



Viewpoint

Public–private partnerships as enablers of progress in the fight against mental disorders: The example of the European Innovative Medicines Initiative

Mental illness comprises a class of conditions which impact a significant use of health care, lost productivity, and human suffering for the patients, their families and carers. Their burden of disease is rising globally and comparable, or higher, to that of cardiovascular diseases and cancer [1]. In Europe, about 165 million people are affected each year by mental disorders. Overall, more than 50% of the general population in middle- and high-income countries will suffer from at least one mental disorder at some point in their lives. This implies tremendous economic costs, especially indirectly via proportionally high productivity losses and thus impact on economic growth [2]. The unmet social, clinical and economic need for improved therapies for such conditions is therefore significant. Indeed, while in the last six decades there have been important advances of both medication and non-pharmacotherapeutic strategies for mental diseases, these are mostly been incremental and not game changing. There is therefore a critical need for increased treatment effectiveness both in refractory and in partially-responsive subjects, and for treatments capable of slowing or preventing disease onset and progression [3].

The last decade has witnessed exciting and important advances in the neuroscience of mental health including the mapping of neural circuitry and neurochemical mechanisms, identification of multiple genetic loci and the application of novel technologies to both the pathophysiology and treatment of mental disorders. While this should pave the way to innovative treatments, the translation so far has failed to happen. The research has uncovered the true complexity of neurological and psychiatric conditions which has somehow dampened the appetite of drug developers. Drug development for mental disorders remains highly challenging, and at higher attrition rate compared with other indications [4]. The key challenges are mechanisms of disease, target identification and validation, predictive models, biomarkers for patient stratification and as endpoints for clinical trials, clear regulatory pathways, reliability and reproducibility of published data, and, importantly, data sharing and collaboration [5]. Such complex and multifactorial issues cannot be solved by a single organisation, research group, or sector, but require a concerted collaborative strategic effort of all stakeholders. Collaborative public–private partnerships (PPPs) are powerful instruments to drive innovation in health research and development. PPPs provide the necessary non-competitive space for knowledge sharing and

dialogue between regulatory agencies and other stakeholders, including academia, industry and patients' organisations for successful translation of scientific knowledge to innovative treatments [6]. In Europe the Innovative Medicines Initiative (IMI)¹ is the largest public–private partnership in health science [7]. IMI is a joint undertaking between the European Union (EU) and the European pharmaceutical industry, represented by the European Federation of Pharmaceutical Industries and Associations (EFPIA). For the IMI2 programme (2014–2024), the total budget is €3.276 billion. Half of the budget comes from the EU's research and innovation programme, Horizon 2020. The other half comes mostly from large pharmaceutical companies, and to a less extent from other life science industries or organisations; these do not receive any EU funding, but contribute to the projects 'in kind', for example by donating their researchers' time or providing access to research facilities or resources. IMI funding is awarded via competitive open calls (Fig. 1).

The aim of IMI is to enable an appropriate European-level research and innovation capacity that will make a crucial contribution to delivering better health and wellbeing for all, while positioning Europe as a leader in the rapidly expanding global markets for health and wellbeing innovations. IMI is working to improve health by speeding up the development of, and patient access to, innovative medicines, particularly in areas where there is an unmet medical or social need. In this context indeed mental/psychiatric disorders are one of the priority areas of the IMI Strategic Research Agenda [8], and IMI via its projects is contributing significant new insights and enabling resources to the area.

The NEWMEDS² project has been the first IMI project in this area. As psychiatric disorders may be 'connectopathies', disorders of neuronal connectivity, the project was framed to identify novel discovery paradigms to explicitly assess brain circuits involved in the pathophysiology and treatment of major depression and schizophrenia, using electrophysiology, behavioural assays and translational neuroimaging. The project has contributed significantly to the understanding of the brain circuits involved in psychiatric disorders and its translation into novel research

¹ <http://www.imi.europa.eu/>.

² Novel methods leading to new medications in depression and schizophrenia: <http://www.newmeds-europe.com/en/news.php>.

Two Stages Call process

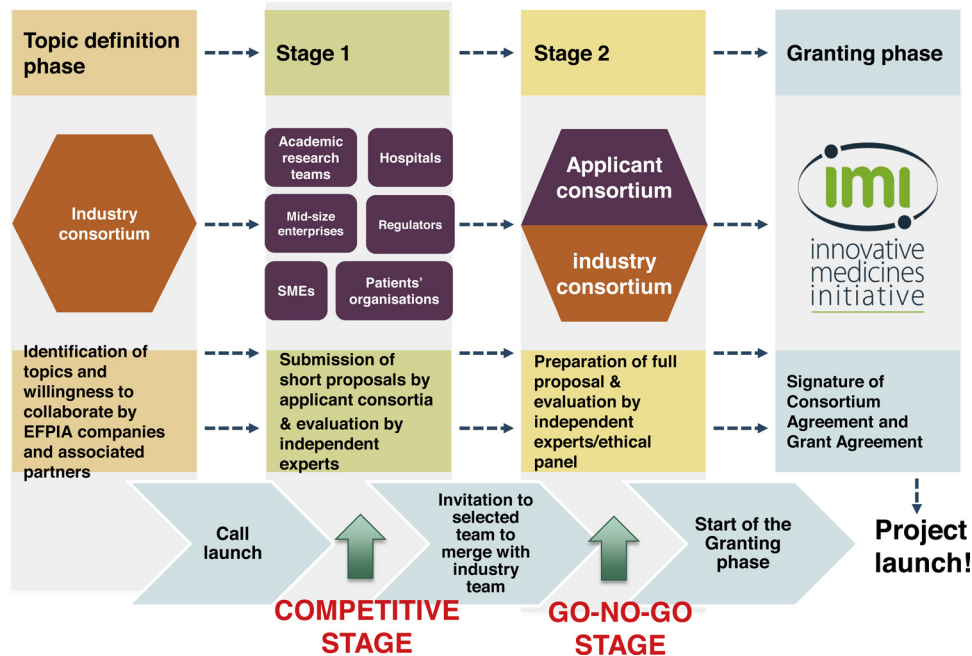


Fig. 1. The two stages IMI Call process. Drawing on the annual priorities, a consortium of EFPIA companies and, in some cases, other large companies or organisations active in health research (the “Industry consortium”), agrees on the need to work together and with other stakeholders on a specific issue: a topic text is drafted. Following consultation with various groups (including the IMI Scientific Committee and the States Representatives Group), and the IMI Governing Board approval, IMI launches an open competitive Call for proposals. The applicant consortium which short proposal is ranked first at Stage One is invited to prepare a full proposal submission with the Industry consortium. If the go/no go evaluation at Stage Two is successful the grant is awarded.

platforms for drug R&D. This has been critically enabled by synergies created by putting together scientists from different EFPIA companies, biotech and academia. The teams cross-validated each other's work, independently, which supported key concepts, particularly the precise brain circuits at risk [9].

The EU-AIMS³ project, now entering its final phase, has developed from scratch a unique research and development platform for autism spectrum disorders (ASD); including novel in vitro assays based on patient derived inducible pluripotent stem cells, in vivo models, translational imaging tools and unique clinical resources. The consortium importantly engaged with the European Medicines Agency and obtained scientific qualification advice to guide its work and maximise potential impact of science generated in its clinical study on the regulatory requirements for future clinical trials. The output is its Longitudinal European Autism Project (LEAP) which is the worldwide largest multicentre, multidisciplinary study to identify stratification biomarkers for ASD and biomarkers that may serve as surrogate endpoints [10].

An important issue hampering the development of new treatments for mental disorders is that most of these conditions are still classified and diagnosed solely based on the symptoms observed, as there are few objective biomarkers for these illnesses compared to others, such as diabetes. But many different neuropsychiatric diseases share symptoms, which complicates understanding what the underlying biological cause of a specific disease is. For example, we do not really know if social withdrawal, an early sign of both schizophrenia and Alzheimer's disease, has a common biological cause in the two diseases. The PRISM⁴ project is developing a quantitative biological approach to determine if social withdrawal has a different biological signature in Alzheimer's

disease versus schizophrenia. The project, still in early phase, if successful will provide important insights for the understanding and classification of neuropsychiatric diseases to accelerate the discovery and development of better treatments for patients. This will be critically enabled by its strong multidisciplinary team of researchers from pharmaceutical companies, research institutions and small and medium enterprises, the inclusion in the consortium of the European College of Neuropsychopharmacology (ECNP), and patient organisations as well as strong links with regulators.

A challenge in understanding and treating mental disorders is that they are chronic conditions in constant evolution, alternating periods where disease symptoms are well managed and periods of deterioration and acute illness (relapse). The technological progress in smartphones and wearable devices now allows for continuous remote assessment and provides a complete picture of a patient's condition at a level of detail which was previously unachievable. Moreover, it could potentially allow treatment to begin before a patient's health deteriorates, preventing the patient relapsing or becoming more ill before they seek treatment. The RADAR-CNS⁵ project is setting up a pipeline for developing, testing and implementing remote measurement technologies for depression, multiple sclerosis and epilepsy. This project comprises clinical and technical platforms and a dedicated cluster for efficient and effective translation of results into real-world clinical applications. To achieve this, the consortium includes and constantly engages with patients, clinical services and regulators. The ambitious aim of RADAR-CNS is to have workable clinical devices entering health services by 2020.

The IMI has still a significant budget to invest and scope of initiatives to implement during its run under H2020. There is therefore opportunity to further impact the area of mental

³ European Autism Interventions – a Multicentre Study for Developing New Medications: <https://www.eu-aims.eu/>.

⁴ Psychiatric Ratings using Intermediate Stratified Markers: <https://prism-project.eu/en/prism-study/>.

⁵ Remote Assessment of Disease and Relapse – Central Nervous System: <https://www.radar-cns.org/>.

disorders. This should be accomplished by building on what already achieved by previous projects both in IMI and elsewhere in Europe, and at national level and globally, and addressing the most critical challenges as collaboratively as possible. For example on the foundations of the results of the EU-AIMS project IMI is now progressing towards the launch of a new transatlantic initiative for the validation of ASD biomarkers and the development of a clinical trial ready cohort for the testing of ASD treatments. Another important initiative is the EQIPD project, which will start early in 2018 focussing on the factors that hamper data reproducibility in preclinical neuroscience research.

The recent “Workshop on Schizophrenia and other mental disorders” has been a very valuable opportunity for collaborative research consortia funded at European level to meet and learn about each other work, partnerships and research approaches. This has been a critical first step to build the basis for further really impactful collaborative initiatives. Leveraging on all available results and engaging all critical public and private stakeholders, in an open innovation spirit, is the only recipe for a really transformative progress against mental illness.

1. Disclosure of interest

The authors declare that they have no competing interest.

Acknowledgements

The author gratefully acknowledges Pierre Meulien and Nathalie Seigneuret for critically reading the manuscript.

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Received 28 September 2017

Received in revised form 4 October 2017

Accepted 4 October 2017

Available online 3 February 2018