Topic 8 of IMI2 JU Call 15 will result in an action that will create a group to profile and progress anti-TB compounds from advanced lead through phase 1 and to collect, share, and analyse TB clinical trial data. Additionally, it will address the development of new alternative anti-tubercular drugs (for example, host-defence or virulence approaches).

Pillar C: Portfolio Building Networks (PBN) to advance the R&D pipeline of new and innovative agents to address AMR.

As in the CBN, the overall scientific scope in the PBN will be broad, including prevention (vaccines, mAbs, immunoprophylaxis, and others) and treatment (new antibiotics, non-antibiotic alternatives,

formulation strategies, and combinations). Within this broad scope, the PBN will provide a mechanism for dedicated partnerships between EFPIA companies and SMEs and/or academic teams for the discovery and development of new antibacterial assets, including in select cases TB and NTM. Assets and projects can originate from SMEs, academia, or EFPIA companies, and will be jointly progressed or studied, including both pre-clinical work and potentially phase 1-3 clinical development. The PBN will also potentially be useful to generate new clinical/regulatory phase 3 pathways for pathogens such as NTM and to conduct phase 2 trials in TB.

Consortia selected under this pillar may have a limited number of partners, and will require the participation of an EFPIA partner (e.g. 1 EFPIA partner + 1 SME/academic partner)[2]. IMI2 JU Call 16, the first call under Pillar C, is divided in several topics, each dedicated to specific individual asset or research area. Additional single-stage calls, one or two per year, may be launched in the future pending available budget. A total of at least 8-10 grant agreements are anticipated in the PBN (indicative number only).

Collaboration agreements

To ensure smooth operation of the projects in the AMR Accelerator, the grant agreement of the first CBN action (selected under Pillar A from IMI2 JU Call 15 topic 7, and containing the coordination and support group[3]) will be complementary to all the grant agreements of actions selected under Pillars B and C (via IMI2 JU Call 15 topic 8 and IMI2 JU Call 16 topics, and potential future additional calls for proposals), as well as probable future grant agreements from actions selected under Pillar A. In addition, grant agreements of actions under pillar B, if more than one, will be complementary between them. The respective options of Article 2, Article 31.6 and Article 41.4 of the IMI2 JU Model Grant Agreement[4] will be applied. Accordingly, the consortia selected under Pillars A, B, and C will conclude collaboration agreements with the CBN consortium selected from IMI2 JU Call 15 topic 7. These collaboration agreements will provide the framework for the CBN to provide day-to-day support of projects in the Accelerator, and will ensure exchange of relevant information, exploration of synergies, collaboration where appropriate, and avoid duplication of efforts.

Furthermore, a memorandum of understanding (MoU) will be pursued between the Pillar B TBDDN action(s) and the Integrated Research Platforms (IRP) action of IMI2 JU Call 15 topic 1 to cover collaboration and sharing of information on TB-related activities. The MoU should constitute one deliverable of the action resulting from topic 8 of IMI2 JU Call 15. Similarly, when reasonable, a MoU should be pursued between potential TB-focused actions under Pillar C of the Accelerator (resulting from IMI2 JU Call 16) and TBDDN action(s), as well as the IRP action of IMI2 JU Call 15 topic 1, with appropriate provisions to protect confidentiality and intellectual property of the interactions between those consortia.

Need and opportunity for public-private collaborative research

The discovery and development of new antibiotics and alternative treatment and prevention options for multi-drug resistant infections is a high medical and societal need. The AMR Accelerator will address multiple challenges in a coordinated programme, which offers excellent opportunities for collaborative work between different sectors and disciplines. Moreover, operating with the support of the coordination and support group in the CBN will allow for greater efficiency, by reducing the need for duplicative management structures or processes.

Due to the current low return on investment that developers can expect for agents to address AMR, this scientific area has not received the investment that was seen in the ‘call to action’ to address HIV/AIDS and on par with the public health threat. Consequently, public-private partnerships (PPPs) such as the framework provided by the IMI2 JU continue to be critical to that effort.

Excellent examples have been the previous and current investments by the European Union and IMI (ND4BB, Model-based preclinical development of anti-tuberculosis drug combinations (PreDiCT-TB),

2 See ‘Applicant consortium’ section of IMI2 JU Call 16 topic text (Pillar C, “Portfolio Building Networks”).
3 For additional details see the topic 7 “Capability Building Network” of IMI2 JU Call 15.
4 See: https://www.imi.europa.eu/sites/default/files/uploads/documents/reference-documents/h2020-mga-imi_en_v5.pdf

More Medicines for Tuberculosis (MM4TB), Open Collaborative Model for Tuberculosis Lead Optimisation (ORCHID), anTBiotic), the NIH (Tuberculosis Research Units Network, TBRU-N) and the Bill & Melinda Gates Foundation (TB Drug Development Accelerator and TB Alliance discovery portfolio)). Multiple new drug candidates are in the pipeline for the treatment of TB for the first time in decades, and are reaching or about to reach the clinic. Existing drugs are being repurposed or optimised for TB with the potential of shortened treatment duration for drug-sensitive TB and safer, shorter treatments for MDR-TB. In ND4BB, immense progress has been made from basic science to discovery of novel lead molecules through to running interventional clinical trials.

However, more work is critical to continue to address the constantly emerging global challenge of AMR. For example, there is a challenge of maturing the TB pipeline from the selection of candidates to progression through phase 1 studies, in addition to parallel studies to determine the optimal combinations to create new pan-TB regimens. Also, the ever-evolving resistance landscape requires additional investment to validate new tools and approaches, in addition to progressing potential new therapies to prevent and treat bacterial infections.

Acting to address these challenges in a single, coordinated Accelerator offers excellent opportunities for collaborative work between different sectors and disciplines on an area of critical scientific need.

The development of the Accelerator will contribute to a vibrant AMR community in Europe and will offer potential opportunities for individual partners, such as:

- Capability Building Network:
  - play key role in a EU AMR programme with connectivity into the broader global agenda on AMR;
  - enable SME, and/or academic groups to progress pre-competitive basic science project in the AMR field;
  - opportunity to work within a broad network of researchers focused on AMR science and gain additional experience in AMR science and drug discovery.
- Tuberculosis Drug Development Network:
  - enable SME and/or academic groups to progress pre-competitive basic science project in the TB field;
  - enable SME and/or academic groups to progress potential drugs from pre-candidate status through to ‘ready for phase 2’ status, including, but not limited to GLP and GMP scale up, formulation, toxicology studies, and phase 1 clinical studies, including preclinical combinations of drugs;
  - opportunity to work within a broad network on researchers focused on TB drug discovery.
- Portfolio Building Network:
  - opportunity for SMEs and/or academic groups to partner with EFPIA companies to enable progression of promising assets or technologies to key milestones, creating value, and sharing risk. There will be potential to further extend such partnerships with EFPIA companies beyond the scope of the Accelerator following completion of project;
  - will allow a vibrant partnering ecosystem that will benefit SMEs or academics with early stage assets based on pre-agreed conditions and milestone decision points.

Applicants to Calls launched as part of the Accelerator should consult the IMI2 JU Model Grant Agreement and IMI2 JU Annotated Model Grant Agreement, as well as a short questions and answers document available at https://www.imi.europa.eu/sites/default/files/uploads/documents/apply-for-funding/open-calls/Questions_and_answers_on_the_AMR_accelerator_programme.pdf.

Topic 7: AMR Accelerator programme Pillar A: Capability Building Network to accelerate and validate scientific discoveries

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Part of IMI2 AMR Accelerator programme

Topic details

Action type	Research and Innovation Action (RIA)
Submission and evaluation process	2 stages

Specific challenges to be addressed

The Capability Building Network (CBN), Pillar A of the IMI2 AMR Accelerator programme, will work to address the innovation gap in the AMR space by enabling pre-competitive research in the treatment and prevention of multi-drug resistant infections.

The success of the overall Accelerator relies on a coordinated approach to ensure efficient implementation, management, and strategic alignment across a broad range of topics, partners, and stakeholders. Expert operational support for the programme, via a centralised coordination and support group will address this need and will allow all Accelerator projects to focus on delivering scientific advancements for the field and progressing medicines and therapies to patients. This coordination and support group will also provide a unique opportunity to coordinate large-scale efforts in the AMR space in collaboration with industry and public partners and will be part of the first project in the CBN.

Scope

The dual aim of this first call for the CBN will be to:

- create an operational group to support the delivery of projects across the Accelerator, specifically:
  - support the project coordinators in horizontal administration of projects, including project and alliance management,
  - centrally source and implement IT infrastructures for projects in the Accelerator (e.g. information-sharing portals or databases, such as the framework created for the New Drugs for Bad Bugs (ND4BB) Information Centre, electronic notebooks),
  - act as an interface with stakeholders in the AMR field to explore synergies and collaboration with other initiatives and contribute to coordinating the broader AMR strategy on a global scale;
- conduct pre-competitive research aimed to:
  - provide learnings derived from shared vaccine and/or antibacterial clinical trial data,
  - improve understanding of variability and translatability of animal models of bacterial infection.

An advisory and communications board, (containing independent external experts to be selected by the CBN consortium and representatives from all the actions running in the AMR Accelerator) will be created as part of the coordination and support group within the CBN. This group will meet regularly

to share summary-level, non-confidential progress reports on projects and where appropriate make recommendations to the AMR Accelerator overall including on potential future call topics.

Expected key deliverables

Deliverable 1: Operationalisation of the entire AMR Accelerator portfolio of projects, including:

- framework established for rigorous programme management and coordination of support of all actions in the Accelerator;
- secretariat role established for Accelerator committees as needed;
- interactions between the Accelerator and IMI2 Infection Control Strategic Governing Group, EFPIA, and other key stakeholders supported;
- interactions between Accelerator actions and IMI2 JU streamlined, facilitated, and supported, including support with financial and scientific reporting;
- ethical guidance and data governance and privacy standards facilitated across Accelerator as appropriate;
- sustainability of results of projects within the Accelerator ensured;
- note that some operational support will also be present in the action resulting from IMI2 JU Call 15 topic 8 (Tuberculosis Drug Development Network (TBDDN), pillar B of the Accelerator) and that the coordination and support group established by this action will work collaboratively with TBDDN in many of these areas.

Deliverable 2: Guidelines and tools for collection, integration, and dissemination of knowledge from Accelerator projects:

- IT infrastructure (e.g. information-sharing portals or databases, such as the framework created for the ND4BB Information Centre, electronic notebooks) to be used across projects in the Accelerator; for example, datasets could include:
  - clinical trial data,
  - microbiology data,
  - preclinical screening/profiling data,
  - chemical structures and descriptors,
  - animal infection model data;
- streamlined and appropriate processes for aggregation and sharing of AMR data established;
- historical AMR data to be fed into other Accelerator projects collected as needed;
- plan for distillation of findings and synthesis of key learnings across the Accelerator programme established.

Deliverable 3: Communication and collaboration across AMR funding landscape:

- mechanism for sharing information and strategies across the global AMR funding community to maximise awareness and synergy and minimise redundancy;
- plans for networking and communications across the Accelerator;
- assistance delivered in the implementation of the EU AMR agenda;
- coordination with other stakeholders on the broader AMR strategy on a global scale;
- the action resulting from IMI2 JU Call 15 topic 8 (Tuberculosis Drug Development Network (TBDDN), Pillar B of the Accelerator) and the CBN (this action) will work together to ensure the efficient communication and dissemination of information between these pillars.

Deliverable 4: Learnings derived from shared AMR clinical trial data (e.g. phase 1-3 vaccines trials, and/or antibacterial trials) and associated enabling studies:

- generation and collation of clinical trial data allow for analysis and the translation of preclinical to clinical data with respect to, for example, safety, tolerability, dose prediction, animal models of infection and efficacy, and greater disease understanding.

Deliverable 5: Improved understanding of animal infection model reproducibility and translation to clinical efficacy:

- establishment of a collection of new and/or 'control' bacterial strains to demonstrate virulence and growth *in vivo*;
- validation of rodent pneumonia and pyelonephritis models using benchmarked control compounds;
- more standardised methods of conducting these studies as 'best practices' identified by comparing data, sharing common practices and experiences between different investigators;
- a data set of benchmark control compounds and bacterial isolates to determine, for example:
  - reproducibility (study-to-study and lab-to-lab),
  - improve/optimise translation to clinical efficacy,
  - predictability of PK/PD targets,
  - identify optimal study conditions and practices for minimising variability.

Expected impact

The expected impact of the CBN will be to:

- contribute to the development of a vibrant AMR research environment in the EU and strengthening the competitiveness and industrial leadership of Europe;
- contribute to EU's ambition of being a 'best practice region' for addressing AMR;
- with other elements of the AMR Accelerator, enhance the overall pipeline of medicines for patients with AMR infections;
- strengthen interaction of AMR stakeholders from across EU and globally;
- strengthen the scientific basis on AMR research.

Applicants should indicate how their proposals will impact and strengthen the competitiveness and industrial leadership of Europe by, for example, engaging suitable SMEs.

Potential synergies with existing consortia

Applicants should take into consideration, while preparing their short proposal, relevant national, European (both research projects as well as research infrastructure initiatives), and non-European initiatives. Synergies and complementarities should be considered in order to incorporate past achievements, available data and lessons learnt where possible, thus avoiding unnecessary overlap and duplication of efforts and funding.

Example of relevant IMI/IMI2 JU and non-IMI projects include:

- aspects of the research of ND4BB TRANSLOCATION (http://www.nd4bb.eu/) (e.g. the ND4BB Information Centre as a possible framework for data sharing);
- ND4BB ENABLE project (http://nd4bb-enable.eu/);
- ND4BB COMBACTE projects and iABC Programme, (https://www.combacte.com; http://www.iabcproject.com) in particular, in relation to networks (CLIN-NET, LAB-NET, STAT-NET and EPI-NET);
- projects funded by other organisations/programmes supporting AMR R&D e.g. the Global AMR R&D Hub, the EU Framework Programmes for Research and Innovation FP7 (for example FORMAP, NAREB) and Horizon 2020, the Joint Programming Initiative AMR, Wellcome Trust, Biomedical Advanced Research and Development Authority (BARDA), Medical Research Council (MRC), CARB-X, Global Antibiotic Research and Development Partnership (GARDP), National

Institute of Allergy and Infectious Diseases (NIAID), TB Alliance and TB Drug Accelerator etc. to ensure synergy and avoid duplication of research.

Industry consortium

The industry consortium is composed of the following EFPIA companies:

- GSK (lead)
- AstraZeneca
- Evotec
- Janssen

The industry consortium will provide knowledge and expertise in:

- best practices on resourcing, setting milestones, and project/portfolio management;
- setting up and maintaining active and nimble governance processes;
- data and knowledge management (e.g. potential mechanisms for collection and pooling relevant data sets);
- ethical guidance and data governance and privacy standards as appropriate;
- networking and communication across large programmes such as the Accelerator.

The industry consortium will also:

- generate and share data, samples, and information from industry-sponsored clinical trials (phases 1-3) in the AMR space (e.g. resources associated with vaccine R&D for drug resistant bacteria causing major burden of disease in developing world, including but not limited to clinical trials and enabling studies, manufacturing, toxicology studies, etc. and/or for antibacterial R&D, e.g. phase 3 gepotidacin clinical trials and associated enabling studies such as but not limited to CMC activities, clinical operations);
- assist in the analysis of the output of clinical trials in the AMR space, e.g. efficacy, safety, translation of preclinical data with respect to safety, tolerability, dose prediction, animal models of infection and efficacy;
- conduct, share data, and analyse results from animal infection studies.

Indicative duration of the action

The indicative duration of the action is 72 months.

Future project expansion

Potential applicants must be aware that the Innovative Medicines Initiative 2 (IMI2) Joint Undertaking may, if exceptionally needed, publish at a later stage another call for proposals restricted to the consortium already selected under this topic, in order to enhance and progress the results and achievements by extending the duration and funding by means of another grant agreement. The consortium will be entitled to open to other beneficiaries as it sees fit. One of the purposes of pillar A is to collate data on antibiotic attrition and effectiveness. The analyses that are carried out will generate further knowledge and understanding and will generate further work streams as yet to be identified. The additional work plans will be addressed via a call for proposals restricted or not to the consortium already selected, depending on the resources required.

Indicative budget

The indicative EFPIA in-kind contribution is EUR 17 300 000.

Due to the global nature of the participating industry partners it is anticipated that some elements of the contributions will be non-EU/H2020 Associated countries in-kind contribution[5].

The financial contribution from IMI2 JU is a maximum of EUR 8 000 000.

Applicants should consider allocating a budget in the region of EUR 5 000 000 of IMI2 JU contribution to support the operational component of the CBN, given the need to support multiple projects across the Accelerator.

Applicant consortium

The applicant consortium will be selected on the basis of the submitted short proposals. The applicant consortium is expected to address all the research objectives and make key contributions to the defined deliverables in synergy with the industry consortium which will join the selected applicant consortium in preparation of the full proposal for stage 2. The applicant consortium is expected to mobilise expertise and proven track record in, for the operational group:

- conducting, and capacity for supporting, grant funded research, preferably with respect to working within projects established by the IMI/IMI2 JU or H2020;
- coordinating multiple discovery AMR projects;
- rigorous project and programme management and alliance management for projects of the complexity and scale of the overall AMR Accelerator, preferably with respect to working within projects established by the IMI/IMI2 JU or H2020 (including management of scientific and financial reporting, legal agreements including IP arrangements, meeting facilitation/secretariat role);
- ethics and data governance and privacy in relation to AMR;
- communications and outreach to the scientific community and public;
- collection, collation and curation of data sets and identifying, implementing, maintaining IT systems across large collaborative projects or PPPs,
- business development as applied to large collaborative projects or PPPs;

and in, for the scientific group:

- analysis of preclinical and clinical trial data in the AMR space in relation to e.g. efficacy, safety, translation of preclinical data with respect to safety, tolerability, dose prediction, animal models of infection and efficacy;
- conducting and analysing animal infection models to generate reference data of benchmarked control compounds and bacterial isolates.

It is suggested that, to minimise complexity, maximise stability, and maintain a lean and effective group, the number of participants directly related to the operational objectives described above be minimal in size.

Suggested architecture of the full proposal

The applicant consortium should submit a short proposal which includes their suggestions for creating a full proposal architecture, taking into consideration the industry contributions and expertise.

The final architecture of the full proposal will be defined by the participants in compliance with the IMI2 rules and with a view to the achievement of the project objectives.

In the spirit of the partnership, and to reflect how IMI2 JU call topics are built on identified scientific priorities agreed together with EFPIA beneficiaries/large industrial beneficiaries, these beneficiaries intend to significantly contribute to the programme and project leadership as well as project financial

[5] Note: This does not however constitute the justification referred to in Article 4(2) of Council Regulation (EU) No 557/2014 ('IMI 2 JU regulation').

management. The allocation of a leading role within the consortium will be discussed in the course of the drafting of the full proposal to be submitted at stage 2. To facilitate the formation of the final consortium, until the roles are formally appointed through the consortium agreement, the proposed project leader from among EFPIA beneficiaries/large industrial beneficiaries shall facilitate an efficient negotiation of project content and required agreements. All beneficiaries are encouraged to discuss the project architecture and governance and the weighting of responsibilities and priorities therein.

Applicants to Calls launched as part of the Accelerator should consult the IMI2 JU Model Grant Agreement and IMI2 JU Annotated Model Grant Agreement, as well as a short questions and answers document available at https://www.imi.europa.eu/sites/default/files/uploads/documents/apply-for-funding/open-calls/Questions_and_answers_on_the_AMR_accelerator_programme.pdf.

Sustainability

A plan for aspects related to sustainability, facilitating continuation beyond the duration of the project should also be proposed.

Topic 8: AMR Accelerator programme Pillar B: Tuberculosis drug development network to accelerate and validate scientific discoveries and advance the R&D pipeline of new and innovative agents to address the global tuberculosis epidemic

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Part of the IMI2 AMR Accelerator programme

Topic details

Action type	Research and Innovation Action (RIA)
Submission and evaluation process	2 stages

Specific challenges to be addressed

On the eve of World tuberculosis (TB) Day 2018, the EU Commissioners for Health & Food Safety; Research, Science & Innovation; Employment, Social Affairs, Skills and Labour Mobility; and International Development and Cooperation issued a joint statement[6] highlighting the EU's commitment to eradicating TB and the crucial role research and product development plays in this. TB is the leading cause of death from a single infectious agent worldwide. An estimated 10.4 million people contracted TB in 2016. The lack of efficiency of current TB drugs is emphasised by the nearly 1.8 million annual deaths reported by World Health Organisation (WHO). Of these, 200 000 were confirmed cases of drug resistant TB, although real estimates could be much higher.

The majority of the 1.8 million annual TB deaths are caused by drug-susceptible TB (DS-TB). The current standard of care (SOC), namely HRZE (H=Isoniazid, R=Rifampin, Z=Pyrazinamide, E=Ethambutol) has an efficacy (favourable outcome) in clinical trials of 90-95 %, yet effectiveness in the field in high incident countries is merely ~75 %. The spread of resistant forms of TB is a continuum, with multi-drug resistant (MDR)-TB cases having already been detected in every country where there is an existing TB surveillance programme. Treatment options for MDR-TB are very poor; only 20 % of patients receive an effective treatment which is excessively long and complex (combination treatment of 7-10 drugs given for 18-24 months for a total of 20 000 pills and 240 painful injections). The lack of adequate compliance and the limited efficacy further reduces the success rate of MDR treatments to only 50 %.

Although significant efforts have been made during the last decade, only two novel drugs have been approved by the Food and Drug Administration (FDA) and European Medicines Agency (EMA) since 1975 (Sirturo ® from Janssen and Delamanid® from Otsuka). Additionally, the lack of new drug candidates to combine with makes it challenging to impossible to develop a fully new combination.

[6] http://europa.eu/rapid/press-release_STATEMENT-18-2461_en.htm

As expressed by the United Nations (UN), a massive scale-up[7] and a dynamic, global, multi-sectoral approach[8] is needed if the global target of eradicating tuberculosis by 2030[9] is to be met. At present, there is a strong consensus both in private and public research sectors working on TB that having a large number of new drug candidates, which are ready to enter into clinical combination studies, is the most critical step to achieving this aspirational goal that will have a tremendous impact on global health. These new candidates should be: 1) highly efficacious against all forms of TB; 2) safe for long-term administration to all TB patients; and 3) orally bioavailable. There is currently a lack of compounds that would be active against all forms of drug-resistant TB with no cross resistance and no drug-drug-interaction liability with existing gold standard drugs. Cost of goods that allow a cheap and easy production should also be factored in to prioritise compounds as appropriate.

The sum of initiatives financed by the European Union and IMI (New Drugs for Bad Bugs (ND4BB), Model-based preclinical development of anti-tuberculosis drug combinations (PreDiCT-TB), More Medicines for Tuberculosis (MM4TB), Open Collaborative Model for Tuberculosis Lead Optimisation (ORCHID), anTBiotic), the National Institutes of Health (Tuberculosis Research Units Network, TBRU-N), the Bill and Melinda Gates Foundation (TB Drug accelerator, TBDA), together with the Global Alliance for TB, have worked to create the framework and infrastructure required to support and accelerate the development of new drug candidates in TB. Bringing forward a new generation of candidates through good laboratory practice (GLP) toxicity studies and first time in human (FTIH) and performing early combination studies to explore drug-drug interactions, efficacy and safety will accelerate the discovery of novel combination regimens with a higher probability of success. The TB drug development Network (TBDDN) within the AMR Accelerator brings together the collective will of all pharmaceutical companies involved in TB in a European initiative carefully conceived to be synergistic with other initiatives such as the TBDA platform.

The TB drug development Network (TBDDN), pillar B of the IMI2 AMR Accelerator programme, will function as a platform based on the principles of open innovation to advance discovery, preclinical and early clinical projects in the field of TB and MDR-TB. This component of the Accelerator will work to address the innovation gap in the discovery and early development of a pan-TB regimen by enabling access to both novel drug candidates and innovative tools to accelerate the discovery of new combination regimens for the treatment of TB. One of the objectives of the TBDDN is to become a worldwide reference for the development of novel candidates and regimens by sharing results generated by partners and peers from small and medium-sized enterprises (SMEs), public institutions and pharmaceutical companies following the intellectual property (IP) rules set for the IMI2 JU grants[10].

Scope

The main objective of the TBDDN is to provide a unique platform where discovery, development, and clinical trial readouts will occur allowing maximal engagement across groups in the TB field. Specifically:

- coordinate, profile and progress the portfolio of anti-TB compounds existing within the industry consortium (EFPIA companies and Associated Partners) from the advanced lead stage through Phase 1 (candidates ready to enter into Ph-2 clinical studies);
- identify preferred drug partners for preclinical combination studies that will facilitate the design of combination regimens consisting of new TB drugs with an indication for the treatment of any form, including MDR, of TB (pan-TB regimen);
- create additional tools and technologies to progress anti-TB compounds, and to provide learnings derived from the analysis of shared anti-TB clinical trial data;

[7] https://news.un.org/en/story/2016/10/542712-massive-scale-needed-if-global-targets-tuberculosis-are-be-met-top-un-health
8 https://news.un.org/en/story/2017/10/569592-tuberculosis-worlds-top-infectious-killer-un-health-agency-calls-political
9 http://www.who.int/tb/strategy/en/
10 See https://www.imi.europa.eu/sites/default/files/uploads/documents/reference-documents/h2020-mga-imi_en_v5.pdf and https://www.imi.europa.eu/sites/default/files/uploads/documents/apply-for-funding/call-documents/imi2/Annotated_Model_Grant_Agreement%E2%80%93AGA.pdf

- develop new alternative anti-tubercular drugs (host-defence or virulence approaches);
- act as an interface with stakeholders in the TB field and explore synergies and collaboration with the action resulting from IMI2 JU Call 15, topic 7 and potential TB-focused actions from IMI2 JU Call 16 as well as other AMR initiatives.

Expected key deliverables

Deliverable 1: Development and implementation of new assays and tools to study anti-TB compounds:

- assays that can rapidly measure the efflux, outer membrane penetration, of both mycobacteria, infected macrophages, and caseum to enable the rational design of novel, pan-active anti-TB drug candidates;
- *in vitro* assays taking into account disease complexity, including host cells (foamy macrophages, granulomas, caseum medium, etc.) and relying on recent knowledge of TB pathogenesis and persistence;
- optimised animal infection models for both single drugs and combinations to i) improve / optimise translation to clinical efficacy; ii) improve reproducibility (study-to-study and lab-to-lab); iii) determine predictability of pharmacokinetic/pharmacodynamics (PK/PD) parameters; and iv) identify optimal study conditions and practices for minimising variability;
- imaging platforms (*in vitro/in vivo*) to measure pharmacodynamic responses at the sites of action, including single cell microscopy, MALDI, PET/CT, hollow-fibre;
- standardised specific PK/PD studies/models required to support approval for limited use/accelerated pathways for novel TB investigational new drug (INDs) and combinations of INDs & acceptance with EMA & FDA with a focus on human dose prediction to maximise efficacy and minimise risk of resistance;
- translational PBPK-PD models fed with preclinical and clinical data in the TB space (PBPK, PD and disease progression integrative models) to accelerate development of combination studies, associated with the development of novel biomarkers to assess treatment efficacy, disease evolution and cure at preclinical (MBL assay, CFU counting, microCT scan) and clinical (PET/CT scanning, biomarkers from urine or saliva vs blood, immunological markers) stages;
- new host-defence or virulence approaches: identify possible new targets and provide access to *in vitro* and *in vivo* translational assays to better select the next generation of anti-TB drugs.

Deliverable 2: An advanced portfolio of anti-TB compounds:

- new clinical candidates which have completed Phase 1 and are ready to enter into Phase 2 proof of concept studies in TB patients (note that Phase 2 studies are outside the scope of the TBDDN);
- new potential repurposed medicines ready to enter Phase 2;
- novel combination regimens that will be formed by combining the clinical candidates.

Deliverable 3: Learnings derived from shared TB clinical trial data (e.g. Phase 1-3 clinical trials related to TB) and associated enabling studies:

- generation and collation of clinical trial data to allow for analysis and translation of preclinical to clinical data with respect to, for example, safety, tolerability, dose prediction, animal models of infection and efficacy, and greater disease understanding.

Deliverable 4: Management of TBDDN:

- framework established for rigorous programme management and coordination of the action;
- interactions with the Pillar A action resulting from IMI2 JU Call 15, topic 7, with potential future actions under Pillar B of the Accelerator, and with IMI2 JU;
- support financial and scientific reporting for TBDDN projects;
    - collect and distribute historical preclinical and clinical TB data amongst TB projects within the AMR accelerator;

- administrative tasks to support the TBDDN organisation, including tasks such as the organisation of consortium meetings, intra- and inter-work package meetings, preparation of minutes, progress reports, and the interaction required with the Pillar A action resulting from IMI2 JU Call 15, topic 7 that will provide operational support (particularly in legal, data sharing, communication and dissemination tasks).

Sustainability

A plan for aspects related to sustainability, facilitating continuation beyond the duration of the project should also be proposed.

Expected impact

The impact of the TBDDN will help attain the UN 2030 objective by:

- providing new tools and understandings to progress TB science for the discovery of new preclinical candidates and novel combination regimens across the TB R&D landscape;
- contributing to the development of a vibrant TB research environment in the EU and strengthening the competitiveness and industrial leadership of Europe;
- contributing to EU's ambition of being a 'best practice region' for addressing AMR;
- enabling the progression of potential new treatment solutions for TB patients worldwide using a preferential pricing approach for low- and middle-income countries, with the intent to improve the quality of life and life expectation of TB patients;
- strengthen interaction of TB R&D stakeholders from across the EU and globally.

Applicants should indicate how their proposals will impact and strengthen the competitiveness and industrial leadership of Europe by, for example, engaging suitable SMEs.

Potential synergies with existing consortia

Applicants should take into consideration, while preparing their short proposal, relevant national, European (both research projects as well as research infrastructure initiatives), and non-European initiatives. Synergies and complementarities should be considered in order to incorporate past achievements, available data and lessons learnt where possible, thus avoiding unnecessary overlap and duplication of efforts and funding.

The project funded under TBDDN (facilitated by the coordination and support group within the CBN) will work to maximise synergies with the following AMR projects and other public-private partnerships (PPPs):

- aspects of the research of ND4BB TRANSLOCATION (http://www.nd4bb.eu/) (e.g. the ND4BB Information Centre as a possible framework for data sharing);
- ND4BB ENABLE project (http://nd4bb-enable.eu/);
- ND4BB COMBACTE projects and iABC Programme, (https://www.combacte.com; http://www.iabcproject.com) in particular in relation to the networks CLIN-NET, LAB-NET, STAT-NET and EPI-NET;
- Projects funded by other organisations/programmes supporting AMR R&D e.g. the Global AMR R&D Hub, the EU Framework Programmes for Research and Innovation FP7 and Horizon 2020, the European & Developing Countries Clinical Trials Partnership (EDCTP) (projects such as PanACEA), Joint Programming Initiative AMR, Wellcome Trust, Biomedical Advanced Research and Development Authority (BARDA), Medical Research Council (MRC), CARB-X, Global Antibiotic Research and Development Partnership (GARDP), National Institute of Allergy and Infectious Diseases (NIAID), TB Drug Accelerator etc. to ensure synergy and avoid duplication of research.

Of note the TBDDN will ensure that:

- the current project will, where appropriate, build on the output of the IMI project PreDiCT-TB and FP7-funded projects MM4TB and ORCHID;
- complementarities with TBDA, and other global platforms in TB by involving these organisations directly as Associated Partners in the project;
- experts from the regulatory agencies (EMA) and the public and medical sector are consulted in the project so that the data generated can be used when regulatory filings will be made.

Industry consortium

The industry consortium is composed of the following EFPIA companies:

- GSK (lead)
- Evotec
- Janssen

In addition, the industry consortium includes the following IMI2 Associated Partners:

- Bill & Melinda Gates Foundation
- TB Alliance
- the University of Dundee (Drug Discovery Unit)

Please note that the IMI2 JU matching of in-kind provided by Associated Partners on a specific disease (e.g. TB) will be applied to the same disease if required by the Associated Partners.

The Associated Partners will provide novel potential products from their respective portfolios to be included in the TBDDN and scientific and project management to support their series and combinations thereof. The BMGF will also serve as an interface with the existing TB Drug Accelerator (TBDA) and the centralised hubs to access the clinical data generated in TB.

To achieve the scientific objectives of the TBDDN, the industry consortium will do the following.

- Conduct standard medicinal chemistry, microbiology, pharmacology and early ADMET optimisation programmes for novel anti-TB compounds.
- Conduct and share results and information of enabling studies such as synthesis (up-scales, fermentation), optimisation of lead molecules, computational chemistry, profiling in *in vitro and in vivo* models (marmoset and murine models, cell & lesion penetration, PKPD profiling and modelling, metabolomics), access to enzymology platforms (biochemical and biophysical assays and crystallography) and toxicology of novel pre-candidates[11] from TB portfolios from EFPIA and Associated Partners for further analysis.
- Perform preclinical development studies[12] (e.g. GLP toxicity studies, early pharmaceutical development, development and manufacture of clinical trial material (drug substance and drug product)).
- Where appropriate, provide compounds to support and/or validate the development of assays or approaches including potentially the generation of new natural products (fermentation, extract purification).
- Share historical TB drug discovery and development data where appropriate.
- Provide knowledge and expertise in TB drug discovery and development.
    - Capacity for multi-gram scale up synthesis of non-GMP grade of selected pre-candidates (500g), to assess therapeutic index of preclinical pre-candidates (non GLP toxicity and *in vivo* profiling into advanced TB models):

[11] Pre-candidate studies: discovery activities from Lead optimisation to selection of a molecule as preclinical candidate
[12] Preclinical development: studies performed between preclinical candidate and first time in human.

        - early pharmaceutical development including process chemistry development, pre-formulation, formulation and drug delivery techniques to maximise the evaluation of the therapeutic index of novel compound;
        - capacity for scale-up synthesis of selected candidate compounds of suitable quality (usually GMP grade) (1-5 kg) to perform GLP toxicity studies.

    - If additional throughput is needed, ability to undertake first into human studies (FTIH) on heathy volunteers to determine key pharmacokinetic parameters in humans (half-life, volume of distribution, clearance and potential for accumulation under extensive repeated doses) and to assess an indication of adverse effects (standard for any new IND with special focus on cardiovascular and hepatotoxicity).

- Generate and share data, samples, and information from industry-sponsored clinical trials (Phase 1-3) in the field of TB including drug sensitive, drug resistant, and multidrug resistant tuberculosis, of compounds (e.g. Sirturo (Bedaquiline), Pretomanid, Delamanid, Sutezolid, Leu-tRNA synthetase inhibitor, Mtb cholesterol dependent inhibitor and Mtb DprE1 inhibitors and others), including enabling studies (e.g. synthesis, profiling, and toxicology) of novel precandidates from TB portfolios from EFPIA and associated partners (DDU and TB Alliance) for further analysis.
- Assist in the analysis of the output of clinical trials in the TB space, e.g. efficacy, safety, translation of preclinical data with respect to safety, tolerability, dose prediction, animal models of infection and efficacy.

The TBDDN project will include activities from industry-sponsored studies in Phase 1-3 generating data to be shared by EFPIA with the partners of this action. Studies will be sponsored and funded by the respective contributing partner including the cost of full time equivalents (FTEs) and other expenses to run the studies, including but not limited to contract research organisation (CRO) costs, laboratory costs, and investigator and institutional grants based on respective site contracts. Payments will be based on respective agreements with trial related sites and/or trial related scientific advisory groups.

Indicative duration of the action

The indicative duration of the action is 72 months.

Indicative budget

The indicative industry in-kind contribution is EUR 120 900 000.

This contribution comprises an indicative EFPIA in kind contribution of EUR 53 900 000 and an indicative IMI2 JU Associated Partner in kind contribution of EUR 67 000 000.

Due to the global nature of the participating industry and Associated Partners, it is anticipated that some elements of the contributions will be non-EU/ H2020 Associated Countries in kind contribution.[13]

The financial contribution from IMI2 JU contribution will be a maximum of EUR 89 830 000.

Applicant consortium

The applicant consortium will be selected on the basis of submitted short proposals. The applicant consortium is expected to address all the research objectives and make key contributions to the defined deliverables in synergy with the industry consortium which will join the selected applicant consortium in preparation of the full project proposal for stage 2.

To achieve the scientific objectives of the TBDDN, the applicant consortium is expected to mobilise, as appropriate, expertise and capabilities in the following areas:

[13] Note: This does not however constitute the justification referred to in Article 4(2) of the IMI 2 JU regulation.

- analysis of preclinical and clinical trial data in the TB space in relation to e.g. efficacy, safety, translation of preclinical data with respect to safety, tolerability, dose prediction, animal models of infection and efficacy;
- collection, collation and curation of TB-specific data sets and identifying, implementing, maintaining IT systems (e.g. information sharing portals or databases) across large collaborative projects or PPPs, for example datasets could include:
  - clinical trial data;
  - microbiology data;
  - preclinical screening / profiling data;
  - chemical structures and descriptors;
  - animal infection model data;
- development of assays that can rapidly measure the efflux, outer membrane penetration, of both mycobacteria, infected macrophages, and caseum to enable rational design of novel pan-active anti-TB drug candidates;
- translation of PK/PD and regulatory knowledge to support the development of limited use/accelerated pathways for anti-tubercular drugs;
- conducting and analysing TB-animal infection models for single drugs and combinations;
- imaging platforms to measure pharmacodynamic responses at the sites of action;
- translational PBPK-PD models fed with preclinical data in the TB space (PBPK, PD and disease progression integrative models), expertise in preclinical and clinical TB biomarkers;
- drug discovery optimisation activities, e.g. medicinal chemistry, microbiology, scale up, pharmaceutical formulation, DMPK, toxicology, etc;
- development of *in vitro* and *in vivo* tools to identify, characterise and progress molecules from host-defence or virulence approaches;
- multi-gram scale up synthesis of non-GMP grade of selected pre-candidates (500g), to assess therapeutic index of preclinical pre-candidates (non GLP toxicity and *in vivo* profiling into advanced TB models);
- pharmaceutical development techniques to maximise the evaluation of the therapeutic index of novel compound;
- scale up synthesis of selected candidate compounds of GMP grade (1-5 kg) of active product ingredients of GMP grade to perform GLP toxicity studies;
- ability to conduct in parallel several first into human studies (FTIH) on heathy volunteers to determine key pharmacokinetic parameters in humans (half-life, volume of distribution, clearance and potential for accumulation under extensive repeated doses) and to asses an indication of adverse effects (standard for any new IND with special focus on cardiovascular and hepatotoxicity).

In view of the complexity and size of the action, the applicant consortium must bring expertise and consider appropriate resources to deal with the scientific coordination and daily project management, undertake financial tasks (distribution of budget, cost reporting, etc.), and deal with administrative tasks. In addition, operational support will be provided by the coordination and support group formed in the CBN through IMI2 JU Call 15 topic 7 (particularly in legal, data sharing, communication and dissemination tasks).

In addition, representatives from the selected project will contribute to an advisory and communications board (containing independent experts and representatives from all the projects running in the AMR Accelerator) created as part of the coordination and support group within the CBN. This group will meet regularly to share summary level, non-confidential progress reports on projects and where appropriate make recommendations to the AMR Accelerator overall.

Suggested architecture of the full proposal

The applicant consortium should submit a short proposal which includes their suggestions for creating a full proposal architecture, taking into consideration the industry participation including their contributions and expertise.

The consortium is expected to have a strategy on the translation of the relevant project outputs into regulatory practices, regulatory, clinical and healthcare practice. These strategies be aim to ensure access and uptake in high TB burden countries to secure maximum impact on the TB epidemic. A plan for interactions with regulatory agencies/health technology assessment bodies with relevant milestones and resources allocated should be proposed to ensure e.g. qualification advice on the proposed methods for novel methodologies for drug development.

Note that overall plans and go/no-go milestones for progression of different molecules or approaches in the project will need to be established during the full project proposal phase of the application and should be included in full proposals. These milestones will then assist in the decision-making process to help ensure that the overall TBDDN portfolio remains dynamic and work on compounds is prioritised across the portfolio appropriately. Therefore, applicants should be aware that resources dedicated to a specific phase or piece of work may increase or decrease during the project.

Decision making: Following the first stage of the IMI2 JU Call process and selection of partners to receive IMI2 JU funding, it is expected that the consortium preparing the full proposal for the second stage of the IMI2 JU Call process will agree on a robust decision-making process (including escalation procedures) for progression of different molecules or approaches. Such decisions would be made by a committee that includes representatives from all project partners, e.g. including from the Associated Partners (BMGF, TB Alliance and Dundee Drug Discovery Unit (DDU), the contributing EFPIA partners, and the public partners. The composition of this committee will be detailed and agreed by all partners in the Consortium Agreement. A fair and efficient decision making process will be presented in the full proposal at the second stage of the IMI2 JU Call process. This committee will track the progress of the project against its own internal milestones and will be empowered (to be outlined in the Consortium Agreement) to make progression/termination decisions based on pre-agreed go / no go milestones in a e.g. quarterly, streamlined, single-meeting process. For the avoidance of doubt, any decisions directly affecting an existing compound asset (such as an investigational medicinal product from one of the participants), shall always require consent of the participant who owns the existing compound asset. The decision-making process by the committee may result, in case of a 'no-go' decision, in the recommendation from the committee/consortium to IMI2 JU for terminating the grant based on Art. 50.3.1 (h) of the IMI2 JU MGA. The final decision on project continuation or termination will be taken by IMI2 JU in line with the provisions of the Grant Agreement. However, the JU may also make such a decision without prejudice to any decision-making process at the level of the consortium, i.e., even without the aforementioned recommendation.

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.

In the spirit of the partnership, and to reflect how IMI2 JU call topics are built on identified scientific priorities agreed together with EFPIA beneficiaries/large industrial beneficiaries, these beneficiaries intend to significantly contribute to the programme and project leadership as well as project financial management. The allocation of a leading role within the consortium will be discussed in the course of the drafting of the full proposal to be submitted at stage 2. To facilitate the formation of the final consortium, until the roles are formally appointed through the consortium agreement, the proposed project leader from among EFPIA beneficiaries/large industrial beneficiaries shall facilitate an efficient negotiation of project content and required agreements. All beneficiaries are encouraged to discuss the project architecture and governance and the weighting of responsibilities and priorities therein.

Applicants to Calls launched as part of the Accelerator should consult the IMI2 JU Model Grant Agreement and IMI2 JU Annotated Model Grant Agreement, as well as a short questions and answers document available at https://www.imi.europa.eu/sites/default/files/uploads/documents/apply-for-funding/open-calls/Questions_and_answers_on_the_AMR_accelerator_programme.pdf.