Socio-Economic Impact Report on IMI1 projects

Report by:

Centre for Innovation in Regulatory Science (CIRS)
Clarivate
Friars House
160 Blackfriars Road
London SE1 8EZ
✆: +44 2074334000
✉: https://www.cirsci.org/

Final update: 15.02.21

Contents

Foreword

I am happy to present the second in-depth socio-economic impact report regarding the project portfolio of IMI1. The legislation creating the Innovative Medicines Initiative (IMI) notes that IMI 'should provide socio-economic benefits for European citizens', and this report shows that we are achieving this. For example, our projects have delivered biomarkers, models, tools and resources that are already being used by project partners and, in some cases, researchers outside the initial project.

Furthermore, as experience shows that the greatest impacts often come in the months and years after the final project report has been submitted, it is likely that in the long-term, these projects will have an even greater impact than what is reported here.

Forty four IMI1 projects have now officially completed their work and form the basis of this report. While we have kept the same methodology that was developed and used for the first report, the presentation of this second report is very different. I would like to thank our partners Clarivate for redesigning the presentation in a hopefully more reader friendly manner. I would like to take this opportunity to thank the participants of the projects and the IMI team for providing all of the information needed to carry out this study.

Analysing, quantifying and articulating the socio-economic benefits of research projects is highly challenging. This report represents a key element in IMI's drive to demonstrate the impact our projects are having. Other elements include our revised key performance indicators (KPIs), which focus strongly on impacts, as well as our Annual Activity Reports, where we not only report on our KPIs, but tell the stories behind the numbers. Our website also contains a wealth of project success stories, as well as a catalogue of IMI project outputs that are accessible to the wider scientific community.

We are on a journey in terms of articulating socio-economic benefits of research projects and we look forward to feedback from our stakeholders in order for us to get to the next level and of course to prepare the terrain for the final evaluation of IMI2.

Pierre Meulien, IMI Executive Director

November 2020

Abbreviations

AD	Alzheimer's Disease
API	Active Pharmaceutical Ingredients
ASD	Autism Spectrum Disorders
BCDP	Beta Cell and Diabetes Platform
CDISC	Clinical Data Interchange Standards Consortium
CDR	Central Data Repository
CMR	Center for Medicines Research
CNV	Copy Number Variations
COPD	Chronic Obstructive Pulmonary Disease
COU	Context of Use
CPD	Continued Professional Development
CRO	Contract Research Organization
CT	Computed Tomography
DDS	Drug Delivery System
DEN	Diethyl Nitrosamine
DILI	Drug-Induced Liver Injury
DK	Denmark
DNA	Deoxyribonucleic Acid
DSP	Data Standards Package
EE	Estonia
EEG	Electroencephalogram
EFPIA	European Federation of Pharmaceutical Industries and Associations
EGA	European Genome-Phenome Archive
EHR	Electronic Health Record
EMA	European Medicines Agency
EMR	Electronic Medical Record
ES	Spain
EU	Europe
FDA	US Food and Drug Administration
fMRI	Functional Magnetic Resonance Imaging
GI	Gastrointestinal
HA	Haemophilia A
HTA	Health Technology Assessment
HTS	High Throughput Screening
IB	Imaging Biomarkers
IBD	Intestinal Bowel Disease

iBST	Improper Bagging Survival Tree
IMI	Innovative Medicines Initiative
iPSC	Inducible Pluripotent Stem Cell Lines
IT	Italy
ITTM	Information Technology for Translational Medicine
JECL	Joint European Compound Library
JIA	Juvenile Idiopathic Arthritis
KPI	Key Performance Indicators
LOS	Letters of Support
M&S	Modelling and Simulation
MCI	Mild Cognitive Impairment
MID3	Model Informed Drug Discovery and Development
MRB	Multi Resistant Bacteria
MRI	Magnetic Resonance Imaging
MS	Multiple Sclerosis
NAFLD	Non-Alcoholic Fatty Liver Disease
NASH	Nonalcoholic steatohepatitis
NGC	Non-genotoxic carcinogenesis
NGO	Non-Governmental Organization
NL	Netherlands
PA	Physical Activity
PD	Parkinson's Disease
PE	Pharmacoepidemiology
PET	Positron Emission Tomography
POCT	Point-of-Care Test Platforms
PPP	Public-Private Partnership
PRO	Patient Reported Outcome
R&D	Research and Development
RA	Rheumatoid Arthritis
RAMD	Random Acceleration Molecular Dynamics
RDR	Raw Data Repository
RNA	Ribonucleic Acid
RWE	Real-World Evidence
SAD	Systemic Autoimmune Disease
SD	Signal Detection
siRNA	Small interfering Ribonucleic Acid
SMEs	Small and Medium-Sized Enterprises
SOP	Standard Operating Procedures

SWOT	Strengths-Weaknesses-Opportunities-Threats
TB	Tuberculosis
TMA	Tissue Microarrays
UK	United Kingdom
US/USA	United States of America
VAP	Ventilator-Associated Pneumonia
WHO	World Health Organization
YRN	Young Researchers Network

EXECUTIVE SUMMARY

Introduction

The Innovative Medicines Initiative (IMI) is a public-private partnership between the European Union (EU) and the European Federation of Pharmaceutical Industries and Associations (EFPIA) working to improve health by accelerating the development of, and patient access to, innovative medicines, particularly where there is an unmet medical or social need. As of February 2020, forty-four (44) projects had been completed out of 59 launched during the first phase of the IMI (IMI1), with an overall goal of improving the efficiency and effectiveness of the drug development process, with the long-term aim that the pharmaceutical sector produces more effective and safer innovative medicines. Overall, the budget for the 44 IMI1 projects was €1.24 billion, of which 44% (€544 million) was provided by the EU's research and innovation programme, 42% (€525 million) was provided by EFPIA companies, and 14% (€172 million) was provided from the resources of members of the consortia.

The scope of the projects was defined by the objectives of the IMI Strategic Research Agenda.[1] Each IMI1 project was designed to address a 'bottleneck' that had been identified in the drug discovery and development process. Therefore the IMI1 projects were not focused on bringing new medicines to market. In most cases, the rationale for the project was that there was an area in which individual companies or research organisations had failed to make progress and there was a need for different actors to work together to overcome the challenge. The projects were envisaged as a range of activities that would improve the conditions for medicine development in Europe, and remove barriers to the development of medicines and the growth of the sector. The projects covered areas including efficacy and safety assessment for specific disease areas, knowledge management, education and training, and research and development (R&D) and manufacturing processes.

Objective and Methodology

The scope of this report was to identify, summarise and quantify the outcomes of the 44 completed IMI1 projects based on available information. The projects included were those completed by February 2020 and with final reports available. The data source to assess the impact of the 44 IMI1 projects was the public summary of these final project reports.

Outcomes were assessed as progress achieved in the following four areas:

- Innovation
- Infrastructure and resources for further research
- Structuring the European research area
- Dissemination of information

For each area, progress was measured by assessment of the following activities:

- **Innovation:** Development of new biomarkers, *in vitro*, *in vivo*, and computerised models and assays, identification of new drug targets, candidates, and delivery systems, and improvements in manufacturing processes
- **Infrastructure and resources for further research:** Development of new biobanks, cohorts, preclinical and clinical networks and databases, platforms, tools, and technologies (e.g. assays, software tools), and guidance, recommendations, and standards
- **Structuring the European research area:** Collaborations and partnerships within and between the pharmaceutical industry and academia, creation of spin-off companies to commercialise findings, engagement with regulatory bodies on project findings

[1] https://www.imi.europa.eu/about-imi/strategic-research-agenda

- **Dissemination of information:** Publication and accessibility of project outputs, and education and training of the future European workforce for the pharmaceutical sector and the next generation of (academic) researchers.

The progress shown across the four areas provided a basis for assessment of potential socio-economic impact and six potential socio-economic impact types were identified:

- Increase robustness and reproducibility of research
- Reduce the time and cost of research
- Improve manufacturing processes
- Support environmental sustainability
- Improve standards of care
- Consolidate and expand knowledge base

Each impact type has been labelled with an icon as a visual aid. This methodology was designed taking into account the objective of IMI1 as defined in its legal framework, the IMI1 strategic research agenda and its evolution along the Programme and the lessons learned from the IMI1 Socio-economic Impact Assessment Expert Group report of 2016. This approach can be visualised in Table 1 below.

Table 1: Outcome measures used to evaluate socio-economic impact

Outcome	Activities involved (Measures)	Potential socio-economic impacts
Innovation	Development of new biomarkers, *in vitro*, *in vivo*, and computerised models and assays, identification of new drug targets, candidates, and delivery systems, and improvements in manufacturing processes	**Increase robustness and reproducibility of research** **Reduce the time and cost of research**
Infrastructure and resources for further research	Development of new biobanks, cohorts, preclinical and clinical networks and databases, platforms, tools, and technologies (e.g. assays, software tools), and guidance, recommendations, and standards	**Improve manufacturing processes**
Structuring the European research area	Collaborations and partnerships within and between the pharmaceutical industry and academia, creation of spin-off companies to commercialise findings, engagement with regulatory bodies on project findings	**Support environmental sustainability** **Improve standards of care**
Dissemination of information	Publication and accessibility of project outputs, and education and training of the future European workforce for the pharmaceutical sector and the next generation of (academic) researchers.	**Consolidate and expand knowledge base**

The methodology adopted in this report is subject to some limitations:

- The template for the public summary is the same for all projects, however each project interpreted it depending on its own specificity

- The public summary of each project contains only non-confidential information at the moment of the release of the final report
- Further outcomes may have become available after the publication of this report

Evaluation of the socio-economic impact of IMI1 projects

The 44 IMI1 projects have been analysed and their key outcomes have been summarised in the following sections, looking at the areas of Innovation, Infrastructure and resources for further research, Structuring the European research area, and Dissemination of information. The socio-economic impact summary can be also visualised in Table 2.

Please note that terminology used to summarise the projects' achievements such as "potential", "validation", "validated", etc. to define outputs has been extracted from the individual project reports.

Innovation

The IMI1 projects have delivered several outcomes that will support the development of innovative new technologies and treatments, some examples are listed below:

- **Development of biomarkers:** Biomarkers have been developed, and some validated, as part of many IMI1 projects in areas including: biologic immunogenicity (ABIRISK), neurodegenerative diseases (AETIONOMY, EMIF and PharmaCog), vaccines (BioVacSafe), rheumatoid arthritis (BTCure), autism disorders (EU-AIMS), neuropathic pain (EUROPAIN) diabetes and its complications (EMIF, IMIDIA, and SUMMIT), prediction of adverse effects in potential drug candidates (MARCAR and MIP-DILI), schizophrenia (NEWMEDS), oncology (OncoTrack and QUIC-CONCEPT), systemic autoimmune diseases (PRECISESADS), tuberculosis (PreDiCT-TB), infectious diseases (RAPP-ID), drug-induced organ damage (SAFE-T), and asthma (U-BIOPRED). These biomarkers may be used to enhance understanding of disease processes and improve diagnosis, to identify drug targets and potential drug candidates, to better stratify patients, and to increase efficiency reducing potentially duration and cost of clinical trials.
- **Development of *in vitro*, *in vivo*, and *in silico* computerised models and assays:** New *in vitro*, *in vivo*, and computerised models and assays have been developed, and some validated, as part of IMI1 projects, for example, investigating vaccine (BioVacSafe), rheumatoid arthritis (BTCure), drug delivery systems (COMPACT), autism disorders (EU-AIMS), neuropathic pain (EUROPAIN), prediction of adverse effects in potential drug candidates (eTOX, MARCAR, and MIP-DILI), colorectal cancer (OncoTrack), absorption qualities of drug molecules in the GI tract (OrBiTo), tumour architecture (PREDECT), complications in diabetes (SUMMIT), and drug efficacy in schizophrenia (NEWMEDS), Alzheimer's disease (PharmaCog), and tuberculosis (PreDiCT-TB). These models may improve prediction of the efficacy and safety of new drug candidates earlier in the development process. Once implemented, they will reduce animal testing requirements and human exposure to ineffective treatments, ultimately leading to time and resource savings.
- **Identification of new potential drug targets, candidates, and delivery systems:** New drug targets and candidates for the treatment of rheumatoid arthritis have been identified in BTCure and, with further research, may result in the availability of new innovative treatments. Novel drug delivery systems have also been developed in COMPACT and, if further testing is successful, may allow oral delivery of peptides (e.g. insulin), delivery across blood-brain barrier, delivery across air-lung barrier, and dermal delivery of proteins. These outcomes have the potential to provide new treatment options and improve standards of care across a range of disease areas.
- **Improvements in manufacturing processes to reduce their environment impact:** When implemented, innovations to manufacturing processes developed in CHEM21 will reduce the environmental impact of these processes, while also reducing costs and resource use. During the project, a number of new, cleaner catalysts were supplied to EFPIA members for use in their manufacturing processes.

These outcomes have resulted in improvements to the medicine development process, with further potential improvements anticipated through further research. The improvements made may also result

in efficiencies, leading to reductions in cost and resource requirements. With further research, project outcomes could result in the availability of new innovative treatments.

Infrastructure and resources for further research

The infrastructure that has been put in place for further research and the resources generated as part of the IMI1 projects may facilitate and accelerate further innovation. This includes biobanks, cohorts, and databases, platforms, tools, and technologies for further collaborative research and data sharing, along with guidance and recommendations on best practices in various areas:

- **Biobanks, cohorts, and databases:** Biobanks, cohorts, and databases have been developed as part of many of the IMI1 projects. Examples of biobanks include those developed in the MARCAR and U-BIOPRED projects, in which samples from rodent studies and humans with severe asthma were included, respectively. As an example, the ABIRISK project created for the first time a large prospective cohort targeted to the study of biopharmaceuticals immunogenicity.. Databases were also created in several projects, including for biologic immunogenicity (ABIRISK), neurodegenerative diseases (AETIONOMY), vaccine development (BioVacSafe), rheumatoid arthritis (BTCure), drug delivery systems (COMPACT), diabetes and its complications (EMIF and IMIDIA), autism (EU-AIMS), neuropathic pain (EUROPAIN), toxicology (eTOX), bioactive molecules (K4DD), drug-induced organ damage (MIP-DILI and SAFE-T), oncology (OncoTrack and QUIC-CONCEPT), autoimmune diseases (PRECISESADS), tumour function (PREDECT), tuberculosis (PreDiCT-TB), stem cell research (StemBANCC), and anti-microbial resistance (TRANSLOCATION). The creation of biobanks, cohorts, and databases facilitates the use of the data collected during the IMI1 projects for further research, potentially resulting in cost and resource savings and accelerating the medicine development process.
- **Development of platforms, assays, software tools and technologies:** Tools and technologies were developed by most of the IMI1 projects, in the form of software tools and platforms used for data analysis and sharing, tools and techniques used in pre-clinical and clinical research, tools aimed at improving trial design and drug candidate selection, and a mobile app for tracking adverse reactions to medicines (WEB-RADR). The infrastructure and resources developed during some of these projects are already being used in further research or data collection.
- **Guidance, recommendations, and standards:** Projects have generated guidance, recommendations, and standards on: the environmental impact of solvents used in manufacturing (CHEM21), histological evaluation in models of rheumatoid arthritis (BTCure), development, description, and storing of models (DDMoRe), incentivisation of antibiotic development (DRIVE-AB), routine banking, characterisation, and distribution of iPSC cell lines (EBiSC), use of health data for research (EHR4CR), terminology used in pre-clinical studies (eTOX), use of real-world evidence in drug development (GetReal), protocols for use of magnetic resonance imaging and other technologies (MARCAR and PharmaCog), efficiency of clinical trial conduct (NEWMEDS), *in silico* modelling methods (OrBiTo), clinical trials for autoimmune diseases (PRECISESADS), standard operating procedures for precision-cut tumour slicing (PREDECT), assessment of activity monitoring in trials for COPD (PROactive), methods used in pharmacovigilance and pharmacoepidemiology (PROTECT), working with pluripotent stem cells (StemBANCC), diagnostic criteria for severe asthma (U-BIOPRED), and use of mobile applications and social media data for pharmacovigilance (WEB-RADR). The guidance, recommendations, and standards developed may help to improve and standardise the drug development process, potentially accelerating the development of and reducing the cost of developing innovative new drugs.

The infrastructure that has been put in place for further research as part of the IMI1 project may facilitate and accelerate further innovation, potentially reducing the resources and costs associated with medicine development and, ultimately improving the availability of new, innovative medicines.

Structuring the European research area

IMI1 projects have demonstrated the success of the PPP model – by bringing together experts from industry, academia, small and medium-sized enterprises (SMEs), patient groups, and regulators, to

work together. IMI1 projects have resulted in collaborations and partnerships among all of these stakeholders that extend beyond the project lifetime, including spin-off companies created to commercialise project outputs, and engagement with regulatory bodies. Some examples include:

- **Collaborations and partnerships:** Effective collaborations can minimise duplication of work at different organisations and bring together the resources needed for innovation. The IMI1 projects have provided a platform for effective collaboration within the pharmaceutical industry, between industry and academia, and extending to healthcare payers, patient groups, and regulators. The projects have enabled collaborators to establish and use standards as part of the drug development process, in areas such as vaccine development (BioVacSafe), rheumatoid arthritis (BTCure), and autism disorders (EU-AIMS). Collaboration has continued, both formally and informally, following completion of the IMI1 projects, and not-for-profit foundations have been established by the industrial and academic partners of some projects (DDMoRe and OpenPHACTS) in order to maintain the frameworks and infrastructure developed.
- **Spin-off companies:** Spin-off companies have been created to commercialise the output of some of the IMI1 projects, including ELF, eTOX, K4DD, OncoTrack, OpenPHACTS, and SUMMIT. The establishment of new companies ensures continuation of the development and implementation of innovative technologies, supporting and enhancing scientific research in Europe through the provision of novel R&D services. In addition, the creation of SMEs has wider societal benefits, providing employment and promoting European competitiveness in the pharmaceutical industry.
- **Engagement with regulatory bodies:** IMI1 projects have involved engagement with regulatory bodies on issues including biomarkers/outcomes suitable for use in drug development (EUROPAIN, PreDiCT-TB, PROactive, and SAFE-T), improvement of pre-clinical carcinogenicity testing strategies for new drug candidates (MARCAR), patient involvement across the drug development process (EUPATI), environmental issues associated with medicine manufacturing processes (CHEM21), and good practices for the use of new technologies to gather pharmacovigilance information (WEB-RADR). In some cases, this has already resulted in regulatory acceptability on the use of the tools developed as part of projects (e.g. qualification of PROactive tools) or letters of support for those tools shown to be promising based on preliminary data, EU-AIMS).

Effective collaborations can minimise duplication of work at different organisations and bring together the resources needed for innovation. In addition, engagement with regulatory bodies can help to generate the evidence to support development of regulatory guidance and standards for use in the medicine development process, potentially improving efficiency.

Dissemination of information

Dissemination of the findings from IMI1 projects is critical to ensuring that their outputs can be used for further research. Education and training activities are also important, both to ensure dissemination of findings, and to develop a skilled workforce to put Europe at the forefront of scientific R&D.

- **Catalogue of project tools:** Platforms, tools, and technologies have been developed for collaborative research and data sharing as part of many of the IMI1 projects. As of October 2020, the IMI website provides links to accessible project tools from IMI projects,[2] including 67 tools from IMI projects object of this report.
- **Publications:** The IMI1 projects delivered approximately 4,000 high-quality scientific research publications with an average citation impact of 1.83, which is nearly twice the world average of 1.00 and approximately 60% higher than the EU average of 1.10. Although open-access publication was not a requirement for EU funding and was often not budgeted for in IMI1 projects, on average 56% of publications per project were printed in open access journals. The publication of findings from the IMI1 projects facilitates the application of learnings from these projects to further research.

[2] https://www.imi.europa.eu/projects-results/catalogue-project-tools

- **Education and training:** Five of the IMI1 projects (EMTRAIN, EU2P, EUPATI, PHARMATRAIN, and SafeSciMET) focused specifically on education and training, providing training platforms, supporting lifelong learning for those already working in the pharmaceutical sector, supporting patient representatives to engage with the medicine development process, and offering training courses and qualifications. While it was not their primary focus, many of the other IMI1 projects (e.g. BTCure, CHEM21, COMPACT, DDMoRe, EHR4CR, ELF, EMIF, EU-AIMS, EBiSC, eTRIKS, IMIDIA, GETREAL and PharmaCog) provided education and training outcomes through workshops, events, training courses, work-exchange for young researchers across public-private institutions and funding or enabling academic qualifications. Through these activities, the IMI1 projects have helped to reduce the cost and resource burden associated with re-training professionals moving between institutions, and to develop highly-skilled and mobile current and future workforces, thereby positioning Europe as a hub for scientific research in the longer term.

Table 2: Summary of all outcomes and socio-economic impact

Outcome	Activities involved (measures)	Projects generating outcomes	Potential Socio-economic impacts
Innovation	2,863 validated, standardised, or potential biomarkers	ABIRISK, AETIONOMY, BioVacSafe, BTCure, EMIF, EU-AIMS, EUROPAIN, IMIDIA, MARCAR, MIP-DILI, NEWMEDS, OncoTrack, Pharma-Cog, PRECISESADS, PreDiCT-TB, QUIC-CONCEPT, RAPP-ID, SAFE-T, SUMMIT, U-BIOPRED	
	784 validated or potential *in vitro*, *in vivo* and *in silico*/computerised models	ABIRISK, AETIONOMY, BioVacSafe, BTCure, COMPACT, DDMoRe, EBiSC, EMIF, eTOX, EU-AIMS, ELF, EUROPAIN, IMIDIA, MARCAR, MIP-DILI, NEWMEDS, OncoTrack, OrBiTo, PharmaCog, PRECISESADS, PREDECT, PreDiCT-TB, RAPP-ID, SUMMIT, U-BIOPRED	
	238 potential drug targets and delivery systems	BTCure, COMPACT, EBiSC, EMIF, EU-AIMS, ELF, EUROPAIN, IMIDIA, MARCAR, MIP-DILI, NEWMEDS,	

Outcome	Activities involved (measures)	Projects generating outcomes	Potential Socio-economic impacts
		PRECISESADS, SUMMIT	
	3 potential manufacturing processes	CHEM21	
Infrastructure and resources for further research	167 biobanks, cohorts and databases	ABIRISK, AETIONOMY, BioVacSafe, BTCure. COMPACT, DRIVE-AB, EBiSC, EMIF, EMTRAIN, eTOX, eTRIKS, EU-AIMS, ELF, EUPATI, EUROPAIN, GetReal, IMIDIA, K4DD, MARCAR, MIP-DILI, NEWMEDS, OncoTrack, OpenPHACTS, OrBiTo, PharmaCog, PRECISESADS, PREDECT, PreDiCT-TB, PRO-Active, PROTECT, QUIC-CONCEPT, RAPP-ID, SAFE-T, StemBANCC, SUMMIT, Translocation, U-BIOPRED	
	593 validated or potential platforms, assays, software tools and technologies	ABIRISK, AETIONOMY, BioVacSafe, BTCure, CHEM21, COMPACT, DDMoRe, DRIVE-AB, EBiSC, EMIF, eTOX, eTRIKS, EU2P, EU-AIMS, ELF, EUROPAIN, GetReal, IMIDIA, K4DD, MIP-DILI, NEWMEDS, OncoTrack, OpenPHACTS, OrBiTo, PharmaCog, PRECISESADS, PREDECT, PreDiCT-TB, PROTECT, QUIC-CONCEPT, RAPP-ID, SAFE-T, SUMMIT,	

Outcome	Activities involved (measures)	Projects generating outcomes	Potential Socio-economic impacts
		Translocation, U-BIOPRED, WEB-RADR	
	194 published/validated or potential guidance, best practice recommendations and standard operating procedures	ABIRISK, AETIONOMY, BioVacSafe, BTCure, CHEM21, COMPACT, DDMoRe, EBiSC, EHR4CR, EMTRAIN, eTOX, eTRIKS, EU2P, EU-AIMS, ELF, EUPATI, EUROPAIN, IMIDIA, MARCAR, MIP-DILI, NEWMEDS, OncoTrack, OpenPHACTS, OrBiTo, PharmaCog, PharmaTrain, PRECISESADS, PREDECT, PreDiCT-TB, PRO-Active, PROTECT, SAFE-T, StemBANCC, SUMMIT, U-BIOPRED, WEB-RADR	
Structuring the European research area	213 memoranda of understanding and material transfer agreements signed	AETIONOMY, BioVacSafe, BTCure, CHEM21, COMPACT, DDMoRe, DRIVE-AB, EBiSC, eTOX, EU2P, EU-AIMS, ELF, EUPATI, IMIDIA, K4DD, MARCAR, OncoTrack, OpenPHACTS, PharmaCog, PRECISESADS, PREDECT, PreDiCT-TB, PRO-Active, QUIC-CONCEPT, SAFE-T, StemBANCC, SUMMIT, U-BIOPRED	
	16 SME spin-offs	BTCure, DDMoRe, EHR4CR, eTRIKS, ELF, OncoTrack, OpenPHACTS, SAFE-T, StemBANCC, SUMMIT, Translocation	
	28 spin-off projects to continue research	COMPACT, EU-AIMS, EUPATI, EUROPAIN,	

Outcome	Activities involved (measures)	Projects generating outcomes	Potential Socio-economic impacts
		OrBiTo, SUMMIT, U-BIOPRED	
	17 project with impacts on regulatory pathways and practices	AETIONOMY, BioVacSafe, CHEM21, DDMoRe, EU-AIMS, EUPATI, EUROPAIN, MARCAR, OrBiTo, PharmaCog, PharmaTrain, PreDiCT-TB, PRO-Active, SafeSciMET, SAFE-T, U-BIOPRED, WEB-RADR	
Dissemination of Information	67 accessible project tools	AETIONOMY, BioVacSafe, BTCure, CHEM21, DDMoRe, DRIVE-AB, EBiSC, EHR4CR, ELF, EMIF, EMTRAIN, eTOX, eTRIKS, EUPATI, GetReal, IMIDIA, K4DD, NEWMEDS, OpenPHACTS, OrBiTo, PROactive, PROTECT, QUIC-CONCEPT, U-BIOPRED, WEB-RADR	
	>4,000 publications (56% open access)	All projects	
	>3,000 talks and conferences	All projects	
	>700 trainings, workshops, and PhD activities	All projects	

Abbreviations: PhD, doctorate of philosophy; SME, small- to medium-sized enterprise.

Conclusions

IMI1 provided the unique framework required to drive major and fundamental new innovations by enabling unique collaborative partnerships among public and private stakeholders.

Major challenges in life sciences, in particular within the medicines development process, are the scale of the investment required, the stepwise approach, very long development timelines and the successful involvement of relevant stakeholders.

The 44 IMI1 projects analysed in this report confirm that IMI projects are delivering on IMI's goal of helping to make concrete improvements to the medicines development process, in terms of reduction of resources, time and sometimes costs. The analysis also reinforces the success of IMI1 model in being a platform that builds long-lasting collaborative networks and in leveraging funding amongst different stakeholders, able to drive innovation in life science.

This report highlights how IMI1 projects are changing the manner in which new medicines are developed, improving the R&D infrastructure and streamlining R&D processes, involving collaborative networks, but also disseminating findings to develop a skilled workforce to put Europe at the forefront of scientific R&D.

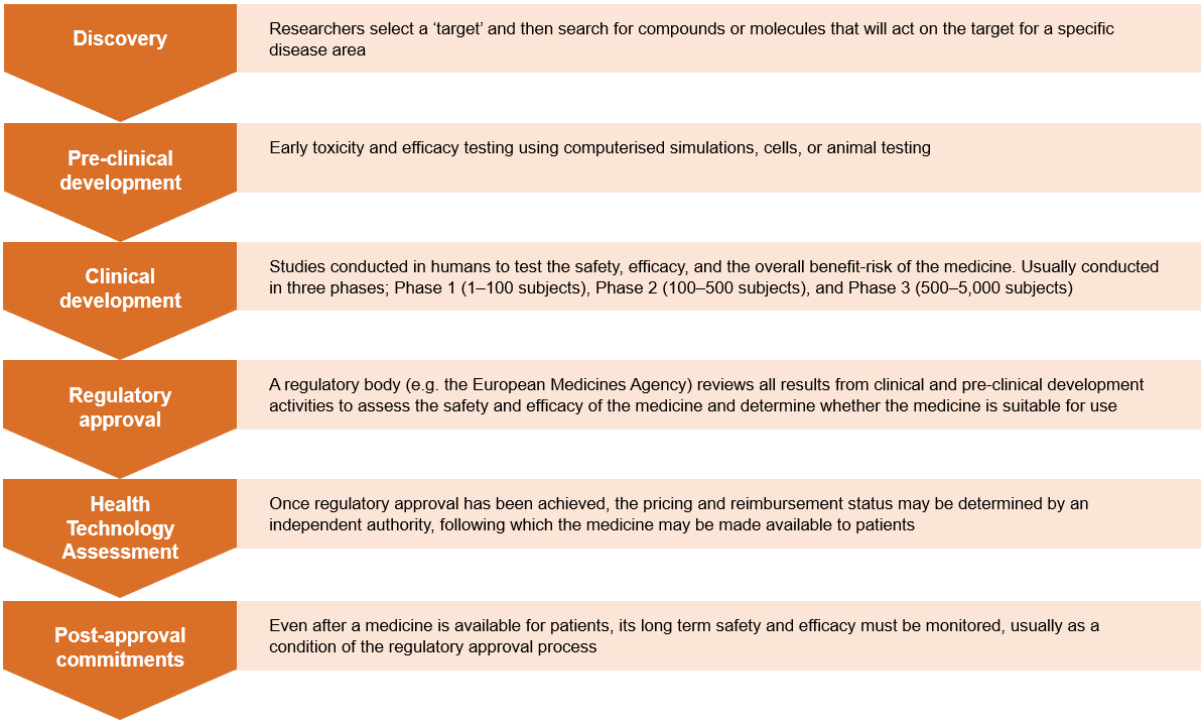
Have IMI projects outcomes translated in socio-economic impact for the society? Based on the information available today, we can affirm that IMI1 projects have produced key outcomes that have the potential to result in socio-economic impact. In some cases, the potential socio-economic benefits generated by the projects are more concrete and visible while, in other projects, the potential benefits are perceivable but not yet tangible. Such a dynamic is in line with the nature of IMI projects, which involve research in the healthcare space, multi-stakeholder partnerships and cross-sector collaboration. It requires time to produce innovative solutions, often happening in the later phases of the project lifecycle and very often even beyond the end date (after projects have been completed). As a result, the impact of IMI projects is expected to evolve with time. Therefore, a future analysis looking at the impact from a longer-term perspective is recommended.

1 INTRODUCTION

1.1 The medicine development process

The medicine development process is complex and involves multiple steps, from discovery of a drug target and then of a potential drug candidate, to pre-clinical and clinical development, regulatory approval, reimbursement, and, finally, fulfilling any post-approval commitments, such as efficacy and safety monitoring (Figure 1).

Figure 1: Medicines development process



The probability of successfully bringing a new medicine to market from pre-clinical research is low, estimated at 9%. Even for successful medicines, it takes approximately 10 years to get from pre-clinical research to launch. With this low probability of success and the substantial time required, it is unsurprising that the medicine development process involves significant resources; in 2018, the cost of developing a new medicine was approximately US$2 billion.[3]

There is potential to optimise the process in order to accelerate and make more efficient the development of new medicines, potentially resulting in reduced costs, faster and increased patient access, and improved value for healthcare payers and providers.

[3] CMR International 2019 Pharmaceutical R&D Factbook. Available at: https://discover.clarivate.com/2019CMRFactbook; CMR Global R&D Performance Metrics Programme. CMR International, a Clarivate Analytics Business.

1.2 Innovative Medicines Initiative (IMI)

The Innovative Medicines Initiative (IMI) was approved in December 2007 as public-private partnership between the European Union (EU) and the European Federation of Pharmaceutical Industries and Associations (EFPIA) and was renewed in 2014 as IMI2. It is the world's largest public-private partnership in health. IMI had €2 billion budget, while IMI2 has a total budget of up to €3.276 billion. This makes IMI total budget more than €5.3 billion. The first IMI projects began in 2009.

The IMI is working to improve health by accelerating the development of, and patient access to, innovative medicines, particularly where there is an unmet medical or social need. It does this by facilitating collaboration between the key players involved in healthcare research, including universities, the pharmaceutical and other industries, small- and medium-sized enterprises (SMEs), patient organisations, and medicines regulators.

1.3 IMI1 projects

In the first phase of the IMI (IMI1), 59 projects were launched of which 44 projects were completed at the time of the analysis of this report (February 2020). Overall, the budget for these projects was €1.24 billion, of which 44% (€544 million) was provided by the EU's research and innovation programme, 42% (€525 million) was provided by EFPIA companies, and 14% (€172 million) was provided by members of the consortium.

The overall goal of the IMI1 programme was to improve the efficiency and effectiveness of the drug development process, with the long-term aim that the pharmaceutical sector produces more effective and safer innovative medicines. The 44 IMI1 projects were designed to address specific 'bottlenecks' related to areas within the medicine development process:[4]

The original Strategic Research Agenda (SRA) for the IMI was released in 2008.In this first version of the SRA four pillars of research were identified:

1. Safety: bottlenecks related to predictivity in safety evaluation and benefit–risk assessment
2. Efficacy: bottlenecks related to predictive pharmacology, the identification and validation of biomarkers, patient recruitment, and benefit–risk assessment
3. Education & training: bottlenecks related to gaps in expertise in biomedical R&D knowledge and skills, enhancing Europe's biomedical education landscape to provide maximum support in revolutionising the conventional medicines discovery and development paradigm
4. Knowledge management: bottlenecks related to gaps in information technology, providing platforms to analyse large amounts of information in an integrated and predictive way

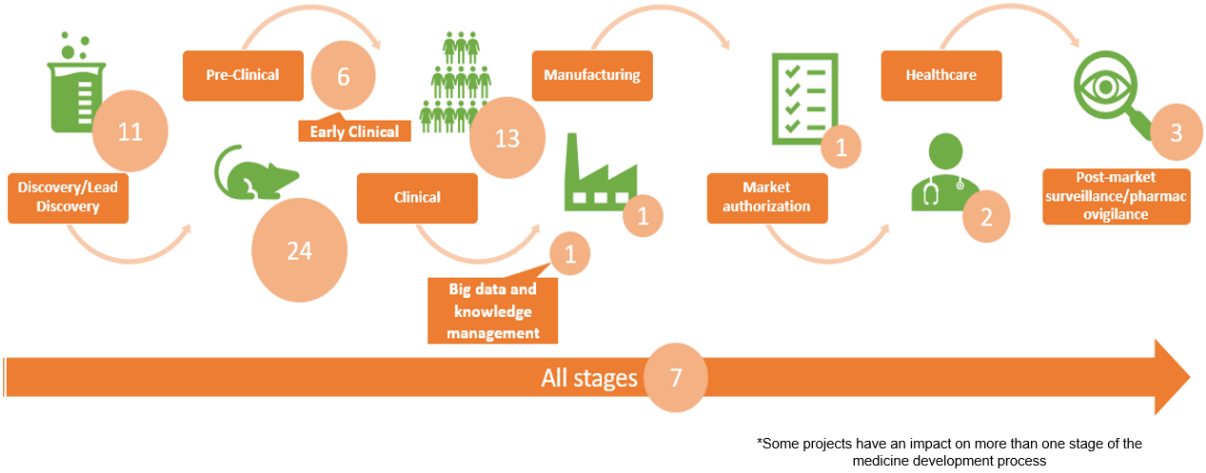
Each project was designed to address an identified 'bottleneck'. In most cases, the rationale for the project was that there was an area in which both public and private sectors were under-investing, but where a problem could be tackled by acting in concert. The projects were envisaged as a range of activities that would improve the conditions for medicine development in Europe, and remove barriers to the development of medicines and the growth of the sector. Based on the first successes of the

[4] IMI Socio-economic Impact Assessment Expert Group. Final Report. May 2016. Available at: https://www.imi.europa.eu/sites/default/files/uploads/documents/reference-documents/SocioeconomicImpactAssessment_FINALMay2016.pdf.

partnership the SRA was further expanded in 2011[5] to include eight new research priorities[6] in order to successfully tackle the challenges and opportunities created by recent major progress in science, and the significant changes in the pharmaceutical industry and healthcare systems in general. This report includes IMI1 projects derived from both versions of the SRA.

As shown in Figure 2, most of the scientific research conducted as part of IMI1 projects was focused on the early phases of the medicine development process. A small number of projects focused on later phases of the process.

Figure 2: Distribution of projects across the medicine development process

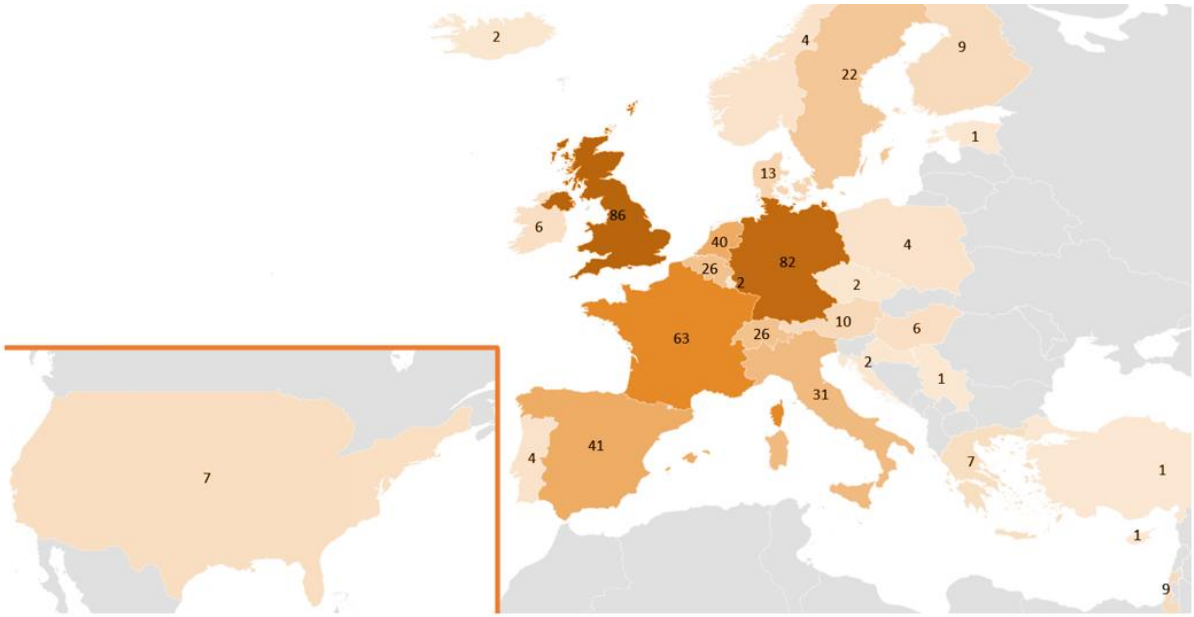


The IMI1 projects involved 49 EFPIA members, 351 research organisations, public bodies, and non-profit organisations, and 108 SMEs across 28 EU and non-EU countries (Figure 3). By bringing together experts from academia, SMEs, patient groups, and regulators in the IMI public-private partnership model, scientific breakthroughs were made in the IMI1 projects that would not have been possible without this collaboration.

[5] IMI Scientific Research Agenda. Revision 2011. Available at: https://www.imi.europa.eu/sites/default/files/uploads/documents/About-IMI/research-agenda/SRArevised2011.pdf.

[6] Pharmacogenetics and taxonomy of human diseases, rare diseases and stratified therapies, system approaches in drug research, pharmacological interactions at the molecular level, drug compound development, advanced formulations, stem cells for drug development and toxicity screening, and integration of imaging techniques into drug research.

Figure 3: Geographical coverage of the IMI1 partners



1.4 Impact assessment of IMI1 projects

While some IMI1 projects focused on specific health issues and disease areas and others focused on broader challenges in medicine development, overall, the projects generated several outcomes with potential short- and long-term socio-economic impacts. To assess this, four key outcome measures with the potential to generate a socioeconomic impact were defined. Project outcomes were then categorised according to these outcomes (Table 3).

Table 3: Outcome measures used to evaluate socio-economic impact of IMI1 projects

Outcome	Activities involved (Measures)	Potential socio-economic impacts
Innovation	Development of new biomarkers, *in vitro*, *in vivo*, and computerised models and assays, identification of new drug targets, candidates, and delivery systems, and improvements in manufacturing processes	**Increase robustness and reproducibility of research** **Reduce the time and cost of research**
Infrastructure and resources for further research	Development of new biobanks, cohorts, preclinical and clinical networks and databases, platforms, tools, and technologies (e.g. assays, software tools), and guidance, recommendations, and standards	**Improve manufacturing processes**
Structuring the European research area	Collaborations and partnerships within and between the pharmaceutical industry and academia, creation of spin-off companies to commercialise findings, engagement with regulatory bodies on project findings	**Support environmental sustainability** **Improve standards of care**
Dissemination of information	Publication and accessibility of project outputs, and education and training of the future European workforce for the pharmaceutical sector and the next generation of (academic) researchers.	**Consolidate and expand knowledge base**

To assess the impact of the IMI1 projects, a survey questionnaire was sent to each project coordinator. However, due to a low response rate (a response was received for eight of 44 projects), the impact assessment was based only on the public summary of project final reports that were available by February 2020. It should be noted that there may have been differences between project reports with regard to reporting of outcomes and that further information on outcomes may have become available following publication of the project reports. In addition in this report some terminology, “e.g. “potential”, validation/validated”, to define outputs has been used reflecting directly, without further elaboration, wording in the individual project reports. Since these terms may have been used differently, depending on the specific context of the project research, this generated some heterogeneity and has to be interpreted broadly.

2 OVERVIEW OF OUTCOMES AND SOCIO-ECONOMIC IMPACTS

2.1 Overview of projects

An overview of areas of focus and objectives of the 44 IMI1 projects analysed by this report is provided in Table 4. The projects cover several areas, including efficacy and safety assessment for specific disease areas, knowledge management, education and training, and R&D and manufacturing processes.

Further information about each specific project, including its objectives, outcomes, and socio-economic impacts is provided in the IMI1 projects assessments sections of this report (Section 3).

Table 4: Overview of IMI1 project areas and objectives

IMI1 project	Area(s)	Objective
ABIRISK†	Safety	Investigation of the clinical relevance of biopharmaceutical-associated immunogenicity in order to increase patient safety, and optimise drug development
AETIONOMY‡	Knowledge management, neurodegenerative diseases	Organisation of mechanistic knowledge about neurodegenerative diseases for the improvement of drug development and therapy
BioVacSafe†	Safety, vaccines	To develop predictive biomarkers for detection of vaccine reactogenicity, develop new ways to identify, classify and record adverse reactions to vaccine administration, and investigate how infectious diseases interact with vaccines
BTCURE†	Efficacy, inflammatory disorders	Development of future curative treatments for early intervention against rheumatoid arthritis
CHEM21‡	Manufacturing methods	To make sustainability improvements in three key synthetic areas: chemical technologies, biocatalysis and synthetic biology
Compact‡	Efficacy, targeted therapies	To explore the obstacles that biologic drugs need to overcome to get to their targets in the body
DDMoRe†	Knowledge management	Establishment of standards for common tools to enhance modelling and simulation technologies
DRIVE-AB‡	Knowledge management, antibiotics	To create, test, and validate new economic models to incentivise the discovery of new antibiotics
EBiSC‡	R&D processes	To create a repository of iPSC cell lines, providing sustainable, quality-assured lines for uptake by researchers across industry and academia
EHR4CR†	Knowledge management	Development of an electronic health records platform to support R&D projects on innovative medicines
EMIF‡	Knowledge management	To develop a common information framework of patient-level data that links up and facilitates access to diverse medical and research data sources, specifically focussing on Alzheimer's disease and obesity
EMTRAIN†	Education and training	Establishment of an European platform for higher education/training on the lifecycle of medicines
eTOX†	Safety, knowledge management	Development of novel strategies and software tools for better prediction of drug side-effects

IMI1 project	Area(s)	Objective
eTRIKS‡	Knowledge management	To create an open, sustainable research informatics and analytics platform for use by IMI (and other) projects with knowledge management needs
EU2P†	Education and training	Establishment of a European platform for education and training in pharmacovigilance and pharmacoepidemiology
EU-AIMS†	Efficacy, brain disorders, autism	To develop specific tools and methods and create a European network of specialised and skilled centres for diagnosis and running of clinical studies and trials in autism
ELF‡	R&D processes	To create a large library of compounds to be used for drug discovery starting points by pooling them from the propriety collections of industry, and complementing them with novel compounds synthesised by ELF chemistry partners
EUPATI†	Education and training	To improve understanding of pharmaceutical research and development among patients and the general public
EUROPAIN†	Efficacy, brain disorders, pain	To improve understanding of chronic pain mechanisms to aid the development of novel drugs
GetReal‡	Knowledge management	To develop new tools and resources for incorporating real-life data into drug development, to increase confidence in new medicines and accelerate patient access
IMIDIA†	Efficacy, metabolic disorders, diabetes	Generation of novel tools, biomarkers and fundamental knowledge on beta-cells to improve diabetes care
K4DD‡	R&D processes	To improve understanding of how potential drugs bind with their target and develop tools to facilitate study of drug-target interactions
MARCAR†	Safety, non-genotoxic carcinogenesis	Identification of new biomarkers for drug-induced tumour formation
MIP-DILI†	Safety	Identification of new assays and models, which can be used during drug discovery and early non-clinical development to support design, ranking and selection of candidates that have low propensity to cause drug-induced liver injury
NEWMEDS†	Efficacy, brain disorders, schizophrenia and depression	Development of biomarkers, tools and models to allow more targeted treatments for schizophrenia and depression
OncoTrack†	Efficacy, cancer	Identification of new models to predict effects and side effects of cancer treatments in defined groups of patients

IMI1 project	Area(s)	Objective
Open PHACTS†	Knowledge management	Development of an open access innovation platform dedicated to drug discovery using a semantic web approach
OrBiTo‡	Safety, efficacy	To enhance understanding of how orally-administered drugs are taken up from the gastrointestinal tract into the body, and apply this knowledge to create new tests and tools that will better predict the performance of these drugs in patients
PHARMA-COG†	Efficacy, brain disorders, Alzheimer's disease	Development and validation of new tools for testing of candidate drugs to treat Alzheimer's disease
PharmaTrain†	Education and training	Establishment of a European masters programme on pharmaceutical medicine and drug-development sciences
PRECISESADS‡	Efficacy, inflammatory autoimmune diseases	To collect data from people with inflammatory autoimmune diseases, specifically on the molecular causes of their disease and their clinical symptoms
PREDECT†	Efficacy, cancer	Development of new models for novel treatments of breast, prostate and lung cancer
PreDiCT-TB†	Efficacy, infectious diseases	Development of an integrated set of pre-clinical *in vitro* and *in vivo* models that provide critical data to design optimised clinical studies in patients with tuberculosis
PROactive†	Efficacy, respiratory disorders	Production of validated patient reported outcome questionnaires to measure physical activity in COPD as a research instrument
PROTECT†	Safety, pharmacovigilance	Enhancement of safety monitoring through new tools and methodologies to evaluate risk-benefit profiles of drugs
QUIC-CONCEPT†	Efficacy, cancer	Standardisation and qualification of imaging biomarkers for Phase 1 oncology clinical drug development
RAPP-ID†	Efficacy, infectious diseases	Development of a point-of-care test for rapid detection of microbes
SafeSciMET†	Education and training	Establishment of an European education and training programme in safety sciences for medicine
SAFE-T†	Safety	Identification of sensitive and predictive biomarkers of liver, kidney and vascular system damages for use in clinical drug development
StemBANCC‡	R&D processes	To generate human iPSCs as a more reliable research tool for *in vitro* disease modelling, toxicology testing, and screening potential new drug candidates

IMI1 project	Area(s)	Objective
SUMMIT†	Efficacy, metabolic disorders, diabetes	Identification of biomarkers to identify diabetic patients at high-risk for cardiovascular complications in diabetes
Translocation‡	Efficacy, knowledge management	To increase understanding of how small molecules (e.g. drugs) penetrate and are effluxed out of Gram-negative bacteria and to create and validate tools and assays that can be used to improve the design of new drugs to treat resistant Gram-negative infections. To facilitate data sharing, TRANSLOCATION created and populated a repository of antibacterial data and the framework to allow the analysis of that data to establish best practices for future antibacterial drug discovery efforts
U-BIOPRED†	Efficacy, respiratory disorders	Development and validation of a biomarker 'handprint' in asthma to predict disease severity and allow more personalised therapies
WEB-RADR‡	Knowledge management, education and training	Development of a mobile application which allows patients to directly report potential medicine side effects and also receive reliable information on their drugs

†Launched under the first SRA and therefore implemented the first SRA priorities. ‡Launched under the second SRA.
Abbreviations: COPD, chronic obstructive pulmonary syndrome; iPSC, induced pluripotent stem cells; R&D, research and development.

2.2 Project outcomes

Overall, the IMI1 projects have delivered a wide range of outcomes that provide a basis for socio-economic impact assessment. In some cases, further outcomes are anticipated; for example, some of the biomarkers developed as part of projects require further validation. As discussed in Section 1.4, to assess the potential socio-economic impacts of projects, four key outcome measures were defined and project outcomes and anticipated future outcomes were then categorised according to these outcomes. The socio-economic impacts associated with each of these outcome measures are summarised in Table 5 and discussed in the following sections.

As discussed in Section 1.4, it should be noted that outcomes were assessed based only on the public summary of project reports that were available by February 2020. It should be noted that there may have been differences between project reports with regard to reporting of outcomes and that further information on outcomes may have become available following publication of the project reports. In addition in this report some terminology, “e.g. “potential”, validation/validated”, to define outputs has been used reflecting directly, without further elaboration, wording in the individual project reports. Since these terms may have been used differently, depending on the specific context of the project research, this generated some heterogeneity and has to be interpreted broadly. The number of accessible project tools was assessed using the catalogue of project tools available on the IMI website, accessed in October 2020.[7]

Some socio-economic impacts of the projects will be observed in the short term, mainly those enhancing productivity or innovations within existing technologies, services and products (incremental innovations). For example, creating new procedures or databases, streamlining processes across organisations, dissemination of knowledge, or providing training to make European research more competitive may be considered incremental yet important innovations with a short-term impact. In addition to the short-term socio-economic impact, some project outcomes may have longer-term socio-economic impacts that will be realised through further research leading to radical innovation.

[7] https://www.imi.europa.eu/projects-results/catalogue-project-tools.

Table 5: Summary of IMI1 project outcomes

Outcome	Activities generated to date†	Anticipated future activities	Projects generating outcomes	Socio-economic impact of outcomes or anticipated future outcomes
Innovation	476 validated or standardised biomarkers	2,387 potential biomarkers	ABIRISK, AETIONOMY, BioVacSafe, BTCure, EMIF, EU-AIMS, EUROPAIN, IMIDIA, MARCAR, MIP-DILI, NEWMEDS, OncoTrack, Pharma-Cog, PRECISESADS, PreDiCT-TB, QUIC-CONCEPT, RAPP-ID, SAFE-T, SUMMIT, U-BIOPRED	
	616 validated *in vitro*, *in vivo* and *in silico*/computerised models	168 potential *in vitro*, *in vivo* and *in silico*/computerised models	ABIRISK, AETIONOMY, BioVacSafe, BTCure, COMPACT, DDMoRe, EBiSC, EMIF, eTOX, EU-AIMS, ELF, EUROPAIN, IMIDIA, MARCAR, MIP-DILI, NEWMEDS, OncoTrack, OrBiTo, PharmaCog, PRECISESADS, PREDECT, PreDiCT-TB, RAPP-ID, SUMMIT, U-BIOPRED	
	–	238 potential drug targets and delivery systems	BTCure, COMPACT, EBiSC, EMIF, EU-AIMS, ELF, EUROPAIN, IMIDIA, MARCAR, MIP-DILI, NEWMEDS, PRECISESADS, SUMMIT	
	–	3 potential manufacturing processes	CHEM21	

Outcome	Activities generated to date†	Anticipated future activities	Projects generating outcomes	Socio-economic impact of outcomes or anticipated future outcomes
Infrastructure and resources for further research	167 biobanks, cohorts and databases	–	ABIRISK, AETIONOMY, BioVacSafe, BTCure. COMPACT, DRIVE-AB, EBiSC, EMIF, EMTRAIN, eTOX, eTRIKS, EU-AIMS, ELF, EUPATI, EUROPAIN, GetReal, IMIDIA, K4DD, MARCAR, MIP-DILI, NEWMEDS, OncoTrack, OpenPHACTS, OrBiTo, PharmaCog, PRECISESADS, PREDECT, PreDiCT-TB, PRO-Active, PROTECT, QUIC-CONCEPT, RAPP-ID, SAFE-T, StemBANCC, SUMMIT, Translocation, U-BIOPRED	
	438 validated platforms, assays, software tools and technologies	155 potential platforms, assays, software tools and technologies	ABIRISK, AETIONOMY, BioVacSafe, BTCure, CHEM21, COMPACT, DDMoRe, DRIVE-AB, EBiSC, EMIF, eTOX, eTRIKS, EU2P, EU-AIMS, ELF, EUROPAIN, GetReal, IMIDIA, K4DD, MIP-DILI, NEWMEDS, OncoTrack, OpenPHACTS, OrBiTo, PharmaCog, PRECISESADS, PREDECT, PreDiCT-TB, PROTECT, QUIC-CONCEPT, RAPP-ID, SAFE-T, SUMMIT, Translocation, U-BIOPRED, WEB-RADR	
	186 published/validated guidance, best practice recommendations and standard operating procedures	8 potential guidance, best practice recommendations and standard operating procedures	ABIRISK, AETIONOMY, BioVacSafe, BTCure, CHEM21, COMPACT, DDMoRe, EBiSC, EHR4CR, EMTRAIN, eTOX, eTRIKS, EU2P, EU-AIMS, ELF, EUPATI, EUROPAIN, IMIDIA, MARCAR, MIP-DILI,	

Outcome	Activities generated to date†	Anticipated future activities	Projects generating outcomes	Socio-economic impact of outcomes or anticipated future outcomes
			NEWMEDS, OncoTrack, OpenPHACTS, OrBiTo, PharmaCog, PharmaTrain, PRECISESADS, PREDECT, PreDiCT-TB, PRO-Active, PROTECT, SAFE-T, StemBANCC, SUMMIT, U-BIOPRED, WEB-RADR	
Structuring the European research area	213 memoranda of understanding and material transfer agreements signed	–	AETIONOMY, BioVacSafe, BTCure, CHEM21, COMPACT, DDMoRe, DRIVE-AB, EBiSC, eTOX, EU2P, EU-AIMS, ELF, EUPATI, IMIDIA, K4DD, MARCAR, OncoTrack, OpenPHACTS, PharmaCog, PRECISESADS, PREDECT, PreDiCT-TB, PRO-Active, QUIC-CONCEPT, SAFE-T, StemBANCC, SUMMIT, U-BIOPRED	
	16 SME spin-offs	–	BTCure, DDMoRe, EHR4CR, eTRIKS, ELF, OncoTrack, OpenPHACTS, SAFE-T, StemBANCC, SUMMIT, Translocation	
	28 spin-off projects to continue research	–	COMPACT, EU-AIMS, EUPATI, EUROPAIN, OrBiTo, SUMMIT, U-BIOPRED	
	17 project with impacts on regulatory pathways and practices		AETIONOMY, BioVacSafe, CHEM21, DDMoRe, EU-AIMS, EUPATI, EUROPAIN, MARCAR, OrBiTo, PharmaCog, PharmaTrain, PreDiCT-	

Outcome	Activities generated to date†	Anticipated future activities	Projects generating outcomes	Socio-economic impact of outcomes or anticipated future outcomes
			TB, PRO-Active, SafeSciMET, SAFE-T, U-BIOPRED, WEB-RADR	
Dissemination of Information	67 accessible project tools	–	AETIONOMY, BioVacSafe, BTCure, CHEM21, DDMoRe, DRIVE-AB, EBiSC, EHR4CR, ELF, EMIF, EMTRAIN, eTOX, eTRIKS, EUPATI, GetReal, IMIDIA, K4DD, NEWMEDS, OpenPHACTS, OrBiTo, PROactive, PROTECT, QUIC-CONCEPT, U-BIOPRED, WEB-RADR	
	>4,000 publications (56% open access)	–	All projects	
	>3,000 talks and conferences	–	All projects	
	>700 trainings, workshops, and PhD activities	–	All projects	

†Definitions used for validated and standardised may have differed between project reports. The outcomes described as validated or standardised are therefore based on the language used in each individual project report and do not necessarily reflect single, specific definitions for these terms.
Abbreviations: PhD, doctorate of philosophy.

2.2.1 Innovation

- The IMI1 projects have delivered several innovations with a direct impact on the medicine development process, including:
  - Development and validation of biomarkers and *in vitro*, *in vivo*, and computerised models and assays, which may be used as part of pre-clinical and clinical research to increase the reproducibility and robustness of results and accelerate the testing of potential new, innovative medicines
  - Identification of new potential drug targets, candidates, and delivery systems, which may result in the development of new, innovative treatments or help to optimise their delivery
  - Improvements in manufacturing processes to reduce costs and resource use, as well as reducing their environment impact

Biomarker development

Biomarkers have been developed, and some validated or standardised,[8] as part of several IMI1 projects across a range of areas, including biologic immunogenicity (ABIRISK), neurodegenerative diseases (AETIONOMY, EMIF and PharmaCog), vaccines (BioVacSafe), rheumatoid arthritis (BTCure), autism disorders (EU-AIMS), neuropathic pain (EUROPAIN) diabetes and its complications (EMIF, IMIDIA, and SUMMIT), prediction of adverse effects in potential drug candidates (MARCAR and MIP-DILI), schizophrenia (NEWMEDS), oncology (OncoTrack and QUIC-CONCEPT), systemic autoimmune diseases (PRECISESADS), tuberculosis (PreDiCT-TB), infectious diseases (RAPP-ID), drug-induced organ damage (SAFE-T), and asthma (U-BIOPRED).

The development of biomarkers during the IMI1 projects is likely to accelerate the development of new vaccines and medicines and improve patient outcomes through:

- Providing guidance in the search for drug targets through improved understanding of disease processes
- Allowing early identification of drug compounds that should not be pursued due to potential safety issues
- Allowing reduction, refinement, or replacement of experimental animal use
- Allowing better prediction of the likely efficacy of drugs early in the development process, potentially reducing clinical trial failure rate and improving cost and time efficiency in the development of new drugs
- Allowing earlier diagnosis of patients to allow earlier treatment
- Allowing stratification of patient populations to allow targeting of novel treatments to patients who are most likely to benefit from them
- Use as part of surrogate endpoints in clinical trials, potentially reducing the length of clinical trials needed to assess the efficacy of new medicines

In vitro, in vivo, and in silico/computerised models

New *in vitro* models have been developed, and some validated, as part of IMI1 projects; examples include projects investigating rheumatoid arthritis (BTCure), drug delivery systems (COMPACT), prediction of drug-induced liver injury in potential drug candidates (MIP-DILI), colorectal cancer (OncoTrack), absorption qualities of drug molecules in the GI tract (OrBiTo), tumour architecture

[8] Definitions used for validated and standardised may have differed between project reports. The outcomes described as validated or standardised are therefore based on the language used in each individual project report and do not necessarily reflect single, specific definitions for these terms.

(PREDECT), and drug efficacy in tuberculosis (PreDiCT-TB). In addition, *in vivo* animal models have been developed, and some validated, for example, in the study of vaccine safety (BioVacSafe), rheumatoid arthritis (BTCure), drug delivery systems (COMPACT), autism disorders (EU-AIMS), neuropathic pain (EUROPAIN), prediction of adverse effects in potential drug candidates (MARCAR and MIP-DILI), prediction of drug efficacy in schizophrenia (NEWMEDS), Alzheimer's disease (PharmaCog), and tuberculosis (PreDiCT-TB), colorectal cancer (OncoTrack), tumour function (PREDECT) and prediction of the development of complications associated with diabetes (SUMMIT). Computerised models have also been developed as part of some projects, such as eTOX and OncoTrack, which explored potential toxicologies and side effects of hypothetical compounds (eTOX) and colorectal cancer (OncoTrack).

Development of these models is likely to enhance pre-clinical research, providing insights into specific disease areas and allowing better prediction of the efficacy and possible safety issues with potential new drugs. Reproducible and robust testing models are critical for successful translation of research into clinical practice in the form of new treatments and knowledge that actually reach the patients or populations The ability to predict the *in vivo* behaviour of drugs from *in vitro* studies may save researchers time and resources, ensuring that only the most promising drugs and their formulations reach the animal/human testing stage. More powerful and insightful animal testing methods are also likely to reduce the need for re-testing on animals, and subjecting human trial participants to ineffective or harmful drugs. In addition, the models developed have been critical to the development of biomarkers in some of the IMI1 projects and may be valuable resources for further research.

Some of the models developed as part of the IMI1 projects have wider implications for future modelling methods. For example:

- In the MARCAR project, human receptors for a drug known to cause cancer in mice but not in humans were inserted into the body of a mouse, creating a 'humanised mouse' model, which may be useful for future research
- In the PRECISESADS project, molecular profiling of a patient cohort was conducted in parallel with profiling of commonly-used pre-clinical animal models to provide insights into the translatability of pathology results from animal testing to clinical testing of humans, facilitating more appropriate model selection for further research

New drug targets and delivery systems

While many of the IMI1 projects have paved the way for the development of potential new treatments through their impact on the medicine development process, potential new drug targets and delivery systems have also been identified in many of the projects, for example:

- In BTCure, five potential drug targets (i.e. molecules with which drugs may interact to inhibit a disease) for rheumatoid arthritis were discovered, two of which have been fully validated. Further study and validation of these biological targets could allow new families of drug compounds to be screened, expanding opportunities for more effective treatment for rheumatoid arthritis. In addition, seven molecules have been identified as potential candidates for further development into novel drugs for rheumatoid arthritis, with another potential candidate requiring further confirmatory studies. These molecules provide a clear path for further validation and optimisation.
- The delivery of the molecule to its specific target is one of the main bottlenecks in biopharmaceutical research. Eleven novel drug delivery systems evaluated as part of the COMPACT project have been progressed to *in vivo* studies. If successful, these delivery systems may allow oral delivery of peptides (e.g. insulin), delivery across blood-brain barrier, delivery across air-lung barrier, and dermal delivery of proteins. Patent protection is being sought for two of these formulations.
- In ELF, a library of over 500,000 compounds was created from the propriety collections of the pharmaceutical industry and novel compounds synthesised by ELF chemistry partners. The library was opened to third parties from European academia and small-medium biotech companies in a newly set up screening centre, where researchers received a 'hit list' of compounds and advice on further research. As of August 2018, the work had generated 109 hit lists, 5,649 qualified hit

molecules (delivered to public and private target owners), three drug discovery programmes in the lead optimisation phase and five patents on ELF compounds.

In addition to the new drug targets and delivery systems explored in IMI1 projects, a novel 'telecoaching' intervention, involving a step counter and smartphone interface, was investigated as a method to improve patient activity levels in patients with COPD in the PROactive study. Despite difficulty in delivering the intervention to certain patients, a small-scale study found a meaningful increase in step count by patients receiving the intervention. Further development and validation of this telecoaching method could result in more widespread implementation, improving the way COPD is managed in clinical settings.

Manufacturing processes

The IMI1 projects have also contributed to the development of improved manufacturing processes, which may help to reduce the cost and resource use associated with pharmaceutical manufacturing, but may also reduce its environmental impact. For example, in the CHEM21 project, the following innovations to manufacturing processes were made:

- A one-step continuous flow method was developed and successfully applied to the synthesis of flucytosine (an essential antifungal medicine). The method involves just one selective reaction, rather than four, resulting in a substantial reduction in energy and raw material use. It also produces less waste than conventional techniques and does not use toxic precious metals for catalysis, which are limited in supply and difficult to recycle. The flow chemistry method was investigated for use in several additional contexts and a large number of new, cleaner catalysts were developed and supplied to EFPIA members for use in development.
- New classes of enzyme biocatalysts were developed, refined, and made available to EFPIA members for in-house evaluation, while existing classes were further optimised. New methods integrating biocatalysis with advanced chemical procedures also demonstrated the potential of biocatalysis for achieving extremely high selectivity in reaction outcomes. In the long term, greater uptake of methods resulting from this work will help to reduce bottlenecks and make chemical reactions within drug manufacturing shorter, less toxic (greener solvents) and less wasteful.
- Synthetic biology (the modification of a microorganism's biochemistry to tailor its metabolism towards the production of specific molecules) was used to establish a 'toolbox' of concepts, methodologies, and biological material for future work. Synthetic biology techniques simplify reactions by reducing the need the multi-step synthesis. Uptake of these techniques will therefore shorten reaction times, whilst also allowing for the use of greener solvents and circumventing the need for harsh reaction conditions and toxic chemicals.

2.2.2 Infrastructure and resources for further research

- The infrastructure that has been put in place for further research as part of the IMI1 projects may facilitate and accelerate further innovation
- Platforms, tools, and technologies are available for further collaborative research and data sharing
- The guidance and recommendations resulting from IMI1 projects may help to improve and standardise the drug development process, potentially accelerating the development of and reducing the cost of developing innovative new drugs

Biobanks, cohorts, and databases

Biobanks, cohorts and databases were created as part of many of the IMI1 projects and may facilitate the use of the data collected during the projects to support further progress in research. Some examples are:

- **Biobanks:** Biobanks were created as part of several IMI1 projects, including MARCAR and U-BIOPRED, which focused on drug-induced tumour formation and severe asthma, respectively. The biobank created in MARCAR comprised tissue and biofluids from rodent studies that could be leveraged by future carcinogenesis research programmes. In U-BIOPRED, biological samples were taken from adults and children with severe asthma to facilitate the clinical investigation of new treatment options for this condition.
- **Cohorts:** The ABIRISK project, which focused on biologic immunogenicity, provides an example of cohort creation. A major achievement of ABIRISK was the creation of the first large prospective cohorts in the study of biologic immunogenicity, which included >700 patients suffering from multiple sclerosis, rheumatoid arthritis, juvenile idiopathic arthritis, intestinal bowel diseases, or haemophilia A, recruited from >70 medical centres across Europe. For the first time ever, this allowed scientists to analyse five different diseases at the same time, partially treated with the same biologics. As a result, best practices for measuring the immunogenicity of therapeutic molecules were established.
- **Databases:** Databases were created across multiple areas, for example, including biologic immunogenicity (ABIRISK), neurodegenerative diseases (AETIONOMY), vaccine development (BioVacSafe), rheumatoid arthritis (BTCure), drug delivery systems (COMPACT), diabetes and its complications (EMIF and IMIDIA), autism (EU-AIMS), neuropathic pain (EUROPAIN), toxicology (eTOX), bioactive molecules (K4DD), drug-induced organ damage (MIP-DILI and SAFE-T), oncology (OncoTrack and QUIC-CONCEPT), autoimmune diseases (PRECISESADS), tumour function (PREDECT), tuberculosis (PreDiCT-TB), stem cell research (STEMBANCC), and anti-microbial resistance (TRANSLOCATION). Some of the databases developed during projects are already being used as part of further research. For example, in EU-AIMS, a comprehensive autism database was created and is already being used to identify new ways for patients with autism to be stratified in clinical trials, which may aid the development of more personalised treatment for autism disorders. In the long term, this may help to reduce the burden of autism disorders on individuals, families, and healthcare systems.

Many of the findings from the IMI1 projects have been made widely available to researchers around the world. In addition to the biobanks, cohorts, and databases created, platforms have been created as part of some of the projects in order to facilitate access to data from the projects. For example, the eTRIKS public platform provides open access to around 200 public domain clinical studies, covering a range of disease areas. The platform facilitates re-use and further analysis of data, potentially advancing subsequent research.

Platforms, tools, and technologies for collaborative research and data sharing

Tools and technologies were developed during the IMI1 projects, in the form of software tools and platforms used for data analysis and sharing, tools and techniques used in pre-clinical and clinical research, tools aimed at improving trial design and drug candidate selection, and a mobile app for tracking adverse reactions to medicines:

- **Data analysis tools:** Data analysis tools and procedures have been established as part of IMI1 projects, some of which may be used as part of further research. For example, in the BioVacSafe project, the R statistical language used was saved as executable documents, making is easy to reproduce the analysis procedures used. Similarly, much of the code used for the development modelling and simulation tools in PreDiCT-TB was made publicly available within the DDMoRe online repository, and modelling and simulation tools developed in the K4DD project are available as a web-based toolbox. As part of the GetReal project, an openly available online tool, the Aggregate Data Drug Information System (ADDIS), was developed to allow users to import or manually input clinical trial data into the structured ADDIS database and use the platform's statistical package to conduct meta-analyses. A suite of software tools for the analysis of rodent behaviour that was developed and validated during the EU-AIMS project is also available to purchase.
- **Knowledge-sharing platforms:** The primary output of the OpenPHACTS project was the OpenPHACTS Discovery Platform, a publicly available, standardised, open-source and open-access platform containing integrated data from 13 data sources. Researchers can use the platform to find information on chemical compounds, targets, biological pathways, diseases and

more, circumventing the need for lengthy data integration from disparate sources by individual companies or research groups. By project completion, the platform was used by several groups in academia and industry, as well as several other IMI projects. The DDMoRe platform was also developed as part of the DDMoRe project and provides a free, open online repository for uploading, storing, and accessing a variety of computational models spanning a range of pharmacometric and disease areas. The repository enables open access to valuable shared knowledge, allowing expertise to be pooled and exploited and making model-informed drug development more efficient, particularly when a model in the library can be used to inform the development of another.

- **New tools for pre-clinical and clinical trials:** In the OrBiTo project, tools were developed and standardised to measure the physical and chemical properties of drug candidates, such as dissolution and solubility, in order to aid better prediction of absorption in the gastrointestinal tract. The tools were largely validated within EFPIA partner laboratories, ensuring industrial applicability. They allow researchers to better understand the properties of drug compounds and to select candidates with suitable properties, potentially reducing failure rates and testing of unsafe drugs on animals. Similarly, a tool developed during the TRANSLOCATION project uses analysis of porin structures to help to predict the ability of a molecule or drug to penetrate the bacterial membrane, potentially saving resources associated with the use of bacterial models to achieve this outcome. As part of the SUMMIT project, a method was developed to standardise optical coherence tomography measurements in multi-centre trials and clinical practice. This new method was validated through several clinical studies, is the first that measures the shift in ultrasound centre frequency to assess atherosclerosis plaque components, and can be used to identify patients with plaques and monitor response to interventions using non-invasive techniques.
- **Tools for improvement of trial design:** An online tool (DupCheck) was developed as part of the NEWMEDS project, which allows clinical trial researchers to check whether participant patients are enrolled twice in the same trial, at a different site, or in another trial. The tool can be used across different sponsors and therapeutic areas and may reduce the risk of harm and false outcomes caused by duplicate enrolments. Two tools aimed at trial design were also developed during the GetReal project. The Sure-Real tool, which contains a data repository and study design models, enables assessment of how real-world evidence can be incorporated into drug development strategies. The PragMagic tool is an interactive online tool that supports researchers in the design and conduct of pragmatic trials (clinical trials that evaluate drug efficacy in real-world healthcare practice). It provides method reviews, case studies, guidance, and recommendations on trial design to maximise generalisability to routine practice.
- **Mobile app development:** A major achievement of the WEB-RADR project was the launch of a mobile app in several countries, which allowed easier and more frequent reporting of adverse reactions to drugs by patients and health care professionals than more traditional methods. The app also provides up-to-date safety information for medicines and facilitates the recording and tracking of adverse events for the pharmaceutical industry and pharmacovigilance entities.

Guidance, recommendations, and standards

Several of the IMI1 projects generated guidance, recommendations, and standards in areas including, for example: the environmental impact of solvents used in manufacturing (CHEM21), histological evaluation in models of rheumatoid arthritis (BTCure), development, description, and storing of models (DDMoRe), routine banking, characterisation, and distribution of iPSC cell lines (EBiSC), use of health data for research (EHR4CR), terminology used in pre-clinical studies (eTOX), use of real-world evidence in drug development (GetReal), protocols for use of magnetic resonance imaging and other technologies (MARCAR and PharmaCog 5), efficiency of clinical trial conduct (NEWMEDS), *in silico* modelling methods (OrBiTo), clinical trials for autoimmune diseases (PRECISESADS), standard operating procedures for precision-cut tumour slicing (PREDECT), assessment of activity monitors in trials for COPD (PROactive), methods used in pharmacovigilance and pharmacoepidemiology (PROTECT), working with pluripotent stem cells (StemBANCC), diagnostic criteria for severe asthma (U-BIOPRED), and use of mobile applications and social media data for pharmacovigilance (WEB-RADR).

The DRIVE-AB project was conducted specifically to provide a set of recommendations for policy makers on how to incentivise the development of new antibiotics in order to mitigate the threat of

antimicrobial resistance to currently available antibiotics. The guidance is drawing attention from governments, policy makers, and public health bodies from around the world and, of the 12 recommendations, six are now being fully or partially implemented. It is anticipated that the influence of the guidance will grow, with more and more policy makers adopting or taking inspiration from the recommendations.

The guidance, recommendations, and standards developed during the IMI1 projects may help to improve and standardise the drug development process, potentially accelerating the development of and reducing the cost of developing innovative new drugs. As discussed in Section 2.2.3, some of the guidance, recommendations, and standards developed as part of the IMI1 projects have been adopted or are under review by regulatory authorities, demonstrating their potential to influence practices in the drug development process.

2.2.3 Structuring the European research area

- IMI1 projects have resulted in ongoing collaborations and partnerships within and between the pharmaceutical industry and academia, as well as with other stakeholders
  - Effective collaborations can minimise duplication of work at different organisations and bring together the resources needed for innovation
- Spin-off companies have been created to commercialise the output of some of the IMI1 projects
  - These companies help to make the outputs of the IMI1 projects available for further use but also have wider societal benefits in Europe by providing employment and promoting European competitiveness in the pharmaceutical industry
- Engagement with regulatory bodies has helped to establish new regulatory guidance to improve and standardise the medicine development process

Collaborations and partnerships

IMI1 projects have demonstrated the success of the PPP model – by bringing together experts from industry, academia, small and medium-sized enterprises (SMEs), patient groups, and regulators, to work together. IMI1 projects have provided a platform for effective collaboration within the pharmaceutical industry, between industry and academia, and extending to healthcare payers, patient groups, and regulators. Among other outcomes, the projects have enabled collaborators to establish and use standards as part of the drug development process, thereby minimising duplication of effort in different organisations. Collaboration has continued, both formally and informally, following completion of the IMI1 projects, building on the networks created during the projects.

Standards that may help to minimise duplication of work have been established as part of projects such as BioVacSafe for vaccine development, BTCure for rheumatoid arthritis, and EU-AIMS for autism disorders, in collaboration with regulators. In some projects, memoranda of understanding have been signed to accommodate collaboration and knowledge sharing between stakeholders. For example, memoranda of understanding in the MARCAR project allowed collaboration between five pharmaceutical companies, seven universities and non-profit research institutions, and one SME. A memorandum of understanding covering the handling of intellectual property, confidentiality, and the transfer of knowledge and materials was also signed to allow collaboration between IMIDIA and SUMMIT, concurrent IMI1 projects focusing on diabetes. The memorandum of understanding enabled efficient and thorough collaboration between the two projects, enhancing the work of each through shared knowledge and resources. To allow development of ToxPHACTS software, an internal IMI memorandum of understanding was also signed between the eTOX and OpenPHACTS consortia, and over 50 were signed with associated partners. The memoranda of understanding and material

transfer agreements signed throughout the projects have facilitated and promoted the sharing of ideas, data and technology, and created lasting ties between project partners and associated organisations.

Not-for-profit foundations have also been established by the project partners of DDMoRe and OpenPHACTS projects in order to maintain the frameworks and infrastructure developed during these projects. Both foundations are supported by industrial and academic partners, facilitating ongoing collaboration and exchange of ideas.

Spin-off companies and projects

Another important outcome of the IMI1 projects is the creation of spin-off companies for the commercialisation of project findings. For example, in the ELF project, seven large pharmaceutical companies pooled compound collections and opened them up to academia and SMEs searching for drug discovery starting points. A library of over 500,000 compounds was developed and the screening results of the project have resulted in the creation of two SMEs, developing treatments for neurodegeneration (Keapstone Therapeutics) and type 2 diabetes (ScandiCure). Two spin-off companies have also been created as a result of the OncoTrack project to commercialise a technology used in the culture of organoids (Cellular Phenomics & Oncology Berlin-Buch GmbH) and project outputs related to diagnostic procedures. Other spin-off companies include Mediscienta, which was created to prepare for effective commercialisation of the imaging technology developed during the SUMMIT project, and Phenaris, which was created to develop software (ToxPHACTS) to combine K4DD and eTOX project outputs with the OpenPHACTS discovery platform in order to improve prediction of drug toxicology to allow reduction of animal testing on toxic drug candidates.

In addition to the spin-off companies established to commercialise project findings, the IMI1 projects have inspired the creation of other spin-off companies established by IMI1 researchers to fulfil market needs identified during projects. For example, while working on the eTRIKS project, researchers at the University of Luxembourg realised that there was high demand in the pharmaceutical sector for cleaning, filtering, hosting, and standardising data. As a result, they created Information Technology for Translational Medicine (ITTM), a small data management consultancy that provides a range of data handling services and contributes to the maintenance of the eTRIKS platform.

The establishment of new companies ensures continuation of the development and implementation of innovative technologies, supporting and enhancing scientific research in Europe through the provision of novel R&D services. In addition, the creation of SMEs has wider societal benefits, providing employment and promoting European competitiveness in the pharmaceutical industry.

As well as spin-off companies, spin-off projects have also resulted from several of the IMI1 projects to build on their findings. As an example, following COMPACT, a project has been planned as part of the second phase of the IMI (IMI2), with the objective of characterising the blood-brain-barrier and identification of new therapeutic or drug delivery targets. Data from COMPACT may be used as part of this project.

Engagement with regulatory bodies

Some of the IMI1 projects have involved engagement with regulatory bodies on issues including outcome measures suitable for use in drug development, improvement of testing strategies for new drug candidates, patient involvement across the drug development process, environmental issues associated with medicine manufacturing processes, and good practices for the use of new technologies to gather pharmacovigilance information. Examples include:

- **Outcome measures suitable for use in drug development:** The development of outcome measures and markers accepted by regulatory authorities as suitable for use in drug development has the potential to improve the drug development process through providing new standard outcome measures for use in clinical trials, which may help to reduce clinical trial length and identify more drug candidates that should be abandoned earlier in the medicine development process. In 2018, the EMA published a document detailing the way in which the tools developed

during the PROactive project can be used to measure physical activity in clinical trials for COPD interventions. In addition, as part of the EUROPAIN project, two new methodologies for the quantitative measurement of pain in early-stage clinical trials are under evaluation by the EMA and, if successfully validated, will provide reliable techniques to be used in future research into analgesics. Engagement with regulatory authorities regarding the outputs of the PreDiCT-TB project ensured that these outputs were well-disseminated and helped to inform regulatory policy around clinical trials in tuberculosis, with EMA qualification advice relating to project outcomes in progress at time of project completion. The SAFE-T project also involved engagement with regulatory authorities, with briefing book packages submitted to both the EMA and FDA to support qualification of the biomarkers developed for the prediction, detection, and monitoring of drug-induced organ damage. Letters of support have since been issued by the EMA and FDA, which indicate the potential of the new biomarkers for use in drug development.

- **Improvement of pre-clinical carcinogenicity testing strategies for new drug candidates:** The MARCAR project has resulted in discussions between regulators and stakeholders from the pharmaceutical industry and academia on the improvement of pre-clinical carcinogenicity testing strategies and proposed changes to the ICH S1 guidance on Rodent Carcinogenicity Testing of Pharmaceuticals (Regulatory Notice Document 8th August 2013). The goal of these potential changes is to introduce a more comprehensive and integrated approach to address the risk of human carcinogenicity of small molecule pharmaceuticals, and to define conditions under which 2-year rat carcinogenicity studies add value to that assessment. This could lead to fewer or no animal carcinogenicity studies in specific circumstances, resulting in reductions in the time and cost of some research.
- **Patient involvement across the drug development process:** As part of the EUPATI project, guidance documents were published, supporting the existing EMA framework for interactions between patients and consumer organisations. The documents cover patient interaction with regulatory agencies, health technology assessment (HTA) bodies, ethics committees and pharmaceutical companies. These documents provide a basis for more effective and consistent patient involvement across the entire drug development process and may help to encourage greater involvement of patients in drug development.
- **Environmental issues associated with medicine manufacturing processes:** Although the CHEM21 project had minimal direct impact on regulatory practices, engagement with regulators resulted in the development of guidance for further research around the green chemistry landscape and ensured that the work of the consortium was targeted as effectively as possible within the regulatory framework.
- **Good practices for the use of new technologies to gather pharmacovigilance information:** As part of the WEB-RADR project, several recommendations were made on the use mobile devices and social media to capture pharmacovigilance information. Adoption of these recommendations as part of the regulatory framework has resulted in the EU becoming a leader in this area.

Engagement with regulatory bodies has meant that the findings from some of the IMI1 projects have contributed to changes in the regulatory guidance for specific areas or diseases. In some cases, regulatory authorities have accepted technologies and measures that can reduce the time taken for and cost of pre-clinical and clinical testing of new medicines, ultimately helping to reduce the time and cost taken to bring new medicines to market, allowing earlier access to these medicines for patients.

2.2.4 Dissemination of information

- A catalogue of tools developed during projects is available and many of these tools can be used free of charge
- Publication of findings from the IMI1 projects facilitates the application of learnings from these projects to further research
- Education and training outputs of the IMI1 projects have helped to develop highly-skilled current and future workforces and facilitate movement of these workforces between organisations
    - Developing a skilled and mobile workforce has wider societal benefits and will help to position Europe as a hub for research in the long term

Availability of project tools

As discussed in Section 2.2.2, platforms, tools, and technologies have been developed for collaborative research and data sharing. As of October 2020, the IMI website provides links to project tools from IMI projects,[9] including 67 tools from IMI projects covered in this report.

Publications

Collectively, the IMI1 projects delivered approximately 4,000 high-quality scientific research publications. These publications had an average citation impact of 1.83, which is nearly twice the world average of 1.00 and approximately 60% higher than the EU average of 1.10. Although open-access publication was not a requirement for EU funding and was often not budgeted for in IMI1 projects, an average of 56% of publications per project were printed in open access journals. In some instances, the final project reports noted that there may be future publications based on work undertaken during the project and the follow-on research. Therefore, the publication numbers and citation rates may also increase over time.

The publication of findings from the IMI1 projects facilitates the application of learnings from these projects to further research.

Education and training

Education and training was the primary purpose of five of the IMI1 projects: EMTRAIN, EU2P, EUPATI, PHARMATRAIN, and SafeSciMET:

- **EMTRAIN:** A pan-European platform for education and training was established, covering the entire life cycle of medicines, from basic research, clinical tests and market authorisation to follow-up research of drugs already on the market. The project strengthened cooperation among industry and academia, enabling faster implementation of new scientific and technological developments into academic teaching, and improving the mobility of professionals across disciplines, sectors and national borders. This was achieved through the development of a comprehensive online course catalogue for pharmaceutical medicine and science across Europe and neighbouring countries, workshops to provide PhD students with a holistic understanding of medicine development, and creation of a community-based platform for lifelong learning (LifeTrain).
- **EU2P:** An e-learning platform dedicated to pharmacovigilance and pharmacoepidemiology training was created as part of the EU2P project. The platform offers courses that can lead to a joint Master's degree or PhD, 25 joint academic certificates, as well as offering short courses. To maximise employability, the emphasis of courses is on 'hands-on training'. Approximately 400 students have been trained and more than 600 professionals have registered for courses.

[9] https://www.imi.europa.eu/projects-results/catalogue-project-tools

- **EUPATI:** A flagship output of the EUPATI project was the development and delivery of freely available training courses to provide patient advocates with expertise in pharmaceutical R&D. The course covers the drug development process from drug discovery to approval processes. Among the 96 individuals who have completed the course to date, the proportion engaging with medicine research has increased dramatically following course completion: the proportion advising pharmaceutical companies, regulatory agencies, and HTA/reimbursement bodies increased from 13% to 44%, 21% to 42%, and 4% to 8%, respectively.
- **PharmaTrain:** By bringing together university training programmes, competent authorities, partner training organisations, and pharmaceutical companies, standards and guidelines were established for the development of post-graduate diplomas and Master's degrees in medicine development, regulatory affairs, clinical trials, investigator training, and clinical trial management. Criteria to recognise and assess the quality of available courses were also developed, along with labels to be awarded to programmes that meet the required standards. Thirteen courses are now recognised as Centres of Excellence and over 150 short courses have been assessed. A freely available online e-learning library was also developed and a not-for-profit organisation (the PharmaTrain Federation) was set up to continue aspects of the project work, including assessment and recognition of courses that meet quality criteria. The PharmaTrain Federation had approximately 50 member institutions at the time of project completion.
- **SafeSciMET:** By bringing together institutes for drug safety education and pharmaceutical industry leaders, accredited training courses were established for post-doctoral toxicology specialists in the EU. More than 800 scientists have already been trained through this new programme.

While it was not their primary focus, several of the other IMI1 projects also provided education and training outcomes. For example workshops, events, and training courses were provided to students and professionals as part of BTCure, CHEM21, DDMoRe, EHR4CR, EMIF, EU-AIMS, EBiSC, eTRIKS, IMIDIA, and PharmaCog projects. Projects such as BTCure, CHEM21, COMPACT, ELF, and PharmaCog have also contributed to training a new generation of scientists through direct funding of academic qualifications and/or through student participation in projects. Online educational resources covering the environmental impact of medicine development and the use of real-world evidence in medicine development have also been developed as part of the CHEM21 and GetReal projects, respectively.

The anticipated socio-economic impacts associated with the education and training outputs of the IMI1 projects include:

- Development of a highly-skilled current and future workforce that is well-equipped to move between different institutions within and between academia and the pharmaceutical industry, helping to position Europe as a hub for scientific research in the longer term.
- Reductions in time and cost of training researchers moving between institutions through shared training standards and protocols.
- Increased focus on the development of and improvement of patient access to medicines with a positive impact on patient lives through increased patient engagement with the pharmaceutical industry, regulatory bodies, and HTA/reimbursement bodies.

2.3 Conclusions

The IMI1 projects delivered important outcomes that are likely to have a positive impact on the medicine development process, as well as other socio-economic effects.

The projects were defined by the objectives of the IMI Strategic Research Agenda (first published in 2008 and updated in 2011), with each designed to address a specific 'bottleneck' that had been identified in the drug discovery and development process. In most cases, the rationale for the project was that there was an area in which both public and private sectors were under-investing, but where a problem could be tackled by acting in concert. The projects were envisaged as a range of activities that would improve the conditions for medicine development in Europe, and remove barriers to the development of medicines and the growth of the sector.

The IMI1 projects should be seen as a first step in this process, with the potential for their outputs to be implemented and/or used in further research in order to improve the medicines development process.

3 IM1 PROJECT ASSESSMENTS

3.1 ABIRISK: Anti-Biopharmaceutical Immunization – Prediction and Analysis of Clinical Relevance to Minimize the Risk

03/2012 – 02/2018

3.1.1 Objectives of the project

Biopharmaceutical products (BPs) offer a great opportunity to treat entirely new classes of disease. However, as BPs are proteins the body can mount an immune response against them in the form of anti-drug antibodies (ADAs). Some ADAs result in the clearance of BPs or neutralise their function reducing the efficacy of treatment, others can result in immune reactions causing adverse reactions such as hypersensitivity reactions. When the BP replaces an endogenous protein with a unique biological function these adverse reactions can lead to life threatening situations.

The aim of the ABIRISK project was to understand the factors behind these immune responses and their molecular origin with the hope of being able to predict and reduce the immunogenic potential of new BPs.. Four chronic diseases were focused on that are treated with biologics: multiple sclerosis (MS), rheumatoid arthritis (RA), intestinal bowel diseases (IBD) and haemophilia A (HA). The primary objective was to build a unique database collecting data both retrospectively from patients suffering from MS, RA, IBD and HA treated with biologics and prospectively from cohorts of patients in dedicated studies during the 5 years of the ABIRISK program. Secondary objectives were to:

- Standardise anti-drug activity (ADA) assays for the BPs assessed in ABIRISK
- Provide novel integrated approaches to characterise anti-drug (AD) lymphocyte responses and biomarkers of immunogenicity from treated patients
- Develop and validate innovative prediction tools for biologics immunogenicity (*in silico*, *in vitro*, and *in vivo*)
- Integrate immunogenicity-related data and clinical relevance of ADA using a single immunogenicity databank

3.1.2 Project coordinator and managing entity

Project Coordinator	Novartis Pharma AG
Managing entity	Institut National de la Santé et de la Recherche Médicale

3.1.3 Participants

Table 6: Project participants

EFPIA companies	
Bayer Pharma AG	Novo Nordisk A/SD
GlaxoSmithKline Research and Development Ltd.	Pfizer Limited

Ipsen Innovation SAS	Sanofi-Aventis Recherche & Developpement
Merck Kommanditgesellschaft Auf Aktien	UCB Pharma SA
Novartis Pharma AG	

Universities, research organizations, public bodies, non-profit groups	
Academisch Medisch Centrum Bij De Universiteit Van Amsterdam (Netherlands)	Karolinska Institutet (Sweden)
Academisch Ziekenhuis Leiden (Netherlands)	Klinikum Rechts Der Isar Der Technischen Universitat Munchen (Germany)
Assistance Publique Hopitaux De Paris (France)	Medical Research Infrastructure Development And Health Services Fund By The Sheba Medical Center (Israel)
Bundesinstitut Fur Impfstoffe Und Biomedizinische Arzneimittel (Germany)	Medizinische Universitat Innsbruck (Austria)
Centre National De La Recherche Scientifique Cnrs (France)	Queen Mary University Of London (United Kingdom)
Commissariat A L Energie Atomique Et Aux Energies Alternatives (France)	Region Hovedstaden (Denmark)
Fondazione Per L Istituto Di Ricerca In Biomedicina (Switzerland)	The Health Corporation – Rambam (Israel)
Fundacio Hospital Universitari Vall D'Hebron - Institut De Recerca (Spain)	Universita Degli Studi Di Firenze (Italy)
Groupe D'Etudes Therapeutiques Desaffections Inflammatoires Digestives Association (France)	Universitatsklinikum Bonn (Germany)
Heinrich-Heine-Universitaet Duesseldorf (Germany)	Universitatsspital Basel (Switzerland)
Institut National De La Sante Et De La Recherche Medicale (France)	University College London (United Kingdom)
Istituto Giannina Gaslini (Italy)	Univerzita Karlova (Czech Republic)
Johann Wolfgang Goethe-Universitatfrankfurt Am Main (Germany)	

Small and medium-sized enterprises (SMEs)	
Alta Ricerca E Sviluppo In Biotecnologie Srlu (Italy)	SciCross AB (Sweden)
Biomonitor A/S (Denmark)	

Patient Organisations
Drk-Blutspendedienst Baden-Wurttemberg-Hessen Ggmbh (Germany)

Third parties	
Universite Paris-Sud (France)	Université François Rabelais De Tours (France)

3.1.4 Project inputs and funding

The ABIRISK project received funding of €19 million from IMI, from a total project cost of €33 million (Table 7).

Table 7: Funding received

Contributions	Financial support, €	% total funding
EU contribution	18,170,217	55.0%
EFPIA contribution	9,573,494	29.0%
IMI contribution	5,107,345	16.0%
Total funding	32,851,056	100.0%

3.1.5 Assessing the socio-economic impact of ABIRISK

Infrastructure for further research

Table 8: Infrastructure for further research

Outcome	Socio-economic impact
A unique database collecting data both retrospectively from patients with MS, RA, IBD, or HA treated with various biologics and prospectively from cohorts of patients in dedicated studies during the 5 years of the ABIRISK programme The major achievement of ABIRISK was the creation of the first prospective cohorts in the study of immunogenicity to biologics. More than 700 patients with MS, RA, IBD and HA, were recruited from more than 70 medical centres across Europe.	**The database is available through an open-source knowledge platform for translational science, based on the tranSMART platform** Cross-comparison of patient data enabled identification of best practices for measuring the immunogenicity of the therapeutic molecules. ABIRISK created a database which brings together clinical and immunogenicity data from trials across Europe. The database is based on the tranSMART platform, an open-source knowledge management platform for translational science.
Standardisation of anti-drug antibodies assays for the biologics assessed in ABIRISK Another important outcome of the project was the standardisation of assays for testing anti-drug antibodies and biological concentrations, as well as the creation of human anti-drug antibody standards. Previously, assays to detect antibodies have used animal standards. However, ABIRISK enabled the production of large quantities of human anti-drug antibody standards. Once validated, these will be available to scientists worldwide through the National Institute for Biological Standards and Control (NIBSC) in the UK.	**These assays can help clinicians to decide to keep a patient on a treatment or to switch to another** The availability of these anti-drug antibody standards allows for the harmonisation of anti-drug antibody assays for biologics and thus enables researchers and clinicians to publish more consistent data. The anti-drug antibody assays developed by the ABIRISK consortium can help clinicians decide to keep a patient on a biologic, switch to another with the same mode of action, or to switch to a different class of biologic, targeting a different part of the disease pathway. ABIRISK researchers also discovered candidates for biomarkers that can predict early anti-drug antibody development. These can be explored further by the pharma industry and academia.

Development and validation of innovative prediction software tools for biologic immunogenicity A novel predictive tool was implemented to analyse the time-to-event outcome data generated in ABIRISK. This method is called improper Bagging Survival Tree (iBST) and has been made freely available in an R package.	**Use in future research** This tool has been made freely available so that other research groups can use it to assess biologic immunogenicity for the development of new treatments

Dissemination of Information

The work of the project was presented to the scientific community through peer-reviewed journal articles and conference presentations (Table 9).

Table 9: Dissemination of information

Outcome	Socio-economic impact
Publications and conference presentations At the time of completion, project findings were reported in 70 publications, 41% of which were open access. The consortium's work was presented at more than 20 scientific conferences and meetings.	Publications had a normalised citation rate of 1.54, which suggests that the results of the project are easily accessible within the academic community.

3.1.6 Conclusion

Despite immunogenicity being one limitation for the treatment of patients with BPs prior to ABIRISK research in Europe in this area was scattered among a relatively few academic groups. And although some research was being performed by companies there was little interaction and collaboration in the basic research to understand the basic immunologic events that drive anti-BP immunisation. ABIRISK brought industry and academia closer together and paved the way for a joint understanding of the challenges surrounding the immunogenicity of BPs.

A major achievement of ABIRISK was the first large prospective cohort study of immunogenicity with biologics, the results of which are available via an open-source knowledge platform to support future research in the field. In addition, the database of data collected both prospectively from patients recruiting during the project and retrospectively will enhance future immunogenicity research. The database is available through a database based on tranSMART platform, an open-source knowledge platform for translational science.

Improving the understanding of the mechanisms behind BP immunogenicity offers the hope that future generations of BPs will display less immunogenicity and ensure patients do not face a loss of efficacy of their treatment due to anti-BP immunisation.

3.2 AETIONOMY: Organising mechanistic knowledge about neurodegenerative diseases for the improvement of drug development and therapy

01/2014 – 12/2018

3.2.1 Objectives of the project

The AETIONOMY project aimed to develop a new approach for the classification of neurodegenerative diseases, particularly Alzheimer's Disease (AD) and Parkinson's Disease (PD), based on the underlying molecular causes. Due to disease heterogeneity, a treatment that works in one patient may be ineffective in another. Biologically distinct diseases may share a common molecular basis. Treatments that target the molecular abnormality may be more effective and have fewer side effects compared with non-targeted treatments.

3.2.2 Project coordinator and managing entity

Project Coordinator	UCB Biopharma SPRL
Managing entity	Fraunhofer-Gesellschaft zur Förderung der angewandten Forschung e.V.

3.2.3 Participants

Table 10: Project participants

EFPIA companies	
Boehringer Ingelheim Internationalgmbh	Sanofi-Aventis Recherche & Developpement
Novartis Pharma AG	UCB Biopharma SPRL
Universities, research organizations, public bodies, non-profit groups	
Consorci Institut D'Investigacions Biomediques August Pi I Sunyer (Spain)	Institut Du Cerveau Et De La Moelle Epiniere (France)
Erasmus Universitair Medisch Centrum Rotterdam (Netherlands)	Karolinska Institutet (Sweden)
Fraunhofer Gesellschaft Zur Foerderung Der Angewandten Forschung E.V (Germany)	Universitatsklinikum Bonn (Germany)
Fundacio Barcelonabeta Brain Research Center (Spain)	Universite D'Aix Marseille (France)

Gottfried Wilhelm Leibniz Universitaet Hannover (Germany)	Universite Du Luxembourg (Luxembourg)

Small and medium-sized enterprises (SMEs)
Pharmacoidea Fejleszto Es Szolgaltato Kft (Hungary)

Patient Organisations
Alzheimer Europe (Luxembourg)

Third parties
Institut National De La Sante Et De La Recherche Medicale (France)

3.2.4 Project inputs and funding

The AETIONOMY project received funding of €8 million from IMI, from a total project cost of €18 million (Table 11).

Table 11: Funding received

Contributions	Financial support, €	% total funding
EU contribution	7,993,234	45.0%
EFPIA contribution	8,021,460	45.0%
IMI contribution	1,797,522	10.0%
Total funding	17,812,216	100.0%

3.2.5 Assessing the socio-economic impact of AETIONOMY

Infrastructure for further research

Table 12: Infrastructure for further research

Outcome	Socio-economic impact
AETIONOMY Knowledge Base (AKB) is a publicly accessible knowledge base to help the development of a mechanism-based taxonomy of diseases and precision medicine drug discovery. The AKB is the most comprehensive knowledge base on AD and PD worldwide. It integrates all study methodology, disease models, web services (tools) and multimodal data resources including knowledge from literature and data generated from the project. It also provides dedicated analysis and visualisation services.	**Increased pace for acquiring evidence-based scientific knowledge for drug discovery**
Virtual Patient Cohorts (VPCs): Synthetic data sets to pre-test in-silico hypotheses prior to lengthy and costly experimental validation in patients. Synthetic patient-level data can be shared without privacy issues for further re-use.	Better prioritisation of resources and therefore potential cost reductions in clinical research

Dissemination of Information

The work of the project was presented to the scientific community through peer-reviewed journal articles and conference presentations (Table 13).

Table 13: Dissemination of information

Outcome	Socio-economic impact
Publications At the time of completion, project findings were reported in 46 publications, 72% of which were open access.	Publications had a normalised citation rate of 1.89, which suggests that the results of the project are easily accessible within the academic community.

3.2.6 Conclusion of impacts

The AETIONOMY project has developed a novel approach for classification of neurogenerative diseases, AD and PD, based on the underlying causes of the symptoms. Through the AETIONOMY Knowledge Base (AKB) and Virtual Patient Cohorts (VPCs), curated data and mechanistic hypotheses have been made available to the biomedical community and regulators to direct the development, approval and use of new diagnostic tests and treatments for AD and PD.

3.3 BioVacSafe: Biomarkers for Enhanced Vaccine Immunosafety

03/2012 - 08/2018

3.3.1 Objectives of the project

Vaccines are one of the cheapest and most effective ways of protecting against infectious disease and are used globally. Vaccine safety is of critical importance to manufacturers, regulators, patients and the public, and new approaches are needed to ensure rapid introduction of novel vaccines by minimising delays due to testing procedures.

BioVacSafe is a consortium consisting of leading vaccine production companies, academic institutions, non-government institutions (NGO)s and SMEs aimed to develop tools, methods and guidelines for the evaluation of vaccine safety from pre-development to post-market surveillance. The aim was to accelerate the introduction of new, safer vaccines, whilst tackling the need for public and private bodies to find new approaches to collaboration in this critically important area.

The objective was to develop predictive biomarkers for detection of vaccine reactogenicity, and develop new ways to identify, classify and record adverse reactions to vaccine administration. The project was designed to exploit the consortium's combined capability in transcriptomics, genotyping, proteomics, metabolomics and data mining, as well as its *ex vivo* and *in vivo* animal models.

3.3.2 Project coordinator and managing entity

Project Coordinator	GlaxoSmithKline Vaccines Srl
Managing entity	The University of Surrey

3.3.3 Participants

Table 14: Project participants

EFPIA companies	
GlaxoSmithKline Vaccines Srl	Islensk Erfdagreining Ehf
Glaxosmithkline Biologicals SA	Sanofi Pasteur SA
Universities, research organizations, public bodies, non-profit groups	
Cdisc Europe Foundation Fondation (Belgium)	St George's Hospital Medical School (United Kingdom)
Chalmers Tekniska Hoegskola AB (Sweden)	Statens Serum Institut (Denmark)

Commissariat A L Energie Atomique Et Aux Energies Alternatives (France)	Universita Degli Studi Di Siena (Italy)
Department Of Health (United Kingdom)	Universiteit Gent (Belgium)
Goeteborgs Universitet (Sweden)	Universiteit Utrecht (Netherlands)
Imperial College Of Science Technology And Medicine (United Kingdom)	University Of Surrey (United Kingdom)
Max-Planck-Gesellschaft Zur Forderung Der Wissenschaften Ev (Germany)	
Small and medium-sized enterprises (SMEs)	
ImmunArray Ltd (Israel)	Vismederi SRL (Italy)
Third parties	
Universitair Ziekenhuis Gent (Belgium)	

3.3.4 Project inputs and funding

The BioVacSafe project received funding of €17.4 million from IMI, from a total project cost of €30.9 million (Table 15).

Table 15: Funding received

Contributions	Financial support, €	% total funding
EU contribution	17,408,770	56.3.0%
EFPIA contribution	7,999,683	25.9.0%
IMI contribution	5,522,917	17.9%
Total funding	30,931,370	100.0%

3.3.5 Assessing the socio-economic impact of BioVacSafe

Innovation

Table 16: Project innovation

Outcome	Socio-economic impact
Increased knowledge base of biomarkers and associated methodologies Through extensive biomedical studies and clinical trials, the project expanded knowledge of responses to vaccines at a range of biological levels. Three novel biomarkers (measurable indicators of the presence/severity of a disease) were characterised and defined, and new methods of predicting vaccine immunosafety were established. Specific innovations include new models of biological responses to vaccines (developed across multiple animal species) and novel *in vivo* techniques such as biopsy of local tissue and radionucleotide scanning.	**Accelerated uptake of improved vaccine safety technologies** The knowledge and techniques generated by BioVacSafe provide an extensive basis for the implementation of new vaccine safety technologies. The results of the project therefore have the potential to benefit public health through the advancement of vaccine safety procedures and increased pace at which new interventions are released to market. In addition, the wide sharing of novel methodologies will encourage more varied and experimental approaches to future research, creating avenues for new technology fields and reducing the need for animal testing.
Novel animal models BioVacSafe researchers developed 10 novel animal models for the study of vaccine safety biomarkers. Some of these models were at the 'identified' stage (requiring further validation), and some fully standardised.	**Improved biomarker research** The animal models were crucial to biomarker study throughout the project and serve as valuable resource for future research.

3.3.6 Infrastructure for further research

Table 17: Infrastructure for further research

Outcome	Socio-economic impact
Archives of selected project datasets A series of clinical trials aimed at identifying predictive biomarkers of vaccine immunosafety were undertaken. After a series of 'training trials', two Phase IV clinical trials were conducted, as well as a comprehensive study of an inactivated influenza vaccine comparing vaccine-induced reactions with those induced by a natural infection. A unique digital archive of RNA sequencing of blood samples collected during these trials, relating to five vaccines, was made available in the public domain, alongside	**Data resources for future biomarker research** The archive serves as a useful basis for subsequent work in this area, ensuring future resources are not wasted by unnecessarily repeating work. This contributes to the acceleration of the release of improved vaccine technologies.

the other clinical and pre-clinical transcriptomics.	
Development of a new data management system As a large-scale, multi-site, multi-study project, BioVacSafe generated a large amount of clinical and pre-clinical data. To support the management of this data and to facilitate a systematic approach to data handling across different project work streams, a platform was developed and refined to serve as a tool for data storage, dataset navigation, file management, exporting dataset analysis and governing data access policy.	**A potential tool for continued work** If the platform remains available to researchers despite project completion (which was the intial desire of the project partners), this could facilitate continued work in the area and serve as a basis for development of data management systems for multi-component projects, thereby increasing the efficiency and pace of future work.
Reproducible data analysis procedures Steps were taken to ensure that the data analysis principles were reproducible and of long-term use to future research. The data analysis procedures, mostly using the R statistical language, were designed to be open and reproducible and the analyses are saved as executable documents. All steps of data normalisation and analysis are included in these documents.	**Improving efficiency and quality of future research** Clear, reproducible data analysis procedures allow future scientists to easily understand the work, and apply the principles in their own research. This facilitates further expansion of the vaccine safety knowledge base, accelerating the introduction of technologies that benefit public health.

Structuring the European research area

Table 18: Structuring the European research area

Outcome	Socio-economic impact
Creation of a 'data standards package' (DSP) Following the development and testing of data capture processes within patient cohorts, an evaluation of existing standards and definitions was performed with input from a variety of stakeholders. The resulting 'Vaccines Therapeutic Area User Guide' was published by the Clinical Data Interchange Standards Consortium (CDISC) and describes the most common biomedical concepts relevant to vaccines, alongside methods of representing data consistently with existing procedures.	**Increasing overall efficiency of vaccine research** The data standards package is available in the public domain for uptake across European organisations. It is a useful resource for codifying vaccine reactogenicity and standardising research on biomarkers and vaccine safety. By guiding EFPIA activity, this has the potential to increase the efficiency and quality of vaccine research in Europe, ensuring more rapid delivery of new vaccine technologies.

Dissemination of information

The work of the project was presented to the scientific community through peer-reviewed journal articles and conference presentations Table 19.

Table 19: Dissemination of information

Outcome	Socio-economic impact
Publications and conference presentations At the time of completion, project findings were reported in 60 publications, 70% of which were open access. The consortium's work was presented at 74 scientific conferences and meetings around the world.	Publications had a normalised citation rate of 1.57, which suggests that the results of the project are easily accessible within the academic community. The conference presentations raised further awareness of vaccine safety issues and European science.

3.3.7 Conclusions of impacts

Accelerated pathway towards improved vaccine safety technologies

The BioVacSafe project combined the expertise and resources of academia and industry to understand mechanisms of adverse reactions to vaccines and develop new biomarkers for the identification of vaccine reactogenicity. Novel biomarkers were characterised, animal models were developed and standardised, and new methods of predicting vaccine immunosafety were established. Continuation of this work will provide public health benefits via the implementation of new vaccine safety technologies, which make the release of new vaccines faster and safer.

Enhancing future vaccine research

Comprehensive datasets were made available to future researchers in the public domain, and data analysis methodologies were clear and reproducible. The project generated and disseminated classifications, guidelines and reference standards for vaccine development, making vaccine research in Europe more efficient.

3.4 BTCure: Be The Cure for Rheumatoid Arthritis

04/2011 – 03/2017

3.4.1 Objectives of the project

Rheumatoid arthritis (RA) is a long-term, progressive autoimmune disease which causes chronic joint inflammation. Amongst other symptoms, it results in painful swelling of affected joints, and can lead to joint erosion and deformity. The precise mechanisms that cause RA are largely unknown and treatment choices are numerous and vary in effectiveness. There is an unmet need to better understand the pathology of RA and improve treatment technologies.

The aim of the BTCure project was to combine rheumatology expertise and resources in academia and the pharmaceutical industry to broaden current understanding of the pathology of RA. The consortium aimed to develop diagnostic processes for RA which could differentiate between subtypes and standardise procedures of generating and interpreting commonly used RA animal models. It was hoped that this would contribute to the development of precise, early and ultimately curative treatments for patients with RA.

3.4.2 Project coordinator and managing entity

Project Coordinator	UCB Biopharma SPRL
Managing entity	Karolinska Institutet

3.4.3 Participants

Table 20: Project participants

EFPIA companies	
Astrazeneca AB	Merck Kommanditgesellschaft Auf Aktien
Boehringer Ingelheim International GmbH	Novo Nordisk A/S
Bristol-Myers Squibb Company Corp	Pfizer Limited
Glaxosmithkline Research and Development LTD.	UCB Biopharma SPRL
Janssen Biologics BV	
Universities, research organizations, public bodies, non-profit groups	
Academisch Medisch Centrum Bij De Universiteit Van Amsterdam (Netherlands)	Institut National De La Sante Et De La Recherche Medicale (France)

Academisch Ziekenhuis Leiden (Netherlands)	Karolinska Institutet (Sweden)
Agencia Estatal Consejo Superior Deinvestigaciones Cientificas (Spain)	King's College London (United Kingdom)
Biomedical Sciences Research Center Alexander Fleming (Greece)	Medizinische Universitaet Wien (Austria)
Centre Hospitalier Universitaire Montpellie (France)	Revmatologicky Ustav (Czech Republic)
Charite - Universitaetsmedizin Berlin (Germany)	Stichting Katholieke Universiteit (Netherlands)
Deutsches Rheuma-Forschungszentrum Berlin (Germany)	The University of Manchester (United Kingdom)
Diakonhjemmet Hospital (Norway)	Universitat Zurich (Switzerland)
Fondazione Humanitas Per La Ricerca (Italy)	Universitatsklinikum Erlangen (Germany)
Idryma Iatroviologikon Ereunon Akademias Athinon (Greece)	University College Dublin, National University of Ireland (Ireland)
University of Glasgow (United Kingdom)	University of Oxford (United Kingdom)
University of Leeds (United Kingdom)	Uppsala Universitet (Sweden)

Small and medium-sized enterprises (SMEs)	
Arthrogen BV (Netherlands)	Firalis SAS (France)
Biomedcode Hellas SA (Greece)	Redoxis AB (Sweden)

Non-EFPIA companies
Phadia AB (Sweden)

3.4.4 Project inputs and funding

The BTCure project received funding of €17.4 million from IMI, from a total project cost of €39.4 million (Table 21).

Table 21: Funding received

Contributions	Financial support, €	% total funding
EU contribution	17,362,872	44.1%
EFPIA contribution	15,604,837	39.7%
IMI contribution	6,387,034	16.2%
Total funding	39,354,743	100.0%

3.4.5 Assessing the socio-economic impact of BTCure

Innovation

Table 22: Project innovation

Outcome	Socio-economic impact
Novel biomarkers Over 10 novel biomarkers of RA were identified, eight of which were validated (tested for accuracy, consistency and disease applicability). Alongside this, assay testing systems were developed to measure these biomarkers for signs of RA, disease progression and response to therapy.	**Research tools for development of new therapies** Biomarkers are used to improve diagnosis accuracy, monitor drug activity/therapeutic response and guide the development of targeted therapies. The significant number of validated RA biomarkers generated by BTCure will therefore facilitate the development of better, more targeted RA therapies and reduce the burden of the disease on public health.
Improved preclinical models A wide range of models (non-human biological systems in which a disease can be studied) were also developed. Nine *in vitro* model systems (microorganisms/cells outside a living organism) were identified, four of which were fully validated. Three *in vivo* models (living organisms, i.e. animals) were also fully validated, with several identified but requiring replication.	**Enhanced vaccine safety research** Biological models are a fundamental part of drug development as they enable experimentation of a disease and its response to interventions in non-human contexts. The expansion of preclinical models of RA will therefore enhance pre-clinical research and provide further opportunities to study disease pathogenesis. Ultimately this will lead

Further development of pre-clinical tools The Phadia-Thermo Fisher ACPA chip was analysed and developed further. Sets of diagnostic tests have been developed such as high throughput , multidimensional flow cytometry .	to better understanding of RA and provide avenues to more effective, targeted treatments.
New knowledge of disease-causing factors The BTCure project increased understanding of the causes of RA. Most significantly, researchers discovered that antibodies contribute to the onset of RA by making joints more sensitive to changes, promoting chronic inflammation. These antibodies can be detected in some individuals years before disease onset.	 **Avenues for novel early-stage therapies** A better understanding of early causes of the disease will contribute to the development of novel treatments and diagnostic tools for early-stage RA. The ability to delay or prevent onset of RA will benefit public health and relieve overburdened healthcare systems.
Identification of novel targets and potential drug compounds Five potential drug targets (e.g. proteins with which drugs interact to inhibit a disease) were discovered, two of which were fully validated. Most notably, a new computer-based drug screening approach identified two small protein targets involved in inflammation processes in RA and other chronic diseases. Several molecules were identified as potential candidates for further development into novel RA drugs. Seven molecules were identified which require further validation.	 **Tangible routes to novel RA treatments** The potential targets and drug compounds identified by BTCure serve as an valuable basis for future work. Further study and validation of the biological targets could allow new families of drug compounds to be screened, expanding opportunities for more effective RA treatments. The 'hit' molecules identified provide a clear path for further validation and optimisation. Ultimately, these achievements could expand the treatments available for RA.

Infrastructure for further research

Table 23: Infrastructure for further research

Outcome	Socio-economic impact
Standard operating procedures for animal models A key objective of the project was to develop an infrastructure to standardise procedures of generating and interpreting commonly used RA animal models. Four workshops were held, in which key opinion leaders within the RA field discussed advantages and disadvantages of various models, and the correlation of different models with human disease. As a result, six reports were produced describing standardised ways to perform and evaluate animal models of RA. Guidelines for histological evaluation (study	 **Enabling higher quality research, leading to better RA treatment and potential cost reduction** The standardisation of procedures relating to RA animal models has enabled quality research and reproducible results between different laboratories. By validating protocols and model descriptions, this work has improved the predictability of preclinical models and identified. the most appropriate models for the various disease stages. Ultimately, this will lead to more robust and reproducible research in RA and potential cost reduction of developing future treatment.

of tissue) of sections of RA models were also generated.	
Databases In total, 42 datasets of clinical data and biomaterials were generated by project completion and stored for future use by various consortium members. A RA-specific database was created for data archiving, representation and validation (www.therabase.eu)	**Supporting future science** The data and database is a resource for future research across the scientific community.

Dissemination of information

The work of the project was presented to the scientific community through peer-reviewed journal articles and conference presentations (Table 24).

Table 24: Dissemination of information

Outcome	Socio-economic impact
Publications and conference presentations At the time of completion, project findings were reported in 645 publications, 60.2% of which were open access. A further 31 publications were ongoing. Numerous presentations were delivered at scientific conferences around the world.	Publications had a normalised citation impact of 1.83, which suggests that the results of the project are easily accessible within the academic community. The BTCure project resulted in a large amount of published research, significantly expanding the scientific literature in the field of RA.
Educational outputs The BTCure projects had significant education and training outputs. In total, 13 workshops were held for consortium members in academia and industry, covering a range of relevant scientific areas. Several PhD and Master's qualifications were obtained by individuals in industry and academia, either through direct BTCure funding or participation in BTCure projects.	**Expertise for future RA research** The skills, knowledge and disease awareness generated by the educational outputs of BTCure will be important for sustained research in the area. The transferable skills gained by scientifically-trained individuals will also have beneficial economic impacts.
The consortium working with the wider scientific community to harmonise data collection for clinical studies of RA has resulted in the formation of a EULAR task force group for standardizing a minimum data collection for RA Observational Research.	This work will result in harmonised data collection, development of common data models and serve as a model for data collection for RA research in clinical practice. These will contribute to a better understanding of disease and its treatment to speed up the development of new therapies for the benefit of patients

3.4.6 Conclusions of impacts

Infrastructure for higher quality, accelerated research

The BTCure project made major contributions to research infrastructure in a number of areas. Techniques and resources were generated for application in future research, including biomarkers for the disease detection and assessment, models for drug testing and several databases for future analyses. Guidelines for more efficient RA research were also created, most notably six standard operating procedures for the use of animal models. Overall, these outputs will accelerate and improve RA research aiming to improve treatments and reduce the socioeconomic burden of the disease.

Better understanding of disease-causing factors

BTCURE made significant progress in furthering fundamental knowledge of the disease and its causes. Important discoveries were made regarding core biological processes, for example the finding that certain antibodies can cause disease onset. New drug targets were also generated and the two fully validated targets provide a clear starting point for the development of novel drugs. Ultimately, the increased disease knowledge resulting from BTCURE expands the scope of subsequent RA research, facilitating the development of more targeted RA treatment.

3.5 CHEM21: Chemical manufacturing methods for the 21st century pharmaceutical industries

10/2012 – 06/2017

3.5.1 Objectives of the project

The CHEM21 project was designed to address key issues relating to the efficiency, sustainability and cost-effectiveness of manufacturing processes for Active Pharmaceutical Ingredients (APIs). The inefficiencies inherent in many drug production processes and the associated environmental concerns make it increasingly important to develop more sustainable synthetic technologies that minimise waste, reduce the need for toxic materials and are more energy-efficient. By partnering 'green' academic communities with industry manufacturers, CHEM21 aimed to make sustainability improvements in three key synthetic areas: chemical technologies, biocatalysis and synthetic biology.

Within the chemical technologies field, the CHEM21 project primarily aimed to develop chemical catalysts based on abundant transition metals, rather than commonly-used precious metals that are in limited supply, more expensive and generally more toxic. Other objectives were investigating the use of more efficient reactors and improved synthetic methodologies to achieve a range of key chemical transformations.

The biocatalysis branch of the project aimed to develop biocatalysts that could be used in a wide range of synthetic steps, where current use of chemical catalysts was in need of replacement or improvement. The objectives of the CHEM21 within the synthetic biology field were to investigate the sustainable production and deployment of microorganisms in the conversion of simple materials to valuable products – simplifying drug production by reducing the need for synthetic steps based on traditional organic chemistry.

Finally, the project aimed to deliver valuable training and educational materials to the next generation of pharmaceutical chemists, to ensure widespread understanding of the sustainable methodologies established during the project. Overall, it was hoped that the fulfilment of these objectives would make pharmaceutical manufacturing cleaner, greener and more cost-effective, whilst enhancing the competitiveness of Europe as a place for drug production.

3.5.2 Project coordinator and managing entity

Project Coordinator	GSK
Managing entity	University of Manchester

3.5.3 Participants

Table 25: Project participants

EFPIA companies	
Bayer Pharma AG	Orion Oyj
Glaxosmithkline Research And Development LTD.	Pfizer Limited

Janssen Pharmaceutica Nv	Sanofi Chimie
Universities, research organizations, public bodies, non-profit groups	
Leibniz - Institut Fur Katalyse Ev An Der Universitat Rostock (Germany)	Universiteit Antwerpen (Belgium)
Stichting Vu, (Netherlands)	University of Durham (United Kingdom)
The University of Manchester (United Kingdom)	University of Leeds (United Kingdom)
Universitaet Stuttgart (Germany)	University of York (United Kingdom)
Small and medium-sized enterprises (SMEs)	
ACIB GmbH (Austria)	Reaxa Limited (United Kingdom)
CatScI Ltd, Wentloog (United Kingdom)	Charnwood Technical Consulting Ltd (United Kingdom)
Evolva AG (Switzerland)	
Third parties	
Technische Universitaet Graz (Austria)	Universitaet Graz (Austria)

3.5.4 Project inputs and funding

The CHEM21 project received funding of €9.8 million from IMI, from a total project cost of €26.7 million (Table 26).

Table 26: Funding received

Contributions	Financial support, €	% total funding
EU contribution	9,829,638	37.0%
EFPIA contribution	13,871,772	52.0%
IMI contribution	3,009,396	11.0%
Total funding	26,710,806	100.0%

3.5.5 Assessing the socio-economic impact of CHEM21

Innovation

Table 27: Project innovation

Outcome	Socio-economic impact
New chemical technologies A new method for the synthesis of flucytosine, an essential antifungal medicine, was developed. A one-step 'continuous flow' method was devised, involving the direct fluorination of a readily available starting product. Flow chemistry was investigated for use in several additional contexts, including oxidation with air and peptide formation. A large number of new, cleaner more sustainable catalysts for use in reactions that are typically catalysed by toxic precious metals (which are limited in supply and have poor recyclable qualities) were developed supplied to EFPIA members for use in development. In addition, progress was made in areas such as C-H activation and amide bond formation.	**Foundations for cleaner, safer and more sustainable manufacturing processes** The new synthetic pathway of cytosine can replace unsustainable methods currently in use. Because it involves just one selective reaction instead of four, it uses significantly less energy and raw materials and produces less waste than conventional techniques. Oxidation with air typically carries risk of explosion and involves highly toxic chemicals, and traditional peptide synthesis requires long, multi-step reactions. Uptake of the flow chemistry techniques circumvents these issues.
New biocatalytical methods New classes of enzyme biocatalysts were developed, refined and made available to EFPIA members for in-house evaluation, and existing classes were further optimised. Notably imine reductases/reductive amination have been developed and adopted by EFPIA partner to a similar level of readiness as transaminases and ketoreductases. New methods integrating biocatalysis with advanced chemical procedures also demonstrated the potential of biocatalysis for achieving high selectivity in reaction outcomes.	**Facilitating widespread uptake of greener, shorter and less wasteful synthetic pathways** In the long term, greater uptake of the sustainable methods resulting from this work will make the drug manufacturing process shorter, less toxic and more environmentally friendly.
New synthetic biology technologies Synthetic biology (the modification of a microorganism's biochemistry to tailor its metabolism towards the production of specific molecules) was used to establish novel pathways towards a range of drug intermediates. A 'toolbox' of concepts, methodologies and biological material was established which included sets of enzymes, DNA parts and host strains, new DNA assembly methods and genome engineering techniques. The engineered enzymes have been made available to all partners and novel pathways	**Reducing the need for long reactions and toxic solvents** Synthetic biology techniques simplify reactions by reducing the need for the multi-step synthesis. Uptake of these techniques will therefore shorten reaction times and allow for the use of greener solvents, circumventing the need for harsh reaction conditions and toxic chemicals.

have been evaluated leading to the synthesis of several compounds for the first time using synthetic biology. The applicability of biosynthetic techniques was demonstrated via the scaling up of a specific novel pathway to a 20 litre bioreactor.	

Infrastructure for further research

Table 28: Infrastructure for further research

Outcome	Socio-economic impact
The CHEM21 sustainability metrics toolkit A unified metrics toolkit agreed by all partners was developed with range of metrics using both qualitative and quantitative criteria to assess sustainability. It can be used in the assessment of all reactions, from lab-bench to industrial scales.	 **Infrastructure for future green research** The toolkit provides a comprehensive basis for assessing sustainability in future research, providing greater insight than the standard metrics system used previously. The toolkit is freely available for use in the scientific community, which will hopefully increase the quality and pace of green chemistry research.
The CHEM21 Solvents selection guide A comprehensive guide for selecting less-toxic solvents was published, ranking both classical and non-classical (bio-derived) solvents based on safety, health and environment criteria and physical properties. Formed through extensive discussions between consortium members, it can also be used to assess and rank new solvents via a free web-based tool.	 **A basis for greener solvent choice** The guide serves as a comprehensive resource for future work. The guide also includes bio-derived solvents, which are not typically assessed for environmental impact. By facilitating sustainability assessment of solvents, this work will help to minimise the impact of solvents on the environment.

Structuring the European Research Area

Table 29: Structuring the European research area

Outcome	Socio-economic impact
Regulatory discussions Regulators were included in discussions about the green chemistry landscape, helping to identify drivers, issues and barriers to implementation.	 **Well-targeted green research** The project had minimal direct impact on regulatory practices, however engagement with regulators generated guidance for future research and ensured that the work of the consortium was targeted as effectively as possible within the regulatory framework.

Dissemination of information

The work of the project was presented to the scientific community through peer-reviewed journal articles and conference presentations (Table 30).

Table 30: Dissemination of information

Outcome	Socio-economic impact
Publications and conference presentations At the time of completion, project findings were reported in 119 publications, 26.9% of which were open access. The project also contributed to the publication of a book on current challenges in green manufacturing. The work of CHEM21 was presented at 132 conferences around the world.	Publications had a normalised citation rate of 1.73, which suggests that the results of the project are easily accessible within the academic community. The conference presentations further increased awareness of green methodologies and helped to promote Europe as a place for collaborative research.
Educational activities Numerous educational workshops and training events were run both internally and for the wider scientific community. A total of 614 people from academia and industry were trained at face-to-face events. An open, free online learning platform was also launched, providing interactive educational material at introductory and advanced levels. A network of ~50 early-career researchers working on CHEM21 projects was established (the 'Young Researchers Network' (YRN)), to increased ease of collaboration and communication between individuals with a range of scientific backgrounds. The consortium contributed to a new Industrial Biocatalysis Massive Open Online Course (MOOC) developed by the university of Manchester	Most of the projects educational activities were held in Europe, helping to embed green principles in the minds of future Europe chemists. The online learning platform is a valuable educational resource which covers a wide range of topics and is part of undergraduate Chemistry courses in several European universities. Many of the YRN members are now working in the pharmaceutical industry, allowing for further collaboration and knowledge-sharing across Europe.

3.5.6 Conclusions of impacts

Foundations for cleaner, safer and more sustainable manufacturing processes

Overall, the CHEM21 project has contributed extensively to the further development and uptake of green manufacturing techniques. New chemical technologies were generated in the fields of chemical catalysis, fluorination and flow chemistry, which have the potential to lead to cleaner, more sustainable manufacturing processes. By developing novel enzyme biocatalysts and making them available to EFPIA members, CHEM21 has also helped facilitate uptake of biocatalytical manufacturing methods, allowing for shorter, greener and less wasteful reaction pathways. This work in the field of synthetic biology has provided a foundation for further development and implementation of synthetic biology techniques.

Toolkit for future green research

Implementation of more sustainable manufacturing processes enables safe and environmentally responsible delivery of medicines to European citizens. CHEM21 has also provided infrastructure for future research. A sustainability metrics toolkit was developed as a novel quantitative tool for assessing reaction sustainability, in addition to a solvent selection guide for the assessments of solvents for environmental impact. This will enhance future research in green chemistry and accelerate the implementation of green technologies in industry.

Green chemistry training for future researchers

The educational impact of CHEM21 is a key attribute of the project, with considerable effort put into the creation of free educational resources and ensuring that the knowledge and principles generated throughout the project were widely disseminated to future generations of process chemists.

3.6 COMPACT: Collaboration on the optimisation of macromolecular pharmaceutical access to cellular targets

11/2012 – 10/2017

3.6.1 Objectives of the project

New therapies based on macromolecules of biological origin such as proteins, peptides and oligonucleotides have a huge pharmacological potential due to their highly selective mode of action and their potential activity against targets that are considered 'non-druggable' by more traditional small organic molecules. However, the ability to develop these potential macromolecular therapeutics has been very limited due to difficulties faced in getting these complex molecules to where they are needed in the body. These barriers often occur at the tissue and cellular level. Therefore, their success in developing future innovative medicines will heavily depend on improvements in both chemistries and delivery technologies that can address these limitations. The main goal of COMPACT was to understand the challenges associated with delivering a biologic to its target, a process known as drug delivery, and develop novel drug delivery systems (DDS).

3.6.2 Project coordinator and managing entity

Project Coordinator	Sanofi-Aventis Deutschland GmbH
Managing entity	Universiteit Utrecht

3.6.3 Participants

Table 31: Project participants

EFPIA companies	
Abbvie Deutschland GMBH & Co Kg	Novo Nordisk A/S
Boehringer Ingelheim Internationalgmbh	Pfizer Limited
Glaxosmithkline Research And Development LTD	Sanofi-Aventis Deutschland GMBH
Merck Kommanditgesellschaft Auf Aktien	
Universities, research organizations, public bodies, non-profit groups	
Bioneer A/S (Denmark)	Universitat Wien (Austria)
Cardiff University (United Kingdom)	Universitat Zurich (Switzerland)
Helmholtz-Zentrum Fur Infektionsforschung GMBH (Germany)	Universiteit Gent (Belgium)

Kobenhavns Universitet (Denmark)	Universiteit Leiden (Netherlands)
Ludwig-Maximilians-Universitaet (Germany)	Universiteit Utrecht (Netherlands)
Norges Teknisk-Naturvitenskapelige Universitet – NTNU (Norway)	University Of Helsinki (Finland)
Stockholms Universitet (Sweden)	University Of Oxford (United Kingdom)
Small and medium-sized enterprises (SMEs)	
Pharmacoidea Fejleszto Es Szolgaltato Kft (Hungary)	

3.6.4 Project inputs and funding

The project received funding of €8 million from IMI, from a total project cost of €21 million (Table 32).

Table 32: Funding received

Contribution	Financial support, €	% total funding
EU contribution	10,184,909	34%
EFPIA contribution	16,561,578	55.2%
IMI contribution	3,237,243	10.8%
Total funding	29,983,730	100%

3.6.5 Assessing the socio-economic impact of COMPACT

Innovation

Table 33: Project innovation

Outcome	Socio-economic impact
Novel drug delivery systems for biologics Novel drug delivery systems (DDS) have been tested during the COMPACT project, 11 of which are being tested *in vivo*. New formulations include oral delivery peptides, dermal delivery proteins and can be delivered across the blood-brain or air-lung barrier. Two of these formulations have suitable novelty and have been filed for patent protection.	**Improved biopharmaceuticals research** One of the main bottlenecks in biopharmaceuticals research is the delivery of a molecule to its specific target. The 11 novel delivery systems developed during the COMPACT project have the potential to improve the delivery of biopharmaceuticals such as siRNAs, macromolecules and peptides (e.g. insulins). The future use of these delivery systems may provide both clinical and economic benefits.
Oral delivery of peptides Some of the novel drug delivery systems are oral formulations for peptides such as human insulin. Transintestinal delivery formulations have been tested *in vivo* with promising results.	**Benefit for patients** Novel oral delivery systems offer patients the option of orally-administered insulins in addition to currently available transdermal delivery treatments. More convenient administration protocols may improve quality of life for patients.
New *in vivo* and *in vitro* models New models have been developed to evaluate drug delivery systems. Both *in vitro* and *in vivo* (transgenic mouse models) systems have been established to study trafficking of drug delivery systems across cell membranes to intracellular targets.	**Better models, less usage** Improved cellular models are fundamental for testing new drug delivery systems. Better *in vitro* models can also reduce the need for *in vivo* models.

Infrastructure for further research

Table 34: Infrastructure for further research

Outcome	Socio-economic impact
Alfresco database An extensive database of the characterisation of the DDS formulations was compiled during the project and is available on request (Alfresco). The database also contains unpublished negative data therefore is more comprehensive than COMPACT publications.	**Comprehensive DDS data and unpublished negative data** Comprehensive sharing of data (including negative data) will benefit scientists in the field and make research more efficient.

Dissemination of information

The work of the project was presented to the scientific community through peer-reviewed journal articles and presentations (Table 35).

Table 35: Dissemination of information

Outcome	Socio-economic impact
Publications At the time of completion, project findings were reported in 70 publications, 37.1% of which were open access. Consortium members also presented as key speakers at multiple conferences.	Publications had a normalised citation rate of 2.21, which suggests that the results of the project are easily accessible within the academic community. The conference presentations raised awareness of the project in the scientific community.
Educational activities More than 36 PhD students and post-doctoral research assistants were trained by experienced researchers.	**Enhancing the skillset of European researchers** Training of the next generation of academic and industrial scientists with an understanding of DDS will support future research in the field.

3.6.6 Conclusions of impacts

Novel drug delivery prototypes have been developed which may lead to the next generation of biologics for a range of diseases. The project also generated a spin-out company and filed two patents, demonstrating the potential for wider socio-economic benefits. New drug delivery systems lead to new biopharmaceuticals as well as expanding administration options for existing treatments, which may improve quality of life for patients.

Project findings were collected in a database that is available on request, which in addition to publications and training of PhD students, will facilitate ongoing and future research in DDS.

3.7 DDMoRe: Drug Disease Model Resources

03/2011 – 08/2016

3.7.1 Objectives of the project

Demonstrating the safety and efficacy of a new drug is a requirement of bringing it to market. This involves testing the drug in large, representative patient cohorts (i.e. conducting clinical trials) and evaluating clinical outcomes and side effects. Modelling and Simulation (M&S) can be used to analyse large amounts of clinical data, an approach known as Model Informed Drug Discovery and Development (MID3).

The MID3 approach involves complex mathematical models which require extensive knowledge to develop and apply. Collaboration between model developers, regulators and other external parties is key to establishing if a model can be applied to a clinical dataset. The DDMoRe consortium identified several barriers to using MID3 in drug development. Firstly, a range of tools and programming languages/software platforms are used for different models, and a lack of common processes and standards hampers shareability and utilisation. Difficulties in sharing models and knowledge across organisations was identified as a key barrier to both consistency and innovation. Inconsistent quality in expertise within modelling teams was also noted.

The aim of the DDMoRe project was to address these issues by developing the infrastructure to facilitate communication, collaboration and greater consistency across modelling teams. Core goals were to develop a framework of standards for developing, describing and storing models; to create a free, open access library of models for sharing of knowledge and methodologies; and to develop training materials to encourage uptake of these deliverables.

By increasing collaboration, transparency and consistency within MID3 activities, the consortium ultimately hoped to accelerate modelling processes within drug development, increase the quality of and credibility of model-informed development projects and as a result make new drugs safer, more effective and more efficiently delivered to market.

3.7.2 Project coordinator and managing entity

Project Coordinator Pfizer Ltd

Managing entity Uppsala Universitat

3.7.3 Participants

Table 36: Project participants

EFPIA companies	
Astrazeneca AB	Novartis Pharma AG
Eli Lilly And Company Limited	Novo Nordisk A/S
F. Hoffmann-La Roche AG	Pfizer Limited

GlaxoSmithKline Research and Development Ltd.	Takeda Pharmaceuticals International AG
Institut De Recherches Internationales Servier	UCB Biopharma SPRL
Merck Kommanditgesellschaft Auf Aktien	
Universities, research organizations, public bodies, non-profit groups	
Consiglio Nazionale Delle Ricerche (Italy)	Universita Degli Studi Di Pavia (Italy)
European Molecular Biology Laboratory (Germany)	Universite Paris Diderot - Paris 7 (France)
Freie Universitaet Berlin (Germany)	Universiteit Leiden (Netherlands)
Institut National De Recherche Eninformatique Et Automatique (France)	University College London (United Kingdom)
Universidad De Navarra, Pamplona (Spain)	Uppsala Universitet (Sweden)
Small and medium-sized enterprises (SMEs)	
Certara Uk Limited (United Kingdom)	Mango Business Solutions Limited (United Kingdom)
Cyprotex Discovery Ltd (United Kingdom)	Optimata Ltd. (Israel)
Lixoft SAS (France)	
Third parties	
Institut National De La Sante Et De La Recherche Medicale (France)	

3.7.4 Project inputs and funding

The DDMoRe project received funding of €10.4 million from IMI, from a total project cost of €23.3 million (Table 37).

Table 37: Funding received

Contributions	Financial support, €	% total funding
EU contribution	10,399,426	44.7%
EFPIA contribution	10,616,336	45.6%
IMI contribution	2,261,506	9.7%
Total funding	23,277,268	100.0%

3.7.5 Assessing the socio-economic impact of DDMoRe

Infrastructure for further research

Table 38: Infrastructure for further research

Outcome	Socio-economic impact
The DDMoRe model repository A free, publicly available online repository was developed for uploading, storing and accessing a variety of computational models. As of March 2018, the repository contained 128 models, spanning a range of pharmacometric and disease areas. The repository is the largest of its kind to date. It is indexed, fully searchable and allows sharing of private models, captures and display annotations for models, and imports publications. It is showcased by a series of 'proof of concept' published models, and its ease of use is further supported by online video tutorials. To ensure its longevity, a 'DDMoRe Foundation' was set up to maintain the platform and ensure continued access.	**Facilitating increased collaboration and higher quality research** The repository enables open access to valuable shared knowledge, impacting the research community and beyond. It facilitates collaboration across organisations within the modelling community, allowing expertise to be pooled. It makes model-informed drug development more efficient, particularly when a model in the library is used to inform the development of novel model. Widespread use of the platform and continued addition of new models will provide long-term benefits in the improvement and acceleration of drug development, making new drugs safer and more rapidly released to market.

Interoperability framework To further facilitate collaboration, the DDMoRe consortium developed an open source online platform for sharing drug and disease models. The platform provides an environment in which researchers can work using the software they know, sharing work through a standard language for describing models. This integration of models circumvents issues created when different modelling languages are by research groups across different organisations. Importantly, the platform can be used by anyone to perform modelling exercises and re-run existing models. The framework is publicly available and free to download.	**Increased collaboration for enhanced innovation** Creating the opportunity for efficient exchange of models and modelling ideas encourages collaboration and innovative approaches to model development. Effective collaboration through the interoperability platform will result in better models and higher quality research. The platform will also facilitate approval processes as regulators and external bodies will be able to use the framework to re-run models for assessment.
Standards for modelling activities A core achievement of DDMoRe was set of publicly available standards for developing, describing and storing models. Model software often varies across research organisations and model types; the DDMoRe standards were designed to address these challenges and facilitate better collaboration between analysts. The standards describe data inputs, outputs and other technical aspects of data modelling, and were incorporated into the core DDMoRe products.	**Facilitating communication and providing a basis for research-enhancing tools** Development of the model repository and online platform would not have been possible without standards for developing, describing and storing models. Adoption of the standards by stakeholders in the M&S arena will also enable greater collaboration between modelling groups in the future.

Structuring the European research area

Table 39: Structuring the European research area

Outcome	Socio-economic impact
The DDMoRe Foundation The not-for-profit 'DDMoRe Foundation' was established by project partners to maintain all of the public domain outputs, including the model repository, the interoperability framework and the modelling standards. The foundation is funded by academic and industrial partners, both financially and through 'in-kind' contributions. The partners also contribute personnel for a variety of roles (conducted alongside roles within their respective organisations), including a software manager and repository curator.	**Continued enhancement of model-informed drug development** The DDMoRe Foundation ensures that the research-enhancing outputs of the project remain in use to the scientific community, maximising its impact on MID3 activities and the efficacy of medicines arising from model-informed drug development. The existence of the foundation also ensures continued collaboration between academia and industry for the enhancement of modelling activities, facilitating further exchange of ideas and expertise.

Dissemination of information

The work of the project was presented to the scientific community through peer-reviewed journal articles and presentations (Table 40).

Table 40: Dissemination of information

Outcome	Socio-economic impact
Publications and conferences At the time of completion, project findings were reported in 76 publications, 63.2% of which were open access. The work was presented at 55 conferences and scientific meetings around the world.	Publications had a normalised citation rate of 1.0, which suggests that the results of the project are easily accessible within the academic community. The conference presentations promoted the work of the consortium and Europe as a place for collaborative research
Educational activities An unmet need was identified for a consensus on the skills and knowledge required to carry out effective M&S activities. A competency framework was established, highlighting the technical and conceptual requirements for M&S. A training program was funded for PhDs and postdoctoral researchers, introducing principles of model-informed drug development across a range of therapeutic areas. The course comprised six face-to-face 5-day courses of lectures, group work and student presentations. The courses were held across a number of European countries and training materials have been made freely available online for widespread use.	**Enhancing the skillset of European researchers** The competency framework serves as guidance for future M&S education and training activities, helping to ensure teaching resources are allocated effectively and efficiently. The educational and training activities delivered during the project will be of value both to the trainees in their future work and those who use the online educational materials. This dissemination of knowledge will promote expertise in the area and ultimately improving model-informed drug development.

3.7.6 Conclusions of impacts

Enhanced model-informed drug development and efficient collaboration within the modelling community

Adoption and utilisation of the DDMoRe outputs can increase the efficiency, pace, scope and quality of drug development programmes that use modelling and simulation techniques. The models contained in the DDMoRe repository can be accessed and adapted by researchers, making model development more efficient. The long-term impacts of the project on model-informed drug development are highly dependable on the success of the sustainability plan, and the continued addition of new models by research groups.

As a public-private partnership, the DDMoRe consortium brought together modelling groups across academia and industry for the purposes of information sharing. The project created new collaborations between groups and increased transparency in modelling research.

The DDMoRe project has developed the infrastructure to facilitate better collaboration across research organisations globally and enhance MID3 research. The modelling standards will maintain consistency

across research groups, improving reproducibility of model findings; and the free, open access library of models provides a resource for future work in the field.

3.8 DRIVE-AB: Driving re-investment in R&D and responsible antibiotic use

10/2014 – 12/2017

3.8.1 Objectives of the project

Bacteria are becoming increasingly resistant to antibiotics, which is global public health threat. The development of new drugs to treat resistant infections is limited by economic and scientific challenges. The is an unmet need for economic models to support market access of new antibiotics and promote development of novel compounds.

DRIVE-AB goal was to create, test and validate new economic models to incentivise the discovery of new antibiotics. DRIVE-AB recommended to governments and policy-makers new models to stimulate innovation in antibiotic research by assessing the value of new antibiotics and defining standards and metrics for responsible antibiotic use.

3.8.2 Project coordinator and managing entity

Project Coordinator AstraZeneca AB

Managing entity Université de Genève

3.8.3 Participants

Table 41: Project participants

EFPIA companies	
Astellas Pharma Europe LTD	Merck Sharp & Dohme Corp
Astrazeneca AB	Pfizer Limited, Sandwich
F. Hoffmann-La Roche AG	Sanofi-Aventis Recherche & Developpement
Glaxosmithkline Research And Development LTD	
Universities, research organizations, public bodies, non-profit groups	
British Society For Antimicrobial Chemotherapy (United Kingdom)	Universite De Geneve (Switzerland)
Eberhard Karls Universitaet Tuebingen (Germany)	Universite De Lorraine (France)
Folkehelseinstituttet (Norway)	Universiteit Antwerpen (Belgium)

London School Of Economics And Political Science (United Kingdom)	University Of Strathclyde (United Kingdom)
Royal Institute Of International Affairs (United Kingdom)	University Of Rijeka Medical Faculty (Croatia)
Ruprecht-Karls-Universitaet Heidelberg (Germany)	Uppsala Universitet (Sweden)
Stichting Katholieke Universiteit (Netherlands)	Wageningen University (Netherlands)
The Foundation For Medical Research Infrastructural Development And Health Services Next To The Medical Center Tel Aviv (Israel)	
Small and medium-sized enterprises (SMEs)	
Ursula Theuretzbacher (Austria)	

3.8.4 Project inputs and funding

The DRIVE-AB project received funding of €8 million from IMI, from a total project cost of €21 million (Table 42).

Table 42: Funding received

Contributions	Financial support, €	% total funding
EU contribution	6,299,987	57.4%
EFPIA contribution	3,105,250	28.3%
IMI contribution	1,563,439	14.3%
Total funding	10,968,676	100.0%

3.8.5 Assessing the socio-economic impact of DRIVE-AB

Infrastructure for further research

Table 43: Infrastructure for further research

Outcome	Socio-economic impact
More responsible use of antibiotics Project partners compiled and assessed definitions and metrics of responsible antibiotic use across diverse socioeconomic, geographic and clinical settings. They also aimed to deliver a systematic review of antibiotic use, analysing barriers to and enablers of responsible use. A conceptual framework was developed for an international guideline for responsible antibiotic use.	**Less antibiotic resistance** Frameworks developed during the DRIVE-AB project promote the responsible use of antibiotics globally. Responsible use of novel antibiotics will be key to limiting antibiotic resistance and ensure long-term effectiveness for patients.
Multidrug resistant pathogen propagation model Mathematical prediction models were developed of multidrug-resistant pathogen spread from first detection to established endemicity. They determined the clinical impact of emerging multi-resistant pathogens was determined across various settings, as well as quantified the economic consequences of antibiotic resistance from the perspectives of patients, health care providers and society.	**Economic planning** Economic models can be used to quantify the societal burden of antibiotic resistance, estimate the need for new antibiotics and inform clinicians and health policy makers.
Antibiotic valuation models The project developed novel valuation models to quantify the value of new antibiotics from the perspectives of different stakeholders.	**Policy recommendations for stakeholders** Policy recommendations were developed and presented to stakeholders to achieve buy-in for development of new antibiotics.

Dissemination of information

The work of the project was presented to the scientific community through peer-reviewed journal articles and presentations (Table 44).

Table 44: Dissemination of information

Outcome	Socio-economic impact
Publications At the time of completion, project findings were reported in 41 publications, 70.7% of which were open access. The work was presented at various scientific meetings and conferences.	Publications had a normalised citation rate of 2.54, which suggests that the results of the project are easily accessible within the academic community. The conference presentations further promoted the work of the project in the scientific community.
The DRIVE-AB conference The DRIVE-AB conference: "Revitalizing the antibiotic pipeline: Stimulating innovation while driving sustainable use and global access" was held in Brussels in 2017 and was a major achievement of the project. The conference attracted approximately 200 participants from a wide range of stakeholder groups, including policy-makers, medical professionals, representatives of the pharmaceutical and biotechnology industries, civil society communities and regulatory and public health experts.	**Promoting innovation in antibiotics** The interactive two-day meeting was focused on the communication of the consortium's research results and recommended options to drive investment in antibiotics that included a combination of incentive mechanisms along with finance and governance options to support their implementation.
Policy recommendations The DRIVE-AB consortium published its final policy recommendations in 2018 in a report: "Revitalizing the antibiotic pipeline: stimulating innovation while driving sustainable use and global access".	**Promoting innovation in antibiotics** All definitions, models and metrics were collected in the policy recommendations report to promote the development of novel antibiotics.

3.8.6 Conclusions of impacts

Promoting innovation in antibiotics

Work of the DRIVE-AB project published and presented at conferences raised awareness of the importance of innovation in current antibiotics for public health globally.

Creating policy recommendations for responsible use of antibiotics

The models developed during the DRIVE-AB project are a resource for policy makers and stakeholders assessing the economic impact of both antibiotic resistance and the introduction of novel treatments. Policy recommendations promote innovation in antibiotics research and provide guidance for the sustainable use of both current and novel treatments.

3.9 EBiSC: European Bank for induced pluripotent Stem Cells

01/2014 – 12/2017

3.9.1 Objectives of the project

Pluripotent stem cells are embryonic cells that can divide into the three primary germ cell layers of the developing embryo, and therefore into any cell of the body. Terminally differentiated cells that retain proliferative potential can only divide into the same cell type. However, terminally differentiated cells can be reprogrammed to generate induced pluripotent stem cells (iPSCs) with the capacity to generate any cell type, depending on external stimuli. iPSC lines (populations of cells descended from a single cell, stored for research purposes) are widely used in biomedical research areas such as developmental biology and oncology; but their use is often limited by insufficient background data, quality-control measures and availability.

The objective of the EBiSC project was to address the challenges associated with using iPSC lines in research by creating a repository of quality-controlled iPSC lines for researchers in industry and academia. To facilitate this, an engagement strategy was planned to attract clinical and scientific stakeholders in a network of cell line derivation centres.

In addition, the consortium aimed to deliver solutions for the standardisation of methodologies relating to iPSC derivation, preservation and recovery, and establish standards for quality control within the banking, characterisation and distribution of cell lines. These objectives were designed to enhance the quality, scope and efficiency of iPSC cell research, and promote Europe as a place for drug development.

3.9.2 Project coordinator and managing entity

Project Coordinator	Janssen Pharmaceutica NV
Managing entity	University of Edinburgh

3.9.3 Participants

Table 45: Project participants

EFPIA companies	
Astrazeneca AB	Janssen Pharmaceutica Nv
Bayer Aktiengesellschaft	Novo Nordisk A/S
Eli Lilly And Company Limited	Pfizer Limited
H. Lundbeck A/S	UCB Biopharma SPRL
Universities, research organizations, public bodies, non-profit groups	

Bioneer A/S (Denmark)	Instituto De Salud Carlos III (Spain)
Charite - Universitaetsmedizin Berlin (Germany)	Klinikum Der Universitaet Zu Koeln (Germany)
Department of Health (United Kingdom)	Koninklijke Nederlandse Akademie Van Wetenschappen - Knaw (Netherlands)
European Molecular Biology Laboratory (Germany)	The University of Edinburgh (United Kingdom)
Fraunhofer Gesellschaft Zur Foerderung Der Angewandten Forschung E.V. (Germany)	Universitatsklinikum Bonn (Germany)
Genome Research Limited (United Kingdom)	University College London (United Kingdom)
Gottfried Wilhelm Leibniz Universitaet Hannover (Germany)	University of Newcastle (United Kingdom)
Small and medium-sized enterprises (SMEs)	
Arttic (France)	Edelweiss Connect GMBH (Switzerland)
DefiniGEN Ltd (United Kingdom)	Roslin Cell Sciences Ltd (United Kingdom)
Third parties	
Fundacio Privada Centre De Medicina Regenerativa De Barcelona (Spain)	Fundacion Publica Andaluza Progreso Y Salud (Spain)

3.9.4 Project inputs and funding

The EBiSC project received funding of €21.8 million from IMI, from a total project cost of €34.3 million (Table 46).

Table 46: Funding received

Contributions	Financial support, €	% total funding
EU contribution	21,840,380	63.6%
EFPIA contribution	7,167,072	20.9%
IMI contribution	5,320,406	15.5%
Total funding	34,327,858	100.0%

3.9.5 Assessing the socio-economic impact of EBiSC

Infrastructure for further research

Table 47: Infrastructure for further research

Outcome	Socio-economic impact
An extensive biobank of iPSC cell lines The primary output of the project was the EBiSC, a large, not-for-profit repository of iPSC cell lines. At the time of project completion, it contained over 800 cell lines covering 35 diseases. Robust quality control procedures and characterisation tests ensured that highest quality standards were met. Ease of access to the bank were also of importance during development, with potential restrictions to use (such as consent form procedures or end user agreements) minimised to ensure wide availability. To facilitate evaluation of the available iPSC lines by users of the biobank, an Information Management System (IMS) was developed, providing data for the iPSC lines and managing documentation. EBiSC has resulted in the distribution of iPSC lines to users across the world, including Europe, USA, Australia, New Zealand, Japan and Korea.	 **Improved quality and increased scope of iPSC cell research** Robust quality control procedures and characterisation tests on iPSC cell lines deposited in the EBiSC have expanded the number of cell lines available to researchers and made make stem cell research more reproducible. Research on iPSCs will also be more efficient as the use of poor quality or poorly characterised cell lines is reduced. Overall, the provision of characterised, research-grade iPSC cell lines will enhance biomedical research in both academia and industry.

Standardisation of methods for biobank storage of iPSCs To address the varying quality of biobanking procedures across different cell line banks, the project established quality control standards for the routine banking, characterisation and distribution of iPSC cell lines. Standardised procedures and protocols were introduced and disseminated to researchers.	**Improved biobank storage of iPSCs** By introducing standards across cell line biobanking, EBiSC serves as a model for the improvement of other existing biobanks, which will ultimately enhance the reproducibility of cell line-based research and facilitate the development of novel medicines.

Dissemination of information

The work of the project was presented to the scientific community through peer-reviewed journal articles, presentations and through training initiatives (Table 48).

Table 48: Dissemination of information

Outcome	Socio-economic impact
Publications and conferences At the time of completion, project findings were reported in 19 publications, 68.4% of which were open access. Over 85 scientific presentations were made in scientific meetings and conferences around the world.	Publications had a normalised citation impact of 1.92, which suggests that the results of the project are easily accessible within the academic community. The conference presentations further promoted the work of the consortium to the scientific community, and will hopefully increase use of the biobank.
Training The EBiSC project provided theoretical and practical training to staff across partner laboratories to promote quality standards and contribute to the standardisation of iPSC methodologies. A number of Standard Operating Procedures (SOPs) covering good lab practice and cell culture techniques were developed and implemented, and a core training manual was created for new and existing EBiSC staff. Five SOPs were video recorded and are available on the EBiSC website. In addition, four 'hands on' training sessions were delivered, covering cell culture techniques and quality control procedures. Lectures were also delivered as part of the training programme.	**Enhancing the skillset of iPSC researchers and technicians in Europe** The education and training outputs of EBiSC disseminated the knowledge and skills that are important both for the effective implementation and use of the EBiSC biobank. The SOPs generated for the expansion and maintenance of the biobank serve as a valuable basis for the training of new EBiSC staff. Overall, an appropriately trained scientists will improve iPSC-based research.

3.9.6 Conclusions of impacts

Improved iPSC-based medicines research

The extensive biobank of iPSC cell lines established by the EBiSC is a long-term resource for scientists. Standardised methodology for the characterisation and storage of iPSCs will facilitate reproducible stem cell-based biomedical research.

The educational outputs of the EBiSC provided researchers with specific training in biobanking techniques and procedures which is important for long-term use of the biobank and expansion of iPSC research in Europe.

3.10 EHR4CR: Electronic Health Records Systems for Clinical Research

03/2011 – 02/2016

3.10.1 Objectives of the project

There are several challenges associated with clinical research and development (R&D) which have significant impacts to cost and project timelines, such as protocol optimisation, patient recruitment and clinical trial execution.

Electronic health record (EHR) systems are used in Europe and worldwide and have the potential to address some of the challenges associated with clinical research. Potential applications of interest include clinical trial feasibility, patient recruitment, clinical trial execution and drug surveillance reporting. However, there is a lack of interoperability between EHR systems which currently prevents efficient compilation of patient records data across large populations for research analysis.

The EHR4CR project has developed a scalable platform using de-identified data from hospital EHR systems, in full compliance with the ethical, regulatory and data protection policies and requirements of each participating country. The EHR4CR platform supports distributed querying to assist in clinical trials feasibility assessment and patient recruitment. The platform can access data within multiple hospital EHR systems and clinical data warehouses across Europe to enable researchers to predict the number of eligible patients for a candidate clinical trial protocol, assess trial feasibility and locate the most relevant hospital sites. Contrary to other initiatives, EHR4CR is compliant with relevant EU legislation and hospital policies regarding data protection and patient confidentiality.

3.10.2 Project coordinator and managing entity

Project Coordinator	AstraZeneca
Managing entity	European Institute for Health Records

3.10.3 Participants

Table 49: Project participants

EFPIA companies	
Amgen	GlaxosmithKline Research and Development LTD
AstraZeneca AB	Janssen Pharmaceutica NV
Bayer Pharma AG	Merck Kommanditgesellschaft Auf Aktien
Eli Lilly and Company Limited	Novartis Pharma AG
F. Hoffmann-La Roche AG	Sanofi-Aventis Recherche & Development

Universities, research organizations, public bodies, non-profit groups	
Assistance Publique (France)	Research In Advanced Medical Information And Telematics Vzw (Belgium)
Cdisc Europe Foundation (Belgium)	The University Of Edinburgh (United Kingdom)
Ethniko Kai Kapodistriako Panepistimio Athinon (Greece)	The University Of Manchester (United Kingdom)
European Institute For Health Records (France)	Tmf - Technologie Und Methodenplattform Fur Die Vernetzte Medizinische Forschung (Germany)
European Molecular Biology Laboratory (Germany)	Universite De Rennes I (France)
European Platform For Patients Oganisations (Belgium)	University College London (United Kingdom)
Friedrich-Alexander-Universitaet Erlangen Nuernberg (Germany)	University Of Dundee (United Kingdom)
Heinrich-Heine-Universitaet Duesseldorf (Germany)	University Of Glasgow (United Kingdom)
Institut National De La Sante Et De La Recherche Medicale (France)	Warszawski Uniwersytet Medyczny (Poland)
King's College London (United Kingdom)	Westfaelische Wilhelms-Universitaet Muenster (Germany)
Les Hopitaux Universitaires De Geneve (Switzerland)	EClinical Forum Association (France)
Small and medium-sized enterprises (SMEs)	
Custodix NV	Xclinical GMBH
Third parties	
Concept Consulting SARL	Neptunus Data Aktiebolag

3.10.4 Project inputs and funding

The EHR4CR project received funding of €7 million from IMI, from a total project cost of €16.6 million (Table 50).

Table 50: Funding received

Contributions	Financial support, €	% total funding
EU contribution	7,194,044	42.1%
EFPIA contribution	7,555,883	44.3%
IMI contribution	2,321,329	13.6%
Total funding	17,071,256	100.0%

3.10.5 Assessing the socio-economic impact of EHR4CR

Infrastructure for further research

Table 51: Infrastructure for further research

Outcome	Socio-economic impact
Creation and launch of operational platform In 2015, the European Institute for Innovation through Health Data (i~HD) was created. The i~HD is a not-for-profit organisation that develops and promotes best practices in the governance, quality, semantic interoperability and uses of health data in research. It provides independent oversight of clinical research platforms and their expanding hospital networks.	**Promotion of new methodologies and practices to optimise clinical research** Reusing digital health can impact the clinical research landscape across all stakeholder groups. Real-world data can inform clinical trial design; and improve patient recruitment and trial execution. The i~HD promotes best practices for accessing and analysing real-world data.
Creation and launch operational platform InSite is a clinical research platform, the main objective of which is to build a network and community of hospitals open to data re-use for research. The platform supports clinical protocol optimisation and helps with patient recruitment. InSite was improved and commercialised by Custodix and SME collaborator spin off (now merged with a US company, TriNetX). The platform is a commercial product now being rolled out across multiple hospitals in Europe,	**Clinical research optimization, reducing time for recruitment** This platform uses real-world data to improve protocol optimisation and patient recruitment, making clinical reach more efficient and cost-effective. The platform also facilitates improved patient screening and management of multicentre clinical trial programmes.

and some pharmaceutical companies have contracted the platform for clinical research.	Due to higher recruitment rates, hospitals have access to more clinical trials and can use their data for patient screening and unprecedented clinical intelligence.
New standard operating procedures EHR4CR drafted and developed new standard operating procedures (SOP)s for the use of EHRs.	**Improvement other research projects** New SOPs have since been applied to other research projects.

Dissemination of information

The work of the project was presented to the scientific community through peer-reviewed journal articles, conference presentations and training initiatives (Table 52).

Table 52: Dissemination of information

Outcome	Socio-economic impact
Publications At the time of completion, project findings were reported in 19 publications, 58% of which were open access. The work of the project was also presented at more than 180 international conferences. A website was also developed to communicate project initiatives and findings.	Publications had a normalized citation rate of 1.01, which suggests that the results of the project are easily accessible within the academic community. The conference presentations further promoted the work of the project.
Workshops Workshops and training events were held for both internal participants and the wider scientific community, including seven workshops for non-academic partners.	**Educational dissemination** Education initiative will increase the commercial use of the platform and ultimately make clinical research processes more efficient.

3.10.6 Conclusions of impacts

Creation of InSite platform to improve and optimise protocol designs and patient recruitment

The InSite platform has to potential to optimise clinical trial and patient recruitment protocols, minimising protocol-related study delays and costs. InSite has been commercialised by Custodix and an EHR4CR spin-off company, which will expand access to the platform for clinical researchers and pharmaceutical companies, ultimately expanding patient access to clinical studies.

Methods for using digital health data in clinical research

The SOPs for using EHRs will ensure best practices are applied across partner organisations and ensure patient data is used in accordance with relevant European legislation.

3.11 EMIF: European Medical Information Framework

01/2017 – 06/2018

3.11.1 Objectives of the project

Huge volumes of healthcare data are being collected and stored electronically in Electronic Healthcare Record (EHR) databases, research-driven cohort studies associated with biobanks and other sources. Due to storage of these data across multiple databases, it is rarely aggregated into larger datasets (for example, to increase patient cohorts in a disease area), where it would be of greater use to clinical research.

The European Medical Information Framework (EMIF) was launched in January 2013 to improve access to patient-level data. Project objectives were to develop common technical and governance solutions to increase access to health data. A common Information Framework (EMIF-Platform) was developed to facilitate access to diverse medical and research data sources.

To ensure immediate applicability, the EMIF project included two specific therapeutic research topics to guide the development of the Information Framework: the onset of Alzheimer's disease (EMIF-AD) and metabolic complications of obesity (EMIF-Metabolic).

3.11.2 Project coordinator and managing entity

Project Coordinator	Janssen Pharmaceutica NV
Managing entity	Erasmus Universitair Medisch Centrum Rotterdam

3.11.3 Participants

Table 53: Project participants

EFPIA companies	
Amgen	Janssen Pharmaceutica Nv
Boehringer Ingelheim Internationalgmbh	Merck Kommanditgesellschaft Auf Aktien
F. Hoffmann-La Roche AG	Novo Nordisk A/S
Glaxosmithkline Research And Development LTD	Pfizer Limited
Institut De Recherches Internationales Servier	UCB Biopharma SPRL

Universities, research organizations, public bodies, non-profit groups	
Aarhus Universitetshospital (Denmark)	The University Of Exeter (United Kingdom)
Agenzia Regionale Di Sanita (Italy)	The University Of Manchester (United Kingdom)
Erasmus Universitair Medisch Centrum Rotterdam (Netherlands)	Universidad Pompeu Fabra (Spain)
European Institute For Health Records (France)	Universidade De Aveiro (Portugal)
European Molecular Biology Laboratory (Germany)	Universita Di Pisa (Italy)
Fondazione PENTA - For The Treatment And Care Of Children With HIV-ONLUS (Italy)	Universitaet Leipzig (Germany)
Fundacio Institut Universitari Pera La Recerca A L'Atencio Primaria De Salut Jordi Gol I Gurina (Spain)	Universitat Zu Lubeck (Germany)
Goeteborgs Universitet (Sweden)	Universitatsklinikum Erlangen (Germany)
Institut National De La Sante Et De La Recherche Medicale (France)	Universiteit Antwerpen (Belgium)
Itä-Suomen Yliopisto (Finland)	Universiteit Maastricht (Netherlands)
Karolinska Institutet (Sweden)	University College London (United Kingdom)
King's College London (United Kingdom)	University Of Glasgow (United Kingdom)
Kobenhavns Universitet (Denmark)	University Of Leicester (United Kingdom)
Leibniz-Institut Für Präventionsforschung Und Epidemiologie - BIPS GmbH (Germany)	University Of Cambridge (United Kingdom)
Provincia Lombardo Veneta - Ordineospedaliero Di San Giovanni Di Dio- Fatebenefratelli (Italy)	University Of Helsinki, University Of Helsinki (Finland)
Sorbonne Universite (France)	University Of Oxford (United Kingdom)
Stichting Vumc (Netherlands)	Vib Vzw, (Belgium)
Tartu Ulikool (Estonia)	Teknologian Tutkimuskeskus VTT Oy (Finland)

Small and medium-sized enterprises (SMEs)	
Cambridge Cognition Limited (United Kingdom)	Maat France SARL (France)
Concentris Research Management GmbH (Germany)	Societa Servizi Telematici SRL (Italy)
Custodix Nv (Belgium)	Stichting Informatievoorziening Voor Zorg En Onderzoek (Netherlands)
Electrophoretics Ltd (United Kingdom)	Synapse Research Management Partners SL (Spain)
Genomedics S.R.L. (Italy)	
Patient Organisations	
Alzheimer Europe (Luxembourg)	Vestische Caritas-Kliniken (Germany)
Third parties	
PHARMO Institute N.V.(Netherlands)	Universitatsklinikum Schleswig-Holstein, (Germany)
-Universite Paul Sabatier Toulouse III (France)	

3.11.4 Project inputs and funding

The EMIF project received funding of €24.4 million from IMI, from a total project cost of €55.8 million (Table 54).

Table 54: Funding received

Contributions	Financial support, €	% total funding
EU contribution	24,356,096	43.7%
EFPIA contribution	24,354,503	43.6%
IMI contribution	7,073,712	12.7%
Total funding	55,784,311	100.0%

3.11.5 Assessing the socio-economic impact of EMIF

Innovation

Table 55: Project innovation

Outcome	Socio-economic impact
New Alzheimer's disease biomarkers New AD biomarkers were identified and validated.	 **Biomarkers to identify larger cohorts** These biomarkers can be used to identify new and larger cohorts of patients for clinical research.
New type 2 diabetes biomarkers New biomarkers predictive of insulin resistance and future development of type 2 diabetes were identified. Biomarkers for macrovascular and microvascular diabetes complications were also identified.	 **Improvement of type 2 diabetes diagnosis and management** These biomarkers have the potential to improve diabetes management and minimise the risk of complications.
Novel targets for the prevention of NASH (non-alcoholic fatty liver disease) Novel drug targets identified to prevent NAFLD/NASH were tested in early-phase clinical trials with promising findings.	 **New treatments for potential cases of NASH** New treatments could prevent worsening NASH.

Infrastructure for further research

Table 56: Infrastructure for further research

Outcome	Socio-economic impact
EMIF-Platform The EMIF-Platform is an efficient framework (technical solutions and governance processes) for accessing patient-level data in research. This platform enables researchers to browse data from over 400 databases across Europe.	 **EMIF-Platform connects researchers to real world data** EMIF-Platform catalogue has over 850 users and includes over 400 databases. The EMIF-Platform has leveraged data on more than 62 million adults and children in Europe from healthcare databases and cohorts from seven countries (Denmark, Italy, Netherlands, UK, Spain, EE), and is representative of existing data sources (for e.g. population-based registries, hospital-based databases, cohorts, national registries, and biobanks). The EMIF Data Catalogue is now available outside of EMIF to researchers. This widely available dataset will expand clinical research in Europe.

Overview of existing Alzheimer's disease cohorts EMIF provided an overview of the existing AD research cohorts. This information was integrated with the EMIF catalogue (EMIF-Platform). In total, 14 European cohorts were linked to the platform, including datasets needed for specific research questions.	**Pooled data from patient cohorts to create omics data for further research** Pooled data from research cohorts were used to create high dimensional omics data (proteomics, metabolomics, genomics). Using these data, EMIF has developed new treatment targets for drug development.
Connecting relevant cohort studies across Europe EMIF has connected relevant research cohorts of patients with AD across Europe.	**By connecting relevant cohorts, EMIF has set up a pan-European platform for large-scale research.** These large-scale studies can lead to new diagnostic and prognostic markers for neurodegenerative disorders.
New prediction rules and definitions of extreme phenotypes. EMIF created and validated new prediction rules for cognitive decline in pre-symptomatic and prodromal AD.	**Earlier diagnosis of patients and improved patient selection for future clinical research.** Earlier diagnosis of AD may improve prognosis for patients. Cognitive decline prediction methods can also support subject selection and stratification in future clinical trials.

Dissemination of information

The work of the project was presented to the scientific community through peer-reviewed journal articles conference presentations and education initiatives (Table 57).

Table 57: Dissemination of information

Outcome	Socio-economic impact
Publications and conference presentations At the time of completion, project findings were reported in 229 publications, 68.6% of which were open access. Numerous scientific presentations were made at conferences around the world.	Publications had a normalised citation rate of 3.60, which suggests that the results of the project are easily accessible within the academic community. The conference presentations further promoted the project to the scientific community.
Training outputs The EMIF project provided several workshops across Europe.	**Enhancing the skillset of the scientific workforce**

	The education and training outputs of EMIF will enable effective implementation and use of the EMIF-Platform.

3.11.6 Conclusions of impacts

EMIF-Platform facilitates the access of real-world data and research tools to European researchers.

EMIF-Platform is a major achievement of the project and enables researchers to use real-world data to inform their research. Researchers can access a variety of data sources such as hospital databases (real-world data), research cohorts (to inform patient recruitment in future studies) and biobanks.

Identification of biomarkers for disease such as dementia and type 2 diabetes

Novel biomarkers can be used to recruit patients into the most appropriate clinical trial cohorts. Biomarkers can also inform disease diagnosis and prognosis, which may improve disease management.

By connecting relevant cohorts, EMIF has set up a platform for large-scale research. Using pool data from the cohorts to create omics data for further research.

These large-scale studies may lead to new diagnostic and prognostic markers for neurodegenerative disorders by using pool data from all cohorts to create omics data (proteomics, metabolomics, genomics) for further research.

3.12 EMTRAIN: European Medicines Research Training Network

10/2009 – 09/2016

3.12.1 Objectives of the project

For Europe to remain at the forefront of biomedical science, the highest quality of education and training must be delivered to future and current researchers. Knowledge transfer between academia and the pharmaceutical industry is important for education and training programmes and ultimately progression in biomedical science.

The 7-year EMTRAIN project established a pan-European network integrating education and training programmes across all aspects of medicines research. Specifically, the key objectives were to create an online catalogue of education courses across Europe, deliver a series of PhD workshops on careers in the pharmaceutical industry and establish a network of public and private bodies for the ongoing discussion of educational issues.

3.12.2 Project coordinator and managing entity

Project Coordinator AstraZeneca

Managing entity Medizinische Universitaet Wien

3.12.3 Participants

Table 58: Project participants

EFPIA companies	
AstraZeneca AB	Janssen Pharmaceutica Nv
Bayer Pharma AG	Laboratorios Almirall S.A.
Boehringer Ingelheim International GmbH	Novartis Pharma AG
Esteve Pharmaceuticals S.A.	Novo Nordisk A/S
F. Hoffmann-La Roche AG	Orion Oyj
Genzyme Europe B.V.	Sanofi-Aventis Deutschland GmbH
Glaxosmithkline Research And Development LTD.	UCB Biopharma SPRL
H. Lundbeck A/S	

Universities, research organizations, public bodies, non-profit groups	
Biobanks And Biomolecular Resources Research Infrastructure Consortium (BBMRI-ERIC)	Medizinische Universitaet Wien (Austria)
Centre Europeen De Recherche En Biologie Et Medecine (France)	Medizinische Universitat Graz (Austria)
European Molecular Biology Laboratory (Germany)	Ministry of Human Resources, Medical Research Council, National Healthcare Service Center (Hungary)
Helmholtz-Zentrum Fur Infektionsforschung GMBH, Braunschweig (Germany)	PharmaTrain Federation (Switzerland)
Helmholtz Zentrum Muenchen Deutsches Forschungszentrum Fuer Gesundheit Und Umwelt GMBH (Germany)	The University of Manchester (United Kingdom)
Institut National De La Sante Et De La Recherche Medicale (France)	University of Oxford (United Kingdom)
Karolinska Institutet (Sweden)	

3.12.4 Project inputs and funding

The EMTRAIN project received funding of €4.3 million from IMI, from a total project cost of €8.0 million (Table 59).

Table 59: Funding received

Contributions	Financial support, €	% total funding
EU contribution	4,324,999€	54.1%
EFPIA contribution	3,664,510€	45.9%
IMI contribution	-	-
Total funding	7,989,509€	100.0%

3.12.5 Assessing the socio-economic impact of EMTRAIN

Innovation

Table 60: Project innovation

Outcome	Socio-economic impact
Online catalogue of biomedical science courses in Europe (now offline) EMTRAIN developed a free-to-use online portal, cataloguing thousands of courses across Europe alongside costs, content, requirements and links to course websites. Over 7,700 courses were listed at the time of project completion, ranging from simple one-day teaching events to Master's, PhD and continued professional development (CPD) courses. Named 'on-course®', the portal was the flagship output of the EMTRAIN project. However, provisions were only made to maintain the portal for 2-3 years after the end of the funding period. It is now offline.	**Guidance for prospective students (limited to platform availability period)** According to consortium figures, on-course® attracted a high number of weekly visits, indicating its value in helping prospective students navigate the large number of available courses. However, the portal is now offline, and unless future resources are committed to re-launching and regularly updating the platform, it will not be of long-term benefit to European citizens.

Structuring the European research area

Table 61: Structuring the European research area

Outcome	Socio-economic impact
'LifeTrain' framework for coordinated CPD delivery across Europe Continued professional development (CPD) is an essential means by which professionals maintain and improve their knowledge and skills. However, the delivery of CPD across European organisations varies considerably. EMTRAIN developed a common framework for the delivery of CPD within Europe. Branded 'LifeTrain', this framework contains four sets of agreed principles - one for each of the following parties: professional/scientific bodies, course providers, employers and individual professionals. Three LifeTrain workshops were held in which delegates from relevant bodies discussed how best to form a coherent approach to CPD, and the resulting framework document is available on the EMTRAIN website.	**Greater mobility across organisations and more effective training** The LifeTrain project provides a valuable basis for future discussion and progress in CPD management. A fourth LifeTrain event, 'The Lifelong Learning Conference' involved a particularly comprehensive discussion about both CPD delivery and the wider professional education landscape. A LifeTrain website was created containing the principles, workshop details, conference presentations, publications, examples of competency profiles, case studies and the list of signatories, however it is now offline, limiting dissemination of new ideas generated by the initiative.

Dissemination of information

Training initiatives included workshops for PhD students and early-career researchers, which raised awareness of career options within the pharmaceutical industry (Table 62).

Table 62: Dissemination of information

Outcome	Socio-economic impact
Public-Private Partner PhD workshops EMTRAIN devised a series of workshops aimed at providing young researchers with a holistic understanding of drug development processes and associated career options in the pharmaceutical industry. Over the course of the project, five Public-Private Partner (PPP) PhD workshops were delivered within industry settings: two in Belgium (Janssen and UCB), two in the UK (GSK and AstraZeneca) and one in Germany (Bayer). In total, 135 students from 17 companies, 56 universities and 22 different countries attended the workshops.	**Raising industry awareness** Feedback from the workshops showed that they had a positive impact in raising awareness of career options in the pharmaceutical industry. The agenda and feedback from each workshop are available on the EMTRAIN website, serving as a basis for future programmes. The impact of this work could have been greater if a larger number of workshops been delivered across a broader range of countries.

3.12.6 Conclusions of impacts

Foundations for future discussion and increased industry awareness for PhD students

IMI identified a lack of interaction between academia and industry in Europe, finding that undergraduate students were not aware of the many career options available within biomedical R&D. This was addressed with PPPs across Europe to educate PhD students on drug development processes and associated career options. In addition, the framework created by the LifeTrain programme for CPD will reduce training costs and enhance mobility of staff across organisations.

Impacts limited by poor sustainability of outputs

The on-course® tool and the LifeTrain website are now offline which limits any long-term benefit of the project.

3.13 eTOX: Integrating bioinformatics and chemoinformatics approaches for the development of Expert systems allowing the in silico prediction of toxicities

01/2010 – 12/2016

3.13.1 Objectives of the project

Predicting side effects of drug candidates is of critical importance in the drug development process. A vast amount of preclinical data are produced by pharmaceutical companies on potential drug side-effects, however, these data are rarely shared with the research community.

The eTOX project aimed to address this by enabling pharmaceutical companies to share their preclinical data in a database. The eTOX project specifically targeted *in silico* data, i.e. data arising from computer simulations for the prediction of the toxicology of molecules, before they are physically tested *in vivo*. The more insight gained from *in silico* data, fewer animal tests are required to determine drug safety.

This dataset was also used to develop computerised models to predict side-effects of future compounds.

3.13.2 Project coordinator and managing entity

Project Coordinator	Novartis Pharma AG
Managing entity	Fundació Institut Mar d'investigacions Mèdiques IMIM

3.13.3 Participants

Table 63: Project participants

EFPIA companies	
Astrazeneca AB	Institut De Recherches Internationales Servier, Suresnes
Bayer Pharma AG	Janssen Pharmaceutica Nv
Boehringer Ingelheim International GmbH,	Novartis Pharma AG
Esteve Pharmaceuticals, SA	Pfizer Limited
F. Hoffmann-La Roche AG	Sanofi-Aventis Deutschland GmbH
Glaxosmithkline Research and Development Ltd.	UCB Biopharma SPRL
H. Lundbeck As, Valby	

Universities, research organizations, public bodies, non-profit groups	
Danmarks Tekniske Universitet (Denmark)	Lhasa Limited (United Kingdom)
Erasmus Universitair Medisch (Netherlands)	Liverpool John Moores University (United Kingdom)
European Molecular Biology Laboratory (Germany)	Stichting Vu (Netherlands)
Fraunhofer Gesellschaft Zur Foerderung Der Angewandten Forschung E.V. (Germany)	Universitat Politecnica De Valencia (Spain)
Fundacio Institut Mar D Investigacions Mediques IMIM (Spain)	Universitat Wien (Austria)
Fundacion Centro Nacional De Investigaciones Oncologicas Carlos Iii (Spain)	University Of Leicester (United Kingdom)
Small and medium-sized enterprises (SMEs)	
Chemotargets SL (Spain)	Molecular Networks GMBH Computerchemie (Germany)
Inte:Ligand Software-Entwicklungs-Und Consulting GmbH (Austria)	Synapse Research Management Partners SL (Spain)
Lead Molecular Design S.L., Sant Cugat Del Vallès (Spain)	
Third parties	
Consorcio Mar Parc De Salut De Barcelona (Spain)	Universidad Pompeu Fabra (Spain)

3.13.4 Project inputs and funding

The eTOX project received funding of €6.9 million from IMI, from a total project cost of €18.8 million (Table 64).

Table 64: Funding received

Financial support	Financial support, €	% total funding
EU contribution	6,910,018	36.8%
EFPIA contribution	10,157,590	54.1%
IMI contribution	1,719,500	9.2%
Total funding	18,787,108	100.0%

3.13.5 Assessing the socio-economic impact of eTOX

Innovation

Table 65: Project innovation

Outcome	Socio-economic impact
New predictive models The consortium used the pooled dataset to build 99 computerised models that could be used to predict the toxicology of compounds not found in the dataset. The models are based on the relationships between the structures of existing compounds in the eTOXsys database and their associated toxicological and clinical data. These models are integrated into the eTOXsys platform, which users to enter structures of hypothetical compounds and gain predictions of potential side effects.	 **Tools to increase research efficiency** The models provide further guidance to researchers assessing drug candidates for clinical development. Widespread use of the models will help to reduce late-stage failure rates, providing cost and time benefits, as well as minimising the use of both animal and human subjects in trials.

Infrastructure for further research

Table 66: Infrastructure for further research

Outcome	Socio-economic impact
The eTOXsys platform eTOXsys is a toxicology database containing information on almost 2000 molecules from over 8000 toxicology studies. The data was derived from proprietary preclinical data donated by the 13 pharmaceutical consortium partners, as well as data in the public domain. A web application – the eTOXsys user interface – was designed for user-friendly access to the database, in which chemical compounds could be searched by name or structure, with the toxicology prediction results presented in a structured layout, with hit lists, study design and dose range presented in table form. As well as retrieving toxicity information for the molecules stored in the eTOX database, the eTOXsys platform also integrated new predictive models to predict toxicity endpoints for molecules for which no appropriate information is available in the database.	 **Increase in drug development efficiency** The eTOXsys database can inform early stage decision making, increasing the efficiency of the drug development process. eTOXsys was only available to consortium members, with access dependent on the 'sensitivity class' of the data, reducing the impact of this work. A commercialisation plan was enacted after project completion, with access to the platform only granted through data sharing/fee paying.
Standardisation of terminologies The consortium identified a critical need to simplify and standardise the scientific terminologies used by different organisations to describe features and outputs of preclinical studies. eTOX researchers therefore carried out a simplification process, reducing around 80,000 terms in initial data sources to under 7000. The new terminology system is stored for future use in a publicly available tool ('OntoBrowser').	 **A basis for more effective data sharing** The standardisation process was required for full use of the pooled data. It provides the basis for any research/healthcare-enhancing impacts of the eTOX products. It also serves as infrastructure for future collaboration within the *in silico* modelling research space, facilitating efficient data sharing through common terminology.
The eTOXlibrary The eTOXlibrary is a web-based, structured library containing links to a variety of online materials of relevance to *in silico* toxicity prediction studies. Materials include articles, public databases, standardised terminology systems and modelling tools. All resources were reviewed, evaluated and grouped into categories. The library is publicly available online and was updated on a monthly basis during the project lifetime.	 **Useful resource for *in silico* studies** The eTOXlibrary is publicly available and easily accessed. It therefore remains of use to the research community, providing a catalogue of scientific resources. Widespread use will result in more informed research decisions and methodologies, leading to more efficient drug development.

Dissemination of information

The work of the project was presented to the scientific community through peer-reviewed journal articles and conference presentations (Table 67).

Table 67: Dissemination of information

Outcome	Socio-economic impact
Publications At the time of completion, project findings were reported in 95 publications, 60% of which were open access. 169 presentations were made at conferences and scientific meetings around the world.	Publications had a normalised citation impact of 1.60, which suggests that the results of the project are easily accessible within the academic community. The conference presentations further promoted the work of the project and the importance of sharing toxicology data.

3.13.6 Conclusions of impacts

More efficient clinical research, dependent on platform availability

The research tools delivered by the eTOX project have the potential to reduce failure rates in drug development, making pharmaceutical research more efficient. The eTOXsys database is a valuable library of toxicology prediction data, which can help researchers choose which drug candidates to pursue based on likely side effects, which otherwise would only be discovered in later stages of testing. The novel computer models can also be used inform early stage decision making. Wider access to the tools within the research community would increase the weight of these impacts.

Reduced animal testing and risk of harm to clinical trial participants

If the eTOXsys tools successfully reduce the number of unsuitable drugs candidates that are selected for further development, it will result in fewer animals being used for *in vivo* toxicity testing of harmful drug candidates. It also reduces the risk of unnecessary exposure of clinical trial participants to harmful/unsuitable treatments.

Infrastructure for further collaboration

The eTOX project set a precedent for future projects involving data sharing collaborations, demonstrating the feasibility and benefits of sharing proprietary data. The project also left infrastructure for further collaboration within the *in silico* prediction field, with a standardisation terminology framework made publicly available online.

3.14 ETRIKS: European Translational Information and Knowledge Management Services

10/2012 – 09/2018

3.14.1 Objectives of the project

Complex research projects involving collaborations between organisations need infrastructure to facilitate the sharing and management of data from numerous different sources. At the start of the eTRIKS project, each IMI consortia had to develop its own information management system, using resources and risking loss of data after project completion.

The eTRIKS project was devised to address this burden on time and resources by creating an open information analytics/management platform and providing sustainable knowledge management services to consortia clients. Services included data curation and custom analysis. The eTRIKS consortium also aimed to develop standards and training materials for effective implementation and use of the eTRIKS platform.

The ultimate goal of the work was to increase the efficiency of IMI and other consortium-based research projects, allowing greater scientific and socio-economic value to be derived from the work. It was also hoped that the use of an open platform with consistent standards would also facilitate greater re-use of data, enhancing the reproducibility and long term impacts of the research projects.

3.14.2 Project coordinator and managing entity

Project Coordinator AstraZeneca AB

Managing entity Imperial College London

3.14.3 Participants

Table 68: Project participants

EFPIA companies	
AstraZeneca AB	H. Lundbeck As
Bayer Aktiengesellschaft	Janssen Pharmaceutica Nv
Eli Lilly And Company Limited	Merck Kommanditgesellschaft Auf Aktien
F. Hoffmann-La Roche AG	Pfizer Limited
Glaxosmithkline Research and Development Ltd.	Sanofi-Aventis Recherche & Developpement

Universities, research organizations, public bodies, non-profit groups	
Association Eisbm (France)	Imperial College of Science Technology And Medicine (United Kingdom)
Cdisc Europe Foundation Fondation (Belgium)	Universite Du Luxembourg (Luxembourg)
Centre National De La Recherche Scientifique Cnrs (France)	University of Oxford (United Kingdom)
Small and medium-sized enterprises (SMEs)	
Biosci Consulting Bvba (Belgium)	
Non-EFPIA companies	
ID Business Solutions Limited (United Kingdom)	

3.14.4 Project inputs and funding

The eTRIKS project received funding of €17.4 million from IMI, from a total project cost of €39.4 million (Table 69).

Table 69: Funding received

Contributions	Financial support, €	% total funding
EU contribution	10,309,818	42.5%
EFPIA contribution	10,795,178	44.5%
IMI contribution	3,139,745	13.0%
Total funding	24,244,741	100.0%

3.14.5 Assessing the socio-economic impact of ETRIKS

Innovation

Table 70: Project innovation

Outcome	Socio-economic impact
eTRIKS Translational Research Information Platform & supporting services The platform at the core of the eTRIKS project is an open, sustainable research informatics/knowledge management platform, based on previously existing data warehouse software. The data management needs of 61 EU public-private partnerships (both IMI and external public-private partnerships) were supported by the platform. Six IMI consortia clients were comprehensively supported with platform provision, training, data curation and custom development and analysis. A further 34 clients were provided with more basic enabling support and the remaining clients used the platform without the direct support of eTRIKS personnel. The information management was conducted based on agreed standards, and business plans were put in place for platform maintenance beyond project completion.	 **Greater time and cost efficiency for public-private research projects** Without the eTRIKS platform, the public/private users would have had to expend significant resources on the development of their own, single-use data management tools. Significant time and cost savings were therefore made as a result of the immediately available eTRIKS platform, accelerating projects and providing greater return on public investment on IMI project. The use of the platform provided further benefit in circumventing the risk of data loss that often occurs with projects that have used project-specific knowledge management systems. The use of a common platform, based on agreed standards, therefore enhances the long-term impacts of the projects by increasing transparency and reproducibility.
eTRIKS Labs eTRIKS labs is an online portal designed for the open-license distribution of the applications and analysis methods developed supplementary to the translational research platform. The applications include a data harmonisation/mapping service and a data analysis environment developed by Imperial College London.	 **Open tools for greater research efficiency** eTRIKS labs provides the research community with open access to a variety of tools that facilitate the management of multi-source datasets. As such, the platform further enhances the efficiency of public-private partnership research projects, furthering the socio-economic benefits of each one.

Infrastructure for further research

Table 71: Infrastructure for further research

Outcome	Socio-economic impact
eTRIKS Public Platform The eTRIKS public platform provides open access to around 200 public domain clinical studies, curated to the quality standards established by the consortium. The studies cover a range of disease areas. The platform also serves as an educational environment for researchers seeking to use the core eTRIKS platform.	**Increasing accessibility and re-use of clinical data** The public platform increases the long-term value of existing clinical studies by enhancing accessibility and standards of curation of the datasets. This promotes re-use and further analysis, advancing subsequent research.

Structuring the European research area

Table 72: Structuring the European research area

Outcome	Socio-economic impact
Commercial spin-off: ITTM Operationalising eTRIKS curation support for comprehensively supported IMI projects led in part to the creation of ITTM (Information Technology for Translational Medicine) a small (<5 FTE) data management consultancy. A spin-off from the University of Luxembourg, ITTM provides a range of data handling services, and contributes to the maintenance of the eTRIKS platform.	**Business creation and high-quality support for data management** In addition to its economic impacts as a new business, ITTM enhances large-scale research projects through high-quality data curation and management. It also consolidates the long-term benefits of eTRIKS though its activity within the sustainability plans for the platform.

Dissemination of information

The work of the project was presented to the scientific community through peer-reviewed journal articles, conference presentations and training initiatives (Table 73).

Table 73: Dissemination of information

Outcome	Socio-economic impact
Publications and presentations At the time of completion, project findings were reported in 35 publications, 65.7% of which were open access. The consortium's work was presented at over 140 conferences, seminars and other scientific meetings, predominantly in Europe.	The dissemination of the project's work to the scientific community encouraged use of the eTRIKS platform, raised awareness of data management issues and promoted Europe as a place for innovative research.

Training activity In total, 444 individuals received training on concepts and processes fundamental to eTRIKS outputs. Areas covered included data curation, data privacy and re-use, application of data standards and database mapping. The training materials were not licensed for open use beyond project completion.	 **Enhanced skillset of research workforce** Whilst the training was largely specific to eTRIKS tools, enhanced knowledge of data sharing concepts and processes can be applied by trainees in future work, increasing their competitivity in the job market. Open sharing of the training materials could have further enhanced this impact.

3.14.6 Conclusions of impacts

Greater cost and time efficiency of public-private research projects

The provision of the eTRIKS platform to public-private research consortia circumvented the need for each one to create its own data management system – a task that typically requires significant time and resources. As such, the eTRIKS project allowed greater focus to be placed on research, rather than research infrastructure - increasing the value and return on investment of IMI (and other) projects.

Infrastructure for information management of needs of future partnerships

The outputs of the eTRIKS project provide infrastructure for the continued enhancement of translational research. The eTRIKS Translational Research Information Platform is being sustained by a number of entities, and the spin-off company Information Technology for Translational Medicine (ITTM) offers high-quality data management services. Alongside this, eTRIKS Labs provides open-license access to applications and analysis methods developed throughout the project. These outputs will increase the efficiency of future multi-partner projects, contributing to the socio-economic impacts of each one.

3.15 EU2P: European programme in Pharmacovigilance and Pharmacoepidemiology

09/2009 – 06/2016

3.15.1 Objectives of the project

The European Programme in Pharmacovigilance and Pharmacoepidemiology (EU2P) project aims to increase the knowledge and understanding of medicines-related risk and integrated benefit-risk by implementing a European training and education platform in Pharmacovigilance and Pharmacoepidemiology for academia, industry and regulatory bodies.

This programme offers courses in Pharmacovigilance and Pharmacoepidemiology with specialties in benefit assessment, regulatory aspects, risk identification and quantification, benefit-risk assessment, public health and risk communication. Courses are recognised by academia, industry and regulatory bodies, with postgraduate diplomas in the framework of the Bologna process awarded. Eu2P targets specialists such as pharmacists, physicians, scientists and experienced professionals but also non-specialists such as media representatives, laypersons and patients for risk communication training.

3.15.2 Project coordinator and managing entity

Project Coordinator	F. Hoffmann-La Roche AG
Managing entity	Université de Bordeaux

3.15.3 Participants

Table 74: Project participants

EFPIA companies	
Amgen	Janssen Pharmaceutica Nv
AstraZeneca AB	Laboratorios Almirall
Bayer Pharma AG	Novartis Pharma AG
Boheringer Ingelheim Internatinal gmbh	Novo Nordisk AS
Eli Lilly And Company Limited	Orion Oyj
F. Hoffmann-La Roche AG	Sanofi-Aventis Rescherche and Developpment
Glaxosmithkline Research and Development LTD	UCB Pharma

H. Lundbeck AS

Universities, research organizations, public bodies, non-profit groups	
Erasmus Universitair Medisch Centrum Rotterdam (Netherlands)	The University of Hertfordshire Higher Education Corporation (United Kingdom)
Fundacio' Institut Català De Farmacologia (Spain)	Universita Degli Studi Di Verona (Italy)
Karolinska Institutet (Sweden)	Universite De Bordeaux (France)
The European Medicines Agency (United Kingdom)	Universiteit Utrecht (Netherlands)
Third parties	
Association Pour Le Développement De L'Enseignement Et Des Recherches Auprès Des Universités, Des Centres De Recherche Et Des Entreprises D'Aquitaine (France)	
Non-EFPIA companies	
Agence Nationale De Sécurité Du Médicament Et Des Produits De Santé (France)	

3.15.4 Project inputs and funding

The EU2P project received funding of €6.0 million from IMI, from a total project cost of €13.1 million (Table 75).

Table 75: Funding received

Contributions	Financial support, €	% total funding
EU contribution	3,708,225	46.0%
EFPIA contribution	4,019,661	50.0%
IMI contribution	291,018	4.0%
Total funding	8,018,904	100.0%

3.15.5 Assessing the socio-economic impact of EU2P

Structuring the European research area

Table 76: Structuring the European research area

Outcome	Socio-economic impact
Memorandum of Understanding until 2021 EU2P have a memorandum of understanding (valid until June 2021) which is the legal framework of cooperation between the Eu2P Academic partners (delivering courses and awards and providing the pedagogical accreditation of all training programs) and associated partners providing support in the training content and organisational aspects. Separate agreements were signed for the organisation, delivery and partnership management for each of the different types of training (Eu2P Master's degree, Eu2P Certificates, and Eu2P).	**Academic agreements to facilitate education in Europe** Most of the projects are based on educational activities, facilitating regulated courses, Master's degrees and certificates in Europe. Improves and facilitates interaction between public, regulatory and private stakeholders and meets the needs of industry and regulators for tailored training,
SOPs for pharmacovigilance and pharmacoepidemiology Researchers have established quality standards and best practices in various European (ENCePP network) and international bodies (ISoP and ISPE societies) as active members, including presidents.	**Applying knowledge** All of the pharmacovigilance and pharmacoepidemiology information shared by the EU2P improved the understanding of the risks and benefits of medicines globally. SOPs facilitate application of this knowledge into practice.

Dissemination of information

The work of the project was presented to the scientific community through peer-reviewed journal articles, conference presentations and education initiatives (Table 77).

Table 77: Dissemination of information

Outcome	Socio-economic impact
Publications and conferences At the time of completion, project findings were reported in three publications.	Publications had a normalised citation rate of 1.88, which suggests that the results of the project are easily accessible within the academic community.

Pharmacovigilance and pharmaco-epidemiology educational activities The EU2P consortium created an e-learning platform dedicated to pharmacovigilance and pharmaco-epidemiology training for students and professionals. EU2P offers a Master of Science program, 25 certificate courses, 65 short courses and 3-year PhD programmes. To date, approximately 400 students have been trained in either Master's or PhD programs and 685 professionals have registered for short courses.	 EU2P has an impact on future work in the field by training medicines-related stakeholders. Provide well-trained professionals in pharmacovigilance and pharmacoepidemiology, which fulfils the need of having Qualified Persons for the pharmaceutical industry, well trained persons in regulatory authorities and future experts who boost methods research in the academic centres,

3.15.6 Conclusions of impacts

EU2P improved the understanding of medicines-related risk and benefit globally by developing an online training and education platform in pharmacovigilance and pharmacoepidemiology.

By bringing together academic, regulatory and industry partners, the project developed the first pan-European, internationally recognised programme in pharmacovigilance and pharmacoepidemiology. This framework enabled the involvement of regulatory agencies (including the EMA) and EFPIA pharma industry partners to enrich the programme curricula with different stakeholders' perspectives, international experts' involvements and real-life case learning materials.

The project also aims to reach the North American and Middle East markets through new partnerships in 2020.

3.16 EU-AIMS: European Autism Interventions – a Multicentre Study for Developing New Medications

04/2012 – 03/2018

3.16.1 Objectives of the project

Autism spectrum disorders (ASD) are a group of development disorders associated with inhibited social interactions, difficulties with communication and atypical repetitive behaviours. The prevalence of ASD is increasing, with 1 child in 110 currently affected. Despite this, there are no treatments for the specific symptoms of ASD and little is known about the causes of the condition.

EU-AIMS project objective was to conduct research on the genetics, biological causes and indications of ASD, including a large, Europe-wide clinical study of people with autism. The project also aimed to generate new tools for the diagnosis and assessment of ASD, as well as research tools such as animal models and *in vitro* cell lines for the development of effective ASD treatments.

Through increased knowledge of ASD and the generation of research tools, the EU-AIMS consortium aimed to accelerate the development of effective ASD treatments, reducing the burden associated with treating patients with ASD whilst increasing the quality of life of those living with the condition.

3.16.2 Project coordinator and managing entity

Project Coordinator	F. Hoffmann-La Roche AG
Managing entity	King's College London

3.16.3 Participants

Table 78: Project participants

EFPIA companies	
Eli Lilly and Company Limited	Janssen Pharmaceutica Nv
F. Hoffmann-La Roche AG	Pfizer Limited
Institut De Recherches Servier	Vifor SA
Islensk Erfdagreining Ehf	
Universities, research organizations, public bodies, non-profit groups	
Birkbeck College - University of London (United Kingdom)	Universita Campus Bio Medico di Roma (Italy)

Commissariat A L Energie Atomique Et Aux Energies Alternatives (France)	Stichting Katholieke Universiteit (Netherlands)
European Molecular Biology Laboratory (Germany)	Universitaet Ulm (Germany)
Institut Pasteur (France)	Universitair Medisch Centrum Utrecht (Netherlands)
Karolinska Institutet (Sweden)	Universitat Basel (Switzerland)
King's College London (United Kingdom)	University of Cambridge (United Kingdom)
Max-Planck-Gesellschaft Zur Forderung Der Wissenschaften Ev (Germany)	Zentralinstitut Fuer Seelische Gesundheit (Germany)
Small and medium-sized enterprises (SMEs)	
Arttic (France)	Noldus Information Technology BV (Netherlands)
Laeknisfraedileg Myndgreining Ltd (Iceland)	
Patient organisations	
Autism Speaks Inc. Non Profit Corporation, Princeton, NJ, United States	
Third parties	
Koninklijke Nederlandse Akademie Van Wetenschappen (Netherlands)	

3.16.4 Project inputs and funding

The EU-AIMS project received funding of €20.5 million from IMI, from a total project cost of €37.5 million (Table 79).

Table 79: Funding received

Financial support	Financial support, €	% total funding
EU contribution	20,490,981	54.7%
EFPIA contribution	9,773,543	26.1%
IMI contribution	7,216,089	19.3%
Total funding	37,480,613	100.5%

3.16.5 Assessing the socio-economic impact of EU-AIMS

Innovation

Table 80: Project innovation

Outcome	Socio-economic impact
Advancement of *in vitro* testing capabilities The EU-AIMS consortium made significant progress in developing resources for *in vitro* ASD studies (*in vitro*: studying the condition in cells/microorganisms, outside of living organisms). A significant achievement in this field was the use of *in vitro* testing to understand how viral infections in pregnant mothers increases the likelihood of ASD in the unborn child. Extensive materials for future *in vitro* testing were also developed, including 339 stem cell biosamples. Six *in vitro* models were standardised and validated.	**Enabling greater insight from early-stage ASD research** *In vitro* testing is a fundamental process in drug development and can be used to identify candidate drugs for further preclinical testing. EU-AIMS has widened the scope of early stage ASD drug development and enabled higher quality, more efficient research than was achievable previously. Ultimately, this will help accelerate the introduction of novel treatments for ASD.
Novel animal models and biomarkers for ASD Two new animal models were developed to study ASD, in addition to a comprehensive knowledge base for the development of further models. Four new candidate biomarkers for ASD were discovered.	**Increasing the scope of ASD research for more effective treatments** The greater number of animal models and biomarkers that are available for ASD research, the better scientists can understand the condition and develop new treatments. The development and validation of new animal models by EU-AIMS has increased the potential of research h in ASD, accelerating the development of treatments for autism disorders.

Imaging technologies The EU-AIMS consortium made significant progress in developing neuroimaging methodologies for the study of brain activity in individuals with ASD. These techniques were used in studies on both animals and humans to understand the neurological basis of the condition.	**Techniques for detailed study of ASD** The neuroimaging methodologies were used to understand the neurological processes associated with ASD. The techniques can be used in further studies, boosting ASD drug development.
Increased fundamental knowledge of ASD Project findings included a link between eye movement in babies looking at a still image and ASD, differences in the effects of autism between the male and female brain, and a link between increased paternal age and risk of ASD.	**Foundations for more targeted ASD research** Since relatively little is known about the biological causes of ASD, knowledge generated by EU-AIMS may guide future research and ultimately accelerate the development of potential new treatments for ASD.

Infrastructure for further research

Table 81: Infrastructure for further research

Outcome	Socio-economic impact
Autism database EU-AIMS researchers created one of the world's most comprehensive autism databases, containing data from hundreds of individuals with ASD. Data was collected through two large clinical studies, in which each participant was characterised by their medical history, family history, behaviour, cognitive profile and brain scans. In total, 450 people with ASD, 300 babies at high risk of developing autism and 450 individuals with typical development or other mental disabilities were included. The database is being shared with five international organisations and will be made available to the research community in 2020.	**Avenues for more personalised treatment for autism disorders** This work provides a source of data for further analysis to better understand ASD conditions. Significantly, it is already being used to identify new ways for patients with autism to be stratified in clinical trials, enabling development of more personalised medication for ASD disorders. In the long term, this will help reduce the burden of ASD on individuals, families and healthcare systems. The widespread availability of the database will secure the long-erm impacts of the project.
New software package for analysis of animal behaviours A suite of software tools for the analysis of rodent behaviour were developed and validated by EU-AIMS, through Noldus Information Technology (a partner SME). The tools were designed for the detailed study of the behaviour of ASD animal models, and comprise a video tracking system, a call-analysing system and a platform for the coding and analysis of behaviours. The 12 EU-AIMS partners defined	**Greater insight from animal testing, leading to higher quality research** The software tools developed through EU-AIMS will help researchers gain disease and treatment insights from ASD animal testing. This will enhance ASD drug development, potentially leading to safer, more effective ASD treatments. The extent of these impacts depends on the

the requirements, gave feedback and tested and validated the tools. The tools are available for purchase.	level of uptake of the technologies by pharmaceutical companies.

Structuring the European research area

Table 82: Structuring the European research area

Outcome	Socio-economic impact
EMA qualification advice A genetic profiling study conducted by EU-AIMS (the 'LEAP' trial) became the first study in autism research to receive official qualification advice and letters of support from the EMA. The advice relates to the identification and validation of biomarkers for ASD.	**Improved guidelines for autism research** The qualification advice published by the EMA provides scientists in academia and industry with clear guidelines for biomarker research, making ASD drug development more efficient and wider in scope.

Dissemination of information

The work of the project was presented to the scientific community through peer-reviewed journal articles conference presentations and training initiatives (Table 83).

Table 83: Dissemination of information

Outcome	Socio-economic impact
Publications and conference presentations At the time of completion, project findings were reported in 346 publications, 63.6% of which were open access. Numerous presentations were made by consortium partners at internal conferences and scientific meetings.	Publications had a normalised citation impact of 1.98, which suggests that the results of the project are easily accessible within the academic community. The presentations further raised awareness and promoted Europe as a place for collaborative research.
Training outputs The consortium conducted a range of training courses for autism research. Noldus IT delivered 300 one-day training courses on the software tools developed by the project. In total, 30 trainees completed continuous professional development training programs and 30 students graduated from various training programmes across five countries.	**Expanded skills base** The educational outputs of the project enhance the skills of researchers in Europe, improving the efficiency and quality of research and increasing competitivity of Europe within autism research.

3.16.6 Conclusions of impacts

Enhanced understanding of autism spectrum disorders

The EU-AIMS project increased understanding of ASD through research and has provided a basis for continued work. Project research comprised fundamental biological processes such as the neurological activity of individuals with ASD and early signs of the condition in babies.

Tools for accelerated, higher quality ASD research

The project generated valuable tools and infrastructure for future work. These included 339 stem cell lines, six *in vitro* models, two animal models, a comprehensive database for data mining and clinical trial design and a software package for the analysis of animal behaviours. These outputs will accelerate and enhance future research, which may lead to novel treatments for patients with ASD.

3.17 ELF: European Lead Factory

01/2013 – 05/2018

3.17.1 Objectives of the project

In drug development, high throughput screening (HTS) is a process by which a large number of compounds are robotically tested for activity against a biological target. Researchers can use HTS to rapidly conduct millions of tests to identify compounds with anti-disease activity; these compounds, termed 'hits', will undergo further testing and validation.

During this stage, pharmaceutical companies expend significant resources building libraries of compounds as potential candidates for future drugs. These libraries are typically not made available to external organisations due intellectual property interests. Often the industrial facilities required to perform HTS are not available to researchers slowing their ability to screen novel targets quickly and against good quality compounds considerably impacting the process of novel drug discovery.

The European Lead Factory (ELF) project created a large library of compounds both from the propriety collections of the pharmaceutical industry and novel compounds synthesised by ELF chemistry partners. The library was opened to third parties from European academia and small-medium biotech companies in a newly set up screening centre, where researchers received a 'hit list' of compounds and advice on further research.

Overall, the aim of the project was to increase the speed and likelihood of success of the first step of drug development and boost the rate of discovery of new molecular entities (drug compounds that are not versions or derivatives of existing ones), which will increase the number of effective of treatments for a range of diseases and improve healthcare globally.

3.17.2 Project coordinator and managing entity

Project Coordinator	Bayer Aktiengesellschaft
Managing entity	Universiteit Leiden

3.17.3 Participants

Table 84: Project participants

EFPIA companies	
Astrazeneca AB	Merck Kommanditgesellschaft Auf Aktien
Bayer Aktiengesellschaft	Sanofi-Aventis Deutschland GmbH
H. Lundbeck As	UCB Biopharma SPRL
Janssen Pharmaceutica Nv	

Universities, research organizations, public bodies, non-profit groups	
Academisch Ziekenhuis Leiden (Netherlands)	Stichting Vu (Netherlands)
Danmarks Tekniske Universitet (Denmark)	The University of Nottingham (United Kingdom)
Max-Planck-Gesellschaft Zur Forderung Der Wissenschaften Ev (Germany)	Universitaet Duisburg-Essen (Germany)
Pivot Park Screening Centre BV (Netherlands)	Universiteit Leiden (Netherlands)
Rijksuniversiteit Groningen (Netherlands)	University of Dundee (United Kingdom)
Stichting Katholieke Universiteit (Netherlands)	University of Leeds (United Kingdom)
Stichting Lygature (Netherlands)	University of Oxford (United Kingdom)
Small and medium-sized enterprises (SMEs)	
Arttic (France)	Mercachem B.V. (Netherlands)
Bioascent Discovery Limited (United Kingdom)	Sygnature Discovery Limited (United Kingdom)
ChemAxon Kutató-Fejlesztő Korlátolt Felelősségű Társaság (Hungary)	Syncom BV (Netherlands)
Edelris SAS (France)	Taros Chemicals GmbH & Co Kg (Germany)
Lead Discovery Center GmbH (Germany)	
Third parties	
Mercachem Holding BV (Netherlands)	Mercatorial BV (Netherlands)
Mercaleads BV (Netherlands)	

3.17.4 Project inputs and funding

The ELF project received funding of €80.0 million from IMI, from a total project cost of €196.6 million (Table 85).

Table 85: Funding received

Contributions	Financial support, €	% total funding
EU contribution	79,999,157	40.7%
EFPIA contribution	91,657,070	46.6%
IMI contribution	24,922,388	12.7%
Total funding	196,578,615	100.0%

3.17.5 Assessing the socio-economic impact of ELF

Innovation

Table 86: Project innovation

Outcome	Socio-economic impact
Joint European Compound Library (JECL) and compound screening The JECL contained over 500,000 compounds available for screening against biological targets. 300,000 of these came from the proprietary libraries of the seven pharmaceutical company partners, while 200,000 were added through a synthetic chemistry programme devised by the project. The compounds were chosen for their 'drug likeness' - i.e. high likelihood of exhibiting properties important for drug molecules (e.g. solubility). The library was available to researchers from academia and SMEs who could submit their biological target for high-throughput screening against the compound collection at the specialist European Screening Centre. As of August 2018, the work had generated 109 hit lists, 5,649 qualified hit molecules (delivered to public and private target owners), three drug discovery programmes in the lead optimisation phase and five patents on ELF compounds.	**Enhanced, accelerated drug development** Given the 10-15-year timescale of drug development, tangible public health benefits of this early stage research boost cannot be assessed. However, the work was successful in accelerating drug discovery across a range of therapeutic areas, providing SMEs and public bodies with screening capabilities that otherwise would have been unavailable. Extensive further work is being conducted based on the screening results and whole drug development programmes based on hit compounds from the JECL have been launched. These would not have been possible had the library not been made available. As such, the scope and quality of current drug development within Europe has been enhanced, making the approval and release of novel treatments for unmet clinical needs more likely. These compounds also provide better starting points for the discovery of new treatments saving time and money in future research. In the long term, the acceleration of innovative medicines research will reduce help the socio-economic

	burdens of diseases for which current treatment is lacking.

Infrastructure for further research

Table 87: Infrastructure for further research

Outcome	Socio-economic impact
Infrastructure for the ESCulab project (IMI2) and beyond The tools, assets, procedures and technology developed for the ELF project are the basis for an ongoing IMI project, the 'European Screening Centre; unique library for attractive biology' (ESCulab). Researchers submit biological samples for screening against the compound collection, receiving hit lists for further development. In addition, sustainability plans are being developed for the European Screening Centre to continue providing screening services beyond completion of this project in 2023.	**Continued advancement of medicines research in Europe** The continued use of the ELF infrastructure for drug discovery will further accelerate drug development, adding to the long-term benefits of the ELF project. It also boosts the competitivity of Europe as a place for drug discovery research, helping it remain attractive to researchers, companies and investors.

Structuring the European research area

Table 88: Structuring the European research area

Outcome	Socio-economic impact
New small and medium-sized enterprises (SMEs), jobs and partnering deals The screening results of the ELF project lead to two spin-out SME companies: Keapstone Therapeutics (developing novel treatment for neurodegeneration) and ScandiCure (targeting type 2 diabetes), hiring 172 members of staff. Two partnering deals were made between companies.	**Increasing Europe's research competitivity** The contributions of the ELF project to research activity and infrastructure and activity in the European Research Area help make it a richer, more attractive place for research, helping boost competitivity within the global scientific community and leading to the creation of new businesses and jobs.

Dissemination of information

The work of the project was presented to the scientific community through peer-reviewed journal articles, conference presentations and training initiatives (Table 89).

Table 89: Dissemination of information

Outcome	Socio-economic impact
Publications and conferences At the time of completion, project findings were reported in 103 publications, 45.6% of which were open access. The work of the project was shared in over 200 scientific conferences and events.	Publication had a normalised citation impact of 1.18, which suggests that the results of the project are easily accessible within the academic community. Presentation of findings to the scientific community, raises awareness of the consortium's work and promotes Europe as a place for medicines research.
Education and training The ELF project's educational activities resulted in the training of around 100 academic postdoctoral fellows in industry methods related to drug discovery and screening processes. Four PhD theses enhanced by ELF activity and results.	**A more competitive research workforce** Skills and expertise were developed that were transferable to both the ESCulab project and wider industry.

3.17.6 Conclusions of impacts

Accelerated drug development

The ELF project boosted drug discovery across a range of therapeutic areas. HTS capabilities were offered to research groups within SMEs and academia, and biological targets were tested against compounds from previously inaccessible proprietary collections of pharmaceutical companies. Extensive follow-up work is being conducted on the 'hit' compounds generated by the screening activities, including three drug development programmes in the lead optimisation phase. The drug candidates in company pipelines as a result of the ELF project could address unmet clinical needs.

Economic impacts

The project provided a number of economic benefits. Two spin-out SMEs were created for the further development of hit compounds generated by ELF high-throughput screening and a large number of jobs were created for skilled researchers. Two partnering deals were made between ELF-associated companies and external pharma. The project also reduced the cost of HTS for partner businesses and academic bodies.

Infrastructure for further drug discovery research

The tools and assets of the ELF project, including the European Screening Centre, remain in operation at the centre of an ongoing IMI2 project, ESCulab. The ELF project therefore has provided infrastructure for further drug discovery, further enhancing Europe as a place for medicines research.

3.18 EUPATI: European Patients' Academy on Therapeutic Innovation

02/2012 – 01/2017

3.18.1 Objectives of the project

Despite the increasing demand for improved healthcare, knowledge of the drug development process amongst patients is lacking. Involving patients in medicines research and integrating their priorities and perspective may drive development of more effective treatments and increase public support for medicines research.

Patient involvement in drug development requires an understanding of the many R&D and regulatory processes involved. The EUPATI project aimed to bring together academic groups, NGOs, patient organisations and pharmaceutical companies for extensive educational activities aimed at patient experts, journalists, the broader patient community and the wider public.

The consortium aimed to cover six key areas: medicines discovery and development planning, non-clinical testing/pharmaceutical development, exploratory/confirmatory clinical development, clinical trials, regulatory affairs/safety issues, and Health Technology Assessment (HTA) principles and practices. It was hoped that educating patients and the public on drug development processes would empower them to work with drug developers, regulatory authorities and healthcare professionals to improve medicines research for the benefit of patients.

3.18.2 Project coordinator and managing entity

Project Coordinator	European Patients Forum FPE EPF
Managing entity	European Patients Forum FPE EPF

3.18.3 Participants

Table 90: Project participants

EFPIA companies	
Amgen	Janssen Pharmaceutica Nv
Asociacion Nacional Empresarial De La Industria Farmaceutica	Merck Kommanditgesellschaft Auf Aktien
Astrazeneca AB	Merck Sharp & Dohme Corp
Bayer Pharma AG	Novartis Pharma AG
Boehringer Ingelheim Internationalgmbh	Novo Nordisk A/S

Bristol-Myers Squibb Company Corp	Pfizer Limited
Chiesi Farmaceutici S.P.A	Sanofi-Aventis Groupe
Eli Lilly And Company Limited	The Employers' Union of Innovative Pharmaceutical Companies INFARMA
Esteve Pharmaceuticals	UCB Biopharma SPRL
F. Hoffmann-La Roche AG	Verband Forschender Arzneimittelhersteller Ev
Glaxosmithkline Research and Development LTD.	

Universities, research organizations, public bodies, non-profit groups	
DIA Europe GmbH (Switzerland)	International Society for Pharmacoeconomics and Outcomes Research Inc (United States)
European Forum for Good Clinical Practice (Belgium)	Kobenhavns Universitet (Denmark)
European Organisation for Research and Treatment of Cancer Aisbl (Belgium)	The University of Manchester (United Kingdom)
Hibernia College (Ireland)	

Patient organisations	
European Aids Treatment Group Ev (Germany)	Eurordis - European Organisation for Rare Diseases Association (France)
European Genetic Alliances' Network (Belgium)	Irish Platform for Patients' Organisations Science and Industry (Ireland)
European Patients’ Forum (EPF) (Belgium)	

Third parties	
Central Manchester University Hospitals NHS Foundation Trust (United Kingdom)	Vereniging Samenwerkende Ouder - En Patientenorganisaties (Netherlands)
Genetic Alliance UK Ltd (United Kingdom)	

3.18.4 Project inputs and funding

The EUPATI project received funding of €5.25 million from IMI, from a total project cost of €11.0 million (Table 91).

Table 91: Funding received

Financial support	Financial support, €	% total funding
EU contribution	5,250,000	47.9%
EFPIA contribution	5,701,178	52.1%
IMI contribution	-	-
Total funding	10,951,178	100.0%

3.18.5 Assessing the socio-economic impact of EUPATI

Structuring the European research area

Table 92: Structuring the European research area

Outcome	Socio-economic impact
Guidance documents on patient involvement Guidance documents supporting the existing EMA framework for interactions between patients and consumer organisations were published by the EUPATI consortium. The documents cover patient interaction with regulatory agencies, Health Technology Assessment (HTA) bodies, ethics committees and pharmaceutical companies. Amongst other things, each document suggests key areas with opportunities for patient involvement.	**More effective integration of patient involvement** The guidance documents provide a basis for more effective and consistent patient involvement across the entire drug development process. They are freely available on the EUPATI website, maximising dissemination and uptake. This output has the potential to accelerate greater public and patient involvement in drug development.

Dissemination of information

The work of the project was presented to the scientific community through peer-reviewed journal articles, conference presentations and training initiatives (Table 93).

Table 93: Dissemination of information

Outcome	Socio-economic impact
The Patient Expert Training Course A flagship output of the EUPATI project was the development and delivery of a series of 14-month training courses ('The Patient Expert Training Course'), providing patient advocates with expert-level training in medicines R&D. Three courses have been delivered since 2015, with recruitment for a fourth completed in October 2019. The course covers 103 topics across six modules, covering the drug development process from drug discovery to approval processes. Each course was delivered through 81 online lessons, further reading, 14 videos, 65 quizzes, six assessments and eight days of face-to-face training. The content of the course is available for free download from the EUPATI website.	**More informed patient advocate with greater involvement in drug development processes** 96 patient experts from 31 different countries, with expertise in 58 disease areas completed the first two EUPATI courses, and 56 completed the third. A survey of these individuals before and after course completion showed a notable increase in involvement with medicines research. The proportion of course graduates advising a pharmaceutical company grew from 13−44%, a regulatory agency from 21−42% and an HTA/reimbursement body from 4−8%. The courses therefore enhanced patient advocate involvement within pharmaceutical R&D. The fact that the course is freely available to the public maximises its outreach and value.
R&D Toolbox Comprehensive educational material on the drug development process was also published in the form of an online 'toolbox'. It is freely available in seven languages and contains 254 presentations, 1463 articles, 97 videos, five webinars, 148 infographics, 246 images, 4,708 glossary items and more. The material spans the entire drug development cycle, covering all the 'tools' needed for effective patient engagement and advocacy. All material was released under Creative Commons, allowing any third party to use and adapt the material for non-commercial purposes.	**Widely used educational resource for patients and the public** The toolbox received higher than expected traffic, with 108,869 unique users in 144,000 sessions having visited the website by the end of January. Requests for translations outside the eight existing languages. Most users came from Europe (76,000), showing that the platform provided most educational value for European citizens. The toolbox facilitates greater engagement of patients with drug development processes.
Conferences and workshops Considerable effort was made to increase outreach and deliver further educational material to complement the training programme and toolbox. The consortium organised annual conferences and workshops which attracted around 1200 participants, 50% of which were patient advocates. Different aspects of patient	**More effective patient education activity** By reaching out to patients and patient advocates, the EUPATI consortium generated valuable, patient -led advice on both the direction of the project and how patient education can be improved. The outputs of this will help increase patient awareness of and involvement in drug development processes.

education were discussed and outcomes were widely disseminated.	
National platforms for patient education The consortium established national platforms in 18 European countries, each based on the broader EUPATI model. The platforms are public-private partnerships between industry, academia and in some cases regulators. At time of project completion, the platforms had organised and delivered a range of educational activities, including webinars, information days and social media campaigns. Platforms were set up in Austria, Belgium, Denmark, France, Germany, Greece, Ireland, Italy, Luxembourg, Malta, Norway, Poland, Portugal, Romania, Slovakia, Spain, Switzerland and UK.	**More targeted patient engagement** The delivery of patient education on a national, rather than Europe-wide level allows for greater outreach and more targeted patient involvement. It promotes further patient advocacy within drug development and regulatory affairs, raising awareness of the processes involved in bring a drug to market.

3.18.6 Conclusions of impacts

Greater understanding of drug development processes amongst patients and public

The educational outputs of EUPATI had significant outreach and increased understanding of key drug development processes amongst patient advocates and the public. Patient advocates benefitted from this via the Patient Expert Training Course and the online toolbox providing key knowledge for effective patient advocacy.

Enhanced patient engagement with medicines R&D

The Patient Expert Training Course was effective in increasing the R&D involvement of its graduates, as shown by the significant increase in participants advising pharmaceutical companies, regulatory agencies and HTA bodies. The online toolbox also disseminated key knowledge required for effective advocacy, contributing further to patient involvement. Infrastructure facilitated further engagement, including guidelines for patient involvement and 18 national platforms for the delivery of further educational activity. Ultimately, more effective integration of patients within medicines research will help ensure that drug development is targeted to patient needs.

Sustainability issues

The long-term impacts of the project are dependent on continued activity, which requires further continued development and funding. The toolbox remains available online in eight languages, however the delivery of the Patient Expert Training Courses is set to terminate three years after project completion. The national platforms also require continued resource input if they are to continue to function.

3.19 EUROPAIN: Understanding chronic pain and improving its treatment

10/2009 – 09/2015

3.19.1 Objectives of the project

Chronic pain affects approximately 19% of adults in Europe and causes personal and financial problems amongst sufferers. It also places a significant burden on already stretched public health systems. Only 36% of patients with chronic pain receive effective treatment, therefore there is an unmet need for innovation in treatment. For neuropathic pain, which affects 7–8% of people, even fewer patients receive effective treatments. It has been over 20 years since last new treatment for neuropathic pain was released.

The EUROPAIN project aimed to address this by reducing a number of R&D bottlenecks that are currently hampering development of new analgesics (pain-relieving drugs). Bottlenecks included a lack of adequate animal models for the testing of candidate drugs, methods to quantitively assess pain in humans, pain-measuring techniques that can be applied to animal and human subjects and patient cohort stratification in clinical trials for pain medications.

It was hoped that the outputs of the project would significantly enhance future research conducted in the chronic pain field, ultimately leading to more effective treatments and reducing the socioeconomic burden of chronic pain.

3.19.2 Project coordinator and managing entity

Project Coordinator	H Lundbeck A/S
Managing entity	Kings College London

3.19.3 Participants

Table 94: Project participants

EFPIA companies	
Abbvie Deutschland GmbH & Co Kg	Grunenthal GmbH
Astellas Pharma Europe BV	H. Lundbeck As
Astrazeneca AB	Pfizer Limited
Boehringer Ingelheim International GmbH	Sanofi-Aventis Recherche & Developpement
Eli Lilly And Company Limited	UCB Biopharma SPRL
Esteve Pharmaceuticals	

Universities, research organizations, public bodies, non-profit groups	
Aarhus Universitetshospital (Denmark)	Klinikum Rechts Der Isar Der Technischen Universitat Munchen (Germany)
Berufsgenossenschaftliches Universitätsklinikum Bergmannsheil GmbH (Germany)	Region Hovedstaden (Denmark)
Christian-Albrechts-Universitaet Zu Kiel (Germany)	Ruprecht-Karls-Universitaet Heidelberg (Germany)
Imperial College London (United Kingdom)	Syddansk Universitet (Denmark)
Johann Wolfgang Goethe-Universitatfrankfurt Am Main (Germany)	University College London (United Kingdom)
King's College London (United Kingdom)	University of Oxford (United Kingdom)
Small and medium-sized enterprises (SMEs)	
Neuroscience Technologies Limited (United Kingdom)	Neuroscience Technologies (Spain)
Non-EFPIA companies	
Universitatsklinikum Schleswig-Holstein (Germany)	

3.19.4 Project inputs and funding

The EUROPAIN project received funding of €6.2 million from IMI, from a total project cost of €22.6 million (Table 95).

Table 95: Funding received

Financial support	Financial support, €	% total funding
EU contribution	6,229,343	27.6%
EFPIA contribution	11,165,740	49.5%
IMI contribution	5,155,000	22.9%
Total funding	22,550,083	100.0%

3.19.5 Assessing the socio-economic impact of EUROPAIN

Innovation

Table 96: Project innovation

Outcome	Socio-economic impact
Improved animal models for pain The EUROPAIN consortium identified an unmet need for animal models for a range of neuropathic pain states, with the current method of modelling neuropathy through nerve injury judged to be poorly predictive of drug efficacy. To address this, seven rodent models of a range of neuropathic pain conditions were validated. The consortium also addressed the need for methods to assess pain levels in rodents through their behaviour. By inducing nerve injury in rats and observing their behavioural response, researchers validated four ways to quantitively evaluate pain levels, for example through burrowing rates and social interactions. It was also found that sleep deprivation increased sensitivity to chronic pain.	**Insights from animal models** The use of more reliable and predictive animal models of neuropathological pain will benefit pain research. Suitable animal models minimise waste associated with poorly characterised models and research findings that are not reproducible. Results of this work will increase the value of animal testing in future neuropathic pain research.
Methods for quantitatively assessing pain A variety of methods for the quantitative assessment of pain were evaluated and validated for use in clinical studies. For example, researchers showed that certain areas of the brain are activated when an individual is experiencing pain, and this activity can be measured to assess pain. Other validated quantitative methods included Corneal Confocal Microscopy (imaging nerve cells in the eye) and Quantitative Sensory Testing (a method to investigate nerve endings through changes in sensitivity to heat, touch or pressure).	**Techniques for more effective clinical trials** Traditionally, pain is measured through patient feedback, which can be subjective and unreliable. Quantitative assessment of pain levels in patient cohorts is important when measuring the efficacy of pain medication in clinical trials. The validation of numerous pain-measuring techniques may improve the assessment of treatments in clinical trials and lead to more effective drugs for chronic pain.
Translating pain measurements from animals to humans A key obstacle in the development of new pain medication is translating findings from animal models to humans. To overcome this, pain measuring techniques that can be used in both animals and humans are needed. EUROPAIN validated a technique for this purpose called microneurography, which involves measuring nerve impulses with a needle electrode.	**Better understanding of pain models in early stage development, enabling more efficient research** The EUROPAIN project demonstrated that microneurography can be used to predict whether the effects of analgesics occur humans. The EMA approved the technique for this purpose. It will help reduce failure rates in later stages of development, cutting time, cost and unnecessary human risk in the development of new analgesics.

Infrastructure for further research

Table 97: Infrastructure for further research

Outcome	Socio-economic impact
Methods to minimise placebo effect The placebo effect is a challenge in pain research. EUROPAIN carried out meta-analysis studies to better understand the placebo effect in pain research, and found that the patient's expectation of treatment efficacy had the biggest influence on the magnitude of the placebo effect.	 **More reliable clinical trials** By determining the factors that influence the placebo effect, EUROPAIN researchers were able to suggest methods to minimise it in future pain trials (for e.g. managing patients' expectations of the candidate drug through more neutral consent forms). Managing the placebo effect will enable more reliable and effective clinical trials.
Database analysis for new clinical trial methodologies EUROPAIN researchers assembled a database of 2,300 patients with neuropathic pain and 1000 healthy volunteers to investigate how patients could be classified by their sensitivity to pain, rather than the pain-causing condition. Analgesics were more effective in patients with high pain sensitivity, thus validating this approach for stratifying patients in clinical trials.	 **Foundations for more targeted pain treatment** The EMA approved EUROPAIN's method of stratifying patients in clinical trials and included it in their guidelines for drug development. This provides the basis for companies to develop more targeted drugs, for e.g. drugs that are more effective in patients with high sensitivity to pain. This could lead to more effective treatment of chronic pain, reducing its burden on both individuals and healthcare systems.

Structuring the European research area

Table 98: Structuring the European research area

Outcome	Socio-economic impact
EMA qualification advice Four methodologies generated by the EUROPAIN project for the quantitative measurement of pain were submitted to the EMA for official qualification advice. Two of these, Quantitative Sensory Testing and microneurography, were suitable for early stage clinical trials. One was judged to be suitable for 'proof of concept' studies, and the other needed further evidence before EMA validation.	 **Regulatory validation of new tools for better research** The validation of QST and microneurography by the EMA to measure pain allows future research organisations to use these novel tools in for early stage research. These guidelines will therefore advance development of new analgesics, and widen the scope of future clinical trials. The need for further evidence on other methodologies provides a clear foundation for future work.

Dissemination of information

The work of the project was presented to the scientific community through peer-reviewed journal articles and conference presentations (Table 99).

Table 99: Dissemination of information

Outcome	Socio-economic impact
Publications and conferences At the time of completion, project findings were reported in 167 papers, 29.3% of which were open access. Over 200 presentations were made to scientific audiences at conferences and meetings around the world.	**Dissemination to the scientific community** Publications had a normalised citation rate of 2.22, which suggests that the results of the project are easily accessible within the academic community. The large number of scientific presentations raised awareness the project's work and the opportunities for collaboration across Europe.

3.19.6 Conclusions of impacts

More relevant animal models for pain research

The EUROPAIN project developed and validated new ways to measure pain in rodents based on their spontaneous behavioural responses, such as burrowing rates and interactions with other individuals. This will help future researchers using rodents in analgesic development, and minimised waste associated with inappropriate animal models. EUROPAIN researchers also showed that microneurography can be used in animals to predict whether humans will show similar responses to drugs, helping to decrease drug development failure rates and unnecessary re-testing and gain insights from animal-based research.

Increased scope and effectiveness of future clinical trials

The consortium provided infrastructure for improved clinical trials. Through comprehensive meta-analysis it was shown that stratifying patients by pain sensitivity is a valid approach in analgesics trials, enabling the development of more targeted pain medicines. Methods to minimise the placebo effect were also established, further enhancing future trials and the reliability of their conclusions.

Validated methodologies for better analgesics research

A variety of techniques to quantitively measure pain in humans were validated. This provides researchers with the capabilities to assess the pain-relieving effects of candidate drugs, in more detailed and reliable ways than previous methods. Ultimately, this will help reduce the socioeconomic burden of chronic pain through the introduction of more reliable and effective analgesics.

3.20 GetReal: Incorporating real-life clinical data into drug development

10/2013 – 03/2017

3.20.1 Objectives of the project

Before a new drug is available to patients, it must be approved for market access by regulators who draw on (mostly) clinical trial data to determine its safety and efficacy. It is then reviewed by Health Technology Assessment (HTA) bodies, who evaluate cost effectiveness and determine if it should be approved for reimbursement by a healthcare system.

To determine how effective a drug will be in a typical healthcare setting, HTA bodies often require real-world data, routinely collected from sources such as electronic health records and disease registries. Despite the importance of the real-world evidence (RWE) that this generates, there is little guidance on how RWE should be generated and integrated into drug development. Insufficient evidence on drug efficacy can delay or restrict patient access to new drugs.

The GetReal project aimed to address this issue by generating tools, methodologies, policy frameworks and training to improve the way RWE is incorporated drug development, with a particular focus on exploring how it can be incorporated as early as possible into drug development timelines. Specific deliverables included a guidance framework for the inclusion of alternate study designs in drug development strategies, tools for evidence generation and an e-learning platform to increase knowledge and skills relating to RWE use in drug development.

These objectives were devised with the goal of increasing the approval rate of new treatments and enabling greater evidence-based decision making in clinical practice.

3.20.2 Project coordinator and managing entity

Project Coordinator	GlaxoSmithKline Research and Development Ltd.
Managing entity	Universitair Medisch Centrum Utrecht

3.20.3 Participants

Table 100: Project participants

EFPIA companies	
Amgen	Janssen Pharmaceutica Nv
Astrazeneca AB	Merck Kommanditgesellschaft Auf Aktien
Bayer Pharma AG	Merck Sharp & Dohme Corp
Boehringer Ingelheim International GmbH	Novartis Pharma AG

Bristol-Myers Squibb Company Corp	Novo Nordisk A/S
Eli Lilly And Company Limited	Sanofi-Aventis Recherche & Developpement
F. Hoffmann-La Roche AG	Takeda Development Centre Europe Ltd.
Glaxosmithkline Research And Development Ltd.	
Universities, research organizations, public bodies, non-profit groups	
Academisch Ziekenhuis Groningen (Netherlands)	The University of Manchester (United Kingdom)
European Organisation for Research and Treatment of Cancer (Belgium)	Universitaet Bern (Switzerland)
National Institute for Health and Care Excellence (United Kingdom)	Universitair Medisch Centrum Utrecht (Netherlands)
Panepistimio Ioanninon (Greece)	University of Leicester (United Kingdom)
The European Medicines Agency (United Kingdom)	
Small and medium-sized enterprises (SMEs)	
L.A Sante, Epidemiologie, Evaluation Et Recherche L.A.S.E.R. (France)	
Non-EFPIA companies	
Haute Autorite De Sante (France)	Zorginstituut Nederland (Netherlands)
International Alliance of Patients' Organizations (United Kingdom)	

3.20.4 Project inputs and funding

The GetReal project received funding of €8.0 million from IMI, from a total project cost of €17.0 million (Table 101).

Table 101: Funding received

Contributions	Financial support, €	% total funding
EU contribution	8,000,000	47.2%
EFPIA contribution	6,910,397	40.8%
Beneficiaries' own contribution	2,041,883	12.0%
Total funding	16,952,280	100.0%

3.20.5 Assessing the socio-economic impact of GetReal

Infrastructure for further research

Table 102: Infrastructure for further research

Outcome	Socio-economic impact
ADDIS data management tool The Aggregate Data Drug Information System (ADDIS) is an openly available online tool designed to help healthcare policy makers and researchers evaluate the effects of treatments. Users can import or manually input clinical trial data into the structured ADDIS database, and use the platform's statistical package to conduct meta-analyses (MAs) on the trials, combining data to generate evidence on the relative benefits and risks of treatments.	**More robust evidence-based decision making** The ADDIS tool greatly facilitates the conduct of network meta-analysis (NMA) and multi-criteria decision analysis (MCDA) using data from randomised controlled trials, providing evidence synthesis capabilities that allow for more robust differentiation between medicines. This helps healthcare policy experts make more informed decisions about the benefits and risks of alternative treatments, leading to more robust medicines approval and ultimately safer medicines. It is also a valuable educational resource, with clear tutorials and all uploaded datasets available for analysis.
Sure-Real simulation tool The freely available Sure-Real tool enables evidence development planners in research teams and other stakeholders to assess how real-world evidence can be incorporated into drug development strategies. Containing a data repository and models of different study designs, the tool provides visual trial simulation outputs, giving insight into the impacts of implementing alternative evidence generation strategies.	**Facilitating more informed drug development** The Sure-Real tool provides valuable guidance for researchers seeking to implement RWE strategies within drug development. Wide utilisation could result in earlier adoption of RWE, increasing the quality of evidence behind new medicines and leading to broader acceptance of treatments by HTA bodies.

PragMagic decision support tool The PragMagic tool is an interactive online tool that supports researchers in the design and conduct of pragmatic trials (clinical trials that evaluate drug efficacy in real-world healthcare practice). Aimed at trial design teams, the tool provides method reviews, case studies, guidance and recommendations on how trials can be designed to maximise generalisability to routine practice, and how the resulting operational challenges can be navigated. The tool can be freely accessed online.	 **Greater knowledge of RWE in drug development** The PragMagic tool provides researchers with valuable knowledge of how clinical trials can be designed to better predict drug efficacy in healthcare, and promotes the use of RWE in the drug development process. It therefore facilitates earlier and more effective incorporation of real-world data into clinical research, ultimately increasing the pace of drug approval processes and allowing for better evidenced-based decision making by healthcare professionals.

Structuring the European research area

Table 103: Structuring the European research area

Outcome	Socio-economic impact
Policy recommendations A GetReal Policy Expert Group was established to produce recommendations on how RWE generation can be advanced. Policy recommendations were published across seven key areas, including education and training, stakeholder involvement. The recommendations are available to view online.	 **Foundations for further advancement of evidence generation** The policy recommendations provide a robust basis for further efforts to enhance the use of real-world evidence in drug development. Depending on uptake, this could foster continued collaboration between industry, regulatory bodies and academia.

Dissemination of information

The work of the project was presented to the scientific community through peer-reviewed journal articles and conference presentations (Table 104).

Table 104: Dissemination of information

Outcome	Socio-economic impact
RWE Navigator and online course The RWE navigator is an extensive online educational resource designed to increase knowledge of real-world evidence and how it can be incorporated into drug development strategies. Freely available, its content includes interactive information pages, case studies and links to further resources. As a multi-stakeholder tool, it aids industry researchers develop RWE strategies, regulatory bodies understand the RWE analyses conducted and healthcare professionals and patients understand the	 **More effective integration of RWE into drug development strategies** The educational outputs of the GetReal project supports researchers in identifying where and how RWE can be used to enhance drug development strategies. The RWE Navigator is a common source of information for individuals across industry and regulatory bodies, reducing barriers to RWE integration through the alignment of stakeholder

importance and use of RWE in drug development. GetReal also conducted an online remote learning course: 'Real World Evidence in Drug Development', delivering similar content to individuals across many organisations and disciplines.	perspectives. The online course further contributes to this.
Publications At the time of completion, project findings have been reported in 40 publications, 57.5% of which are open access. Presentations were made by consortium partners at scientific meetings and conferences.	Publications had normalised citation impact of 2.03, which suggests that the results of the project are easily accessible within the academic community. Findings of the GetReal project provides the scientific community with valuable novel information within the RWE field, with dissemination enhanced by presentations at scientific events.

3.20.6 Conclusions of impacts

More effective incorporation of real-world evidence into drug development strategies

The outputs of the GetReal project facilitate earlier and more effective RWE generation within drug development. The ADDIS data management tool, Sure-Real simulation tool and PragMagic decision support tool help drug development researchers understand the importance of RWE and how development strategies can be devised to incorporate it. HTA and regulatory bodies can also use these tools to further their understanding of the analyses used. More widespread use of RWE will make the evidence generated during drug development more predictive of real-world effectiveness, resulting in more informed HTA approval processes. GetReal has created a network of regulators, HTA organisations, companies, academics, healthcare professionals, patients and other societal stakeholders working in the field of RWE generation, analysis and use. The GetReal Initiative is a follow-up project launched in 2018 that drives the adoption of tools, methodologies and best practices of GetReal

Educational impacts

The GetReal project had educational benefits for a range of stakeholders. The RWE navigator is a comprehensive resource, providing researchers with information to develop RWE strategies, and helping regulatory bodies and healthcare professionals understand the processes and analyses used. This further lowers the barrier to RWE implementation. The online course contributes to this, consolidating the above benefits.

Guidance for continued collaboration in Europe

GetReal serves as a blueprint for future projects, showing how industry, academia and business can efficiently collaborate to advance RWE issues. The policy recommendations produced by the consortium provide a concrete basis for future work.

3.21 IMIDIA: Improving beta-cell function and identification of diagnostic biomarkers For treatment monitoring in diabetes

02/2010 – 09/2015

3.21.1 Objectives of the project

Diabetes is the seventh leading cause of death in the world, and the number of people living with the condition is rising. Type 2 diabetes accounts for 90% of cases, and occurs when insulin-producing cells in the pancreas (beta-cells) become dysfunctional. As a result, the body produces increasingly less insulin and blood sugar levels rise. There are treatments available for the management of type 2 diabetes, but none prevent or cure the disease.

The IMIDIA project aimed to address the lack of understanding of the biological and molecular mechanisms behind beta-cell dysfunction and create tools and infrastructure to aid further study and development of beta cell-focused drugs. Ultimately, the consortium aimed to accelerate the development of therapies for diabetes management and lay foundations for the discovery of curative treatments. In the long term, this would help reduce the significant burden of diabetes on patients and healthcare systems.

3.21.2 Project coordinator and managing entity

Project Coordinator	University of Lausanne
Managing entity	University of Lausanne

3.21.3 Participants

Table 105: Project participants

EFPIA companies	
AstraZeneca AB	Institut De Recherches Servier (France)
Boehringer (Germany)	Novartis Pharma AG (Switzerland)
Eli Lilly And Company Limited	Novo Nordisk A/S (Denmark)
F. Hoffmann-La Roche AG	Sanofi-Aventis Deutschland GMBH (Germany)
Universities, research organizations, public bodies, non-profit groups	
Centre National De La Recherche Scientifique Cnrs (France)	Technische Universitaet Dresden (Germany)

Commissariat A L Energie Atomique Et Aux Energies Alternatives (France)	Universita di Pisa (Italy)
Imperial College London (United Kingdom)	Universite de Geneve (Switzerland)
Institut National de la Sante et de la Recherche Medicale (France)	Universite de Lausanne (Switzerland)
Medizinische Hochschule Hannover (Germany)	Universite Paris Diderot (France)
SIB Institut Suisse De Bioinformatique (Switzerland)	Vrije Universiteit Brussel (Belgium)
Small and medium-sized enterprises (SMEs)	
SARL Endocells (France)	

3.21.4 Project inputs and funding

The IMIDIA project received funding of €8.1 million from IMI, from a total project cost of €27.4 million (Table 106).

Table 106: Funding received

Contributions	Financial support, €	% total funding
EU contribution,	8,060,760	29.4%
EFPIA contribution	16,940,659	61.7%
IMI contribution	2,445,590	8.9%
Total funding	27,447,009	100.0%

3.21.5 Assessing the socio-economic impact of IMIDIA

Innovation

Table 107: Project innovation

Outcome	Socio-economic impact
New biological knowledge of diabetes pathology The IMIDIA project generated new scientific knowledge of the biological entities (e.g. enzymes, cells, genes) involved in diabetes, and the various biochemical processes relating to beta-cell function. Particularly notable amongst these achievements was the elucidation of the roles of a range enzymes, genes and small molecules in biological pathways relating to the activity and function of beta-cells.	**Foundations for accelerated drug discovery** The fundamental knowledge of the biochemical processes relating to beta-cells provides subsequent researchers with information required for further targeted research on beta-cells, and ultimately potential treatments in diabetes. In the long term, this work therefore accelerates discovery of new medicines for the prevention and cure of diabetes.
A biobank of islets and pancreatic tissues IMIDIA researchers created an extensive repository of pancreatic tissue and islets (regions that contain hormone-producing cells, including beta-cells), obtained from ~200 diabetic patients and ~300 healthy individuals. A wide range of analyses were conducted on the islets, leading to the discovery of 19 genes expressed differently in the diabetic and healthy islets. These genes serve as potential candidate targets for drugs aiming to restore beta-cell function.	**Broadened drug development through identification of potential drug targets** As well as serving as a valuable resource for future projects and collaborations, the pancreatic islet repository generated knowledge that can provide the basis for focused research on new drugs. The biobank therefore accelerates and enhances diabetes research, broadening the search for effective preventative treatment.

Infrastructure for further research

Table 108: Infrastructure for further research

Outcome	Socio-economic impact
Advancement of research tools and methodologies The IMIDIA project resulted in a number of technical advancements across a range of tools and methods relating to the study of beta-cell function. These include validation of beta-cell probes and imaging techniques, and a verified biomarker for the prediction of type 2 diabetes development.	**Enhanced, more efficient diabetes research** The development and validation of innovative research tools increases the quality and efficiency of subsequent research into beta-cell functionality. As such, this work advances the development of diabetes drugs.

Tissue/knowledge platform The non-profit Beta Cell and Diabetes Platform (BCDP) was established to ensure that the major assets and results of IMIDIA remained available to subsequent IMI projects and other collaborations. Assets include tissue samples and annotated datasets.	**Supporting further collaboration** The BCDP platform is a valuable resource for continued validation of drug targets, biomarkers and models. It also facilitates ongoing collaboration within Europe, advancing innovation within diabetes research.
A validated human beta-cell line To study the biochemical mechanisms of beta-cell dysfunction in diabetic people, researchers require access to diabetic beta-cell lines (stored cultures of diabetic beta-cells that will proliferate in a medium). Before IMIDIA, only beta-cell lines from rodents existed. Consortium researchers developed the first human beta-cell line, which was validated by the pharmaceutical industry and patented, commercialised and developed further by Endocells SARL, an SME project partner. The line was made available to other IMI projects and for further industry/academia collaboration.	**Enhanced development of diabetes drugs** The biology of rodent beta-cells differs significantly from human beta-cells, creating obstacles when using rodent cells in the search for new drugs. The human cell line allows researchers to study beta-cell function in the context of human diabetes, creating opportunities to identify and develop drugs that specifically target beta-cells in diabetic patients. Ultimately, this could result in the release of effective preventative treatment for diabetes, reducing the burden of the disease on healthcare systems and individuals.

Structuring the European research area

Table 109: Structuring the European research area

Outcome	Socio-economic impact
Memorandum of understanding A memorandum of understanding was signed between IMIDIA and SUMMIT, a concurrent IMI project focusing on the development of new treatments for the complications caused by diabetes. The memorandum of understanding covered the handling of intellectual property, confidentiality and the transfer of knowledge and materials.	**Deeper collaboration between European organisations** The memorandum of understanding enabled efficient and thorough collaboration between two large-scale diabetes projects, enhancing the work of each through shared knowledge and resources. The memorandum of understanding also serves as a template/precedent for further memoranda of understanding within IMI.

Dissemination of information

The work of the project was presented to the scientific community through peer-reviewed journal articles, conference presentations and training initiatives (Table 110).

Table 110: Dissemination of information

Outcome	Socio-economic impact
Publications and scientific presentations At the time of completion, project findings were reported in 141 publications, 72.3% of which were open access. Nine presentations were made at various scientific meetings.	**Broadened knowledge base within scientific community** Publications had a normalised citation impact of 1.66, which suggests that the results of the project are easily accessible within the academic community. The presentations raised further awareness of the work of the project.
Training activities Training courses and workshops were delivered in order to provide IMIDIA researchers with the technical skills required to carry out effective project work. Approximately 50 individuals across partner organisations were reached by this activity.	**Increased skillset of project workers** The technical skills gained by project researchers can be applied in their future careers. This makes them more competitive in the European scientific jobs market and contributes to Europe's attractiveness as a place to conduct research.

3.21.6 Conclusions of impacts

Scientific knowledge for accelerated drug discovery

The IMIDIA project generated knowledge of diabetes pathology which provides a valuable basis for research into new treatments. Findings were made across a range of biological and biochemical areas, for example the roles of specific enzymes and genes in beta-cell dysfunction. This enriched knowledge base provides valuable guidance in the search for drug targets, accelerating the development of effective diabetes treatments.

Infrastructure for advanced diabetes research in Europe

The consortium delivered tools and infrastructure for future research. Most notably is the first human beta-cell line to conduct *in vitro* studies of beta-cell function in the context of human, rather than rodent diabetes. Other outputs that accelerate the development of novel diabetes treatment included an extensive pancreatic tissue biobank, verified biomarkers and validation of beta-cell probes and imaging techniques.

Support for continued collaboration

The IMIDIA project demonstrated the benefits and feasibility of collaboration between industry and academia for the benefit of diabetes research, serving as a model for future diabetes projects. The Beta Cell and Diabetes Platform facilitates further collaboration through the provision of data and resources, while the memorandum of understanding signed between IMIDIA and SUMMIT serves as a precedent for future IMI collaborations.

3.22 K4DD: Kinetics for Drug Discovery

11/2012 – 10/2017

3.22.1 Objectives of the project

Drugs work by binding with molecules in the body and either blocking or altering the action of the target molecule. IMI's K4DD project objective was to improve understanding of how potential drugs bind with their target and develop methods and tools to allow researchers to study drug-target interactions and determine whether a drug candidate is likely to be safe and effective earlier in the drug development process.

Many recently marketed drugs possess improved kinetic profiles. Lack of attention kinetic profiles may be one of the reasons for the high attrition rates in drug discovery. K4DD strived to develop techniques, structure-kinetic relationships (SKRs), data and models that are accessible to and used by the drug development community and to enable reliable predictions of kinetic properties *in silico*. Ultimately the goal was to improve the *in vitro* to *in vivo* translation of future medicines.

3.22.2 Project coordinator and managing entity

Project Coordinator	Anke Mueller-Fahrnow (Bayer AG)
Managing entity	Ton Brouwer (Universiteit Leiden)

3.22.3 Participants

Table 111: Project participants

EFPIA companies	
Astrazeneca AB	Janssen Pharmaceutica Nv
Bayer Aktiengesellschaft	Merck Kommanditgesellschaft Auf Aktien
F. Hoffmann-La Roche AG	Sanofi-Aventis Deutschland GMBH
Glaxosmithkline Research and Development Ltd	
Universities, research organizations, public bodies, non-profit groups	
Fraunhofer Gesellschaft Zur Foerderung Der Angewandten Forschung E.V., Germany	The University Of Nottingham, United Kingdom
Hits Ggmbh, Germany	Universitat Wien, Austria

Imperial College Of Science Technology And Medicine, United Kingdom	Universiteit Leiden, Netherlands
Ruhr-Universitaet Bochum, Germany	University Of Dundee, United Kingdom
Stichting Lygature, Netherlands	University Of Oxford, United Kingdom
Stichting Vu, Netherlands	
Small and medium-sized enterprises (SMEs)	
Heptares Therapeutics Limited, United Kingdom	Sierra Sensors GmbH, Germany

3.22.4 Project inputs and funding

The K4DD project received funding of €8 million from IMI, from a total project cost of €21 million (Table 112).

Table 112: Funding received

Contributions	Financial support, €	% total funding
EU contribution	8,286,930	39.7%
EFPIA contribution	9,831,318	46.5%
IMI contribution	2,742,002	13.1%
Total funding	20,860,250	100.0%

3.22.5 Assessing the socio-economic impact of K4DD

Innovation

Table 113: Project innovation

Outcome	Socio-economic impact
New commercialised assays Off-the-shelf kits for analysing drug protein binding kinetics were developed and commercialised e.g., the BRETT assay to measure the binding kinetics of GPCRs. An SME within the consortium, Sierra Sensors, also developed a molecular affinity screening machine that can be used for measuring drug-	 **Economic benefit from tools developed by the project** Some of the tools have been standardised and commercialised. These kits facilitate the use of K4DD findings by other

protein binding kinetics data in a high-throughput format.	research groups, and at the same time providing economic benefit.

Infrastructure for further research

Table 114: Infrastructure for further works

Outcome	Socio-economic impact
New modelling and simulation tools K4DD successfully developed and deployed an array of powerful modelling and simulation tools, including Random Acceleration Molecular Dynamics (RAMD) for computational prediction of relative residence times. These and other computational approaches developed and applied by other members of K4DD are collected in a web-based toolbox.	**Sharing tools in a web-based toolbox** K4DD web-based toolbox is a comprehensive compilation of all K4DD developed tools. There are also guidelines so the scientific community can adopt the same standards.
Comprehensive kinetic database A comprehensive database of kinetic data which is now publicly available through the publicly accessible ChEMBL database. ChEMBL is a manually curated database of bioactive molecules with drug-like properties. It brings together chemical, bioactivity and genomic data to aid the translation of genomic information into effective new drugs.	**Publicly available data** All kinetic data has made publicly available into an existing data base. Implementing the K4DD database in ChEMBL is a great achievement and ensures the results of the project are available to all researchers.

Structuring the European research area

Table 115: Structuring the European research area

Outcome	Socio-economic impact
Creation of spin off project in collaboration with other IMI1 project The project also resulted in the creation of a spin off. Called Phenaris, it will develop ToxPHACTS, a software that will combine K4DD and eTOX project outputs with the Open PHACTS discovery platform.	Collaboration with other IMI1 project to promote a web-service free service for non-commercial use.

Dissemination of information

The work of the project was presented to the scientific community through peer-reviewed journal articles, conference presentations and training initiatives (Table 116).

Table 116: Dissemination of information

Outcome	Socio-economic impact
Publications By the time of project completion, findings were reported in 53 publications, 55.0% of which were open access.	The body of literature had a normalised citation rate of 2.43, which suggests that the results of the project are easily accessible within the academic community.
Training and courses An important part of the K4DD project has been its educational programme which has funded more than 20 post-docs and PhD students in the last five years. The programme has provided fellows with the opportunity to gain a thorough understanding of the connection between drug-discovery and drug development by offering them an extensive drug discovery course and several "binding kinetics" oriented symposia. Fellows also got the opportunity to improve their soft skills by taking a scientific writing course, career workshops and a presentation workshop. The first fellows have defended their thesis successfully and more PhD theses are expected.	Increasing opportunities for post-docs and PhD students in Europe.

3.22.6 Conclusions of impacts

K4DD web-based toolbox is a comprehensive compilation of all K4DD developed tools. There are also guidelines so the scientific community can adopt the same standards

The main impact of K4DD project is raising the awareness of target binding kinetics. The project will also continue to have impact through assays and technologies developed within the project and through the K4DD database, which will be an invaluable asset for future research.

New commercialised assays facilitate the use of K4DD findings by other research groups and have economic benefits

K4DD developed several assays which have now been published and for routine use in the scientific community. Furthermore, K4DD project scientists have already been using these systems to deepen their understanding of compound properties that trigger certain behaviours, therefore laying the foundation for a broader use.

SMEs outside of the project have further built on these ideas by developing and commercialising several off-the-shelf kits for analysing drug protein binding kinetics. An SME within the consortium, Sierra Sensors, also developed a molecular affinity screening machine that can be used for measuring drug-protein binding kinetics data in a high-throughput format.

Creation of a spin off project in collaboration with other IMI1 project

The project also resulted in the creation of a spin off company, Phenaris, which will develop ToxPHACTS, a software that will combine K4DD and eTOX project outputs with the Open PHACTS discovery platform.

3.23 MARCAR: Biomarkers and molecular tumor classification for non-genotoxic carcinogenesis

01/2010 – 06/2015

3.23.1 Objectives of the project

Current methods used in drug development lead to a large number of drugs not reaching the market due to the late discovery of cancerous effects during pre-clinical trials. Such cancers are not the result of direct genetic toxicity, as drugs that exhibit such characteristics are eliminated from consideration early in their development. They can however result from changes in gene expression or cellular phenotypes caused by mechanisms other than changes in the underlying DNA sequence. Drugs that induce such cancers are called non-genotoxic carcinogens (NGC). Due to a lack of validated short-term study techniques, such non-genotoxic cancer causing drugs tend to be identified following prolonged pre-clinical studies. Using the liver, the major target organ for such drug-induced tumours, the MARCAR project aims to advance the understanding of NGC mechanisms and the availability of early "biomarkers" of NGC action to help in the design of more predictive short-term assessment tools to reduce the requirement for costly long-term biological testing including reduction of animal numbers and help to deliver safer and faster medicines to patients.

3.23.2 Project coordinator and managing entity

Project Coordinator	Novartis Pharma AG
Managing entity	University of Dundee

3.23.3 Participants

Table 117: Project participants

EFPIA companies	
Bayer Pharma AG	Novartis Pharma AG
Boheringer Ingelheim International gmbh	UCB Pharma SA
H. Lundbeck AS	
Universities, research organizations, public bodies, non-profit groups	
Eberhard Karls Universitaet Tuebingen (Germany)	Naturwissenschaftliches Und Medizinisches Institut An Der Universitaet Tuebingen (Germany)
Institut National De La Sante Et De La Recherche Medicale (France)	The University Of Edinburgh (United Kingdom)

Medizinische Universitaet Wien (Austria)	University Of Dundee (United Kingdom)

Small and medium-sized enterprises (SMEs)
Cxr Biosciences Limited (United Kingdom)

3.23.4 Project inputs and funding

The MARCAR project received funding of €6.0 million from IMI, from a total project cost of €13.1 million (Table 118).

Table 118: Funding received

Financial support	Financial support, €	% total funding
EU contribution	6,049,578	46%
EFPIA contribution	5,155,604	39%
IMI contribution	1,905,508	15%
Total funding	13,110,690	100%

3.23.5 Assessing the socio-economic impact of MARCAR

Innovation

Table 119: Project innovation

Outcome	Socio-economic impact
New epigenetic biomarkers identified Early efforts in MARCAR focused on optimising methods and technologies which allow scientists to investigate the relationship between drug exposure and measurable epigenetic changes in liver cells transitioning to a tumour. The goal of the research was to identify early epigenetic biomarkers which could signal that a specific drug might cause non-genotoxic changes, and ultimately create an environment in which cancer occurs. At least two classes of such potential biomarkers were identified.	 **Improved preclinical safety studies, reducing cost and time** These biomarkers are currently being evaluated with a broader range of drugs and has the potential to explain the molecular basis of species differences in responses to non-genotoxic carcinogens, a key consideration for interpreting human relevance of animal studies. On this basis, the scientists postulated that the studied biomarkers represent a powerful early marker for predicting tumour growth. Both novel biomarker discoveries have the potential to underpin the design of improved preclinical safety studies that should ultimately

	reduce the cost and accelerate the development of innovative medicines.
New animal model method The new method involves a special magnetic resonance imaging (MRI) technique which allows researchers to scan mice and locate tiny tumours early in the screening process that are 1 mm in size. Scientists can then track the subsequent growth of the tumours by rescanning the same animals.	**Reduction in animals needed in testing** The MARCAR project scientists developed a new method which is non-invasive and significantly reduces the number of animals used in mechanistic carcinogenicity studies.
New animal model with human receptor Another innovation focused on a well-characterised epilepsy drug which causes cancer in mice, but not in humans. To understand this, MARCAR scientists inserted a human receptor for this drug into the body of a mouse, creating a 'humanised mouse' model.	**Knowledge useful for future drug development** While further research is required to prove the carcinogenic effect of the epilepsy drug, the activity proved that the use of such humanised mouse models could be useful in the further study of the mechanisms of how cancer develops and improve new drugs development.

Infrastructure for further research

Table 120: Infrastructure for further research

Outcome	Socio-economic impact
Databases and tools MARCAR has generated a biobank of tissue and biofluids from rodent NGC *in vivo* studies that could be used by future carcinogenesis research programs. MARCAR has developed/ updated three bio-informatic tools for interpretation of study outcomes.	**Biobanks, tools for future research programs** The technology and models developed during the MARCAR project have the potential to improve cancer risk assessment studies, improve drug safety, reduce animal use and reduce the time it takes for new innovative medicines reach patients.
New Standard Operating Procedures for MRI An MRI protocol was created for tumour monitoring in animal studies. MARCAR induced liver tumours in mice by single injection of diethyl nitrosamine (DEN) either in 2-week, or 6-week-old male C3H mice. In the latter, mice were also chronically treated with 0.05% phenobarbital in diet according to an initiation/promotion protocol. Liver tumours became detectable in both experiments when they exceeded a diameter of ~1 mm using MRI.	**Early detection of tumour onset and reduction of animals needed** Non-invasive methods for the early detection of tumour onset and progression in animal studies could be used in drug development and would reduce the number of animals used in research.

Structuring the European research area

Table 121: Structuring the European research area

Outcome	Socio-economic impact
Partnerships The project involved extensive collaboration between pharmaceutical companies, SME enterprises and academic partners. By drawing on expertise and resources made available by the partners, the consortium has been instrumental in the development of new tools for the identification and validation of candidate biomarkers. MARCAR partnerships with five pharmaceuticals (memoranda of understanding outside the IMI), seven universities and non-profit research institutions, and one SME.	 Material transfer agreements ensure continued collaboration past the project lifetime.
Contributions to regulatory discussions The MARCAR project has contributed to discussion on the enhancement of preclinical carcinogenicity testing strategies with regulators/pharmaceutical industry and academic stakeholders via several international workshops (including FDA and EMA representatives). The discussions have been in the context of the proposed changes to the ICH S1 guidance on Rodent Carcinogenicity Testing of Pharmaceuticals (Regulatory Notice Document 8th August 2013). The goal of this potential change is to introduce a more comprehensive and integrated approach to address the risk of human carcinogenicity of small molecule pharmaceuticals, and to define conditions under which animal carcinogenicity studies address the research question.	  **Regulatory changes can lead to fewer or no animal studies** If the regulators take on board the changes suggested by MARCAR then this change could lead to fewer or no animal carcinogenicity studies in specific cases therefore improving efficiency in clinical research.

Dissemination of information

The work of the project was presented to the scientific community through peer-reviewed journal articles and conference presentations (Table 122).

Table 122: Dissemination of information

Outcome	Socio-economic impact
Publications At the time of completion, project findings were reported in 52 publications, 72% of which were open access. The project was present at 33 conferences around the world.	Publications had a normalised citation rate of 1.17, which suggests that the results of the project are easily accessible within the academic community. The conference presentations raised further awareness of the work of the project.

3.23.6 Conclusions of impacts

A good understanding of the effect of a drug at the molecular level will ensure a better safety assessment and lead to safer drugs with less adverse effects. In addition, knowledge about the mechanisms underlying carcinogenesis may also help in treating cancer patients. Better understanding of the associated pathways that respond to drug exposure offers the promise of new therapeutics that bypass these steps. If this can be achieved, it will represent significant savings, both in time and costs, in the drug development process and be of considerable benefit to patients in terms of drug safety.

Identifying biomarkers and developing animal models for NGC research

MARCAR developed animal models to understand early tumour onset, as well as biomarker to indicate that a drug candidate may cause non-genotoxic changes. The tissue samples and resulting data generated by the project have been used to understand the mechanism of action of NGCs.

New tools for future research

Biobanks, databases and tools created during the project will be assets for future research.

3.24 MIP-DILI: Mechanism-Based Integrated Systems for the Prediction of Drug-Induced Liver Injury

02/2012 – 03/2017

3.24.1 Objectives of the project

Almost all classes of medication can cause liver disease, and drug-induced liver injury (DILI) is one of the most common cause of liver failure. The scientific and medical communities recognise two classes of DILI: dose-dependent DILI, which is typically detected early in the drug development process, and idiosyncratic DILI, which is not dose-dependent, only occurs in certain patients and is usually detected very late in the development process – or even after approval.

Predicting which drugs will cause these idiosyncratic adverse reactions is very difficult. MIP-DILI aimed to bring together expertise from industry and academia to better understand DILI, and to improve the tools and methodologies used to measure potential effects of drugs on the liver. Particular focus was placed on improving methods of testing the effects of drug candidates in human cells in the laboratory (*in vitro* testing).

This work was hoped to improve early-stage decision making within drug development, enhancing pharmaceutical productivity by reducing late-stage discontinuation of drug candidates due to unforeseen effects on the liver. As well as delivering cost and time savings, this was hoped to also increase the safety of drugs delivered to patients, reducing the socioeconomic burden of complications caused by DILI.

3.24.2 Project coordinator and managing entity

Project Coordinator	AstraZeneca AB
Managing entity	The University of Liverpool

3.24.3 Participants

Table 123: Project participants

EFPIA companies	
Abbvie Deutschland GmbH & Co Kg	Institut De Recherches Internationales Servier
AstraZeneca AB	Janssen Pharmaceutica Nv
Bristol-Myers Squibb Company Corp	Merck Kommanditgesellschaft Auf Aktien
Eli Lilly And Company Limited	Orion Oyj, Espoo
Glaxosmithkline Research and Development	Sanofi-Aventis Recherche & Developpement

H. Lundbeck As	UCB Biopharma SPRL
Universities, research organizations, public bodies, non-profit groups	
Albert-Ludwigs-Universitaet Freiburg (Germany)	Stichting Vu (Netherlands)
Deutsches Krebsforschungszentrum (Germany)	The University of Liverpool (United Kingdom)
Karolinska Institutet (Sweden)	Universiteit Leiden (Netherlands)
Klinikum Rechts Der Isar Der Technischen Universitat Munchen (Germany)	Universiteit Utrecht (Netherlands)
Lhasa Limited (United Kingdom)	Université de Rennes 1 (France)
Small and medium-sized enterprises (SMEs)	
Interface Europe (Belgium)	Solvo Biotechnology Zrt (Hungary)
KaLy-Cell (France)	Takara Bio Europe AB (Sweden)
Third parties	
Institut National de la Sante et de la Recherche Medicale (France)	

3.24.4 Project inputs and funding

The MIP-DILI project received funding of €15.3 million from IMI, from a total project cost of €32.3 million (Table 124).

Table 124: Funding received

Contributions	Financial support, €	% total funding
EU contribution	15,335,538	47.4%
EFPIA contribution	12,648,466	39.1%
IMI contribution	4,335,862	13.4%
Total funding	32,319,866	100.0%

3.24.5 Assessing the socio-economic impact of MIP-DILI

Innovation

Table 125: Project innovation

Outcome	Socio-economic impact
New preclinical models The consortium generated numerous preclinical models for use in predicting potential DILI with candidate drug molecules. These were predominantly *in vitro* models (e.g. cell cultures), many of which were fully validated. Several *in vivo* models were also developed and were undergoing validation at the time of project completion.	 **Lower attrition rates and safer medicines** The novel preclinical models generated by the MIP-DILI project enable researchers to predict which drug candidates are likely to cause DILI. Effective use of these models will therefore help ensure that only the safest drug candidates reach animals, human clinical trial participants, and ultimately patients. In the long term his will increase pharmaceutical productivity and reduce the public health burden of DILI.
Better understanding of DILI mechanisms and detection techniques Research was conducted to further knowledge of the biological mechanisms and processes underpinning DILI. This directly led to new abilities to detect DILI, based on the elucidated mechanisms. Notable achievements include the breakthrough development of a technique to detect a major sub-type of DILI (cholestasis) based on a new mechanism involving bile formation.	 **Development of DILI detection tools** By increasing the fundamental scientific knowledge base of the biology behind DILI, the project provides guidance and information for the development of tools and techniques that can be used to detect and predict the liver injury-inducing effects of drugs. Indirectly, this contributes to the long-term project impacts of lower drug development failure rates and safer medicines.
Biomarkers and assays A range of biomarkers (measurable indicators of disease presence/severity) and assays (testing procedures to determine the presence/amount of a substance, e.g. drug or biomarker) were developed. Standard protocols were established for the majority of the assays and a number are in use within the screening activities of EFPIA company partners. The biomarkers require further validation.	 **Accelerated DILI research** The assays developed by MIP-DILI are available for uptake by industry, and in some instances are already providing cost and time savings by circumventing the need for pharmaceutical companies to develop them from scratch. If validated, the biomarkers identified by the consortium provide potential for similar research-enhancing impacts.

Infrastructure for further research

Table 126: Infrastructure for further research

Outcome	Socio-economic impact
Systematic evaluation of *in vitro* test systems Project partners carried out an extensive systematic evaluation of existing *in vitro* cell systems used to test the effects of drug candidates on liver cells. Researchers examined how each system functioned, establishing which human biological processes could be captured in the laboratory. This resulted in a set of defined models for examination of a range of chemical attacks.	**Guidance for more informed *in vitro* testing** This work increased the physiological relevance of the *in vitro* models used to identify how a broad range of drug molecules may affect the liver. As such, liver toxicity of drug candidates can be predicted earlier future drug development timelines, leading to lower failure rates, more efficient research and safer medicines.
Central Data Repository and Raw Data Repository Two core online data repositories were made available to consortium members for continued research beyond project completion. The Central Data Repository (CDR) contains background/literature information, and data generated throughout the project. The Raw Data Repository (RDR) contains 1640 raw data files. Both are maintained by Lhasa limited (an SME partner), with access lasting until 2022.	**Facilitating continued research by project partners** The data repositories ensure that all data remain available for 5 years beyond project lifetime to project partners for continued DILI research. While this ensures its continued value to European consortium members, granting public access would have increased the utility and value of this data to the general scientific community.

Dissemination of information

The work of the project was presented to the scientific community through peer-reviewed journal articles and conference presentations (Table 127).

Table 127: Dissemination of information

Outcome	Socio-economic impact
Publications and conferences At the time of completion, project findings were reported in 105 publications, 52.4% of which were open access. In total, 63 oral and 51 poster presentations were made at scientific meetings internationally.	**Enhanced scientific knowledge base** Publications had a normalised citation rate of 1.65, which suggests that the results of the project are easily accessible within the academic community. The numerous presentations raised awareness of the project and promoted Europe as a place for collaborative research.

3.24.6 Conclusions of impacts

Tools for more efficient drug development

The tools developed by MIP-DILI scientists allow drug development researchers across multiple disease areas to better predict which drug candidates are likely to cause liver harm. In the long term, earlier detection of these issues will reduce failure rates in the later stages of drug development and reduce the risk of market withdrawal due to DILI issues. This will increase research efficiency and productivity.

More ethical research and safer medicines

Being able to detect DILI problems early in drug development will help researchers ensure that only the safest drug candidates reach the animal testing stage, reducing unnecessary animal suffering. Liver injury risk to human clinical trial participants will also be reduced, as will the risk of DILI occurrence after drugs have been released to market. The project outputs therefore help make drug development more ethical and will benefit patients through increased medicine safety.

Infrastructure and knowledge to guide future research

The MIP-DILI project generated new knowledge of the biological processes involved in DILI, laying foundations for the future development of DILI detection tools and techniques. The biomarkers, assays and preclinical models also serve as resources for further research, whilst evaluations of the research landscape guide future work by identifying the areas in most need of work.

3.25 NEWMEDS: Novel methods leading to new medications in depression and schizophrenia

09/2009 – 02/2015

3.25.1 Objectives of the project

Schizophrenia and depression are highly prevalent mental illnesses, affecting over 320 million people globally. They place huge burdens on sufferers, families, care givers and public health systems, and as such are pressing public health issues. Schizophrenia and depression are hard to treat, with limited progress made in turning recent scientific advancements into effective treatments.

The NEWMEDS project aimed to bring together experts from academia and industry to improve knowledge of the genetic and environmental causes of the psychiatric conditions, and to create new avenues for the development of effective treatments. The consortium planned to carry out research into the genetics behind the illnesses, whilst developing tools such as animal models, biomarkers and imaging techniques to enhance and broaden the development of new medications.

Ultimately, it was hoped that this would accelerate drug development for schizophrenia and depression, leading to a wider variety of available medicines and reducing the socioeconomic burden of the illnesses.

3.25.2 Project coordinator and managing entity

Project Coordinator H. Lundbeck A/S

Managing entity King's College London

3.25.3 Participants

Table 128: Project participants

EFPIA companies	
Abbvie Deutschland GmbH	Islensk Erfdagreining Ehf
Eli Lilly And Company Limited	Janssen Pharmaceutica Nv
F. Hoffmann-La Roche AG	Novartis Pharma AG
H. Lundbeck As	Orion Oyj, Espoo
Institut De Recherches Servier	Pfizer Limited

Universities, research organizations, public bodies, non-profit groups	
Agencia Estatal Consejo Superior Deinvestigaciones Cientificas (Spain)	The University of Manchester (United Kingdom)
Bar Ilan University (Israel)	University of Cambridge (United Kingdom)
Karolinska Institutet (Sweden)	Zentralinstitut Fuer Seelische Gesundheit (Germany)
King's College London (United Kingdom)	
Small and medium-sized enterprises (SMEs)	
Gabo: Mi Gesellschaft Fur Ablauforganisation:Milliarium MbH & Co. KG (Germany)	Psynova Neurotech Ltd (United Kingdom)

3.25.4 Project inputs and funding

The NEWMEDS project received funding of €9.0 million from IMI, from a total project cost of €24.8 million (Table 129).

Table 129: Funding received

Contributions	Financial support, €	% total funding
EU contribution	8,986,216	36.2%
EFPIA contribution	13,789,412	55.5%
IMI contribution	2,074,047	8.3%
Total funding	24,849,675	100.0%

3.25.5 Assessing the socio-economic impact of NEWMEDS

Innovation

Table 130: Project innovation

Outcome	Socio-economic impact
New animal models To develop effective treatment for schizophrenia, researchers need to test potential treatments on animals that exhibit symptoms of the condition (animal models). NEWMEDS researchers developed new animal models for schizophrenia research. The models are assessed using brain recording and behavioural tests, giving researchers greater ability to predict drug safety and efficacy from animal testing.	**More efficient drug development for schizophrenia** The animal models developed by NEWMEDS provide researchers with better tools to study drug candidates. The ability to more effectively predict drug efficacy in humans will help reduce failure rates in later stages of drug development, reduce the risk of unsafe treatments reaching human clinical trials and accelerate the development of new, effective treatments for schizophrenia.

Infrastructure for further research

Table 131: Infrastructure for further research

Outcome	Socio-economic impact
Greater understanding of biology behind schizophrenia NEWMEDS scientists conducted research on the biological causes of schizophrenia. Amongst other findings, a breakthrough was made in the demonstration that particular genetic variations ('copy number variations' (CNV)) are closely linked with schizophrenia (amongst other cognitive disorders). By examining CNVs in animal and human models, researchers identified which brain mechanisms are affected by the variations.	**New scientific foundations for medicine development** By generating new knowledge of the neurological causes of schizophrenia, the NEWMEDS project has provided new avenues for drug discovery. In the long term, this will help broaden the available treatment for the disorder, reducing its burden on individuals and healthcare systems.
Search for genetic biomarkers NEWMEDS researchers compiled a database of over 2000 individuals from five studies and conducted analysis to identify DNA sequences ('genetic biomarkers') whose presence in patients could be used to predict their response to antidepressants. This was done with a view to use the information to stratify patients in antidepressant trials, allowing development of more targeted treatments. No major stratifying genetic biomarkers were found; however, an	**Guidance for future work** This work did not return any stratifying biomarkers. However, it is a valuable piece of research, accelerating future development of more targeted antidepressants through the guidance it provides for further work. The publicly available online tool enhanced research by supporting researchers in their assessment of new biomarkers, however its impact is limited by its current unavailability.

online tool was built for the assessment of clinical relevance of future biomarkers.	
Imaging techniques The NEWMEDS consortium developed imaging tools and models for the early testing of drug efficacy. Positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) techniques were established.	**Tools for enhanced drug development** The imaging tools and techniques developed by the consortium provide researchers with greater power to test drug efficacy earlier in drug development timelines. This work will therefore increase the efficiency and scope of further research.
DupCheck tool NEWMEDS developed and released an online tool ('Dup Check', www.dupcheck.org) which allows clinical trial researchers to check whether participant patients are enrolled twice in the same trial, at a different site, or in another trial. The tool can be used across different sponsors and therapeutic areas and was given a favourable Qualification Advice review by the European Medicines Agency.	**Safer, more robust trials** By enrolling in duplicate studies, patients expose themselves to a higher risk of harm. The validity of the clinical trial results are also compromised, with even a small number of duplicate patients potentially leading to failed or negative trials. The DupCheck tool therefore decreases the likelihood of harm caused by duplicate enrolments and reduces the risk of false outcomes across all medicine areas.
Database analysis Project workers constructed and analysed anonymised databases of patient-level data from clinical trials in schizophrenia and depression to determine ways of conducting more efficient trials. Analysis of the databases produced several findings, including that for trials of schizophrenia and depression medication, detection of patterns in adverse events can be improved, and sample size can be reduced, by altering cohort characteristics. It was also found that trials can be made shorter and give similar results.	**Information for improved clinical trials** The findings made from the database analyses allow clinical trial researchers and planners to structure trials more efficiently, with trials lasting no longer than necessary. Smaller sample sizes would provide cost and time savings while subjecting fewer individuals to the risks involved in clinical studies.

3.25.6 Dissemination of information

The work of the project was presented to the scientific community through peer-reviewed journal articles and conference presentations (Table 132).

Table 132: Dissemination of information

Outcome	Socio-economic impact
Publications and scientific presentations At the time of completion, project findings were reported in 187 publications, 51.3% of which were open access. 161 presentations were made at scientific meetings around the world, including conferences and workshops.	Publications had a normalised citation impact of 2.13, which suggests that the results of the project are easily accessible within the academic community. The scientific presentations raised awareness of the project and promoted Europe as a place for drug development research.

3.25.7 Conclusions of impacts

Expanded knowledge base for schizophrenia and depression drug development

The NEWMEDS project generated knowledge and research tools for enhanced and accelerated development of treatments for schizophrenia and depression. The knowledge base of the biology behind the conditions was expanded in multiple areas, with key findings made regarding genetic variations in individuals with schizophrenia. This knowledge can be used for the development of new, targeted treatments.

Resources for accelerated medicines research

New tools and techniques were established by NEWMEDS researchers for direct application in future research. New animal models were developed and validated to predict the safety and efficacy of candidate drugs in humans. Novel imaging techniques were also developed, giving researchers greater power to predict drug efficacy during early drug development. Overall, these resources help reduce failure rates of the drug development process and increase the quality and efficiency of subsequent research.

Shorter, more informative and safer trials

Valuable information was generated for the optimisation of future clinical trials. The largest databases to date of patient-level data within schizophrenia and depression were created and analysed, and methods for making trials shorter, smaller and more informative were established. Alongside this, an online tool was created to screen for duplicate patient enrolment, which can harm patients and invalidate trial results. The project therefore contributed to the safety and quality of clinical trials for schizophrenia and depression.

3.26 OncoTrack: Methods for systematic next generation oncology biomarker development

01/2011 – 12/2016

3.26.1 Objectives of the project

Colorectal cancer is one of the leading causes of death worldwide and places huge burdens on patients, carers and healthcare systems. As colorectal cancer tumours grow, they undergo genetic changes which vary between patients, making response to treatments highly variable.

The OncoTrack project aimed to develop models to predict the effects of drugs on different colon cancers by collecting tumour tissue samples from patients at different stages of the disease and analysing them for biomarkers (molecules within tumour cells that are indicative of the sub-group to which the tumour belongs). This would allow scientists to create 'molecular fingerprints' of the tumours, which could be correlated with the tumour's response to drug compounds and used to predict the efficacy of drugs against certain tumour types.

It was hoped that this work would enable healthcare professionals to make more informed decisions on which treatment to give individual patients with colorectal cancer, based on blood tests from the tumour. This would result in more targeted treatment for colorectal cancer, and lessen the socio-economic burden of the disease.

3.26.2 Project coordinator and managing entity

Project Coordinator	Bayer Pharma AG
Managing entity	Max-Planck-Gesellschaft zur Foerderung der Wissenschaften e.V.

3.26.3 Participants

Table 133: Project participants

EFPIA companies	
AstraZeneca AB	F. Hoffmann-La Roche AG
Bayer Pharma AG	Janssen Pharmaceutica Nv
Boehringer Ingelheim International GmbH	Merck Kommanditgesellschaft Auf Aktien
Eli Lilly And Company Limited	Pfizer Limited
Universities, research organizations, public bodies, non-profit groups	
Charite - Universitaetsmedizin Berlin (Germany)	Stockholms Universitet (Sweden)

Dahlem Center For Genome Research And Medical Systems Biology GMBH (Germany)	Technische Universitaet Dresden (Germany)
Fundacio Privada Institut D'Investigacio Oncologica De Vall-Hebron (Spain)	Universite Paris-Sud (France)
Max-Planck-Gesellschaft Zur Forderung Der Wissenschaften Ev (Germany)	University College London (United Kingdom)
Medizinische Universitat Graz (Austria)	Uppsala Universitet (Sweden)
Small and medium-sized enterprises (SMEs)	
Alacris Theranostics GmbH (Germany)	International Prevention Research Institut-Ipri Management (France)
Experimentelle Pharmakologie Und Onkologie Berlin-Buch GMBH (Germany)	
Third parties	
Ipri Services (France)	

3.26.4 Project inputs and funding

The OncoTrack project received funding of €16.8 million from IMI, from a total project cost of €29.4 million (Table 134).

Table 134: Funding received

Contributions	Financial support, €	% total funding
EU contribution	16,757,282	56.9%
EFPIA contribution	10,976,55	37.3%
IMI contribution	1,697,375€	5.8%
Total funding	29,431,214	100.0%

3.26.5 Assessing the socio-economic impact of OncoTrack

Innovation

Table 135: Project innovation

Outcome	Socio-economic impact
Biomarkers to predict efficacy of colorectal cancer drugs OncoTrack scientists collected tumour samples from 106 colorectal cancer patients and grew them *in vitro* and *in vivo* using mouse strains. The samples were then analysed for biomarkers and the resulting 'molecular fingerprints' of the tumour systems were correlated with drug response. Four biomarkers were identified as efficacy predictors for four common colorectal cancer drugs: 5FU, Cetuximab (validated), afatinib and AZD8931.	 **Progress towards predictive diagnostic tools** The extensive study of the molecular landscape of colorectal cancer tumours provides data, knowledge and resources for further investigation of methods to predict efficacy of drugs based on biomarker measurements within tumours. In effect, this accelerates the pathway towards more effective, patient-specific treatment of colorectal cancer. The biomarkers identified can be further developed for routine clinical use. Furthermore, the analysis of the tumour samples of the 106 patients involved in the study can be used to guide and improve their treatment.
Elucidation of new treatment pathway for colorectal cancer OncoTrack researchers discovered the biological process that controls the survival of stem cells in colorectal cancer (the 'Hedgehog' signalling pathway), by studying genetic sequences within the cells. Since stem cells have an important role in the growth of cancer tumours, inhibition of this pathway could be a viable way of eliminating cancer cells and preventing reoccurrence.	 **Knowledge base for further development** This work provides concrete foundations for further research into how the Hedgehog biological pathway controls stem cell survival, paving the way for the development of interventions that inhibit this process. This output therefore provides a potential pathway to novel colorectal cancer treatment and increased survival rates amongst patients.
New biological models of colorectal cancer Many biological models of colorectal cancer were developed by the consortium over the course of the project. In total, 93 organoid models (small groups of cells that mimic tumour biology) and 211 xenograft models (tumour tissue transplanted into an animal, in this case mice) were generated, alongside 66 *in silico* models (computer models).	 **Enhanced industry research** The models generated are tools for further biomarker and drug discovery research, with some companies already using them in R&D programmes. This output therefore accelerates and enhances further research into novel colorectal cancer treatments.

Infrastructure for further research

Table 136: Infrastructure for further research

Outcome	Socio-economic impact
Sustainability plan for resource provision A sustainability plan was put in place to ensure that as many of the scientific resources generated throughout the project as possible were made available to the scientific community beyond project completion. The electronic data was archived in the European Genome-phenome Archive (EGA) and biological models and samples were retained by project partners.	 **Broadened colorectal cancer research** The provision of valuable data and resources to the scientific community widens the scope of further research into colorectal cancer biomarkers, animal models, biological causes and ultimately novel treatments. In doing so it accelerates the development of more targeted interventions and makes Europe a more competitive place within this area.

Structuring the European research area

Table 137: Structuring the European research area

Outcome	Socio-economic impact
Spin-off SME companies Two spin-off companies were created as a result of the OncoTrack project. The first, 'Cellular Phenomics & Oncology Berlin-Buch GmbH' (CPO) was established in 2014 to commercialise a technology relating to the culture of organoids. The company offers these technologies to pharmaceutical companies for drug testing purposes. A second was set up in 2018 to commercialise project outputs relating to diagnostic procedures.	 **Business creation and continued technology development** The establishment of new SMEs increases productivity in Europe and provides economic benefits such as job growth and expansion of the tax base. It also ensures continuation of the development and implementation of innovative technologies; supporting and enhancing scientific research in Europe through the provision of novel R&D services.

Dissemination of information

The work of the project was presented to the scientific community through peer-reviewed journal articles and conference presentations (Table 138).

Table 138: Dissemination of information

Outcome	Socio-economic impact
Publications and scientific presentations At the time of completion, project findings were reported in 57 publications, 59.6% of which were open access. Over 200 presentations were made at scientific meetings across the world.	 Publications had a normalised citation rate of 2.43, which suggests that the results of the project are easily accessible within the academic community. The scientific presentations raised awareness of the project and promoted Europe as a place for medicines research.

3.26.6 Conclusions of impacts

Accelerated development of more targeted colorectal cancer management

The OncoTrack project made significant advances towards the development of clinical tools that can be used to guide treatment decision making based on the molecular analysis of individual patients' tumours. The landmark study of 106 tumour samples from colorectal cancer patients is particularly notable, producing distinct biomarkers which can predict tumour response to common colorectal cancer treatments. This paves the way for the development of tools that can be used in the clinic to determine which treatment is best for a given patient.

Knowledge and resources for enriched further research

The project produced a body of new knowledge of the biology behind colorectal cancer, which expands the scope of future research. Resources including *in vitro* and animal models, biomarkers, tissue samples and biological data, were generated which can be used in further research by partners and third parties.

Increased European competitivity through business creation

The project led to the development of two spin-off businesses for the commercialisation of technologies generated by the project. This provides the economic benefits of new business, alongside continued development and provision of novel technologies to the scientific community. This increases Europe's competitivity within the global research landscape.

3.27 Open PHACTS: The Open Pharmacological Concepts Triple Store

03/2011 – 02/2016

3.27.1 Objectives of the project

Pharmaceutical companies collect and maintain large amounts of public chemical and biomedical data for drug discovery. The data collected must be in a consistent format to be collectively analysed. The alignment of this multi-source data, which includes information on chemical compounds, biological targets, diseases and tissues, requires significant effort and resources, with standardisation processes repeated internally across companies. This represents a significant cost and time burden.

The Open PHACTS project aimed to address this by bringing together experts in fields such as information handling, data storage, data mining, bioinformatics and biological chemistry to develop a platform that integrates pharmacological data from a range of public sources, with shared standards and identifiers to facilitate searchability and data comparison.

It was hoped that this would significantly shorten the time required for researchers to access required data, thus accelerating early-stage drug development and reducing unnecessary expense of time, cost and resources caused by duplicated data integration efforts by pharmaceutical companies.

3.27.2 Project coordinator and managing entity

Project Coordinator	GlaxoSmithKline Research and Development Ltd
Managing entity	Universität Wien

3.27.3 Participants

Table 139: Project participants

EFPIA companies	
AstraZeneca AB	Janssen Pharmaceutica Nv
Eli Lilly And Company Limited	Laboratorios Almirall S.A.
Esteve Pharmaceuticals	Merck Kommanditgesellschaft Auf Aktien
Glaxosmithkline Research and Development Ltd.	Novartis Pharma AG
H. Lundbeck As	Pfizer Limited
Universities, research organizations, public bodies, non-profit groups	
Academisch Ziekenhuis Leiden (Netherlands)	Stichting Vu (Netherlands)

Consorcio Mar Parc De Salut De Barcelona (Spain)	The Royal Society of Chemistry (United Kingdom)
Danmarks Tekniske Universitet (Denmark)	The University of Manchester (United Kingdom)
European Molecular Biology Laboratory (Germany)	Universidad De Santiago De Compostela (Spain)
Fundacion Centro Nacional De Investigaciones Oncologicas Carlos Iii (Spain)	Universitaet Hamburg (Germany)
Open Phacts Foundation Lbg (United Kingdom)	Universitat Wien (Austria)
Rheinische Friedrich-Wilhelms-Universitat Bonn (Germany)	Universiteit Maastricht (Netherlands)
SIB Institut Suisse De Bioinformatique (Switzerland)	
Small and medium-sized enterprises (SMEs)	
BioSolveIT GmbH (Germany)	Openlink Group Limited (United Kingdom)
Connected Discovery Ltd (United Kingdom)	SciBite Limited (United Kingdom)
Non-EFPIA companies	
Stichting Dtl Projects (Netherlands)	
Third parties	
Fundacio Institut Mar D Investigacions Mediques Imim (Spain)	RSC Worldwide (US) Inc. (United States)
RSC World Wide Ltd (United Kingdom)	Universidad Pompeu Fabra (Spain)

3.27.4 Project inputs and funding

The Open PHACTS project received funding of €11.5 million from IMI, from a total project cost of €21.8 million (Table 140).

Table 140: Funding received

Contribution	Financial support, €	% total funding
EU contribution	11,466,433	52.6%
EFPIA contribution	6,412,905	29.4%
IMI contribution	3,921,792	18.0%
Total funding	21,801,130	100.0%

3.27.5 Assessing the socio-economic impact of Open PHACTS

Infrastructure for further research

Table 141: Infrastructure for further research

Outcome	Socio-economic impact
Open PHACTS Discovery Platform The primary output of the project was the Open PHACTS Discovery Platform, a publicly available, standardised, open-source and open-access platform containing integrated data from 13 data sources. Researchers can use the platform to perform queries for information on chemical compounds, targets, biological pathways, diseases and more, circumventing the need for lengthy data integration from disparate sources by individual companies.	**More efficient drug development** The Open PHACTS Discovery Platform provides significant cost and time-saving benefits to drug developers. The platform allows researchers to rapidly access relevant data to answer scientific questions, without the need for lengthy and resource-heavy data integration tasks. By project completion, the platform was in use by several groups within academia and industry, as well as several other IMI projects. In the long term, the cost and time savings will contribute to faster delivery of new medicines to patients, benefiting public health.

Structuring the European research area

Table 142: Structuring the European research area

Outcome	Socio-economic impact
Spin-off SME business The project contributed to the formation of a spin-off company, Phenaris, based in Austria. Amongst other drug discovery services, Phenaris offers the ToxPHACTS platform, developed through integration of the outputs of Open PHACTS and the eTOX IMI project. ToxPHACTS allows early-stage assessment of the toxicological risk of candidate drug compounds.	 **Business creation and continued technological development** As a new business, Phenaris provides economic benefits such job creation and tax contributions. Importantly, it also contributes to the development of innovative technologies in Europe, enhancing its competitivity within the global R&D landscape. Specific benefits of the ToxPHACTS platform includes better prediction of drug toxicology and reduction of animal testing on toxic drug candidates.
The Open PHACTS Foundation To ensure continued maintenance and utility of the Open PHACTS infrastructure, the Open FACTS foundation was established. Not-for-profit and made up of one academic and three industry partners, the foundation maintains the Discovery Platform, and is currently a partner in multiple Horizon 2020 research projects.	 **Sustained collaboration and further platform development** The existence of the Open PHACTS Foundation ensures continued collaboration between academia and industry, via the member organisations. It also drives further development of innovative data solutions, contributing to the competitivity of Europe in this area.
Memoranda of understanding and material transfer agreements Material transfer agreements were signed for the transfer of Open PHACTS data. An internal IMI memorandum of understanding was signed with the eTOX consortium, and over 50 were signed with associated partners.	 **Infrastructure for collaboration** The memoranda of understanding and material transfer agreements signed throughout the project facilitated the sharing of ideas, data and technology, creating collaboration between project partners and associated organisations. The agreements also serve as blueprints for future collaboration in this area.

Dissemination of information

The work of the project was presented to the scientific community through peer-reviewed journal articles and conference presentations (Table 143).

Table 143: Dissemination of information

Outcome	Socio-economic impact
Publications and conferences At the time of completion, project findings were reported in 73 publications, 80.8% of which were open access. Over 160 presentations were made at scientific conferences around the world.	**Raised awareness within scientific community** Publications had a normalised citation rate of 3.14, which suggests that the results of the project are easily accessible within the academic community. The conference presentations further promoted the work of the project in the scientific community.

3.27.6 Conclusions of impacts

More efficient, less wasteful drug development

The Open PHACTS discovery platform circumvents the need for drug development researchers to conduct lengthy and resource-intensive in-house data integration tasks, allowing resources to be targeted elsewhere in the drug development process. This output increases the cost and time efficiency of drug development, accelerating the release of new treatments to patients.

Sustained collaboration

The project brought together European organisations from industry and academia, with groups from both sides benefitting from insights into the operations of the other. The Open PHACTS Foundation ensures continued collaboration between four of these organisations. Overall, scientific collaboration promotes innovation within the field and increases Europe's competitivity within the global R&D community.

Economic benefits

The time and cost savings resulting from the project outputs increases pharmaceutical productivity within Europe. The project also resulted in a spin-off company, providing further economic benefits and the continued development of innovative technology within the field of database integration.

3.28 OrBiTo: Oral biopharmaceutics tools

10/2012 – 09/2018

3.28.1 Objectives of the project

Pharmaceutical companies collect and maintain large amounts of public chemical and biomedical data for drug discovery. The data collected must be in a consistent format to be collectively analysed. The alignment of this multi-source data, which includes information on chemical compounds, biological targets, diseases and tissues, requires significant effort and resources, with standardisation processes repeated internally across companies. This represents a significant cost and time burden.

The Open PHACTS project aimed to address this by bringing together experts in fields such as information handling, data storage, data mining, bioinformatics and biological chemistry to develop a platform that integrates pharmacological data from a range of public sources, with shared standards and identifiers to facilitate searchability and data comparison.

It was hoped that this would significantly shorten the time required for researchers to access required data, thus accelerating early-stage drug development and reducing unnecessary expense of time, cost and resources caused by duplicated data integration efforts by pharmaceutical companies.

3.28.2 Project coordinator and managing entity

Project Coordinator AstraZeneca AB

Managing entity Uppsala Universitet

3.28.3 Participants

Table 144: Project participants

EFPIA companies	
Abbvie Deutschland GmbH	Janssen Pharmaceutica Nv
Astrazeneca AB	Merck Sharp & Dohme Corp
Bayer Pharma AG	Novartis Pharma AG
Boehringer Ingelheim International GmbH	Orion Oyj
Bristol-Myers Squibb Company Corp	Pfizer Limited
Glaxosmithkline Research and Development Ltd	Sanofi-Aventis Recherche & Developpement
H. Lundbeck As	

Universities, research organizations, public bodies, non-profit groups	
Ethniko Kai Kapodistriako Panepistimio Athinon (Greece)	Johann Wolfgang Goethe-Universitatfrankfurt Am Main (Germany)
Nederlandse Organisatie Voor Toegepast Natuurwetenschappelijk Onderzoek Tno (Netherlands)	Johannes Gutenberg-Universitat Mainz (Germany)
The University of Manchester (United Kingdom)	Katholieke Universiteit Leuven (Belgium)
Universitaet Greifswald (Germany)	Kobenhavns Universitet (Denmark)
University of Strathclyde (United Kingdom)	Lakemedelsverket (Sweden)
Uppsala Universitet (Sweden)	
Small and medium-sized enterprises (SMEs)	
Certara Uk Limited (United Kingdom)	Sirius Analytical Ltd (United Kingdom)
Simulations Plus, Inc. (United States)	
Third parties	
TNO Triskelion (Netherlands)	Universitaetsmedizin Der Johannes Gutenberg-Universitaet Mainz (Germany)

3.28.4 Project inputs and funding

The Open PHACTS project received funding of €11.5 million from IMI, from a total project cost of €21.8 million (Table 145).

Table 145: Funding received

Contribution	Financial support, €	% total funding
EU contribution	11,466,433	52.6%
EFPIA contribution	6,412,905	29.4%
IMI contribution	3,921,792	18.0%
Total funding	21,801,130	100.0%

3.28.5 Assessing the socio-economic impact of OrBiTo

Innovation

Table 146: Project innovation

Outcome	Socio-economic impact
Improved *in vitro* tools for *in vivo* prediction To predict the absorption properties of a drug, researchers can model the chemical processes that compounds undergo in the GI tract. A number of such *in vitro* tools were developed by the consortium, to aid researchers in the prediction of how drug molecules will behave in the body (*in vivo*). 20 *in vitro* preclinical models were developed and several of the tools had been adopted by industry partners by project completion.	 **Increased research efficiency and reduced need for *in vivo* testing** The ability to predict the *in vivo* behaviour of drugs from *in vitro* studies saves researchers time and resources, ensuring that only the most promising and safest drug formulations reach the animal/human testing stage. In the long term this increases the quality of drug formulations reaching patients and helps pave the way to reducing regulatory requirements for *in vivo* testing. The ability to better predict the performance of formulations in in vitro systems reduces the reliance on the use of animals studies therefore contributing to the 3Rs.

Infrastructure for further research

Table 147: Infrastructure for further research

Outcome	Socio-economic impact
Tools for better understanding of physicochemical properties Tools were developed and standardised to measure the physical and chemical (physicochemical) properties of drug candidates such as dissolution and solubility, to aid better prediction of how effectively the drug will be absorbed in the GI tract. The tools were largely validated within EFPIA partner labs, ensuring industrial applicability, and protocols were developed for existing procedures through EFPIA surveys.	 **Accelerated research through improved compound selection** The tools allow researchers to better understand the properties of drug compounds and to select candidates with the best pre-requisites for GI solubility. This will accelerate drug development through lower drug development failure rates and minimise animal testing. It also reduces resource expenditure and increases productivity. Several of the OrBiTo tools were adopted by EFPIA partners by project completion.

Expanded knowledge of GI tract and drug absorption To maximise the predictive power of *in vivo* laboratory test systems for drug behaviour, OrBiTo carried out research to expand scientific understanding of the GI tract and drug permeability. Over 20 studies of the GI tract environment were conducted, providing a body of knowledge that can be used to develop more predictive laboratory tools.	**Greater scientific understanding for development of improved predictive tools** The body of scientific knowledge generated by this work provides a basis for the development of tools that better predict drug absorption, particularly for drugs with low solubility/permeability (of which there are an increasing number). This results in more efficient research and minimises the need for studies involving animals and humans.
Advancing computerised modelling capabilities In order to improve and refine existing computerised (*in silico*) models of human drug absorption, OrBiTo created a database of EFPIA data on the physicochemical properties of a range of drug compounds. The database was used to evaluate existing computational models, with improvements and refinements made based on the analysis.	**Higher quality research and reduced *in vivo* testing** By improving computational models of human drug absorption, this work allows researchers to make more informed decisions during the compound selection stage, reducing the drug discovery failure rate at later stages. *In vivo* animal testing is also reduced.
Industry guidance for use of predictive tools The consortium generated valuable guidance for the implementation of the tools and methods validated throughout the project. Multiple decision trees were created for methods including compound characterisation, *in vitro* testing procedures and *in vivo* modelling. Best practice guidance was also published for *in silico* modelling methods.	**Higher quality drug development** The guidance documents provide tools and methods for the prediction of optimal compound properties. This increases the efficiency and quality of decision making using *in vitro* and *in silico* tools.

Dissemination of information

The work of the project was presented to the scientific community through peer-reviewed journal articles and conference presentations (Table 148).

Table 148: Dissemination of information

Outcome	Socio-economic impact
Publications and scientific presentations At the time of completion, project findings were reported in 130 publications, 20.0% of which were open access. Over 67 presentations were made at scientific meetings, primarily in the EU and US.	Publications had a normalised citation impact of 1.64, which suggests that the results of the project are easily accessible within the academic community. Conference presentations further promoted the work of the project.

3.28.6 Conclusions of impacts

Increased research efficiency

The OrBiTo project developed and validated tools to predict absorption of drug compounds in the GI tract. These tools allow researchers to better predict which compounds have adequate absorptive properties to select for further development, which will hopefully reduce failure rates caused by poor GI tract absorption.

Reduced need for animal testing

The tools developed by the project to predict in-body drug behaviour were specifically *in vitro* or *in silico* in nature. The project outputs reduced the reliance of drug developers on testing drug behaviour in animals, making drug development more ethical and resource-efficient.

Knowledge and infrastructure for future work

The consortium generated a body of scientific knowledge on drug behaviour in the GI tract, providing a basis to develop more models. Guidance was also published for the tools and methods developed and validated by the project, supporting future research.

3.29 PharmaCog: Prediction of cognitive properties of new drug candidates for neurodegenerative diseases in early clinical development

01/2010 – 12/2015

3.29.1 Objectives of the project

Alzheimer's disease (AD) is a neurodegenerative disorder that causes an irreversible decline in memory and cognitive abilities. Over 4 million people in Europe suffer from the disease, placing a huge burden on European healthcare systems, carers and patients. Little is understood about the causes of the disease and most candidate drugs fail during clinical trials. There are currently five drugs on the market for AD treatment, and none can effectively slow disease progression.

The PharmaCog project aimed to accelerate the development of new drugs for AD by developing and validating new tools for faster and more precise testing of candidate compounds. The consortium primarily set out to identify new biological indicators (biomarkers) of disease progression and drug response, organising the work around preclinical animal models, as well as clinical studies of healthy volunteers and patients with early signs of AD.

3.29.2 Project coordinator and managing entity

Project Coordinator	GlaxoSmithKline Research and Development Ltd
Managing entity	Université d'Aix-Marseille

3.29.3 Participants

Table 149: Participants

EFPIA companies	
Astrazeneca AB	H. Lundbeck As
Boehringer Ingelheim International GmbH	Institut De Recherches Servier
Eisai Limited	Janssen Pharmaceutica Nv
Eli Lilly And Company Limited	Merck Kommanditgesellschaft Auf Aktien
F. Hoffmann-La Roche AG	Novartis Pharma AG
GlaxoSmithKline Research and Development Ltd	UCB Pharma SA

Universities, research organizations, public bodies, non-profit groups	
Centre National De La Recherche Scientifique (France)	Universita Cattolica Del Sacro Cuore (Italy)
Consorci Institut D'Investigacions Biomediques August Pi I Sunyer (Spain)	Universita Degli Studi Di Foggia (Italy)
Fondazione Sdn Per La Ricerca E L'Alta Formazione In Diagnostica Nucleare (Italy)	Universita Degli Studi Di Genova (Italy)
Institut National De La Sante Et De La Recherche Medicale (France)	Universita Degli Studi Di Perugia (Italy)
Istituto Di Ricerche Farmacologiche Mario Negri (Italy)	Universita Degli Studi Di Verona (Italy)
Provincia Lombardo Veneta - Ordineospedaliero Di San Giovanni Di Dio- Fatebenefratelli (Italy)	Universitaet Leipzig (Germany)
Stichting Vu (Netherlands)	Universitaetsklinikum Essen (Germany)
The University of Exeter (United Kingdom)	Universite D'Aix Marseille (France)
Universidad De Murcia (Spain)	Universite De Lille Ii - Droit Et Sante (France)
Small and medium-sized enterprises (SMEs)	
Diaxonhit SA (France)	Qualissima (France)
Innovative Concepts In Drug Development (ICDD-Sas) (France)	SAS Alzprotect (France)
Patient Organisations	
Alzheimer Europe (Luxembourg)	Elliniki Etairia Nosoy Alzheimer Kai Syggenon Diatarachon Somateio (Greece)
Third parties	
Centre Hospitalier Regional De Mars Eille Assistance Publique-Hopitaux Marseille (France)	Museum National D'Histoire Naturelle (France)
Centre Hospitalier Regional Et Universitaire De Lille (France)	Universite Paul Sabatier Toulouse Iii (France)

3.29.4 Project inputs and funding

The PharmaCog project received funding of €9.7 million from IMI, from a total project cost of €30.7 million (Table 150).

Table 150: Funding received

Contributions	Financial support, €	% total funding
EU contribution (in €)	9,658,388	31.4%
EFPIA contribution (in €)	11,690,333	38.1%
IMI contribution	9,366,835	30.5%
Total funding	30,715,556	100.0%

3.29.5 Assessing the socio-economic impact of PharmaCog

Innovation

Table 151: Project innovation

Outcome	Socio-economic impact
Biomarkers for assessment of AD drug efficacy Studies were carried out in animal models, patients with mild cognitive impairment and healthy volunteers undergoing a challenge such as sleep deprivation. Biomarkers were identified and validated to measure of disease progression and the response to drugs. Techniques such as MRI and electroencephalogram (EEG) brain scanning were used.	**Evaluation of drug candidates** The biomarkers identified by PharmaCog allow scientists to better predict results of drugs in humans based on studies in animals. This could allow for more informed decision making when selecting which drug candidates to bring through to human clinical trials, increasing the efficiency and pace of AD drug research. At time of project completion, and external SME partner was using the findings to evaluate a new drug candidate.
Validation of new animal models Four new animal models were validated to test new drugs for AD.	**Expanded scope of future work** By increasing the range of animal models available to researchers, this work provides new avenues for AD drug testing and reduces the risk of costly failure at the clinical trial stage.

Infrastructure for further research

Table 152: Infrastructure for further research

Outcome	Socio-economic impact
Patient stratification methods A study was conducted of over 150 individuals with mild cognitive impairment (MCI), one of the early indicators of AD. The study identified AD-predictive biomarkers which can be used to generate new ways of stratifying patients in clinical trials.	**Patient stratification in clinical trials** The effects of MCI cause variability across patients in clinical trials, which risks masking the effects of candidate drugs. Stratifying patients according to MIC may address this issue.
Standard operating procedures Five standard operating procedures (SOPs) were developed for various technologies, including MRI imaging techniques, EEG brain monitoring and blood sampling.	**Higher quality research** The SOPs provide researchers with detailed guidance for the use of complex scientific tools. This contributes to increased efficiency and quality of future work.
Pharmacological database A database containing clinical, biological, pharmacokinetic and neurological information generated by the PharmaCog project was developed and can be used by project partners for further modelling work.	**Data resource for accelerated research** The database provides future researchers with valuable information for future work, enhancing research into AD and new treatments.

Dissemination of information

The work of the project was presented to the scientific community through peer-reviewed journal articles, conference presentations and training initiatives (Table 153).

Table 153: Dissemination of information

Outcome	Socio-economic impact
Publications At the time of completion, project findings had been reported in 76 publications, 27.6%. of which were open access. Presentations were made at scientific meetings.	Publications had a normalised citation rate of 1.20, which suggests that the results of the project are easily accessible within the academic community. The conference presentations further promoted the work of the project in the scientific community.
Educational outputs Eight training courses were conducted across six countries. three PhD projects relating to	**Enhanced skills base of research workforce**

PharmaCog were successfully completed in industry.	The training activities enhanced the technical skills of the recipients, producing a more competitive European scientific workforce.

3.29.6 Conclusions of impacts

Knowledge base for more efficient Alzheimer's drug research

The PharmaCog project generated knowledge and biological tools which increase the time and cost efficiency of subsequent research. The biomarkers identified by the consortium allow translation of findings between animal models and humans, allowing for better prediction of drug efficacy at the animal testing stage and reducing the risk of failure in clinical trials. The stratification methods provide a basis for more targeted clinical trial design, increasing reliability of results and further reducing the number of human participants exposed to potentially harmful treatments.

Infrastructure for enhanced drug development

Research infrastructure was generated in a number of areas. Animal models were identified and validated, SOPs were published and a database containing project results was established for future work. These outputs have the potential to accelerate the development of new AD drugs, in the long term reducing the burden of the disease on individuals and healthcare systems.

3.30 PharmaTrain: Pharmaceutical Medicine Training Programme

01/2009 – 04/2014

3.30.1 Objectives of the project

For Europe to have maximum competitivity within the global pharmaceutical industry, trained experts are needed to oversee all aspects of the drug development timeline, from compound discovery and preclinical study, to clinical trials and regulatory approval. Consistent, high quality education and training in these fields must therefore be provided across Europe.

The PharmaTrain project was established to address the fragmented nature of this education and training in Europe. The consortium aimed to bring together European institutions and experts responsible for delivering educational courses in medicines development, and establish shared guidelines and standards for the development of post-graduate diploma and Master's courses. Assessment criteria for existing courses, and a system of recognising courses that meet the criteria, were also project goals. It was hoped that more consistent education and training in Europe would increase the quality and pace of drug development and make Europe a more attractive place to carry out medicines research.

3.30.2 Project coordinator and managing entity

Project Coordinator PharmaTrain Federation

Managing entity Universitaet Basel

3.30.3 Participants

Table 154: Participants

EFPIA companies	
Amgen	Merck Kommanditgesellschaft Auf Aktien
Astrazeneca AB	Novartis Pharma AG
Bayer Pharma AG	Novo Nordisk A/S
Esteve Pharmaceuticals	Orion Oyj
F. Hoffmann-La Roche AG	Pfizer Limited
Glaxosmithkline Research and Development Ltd	Sanofi-Aventis Recherche & Developpement
Janssen Pharmaceutica Nv	UCB Pharma SA

Laboratorios Almirall S.A.

Universities, research organizations, public bodies, non-profit groups	
Cardiff University (United Kingdom)	PharmaTrain Federation (Switzerland)
DIA Europe GmbH (Switzerland)	Semmelweis Egyetem (Hungary)
European Federation for Pharmaceutical Sciences (Sweden)	Stichting Lygature (Netherlands)
European Forum for Good Clinical Practice (Belgium)	Swissmedic (Switzerland)
European Organisation for Research and Treatment of Cancer Aisbl (Belgium)	Trinity College Dublin (Ireland)
Faculty of Medicine, University of Belgrade (Serbia)	Universidad Autonoma De Barcelona (Spain)
Faculty of Pharmaceutical Medicine of The Royal Colleges of Physicians of the United Kingdom (United Kingdom)	Universidad Pompeu Fabra (Spain)
Fondation Health Sciences E-Training (Switzerland)	Universita Cattolica Del Sacro Cuore (Italy)
Goeteborgs Universitet (Sweden)	Universitaetsklinikum Essen (Germany)
Hibernia College (Ireland)	Universitaetsklinikum Freiburg (Germany)
International Federation of Associations of Pharmaceutical Physicians (Netherlands)	Universitat Basel (Switzerland)
Karolinska University Hospital (Sweden)	Universitat De Barcelona (Spain)
King's College London (United Kingdom)	Universitat Wien (Austria)
Kobenhavns Universitet (Denmark)	Universite Louis Pasteur (France)
Medicines and Healthcare Products Regulatory Agency (United Kingdom)	Universite Lyon 1 Claude Bernard (France)
PHARMED Asbi (Belgium)	University of Newcastle Upon Tyne (United Kingdom)
PME Institute for Education in Pharmaceutical Medicine (Germany)	University of Surrey (United Kingdom)

3.30.4 Project inputs and funding

The PharmaTrain project received funding of €3.5 million from IMI, from a total project cost of €7.6 million (Table 155).

Table 155: Funding received

Contributions	Financial support, €	% total funding
EU contribution	3,510,300	46.0%
EFPIA contribution	3,489,181	45.7%
IMI contribution	632,047	8.3%
Total funding	7,631,528	100.0%

3.30.5 Assessing the socio-economic impact of PharmaTrain

Structuring the European research area

Table 156: Structuring the European research area

Outcome	Socio-economic impact
Course guidelines for shared quality standards The consortium established comprehensive standards for the content and delivery of post-graduate diploma, master and continued professional development (CPD) courses in medicines development. Curricula and syllabi were established for each qualification alongside learning outcomes and assessment requirements. Over the project lifetime, 13 universities implemented these standards, covering 10 countries. 156 Master's degrees/diploma courses were conducted, completed by 497 students. 715 trainees completed accredited CPD programmes.	**High quality medicines development education** By providing consistency in medicines development education, each participant organisation delivers post graduate courses covering the knowledge and skills required for careers in drug development. In the long term, this helps to improve the overall competitivity of the European workforce, making it an attractive place for pharmaceutical research. Drug development education also contributes to higher quality research.

Accreditation systems Systems of accreditation were devised to recognise institutions and courses meeting PharmaTrain quality standards, with standard operating procedures defining the quality assurance processes. In total, 13 universities received the 'Centre of Excellence' label, and 150 courses/modules received PharmaTrain recognition for quality.	**More structured educational landscape** The accreditation systems serve as incentives for institutions to develop courses and qualifications that meet the quality criteria developed by PharmaTrain and structure the delivery of medicines development education. This further raise quality of education and long-term availability of expertise within industry.
Memoranda of understanding Three memoranda of understanding were signed within IMI for the coordination of the development and implementation of shared standards within medicines education.	**Facilitated collaboration between partners** The memoranda of understanding allowed for efficient and open collaboration between consortium partners, strengthening ties between European institutions.
PharmaTrain Federation A self-sustaining not-for-profit organisation, the PharmaTrain Federation, was set up to continue aspects of the PharmaTrain project work, including assessment and recognition of institutions that meet quality criteria. The federation had around 50 member institutions at time of project completion.	**Sustained collaboration for continued education improvement** The network of organisations established to form the PharmaTrain federation ensures continued collaboration between European educational institutions for the purpose of raising quality and consistency of medicines development education.

3.30.6 Dissemination of information

The work of the project was presented to the scientific community through e-learning courses (Table 157).

Table 157: Dissemination of information

Outcome	Socio-economic impact
e-learning courses Online e-learning modules were developed, covering various aspects of medicines development. The modules were designed to be complementary to the PharmaTrain-approved courses, with organisations free integrate them as appropriate. All are accessible online, through a free registration process. By project completion, 610 persons had registered.	**Richer educational resource base** The e-learning library expands the base of freely-available educational resources within the field, enhancing the quality of education and training within drug development. The content is specifically tailored to allow PharmaTrain-approved course providers to develop more specialist modules, helping to increasing the quality of education delivered by these institutions.

3.30.7 Conclusions of impacts

Higher quality standards for drug development education

The PharmaTrain project developed comprehensive infrastructure for the harmonisation and improvement of medicines development education. Curricula and syllabi for post-graduate diploma, Master's and continued professional development qualifications were developed, detailing the content and assessment methods required to meet quality standards established by the consortium. An incentivising accreditation system was devised for institutions offering these courses; 13 received this by end of project completion. Freely-available e-learning materials were also developed. Overall, these outputs serve to improve the quality of drug development education available to European citizens, increasing expertise within industry and the quality of medicines research.

Ties for continued collaboration

The project involved collaboration between organisations within industry and academia. Memoranda of understanding were signed to facilitate project outcomes and a not-for-profit organisation made up of around 50 member bodies was established to sustain project outcomes. This collaboration provides further opportunities for education improvement activities and increases Europe's competitivity in the global educational landscape.

3.31 PRECISESADS: Molecular reclassification to find clinically useful biomarkers for systemic autoimmune diseases

02/2014 – 01/2019

3.31.1 Objectives of the project

Inflammatory autoimmune diseases, rheumatoid arthritis and lupus, occur when the immune system attacks body tissue, causing tissue damage. Autoimmune diseases affect 1−3% of the population. Significantly more women than men are affected, and symptoms are burdensome on patients and healthcare systems.

The PRECISESADS project was established to help expand and improve the treatments available to sufferers of autoimmune diseases, which often lack effectiveness due to poor disease classification methods. The project aimed to analyse a large cohort of patients with systemic autoimmune disease (SAD) and classify patients based on common molecular pathology. This was hoped to provide new opportunities for more targeted and personalised treatments of inflammatory diseases, as well as earlier and more accurate diagnoses.

3.31.2 Project coordinator and managing entity

Project Coordinator	UCB Biopharma SPRL
Managing entity	Marta Alarcon-Riquelme

3.31.3 Participants

Table 158: Project participants

EFPIA companies	
Bayer Aktiengesellschaft (Germany)	Sanofi-Aventis Recherche & Developpement (France)
Eli Lilly And Company Limited (United Kingdom)	UCB Biopharma SRL (Belgium)
Institut De Recherches Internationales Servier Iris (France)	
Universities, research organizations, public bodies, non-profit groups	
Agencia Estatal Consejo Superior Deinvestigaciones Cientificas (Spain)	Medizinische Universitaet Wien (Austria)
Centro Hospitalar Universitario Do Porto Epe (Portugal)	Servicio Andaluz De Salud (Spain)

Charite - Universitaetsmedizin Berlin (Germany)	Servicio Cántabro De Salud (Spain)
Consorci Institut D'Investigacions Biomediques August Pi I Sunyer (Spain)	Szegedi Tudomanyegyetem (Hungary)
Fondazione Irccs Ca' Granda - Ospedale Maggiore Policlinico (Italy)	The Cyprus Foundation For Muscular Dystrophy Research (Cyprus)
Fundacio Institut D'Investigacio Biomedica De Bellvitge (Spain)	Universidad De Granada (Spain)
Fundacion Publica Andaluza Progreso Y Salud (Spain)	Universita Degli Studi Di Milano (Italy)
Karolinska Institutet (Sweden)	Universite Catholique De Louvain (Belgium)
Katholieke Universiteit Leuven (Belgium)	Universite De Bretagne Occidentale (France)
Klinikum Der Universitaet Zu Koeln (Germany)	Universite De Geneve (Switzerland)
Medizinische Hochschule Hannover (Germany)	
Small and medium-sized enterprises (SMEs)	
Atrys Health (Spain)	Quartz Bio S.A. (Switzerland)
Third parties	
Centre Hospitalier Regional Et Universitaire De Brest (France)	

3.31.4 Project inputs and funding

The PRECISESADS project received funding of €10.0 million from IMI, from a total project cost of €23.1 million (Table 159).

Table 159: Funding received

Contributions	Financial support, €	% total funding
EU contribution	9,999,323	43.3%
EFPIA contribution	9,892,425	42.8%
IMI contribution	3,206,544	13.9%
Total funding	23,098,292	100.0%

3.31.5 Assessing the socio-economic impact of PRECISESADS

Innovation

Table 160: Project innovation

Outcome	Socio-economic impact
Novel methods and biomarkers for SAD classification Blood and urine samples from a cohort of 2500 patients with SADs, as well as patients with suspected SAD, were analysed generating individual molecular profiles. The results were used to define clusters of individuals with similar molecular pathways of disease, allowing patient classification based on molecular data, rather than clinical factors. Over 30 novel biomarkers relating to these molecular profiles were identified, with biomarker clusters defined for classification of SAD groups. The biomarkers also have the potential for use in diagnosis, prognosis and response to drug assessments in a clinical setting.	**Progress towards earlier diagnosis, tailored treatment and targeted trials** Disease classification is needed for personalised treatments for SAD conditions. A more precise classification system for autoimmune conditions, based on clinically measurable biomarkers, will ultimately allow for earlier and more precise diagnoses and the delivery of targeted treatment based on specific molecular abnormalities. Classifying SAD on molecular mechanisms can be used for patient stratification in clinical trials. The potential long-term impacts of this work are drug development for autoimmune conditions and SAD classification.
Scientific insight for animal model selection Molecular profiling of patients with SAD was accompanied by parallel profiling of commonly used preclinical animal models. Multi-omics data was generated, giving insight into the translatability of pathology results from animal testing to clinical testing of humans. This facilitates more appropriate animal model selection in future work.	**More efficient drug development** More informed selection of animal models in the development of targeted autoimmune drugs will help to increase drug discovery success rates, boosting pharmaceutical productivity and the pace of innovation in new medicines. It minimises the use of inappropriate animal models in research.

Infrastructure for further research

Table 161: Infrastructure for further research

Outcome	Socio-economic impact
Novel clinical protocols Protocols and methods relating to data quality control procedures and sample collection were developed. Guidelines and procedures were established to help researchers conduct high quality trials for inflammatory autoimmune disease.	**Higher quality clinical research** The protocols, methodologies and guidelines developed by the consortium for autoimmune disease trials provide detailed guidance to future researchers, accelerating development of targeted treatments and ensuring high quality standards across multiple clinical trial sites.
Data resources The PRECISESADS consortium established a large, unique dataset for the analysis and validation of patient stratification, combining data collected from clinical trials and a complete range of biological 'omics' data (genomic, proteomic, transcriptomic etc.). A resource containing all publicly available data for autoimmune diseases, as well as project data, was created. These data resources were made available in secure environments for future projects.	**Enhanced research capabilities within autoimmune disease** Analysis of the datasets by future researchers within the autoimmune disease field has the potential to generate valuable insight that would otherwise be unattainable. This output may therefore open new avenues for research, whilst saving cost and time by reducing the need for researchers to generate novel datasets.

Dissemination of information

The work of the project was presented to the scientific community through peer-reviewed journal articles and conference presentations (Table 162).

Table 162: Dissemination of information

Outcome	Socio-economic impact
Publications and conferences At the time of completion, project findings were reported in 42 publications, 47.6% of which were open access. 163 presentations were made at international scientific meetings.	**Dissemination to scientific community** Publications had a normalised citation impact of 1.18, which suggests that the results of the project are easily accessible within the academic community. The conference presentations further raised awareness of the project, promoting scientific collaboration in Europe.

3.31.6 Conclusions of impacts

Accelerated path towards more targeted autoimmune disease treatment

The PRECISESADS project generated novel methods and a robust set of biomarkers for the classification of autoimmune diseases. This represents significant progress towards earlier diagnoses for patients. It also provides a basis for the development of more personalised treatments, targeting specific molecular pathways associated. This work may help to reduce the burden of autoimmune disease on healthcare systems and patients.

Knowledge for more effective drug development

The project produced data and insight that can be used to accelerate and improve drug development for inflammatory autoimmune disease. New scientific insight was generated for more informed animal model selection, increasing the probability of success at the clinical trial stage. Significantly, the novel biomarkers and classification methods allow for new stratification methods in clinical trials, paving the way for the development of more targeted autoimmune drugs.

Infrastructure for enhanced future work

Research infrastructure such as dataset resources, novel clinical protocols and literature developed during the project will improve productivity and drug development in the autoimmune field.

3.32 PREDECT: New models for preclinical evaluation of drug efficacy in common solid tumours

02/2011 – 04/2016

3.32.1 Objectives of the project

Tumour biology can be modelled in the laboratory and used to test new cancer treatments. Researchers use '*in vitro*' preclinical models to perform early tests with drug candidates, selecting compounds for subsequent animal testing and clinical trial stages.

Preclinical models often do not adequately reflect the biology of human tumours. This inadequacy contributes to the high failure rate of drugs in clinical development. The PREDECT project was established to create more appropriate *in vitro* models for cancer tumours which more accurately mimic human tumour biology.

The long-term aim was to increase success rates in drug development, accelerating the development of novel cancer drugs and increasing the productivity of pharmaceutical research in Europe.

3.32.2 Project coordinator and managing entity

Project Coordinator	Institut de Recherche Servier
Managing entity	University of Helsinki

3.32.3 Participants

Table 163: Project participants

EFPIA companies	
Abbvie Inc	F. Hoffmann-La Roche AG
Astrazeneca AB	Institut De Recherches Servier
Bayer Pharma AG	Janssen Pharmaceutica Nv
Boehringer Ingelheim Internationalgmbh	Orion Oyj
Universities, research organizations, public bodies, non-profit groups	
Cardiff University (United Kingdom)	Stichting Katholieke Universiteit (Netherlands)
Ecole Polytechnique Federale De Lausanne (Switzerland)	Tartu Ulikool (Estonia)

Erasmus Universitair Medisch Centrum Rotterdam (Netherlands)	University Of Helsinki (Finland)
Robert Bosch Gesellschaft Fur Medizinische Forschung Mbh (Germany)	Weizmann Institute Of Science (Israel)
Small and medium-sized enterprises (SMEs)	
Biomedicum Genomics Ltd (Finland)	Instituto De Biologia Experimental E Tecnologica (Portugal)
Charles River Discovery Research Services	

3.32.4 Project inputs and funding

The PREDECT project received funding of €8.8 million from IMI, from a total project cost of €21.4 million (Table 164).

Table 164: Funding received

Contributions	Financial support, €	% total funding
EU contribution	8,756,641	40.9%
EFPIA contribution	9,661,201	45.1%
IMI contribution	3,004,727	14.0%
Total funding	21,422,569	100.0%

3.32.5 Assessing the socio-economic impact of PREDECT

Innovation

Table 165: Innovation

Outcome	Socio-economic impact
Improved *in vitro* modelling Novel 3D models which better capture tumour architecture were generated alongside robust protocols and SOPs detailing their characterisation and use.	**More efficient drug development within oncology** By introducing more predictive *in vitro* tumour models, PREDECT has helped to improve preclinical testing. This may lead to faster

	delivery of novel treatments and improved return on R&D investment.
Advancement of precision-cut tumour slicing technique PREDECT researchers developed a novel 'precision-cut' method of obtaining thin slices of animal tumour for drug candidate testing. Around 18-20 samples can be obtained from one tumour using the precision-cut technique, an improvement on previous techniques (one sample per tumour). The slices better capture the microenvironment of tumours compared with 2D cell cultures.	 **Higher quality research, reduction of animal use** The novel slicing technique is a novel tool for *in vitro* tumour studies, with the potential to increase R&D productivity by providing greater insight into tumour biology. The technique also reduces the number of animals required in preclinical testing.
Enhanced *in vivo* models Advances were made within *in vivo* animal modelling, with two rodent models investigated and characterised. A mouse model was developed to study breast cancer which more accurately mimics tumour biology compared with conventional models.	 **More effective drug development through lower attrition rates** More appropriate animal models will improve preclinical testing of drug candidates in breast cancer.

Infrastructure for further research

Table 166: Infrastructure for further research

Outcome	Socio-economic impact
Protocols and SOPs The consortium produced comprehensive guidance for the generation, characterisation and use of the novel complex 2D and 3D tumour models generated throughout the project, including four open access papers. Standard operating procedures for the precision-cut tumour slicing technique were also generated.	 **Guidance for efficient further research** The SOPs provide researchers with step-by-step guidance for the modelling technologies, ensuring maximum uptake and benefit.
Molecular and systems pathology infrastructure All PREDECT models were archived in tissue microarrays (TMAs), and extensive image analysis resulted in a library of 35245 images. Analysis of these images can provide further insight into the ability of PREDECT models to capture tumour complexity in humans.	 **Expanded scope of future work** The TMAs and image library can be used for new scientific insight into the PREDECT models, further expanding the scientific knowledge base within oncology and opening new opportunities for research.

Dissemination of information

The work of the project was presented to the scientific community through peer-reviewed journal articles and conference presentations (Table 167).

Table 167: Dissemination of information

Outcome	Socio-economic impact
Publications and conferences At the time of completion, project findings were reported in 43 publications, 72.1% of which were open access. 118 presentations were made at international scientific meetings.	**Publications had a normalised citation impact of 1.92,** which suggests that the results of the project are easily accessible within the academic community. The conference presentations further raised awareness of the project, promoting Europe as a place for pharmaceutical research.

3.32.6 Conclusions of impacts

Progress towards lower attrition rates in cancer drug development

The inability of conventional preclinical tumour models to accurately predict drug efficacy in humans is a major cause of drug failure at clinical trial. Continued development and implementation of the models generated by the PREDECT project, which better capture the complexity of tumours in the body, will result in more informed drug candidate selection and ultimately higher clinical trial success rates. This will boost pharmaceutical efficiency and productivity and accelerate the delivery of new treatments to cancer patients.

Better candidate drug selection for further testing

The PREDECT models allow for better prediction of which drugs will succeed in clinical trials, reducing the risk of harm to participants. In addition, implementation of the novel precision-cut tumour slicing method will result in reduced animal use in oncology research.

Infrastructure for future research

The PREDECT project generated new modelling technologies and resources for future research in tumour biology across Europe.

3.33 PreDiCT-TB: Model-based preclinical development of anti-tuberculosis drug combinations

05/2012 – 10/2017

3.33.1 Objectives of the project

Tuberculosis (TB) infects over 10 million people every year, killing 1.7 million people, and is the leading cause of death by infectious disease. It is a major global public health issue, especially in the developing world, and requires long treatment periods involving combinations of at least three drugs.

Little is known about the fundamental mechanisms of TB drugs. Reliable preclinical laboratory models of the disease are lacking, and the significance of preclinical measures (such as blood bactericidal activity) during clinical development is poorly understood. These factors result in high failure rates of candidate drugs in clinical trials and are compounded by the need to develop drugs in combination. Very few novel TB drugs have been approved since the 1970s.

The PreDiCT-TB project was established to accelerate the development of new, effective TB treatments by improving existing preclinical laboratory models of the disease. The consortium aimed to use information from clinical studies to inform *in vitro* and *in vivo* modelling and develop mathematical models to predict clinical efficacy of candidate drug combinations. It was hoped that this approach would help improve the chances of success of drug combinations at late clinical development phases.

3.33.2 Project coordinator and managing entity

Project Coordinator	GlaxoSmithKline Research and Development Ltd.
Managing entity	University of Liverpool

3.33.3 Participants

Table 168: Project participants

EFPIA companies	
Glaxosmithkline Investigacion Y Desarrollo SL	Sanofi-Aventis Recherche & Developpement
Janssen Pharmaceutica Nv	
Universities, research organizations, public bodies, non-profit groups	
Department of Health (United Kingdom)	The University Court of the University of St Andrews (United Kingdom)
Ecole Polytechnique Federale De Lausanne (Switzerland)	The University of Liverpool (United Kingdom)

Erasmus Universitair Medisch Centrum Rotterdam (Netherlands)	The University of Sussex (United Kingdom)
Institut Pasteur (France)	Universidad Carlos III De Madrid (Spain)
Liverpool School of Tropical Medicine (United Kingdom)	University College London (United Kingdom)
Max-Planck-Gesellschaft Zur Forderung Der Wissenschaften Ev (Germany)	University of Leicester (United Kingdom)
St George's Hospital Medical School (United Kingdom)	Uppsala Universitet (Sweden)
Stichting Vumc (Netherlands)	
Small and medium-sized enterprises (SMEs)	
Microsens Medtech Ltd (United Kingdom)	Zf-Screens BV (Netherlands)

3.33.4 Project inputs and funding

The PreDiCT-TB project received funding of €14.8 million from IMI, from a total project cost of €28.6 million (Table 169).

Table 169: Funding received

Contributions	Financial support, €	% total funding
EU contribution	14,778,855	51.8%
EFPIA contribution	9,296,106	32.6%
IMI contribution	4,478,125	15.7%
Total funding	28,553,086	100.0%

3.33.5 Assessing the socio-economic impact of PreDiCT-TB

Innovation

Table 170: Innovation

Outcome	Socio-economic impact
More predictive *in vitro, in vivo* and mathematical modelling Extensive work was carried out to develop new information and tools for improved preclinical modelling. A large database of preclinical data from *in vitro* and *in vivo* (animal) TB models was created, alongside a large database of 31 clinical trials. Comprehensive comparative analysis of this data provided new insights into how effectively the models predict drug efficacy in humans, and new integrated frameworks for preclinical modelling. 10 *in vitro*, 11 *in vivo and* four *in silico* (computerised) models were standardised and validated.	**Foundations for more successful clinical trials of novel TB treatments** The new insights, models, and modelling frameworks produced by the consortium gives developers of novel TB drug regimens greater ability to predict which treatments are likely to succeed at clinical trial based on results of preclinical testing. This significantly improves the efficiency and likelihood of success of subsequent drug development for TB, with less time and fewer resources wasted putting ineffective or unsuitable drug candidates through costly clinical trials. This output helps to accelerate the delivery of novel TB treatments, meeting a significant unmet clinical need.
Novel biomarkers The consortium identified and validated novel biomarkers – biological entities that can be measured as an indicator of disease presence/progression – for use in preclinical and clinical study of TB drugs. Particularly notable was the development of ribosomal RNA as a biomarker for TB, allowing for faster and more accurate measurements of TB in preclinical and clinical trials.	**Faster, more effective drug development** Biomarkers that can more accurately measure TB in *in vitro* and *in vivo* systems allow for more robust and reliable insight into drug efficacy. The RNA biomarkers developed by the project also offer faster diagnoses than traditional methods. Industry uptake of these novel biomarker technologies therefore has the potential to enhance and accelerate the development of novel TB treatments, allowing for more informed drug candidate selection.

Infrastructure for further research

Table 171: Infrastructure for further research

Outcome	Socio-economic impact
Sustainable data sharing A data management framework was established to ensure that the large databases of clinical (31 datasets) and preclinical (28 datasets) generated by the project were made available for future use in sustainable online platforms (the WHO-funded TB-PACTS for clinical data, ELIXIR platform for preclinical). Best practices for data sharing and governance within TB research were also developed and shared at a conference.	**Expanded opportunities for further research** By making key project datasets available to future researchers, the project provided a valuable resource for further analysis. The data can be used for drug development efforts, generating new scientific insight and stimulating further advancement of preclinical TB models. This further contributes to the acceleration of TB drug development.
Sharing of modelling code base Much of the code used for the development modelling and simulation tools was made publicly available within the DDMoRe online repository. Online demonstrations of alternative simulation approaches to clinical trial planning were also developed for interactive use.	**More efficient modelling activity within TB research** Ensuring availability of code and reproducibility of results allows subsequent researchers to adopt the same approaches, modifying and integrating PreDiCT-TB code as needed. This saves time and resources, accelerating TB drug research.
Systematic reviews of TB clinical trials Comprehensive systematic overviews of the efficacy of a defined set of anti-TB drugs and combinations was undertaken, involving extensive analysis of clinical trial outcomes. Several key findings were made regarding improvements to clinical trial design and obstacles to successful drug development.	**Guidance for drug developers, policy-makers and regulatory bodies** The results of the systematic reviews guide TB drug developers in the improvement of clinical trial design. It is also a valuable resource for individuals in policy and regulatory bodies, helping to increase understanding of key problems and obstacles in TB drug development.

Structuring the European research area

Table 172: Structuring the European research area

Outcome	Socio-economic impact
Contribution to regulatory discussions The project contributed to discussions of regulatory practice surrounding TB drug development. Two EFPIA partners presented at an EMA consultation on TB clinical trials on behalf of the consortium, and EMA qualification advice relating to project outcomes was in progress at time of project completion.	**More informed regulatory practice** Engagement with regulatory authorities ensured that project-related outputs were well-disseminated to relevant individuals, helping to inform regulatory policy around TB clinical trials.

Dissemination of information

The work of the project was presented to the scientific community through peer-reviewed journal articles and conference presentations (Table 173).

Table 173: Dissemination of information

Outcome	Socio-economic impact
Publications and conferences At the time of completion, project findings were reported in 95 publications, 76.8% of which were open access. 118 presentations were made at international scientific meetings.	**Dissemination to scientific community** Publications had a normalised citation impact of 1.53, which suggests that the results of the project are easily accessible within the academic community. The international scientific presentations further promoted the work of the project.

3.33.6 Conclusions of impacts

Foundations for faster development of novel TB treatment

The PreDiCT-TB project addressed critical barriers to the development of novel TB treatments. Extensive databases of clinical and preclinical data were created and comprehensively analysed using a mathematical modelling approach, producing new information on the effectiveness of *in vitro* and *in vivo* models in the prediction of drug efficacy in humans. Novel biomarkers were also developed, potentially allowing for faster and more reliable measurements of TB in in *in vitro* and *in vivo* systems. Implementation of these outputs in TB drug development will ultimately save time and resources, shorten the timeframe for the approval of critically-needed new treatments and reduce the public health burden of TB.

Resources and infrastructure for more cost-effective research

The project provided the scientific community with valuable databases and modelling code, allowing for more effective allocation of resources by future research groups. Comprehensive systematic reviews

were also carried out, the results of which can be used to increase the quality and success of TB clinical trials.

3.34 PROactive: Physical Activity as a Crucial Patient Reported Outcome in COPD

09/2009 – 05/2016

3.34.1 Objectives of the project

Chronic Obstructive Pulmonary Disease (COPD) affects 64 million people worldwide and causes 3 million deaths. Symptoms include breathlessness and chronic coughing, and patients often reduce their physical activity (PA) due to loss of lung function. Although the link between a reduction in PA and the severity of disease is well established, when the PROactive project began there were no validated tools to assess how the disease impacts a patient's experience, rather than simply the amount, of physical activity.

The PROactive project was established primarily to develop a patient reported outcome (PRO) method to capture both the amount of PA done by a patient with COPD and their experience of it. The consortium aimed to do this by developing a novel set of questions relating to patients' experience of PA, and combine answers results with results from validated wearable PA monitors.

It was hoped that this tool would be approved for use in clinical trials for novel COPD treatments, to measure the impact of drugs on daily lives of participants as well as clinical outcomes. Ultimately, the project aimed to help improve COPD treatment, with long term benefits for public health and over-burdened healthcare systems.

3.34.2 Project coordinator and managing entity

Project Coordinator	Chiesi Farmaceutici S.p.A
Managing entity	Katholieke Universiteit Leuven

3.34.3 Participants

Table 174: Project participants

EFPIA companies	
Astrazeneca AB	Laboratorios Almirall S.A.
Boehringer Ingelheim International GmbH	Novartis Pharma AG
Chiesi Farmaceutici S.A	UCB Pharma SA
Glaxosmithkline Research and Development Ltd.	
Universities, research organizations, public bodies, non-profit groups	

Academisch Ziekenhuis Groningen (Netherlands)	Royal Brompton and Harefield National Health Service Trust (United Kingdom)
European Respiratory Society (Switzerland)	The University of Edinburgh (United Kingdom)
IS GLOBAL - Barcelona Institute For Global Health (Spain)	Thorax Research Foundation (Greece)
Katholieke Universiteit Leuven (Belgium)	Universitat Zurich (Switzerland)
Small and medium-sized enterprises (SMEs)	
Choice Healthcare Solutions Ltd. (United Kingdom)	
Patient Organisations	
British Lung Foundation (United Kingdom)	Netherlands Asthma Foundation (Netherlands)

3.34.4 Project inputs and funding

The PROactive project received funding of €6.8 million from IMI, from a total project cost of €15.6 million (Table 175).

Table 175: Funding received

Contributions	Financial support, €	% total funding
EU contribution	6,767,597	43.3%
EFPIA contribution	7,230,350	46.2%
IMI contribution	1,637,875	10.5%
Total funding	15,635,822	100.0%

3.34.5 Assessing the socio-economic impact of PROactive

Innovation

Table 176: Project innovation

Outcome	Socio-economic impact
'PROactive Physical Activity in COPD' (PPAC) tools Two Patient Reported Outcome (PRO) tools were developed to capture PA data in patients with COPD in clinical trial settings. Both are 'hybrid' tools, which combine classical questionnaire responses (regarding amount and difficulty of PA) and activity monitor readouts to capture experience of PA from a patient perspective. One tool (**DPPAC)** enables daily data collection, and the other enables a 7-day data collection (**C-PPAC)**. Translations to several languages were completed for both tools. A study evaluating the tools, involving over 1000 patients, was completed, with the results informing EMA qualification opinion on the use of the tools in clinical trials.	**More informative clinical trials of COPD treatments** The PPAC tools can be implemented into clinical trials of novel COPD therapies – both pharmacological and non-pharmacological (e.g. rehabilitation) – as per the restrictions and guidance within the EMA qualification opinion. The PRO scores generated from the tools allow researchers to gain quantitative insight into the impact of drugs on factors more relevant to patients' quality of life (QoL), alongside conventional clinical endpoints – facilitating the development of treatments that more effectively address these factors. In the long term, this output will help to enhance treatment of COPD, benefitting public health and reducing cost and time resources needed to treat the disease.
Systematic reviews of existing literature Five systematic literature reviews were published, highlighting the need to develop PRO-centred tools for COPD treatment and research. The reviews also shed light on factors determining PA in COPD, the consequences of a lack of PA, the suitability of various PA monitors and possible methods to improve PA.	**Knowledge base to support COPD research and treatment** The literature reviews generated new information to guide the development of COPD treatments, establishing the importance of PA measurements. Clinically-relevant information was also generated, benefitting clinicians and patients.
Development of novel intervention A novel 'telecoaching' intervention, involving a step counter and smartphone interface, was investigated as a method to improve PA levels. Despite difficulty in delivering the intervention to certain patients, a small-scale study found a meaningful increase in step count by patients receiving the intervention.	**Foundations for more effective COPD management** Further development and validation of this telecoaching method could result in more widespread implementation, improving the way COPD is managed in clinical settings.

Infrastructure for further research

Table 177: Infrastructure for further research

Outcome	Socio-economic impact
Methodology for evaluation and use of activity monitors Project researchers established a methodology for the assessment of validated activity monitors, allowing researchers to identify which are sensitive enough to be used in clinical trial settings. Procedures for the processing, standardisation and analysis of activity monitor data were also developed for clinical trial use.	**Basis for novel clinical trial methodologies** This output enhances the research landscape within COPD, allowing for efficient incorporation of PA activity monitors in the development of novel treatments. This has the potential to speed up drug development processes, benefitting pharmaceutical companies and patients of COPD.
Memoranda of understanding A memorandum of understanding between consortium partners was signed at project completion, with the aim to allow continued development and safeguarding of project outputs. Five memoranda of understanding with entities external to IMI were also signed.	**Facilitating continued collaboration** The memoranda of understanding benefitted the research community by facilitating the continuation of efficient and open collaboration between partners. This sharing of expertise and resources allows for accelerated development of novel COPD treatment.

Structuring the European research area

Table 178: Structuring the European research area

Outcome	Socio-economic impact
European Medicines Agency (EMA) qualification opinion Qualification opinion regarding the use of PROactive tools in clinical trials was published in 2018 by the EMA. The document details the ways in which the tools can be used to measure PA activity in clinical trials of novel COPD treatment, and how these trials can be structured to include the tools effectively.	**Regulatory guidance for effective COPD trials** The EMA qualification opinion contributes to the European regulatory landscape and provides a basis for effective use of the PROactive tools within COPD trials. It therefore expands the scope of COPD research, accelerating development of novel treatments.

Dissemination of information

The work of the project was presented to the scientific community through peer-reviewed journal articles and conference presentations (Table 179).

Table 179: Dissemination of information

Outcome	Socio-economic impact
Publications and conferences At project completion, project findings were reported in 31 publications, 67.7% of which were open access. Numerous presentations were made at international scientific meetings.	**Dissemination to scientific community** Publications had a normalised citation impact of 1.92, which suggests that the results of the project are easily accessible within the academic community. The scientific presentations further promoted the work of the project and Europe as a place for healthcare research.

3.34.6 Conclusions of impacts

Tools for improved COPD treatment

The PROactive project developed two novel tools to measure the experience of PA in patients with COPD, combining questionnaire responses regarding the amount and difficulty of PA with data from validated activity monitors. The tools have the potential to provide benefits to COPD patients by improving the way PA is measured during treatment and in clinical trials, allowing for more effective management of the disease. The tools can be incorporated into clinical trials – as per the EMA qualification opinion – allowing researchers to develop more effective COPD treatments that target improvements in PA.

Expanded scientific knowledge base

In addition to research-applicable tools, the consortium provided new scientific insight into PA within COPD, alongside knowledge of the research landscape and unmet clinical needs. Comprehensive literature reviews were published which can be used by researchers and clinicians. The project also raised awareness in the medical community of the importance of monitoring and improving PA during COPD treatment.

3.35 PROTECT: Pharmacoepidemiological research on outcomes of therapeutics by a European consortium

09/2009 – 04/2015

3.35.1 Objectives of the project

Continuous analysis of the benefits and risks of a drug after its release to market (pharmacoepidemiology [PE]) and includes monitoring for unexpected adverse effects (pharmacovigilance [PV]). The PROTECT consortium, led by the European Medicines Agency (EMA), was established to address limitations in the methods used within these practices in Europe.

The project aimed to develop a set of tools and methods to enhance early detection of adverse reactions ('signal' detection) and enhance integration of benefit-risk data, validating and testing the tools in real-world situations. These objectives were devised to enhance benefit-risk management of approved medicines, providing health and safety benefits for European citizens.

3.35.2 Project coordinator and managing entity

Project Coordinator	European Medicines Agency
Managing entity	Danish Health and Medicines Authority

3.35.3 Participants

Table 180: Project participants

EFPIA companies	
Amgen	H. Lundbeck As
AstraZeneca AB	Merck Kommanditgesellschaft Auf Aktien
Bayer Pharma AG	Novartis Pharma AG
Eli Lilly and Company Limited	Novo Nordisk A/S
F. Hoffmann-La Roche AG	Pfizer Limited
Genzyme Europe B.V.	Sanofi-Aventis Recherche & Developpement
Glaxosmithkline Research and Development Ltd.	Takeda Development Centre Europe Ltd.
Universities, research organizations, public bodies, non-profit groups	

Aarhus Universitet (Denmark)	Ludwig-Maximilians-Universitaet Muenchen (Germany)
Academisch Ziekenhuis Groningen (Netherlands)	Private Universitaet Witten/Herdecke GGmbH (Germany)
Agencia Espanola De Medicamentos Y Productos Sanitarios (Spain)	Rijksuniversiteit Groningen (Netherlands)
Department of Health (United Kingdom)	Stiftelsen WHO Collaborating Centre for International Drug Monitoring (Sweden)
Fundacio' Institut Català De Farmacologia (Spain)	The European Medicines Agency (United Kingdom)
Fundación Centro Español De Investigación Farmacoepidemiológica (Spain)	Universiteit Utrecht (Netherlands)
Imperial College of Science Technology and Medicine (United Kingdom)	University of Newcastle Upon Tyne (United Kingdom)
Institut National de la Sante at de la Recherche Medicale (France)	Uniwersytet Medyczny Im Karola Marcinkowskiego W Poznaniu (Poland)
Istituto Di Ricerche Farmacologiche Mario Negri (Italy)	

Small and medium-sized enterprises (SMEs)	
L.A Sante, Epidemiologie, Evaluation Et Recherche L.A.S.E.R. (France)	Outcome Europe Sarl (Switzerland)

Patient Organisations
International Alliance of Patients' Organizations (United Kingdom)

Third parties	
Benefit France SNC (France)	Quintiles Limited (United Kingdom)
Institut Catala De La Salut (Spain)	

Non-EFPIA companies
Lægemiddelstyrelsen (Denmark)

3.35.4 Project inputs and funding

The PROTECT project received funding of €6.8 million from IMI, from a total project cost of €15.6 million (Table 181).

Table 181: Funding received

Contributions	Financial support, €	% total funding
EU contribution	6,767,597	43.3%
EFPIA contribution	7,230,350	46.2%
IMI contribution	1,637,875	10.5%
Total funding	15,635,822	100.0%

3.35.5 Assessing the socio-economic impact of PROTECT

Innovation

Table 182: Project innovation

Outcome	Socio-economic impact
Multi-country pregnancy study A feasibility study of 2,521 pregnant women was carried out across four countries to assess the extent to which women recruited without the intervention of health care professionals will provide information useful for PV through direct-to-patient data collection. Direct to patient data collection was a useful method for measuring prescription and non-prescription medication use, including medications that may be administered in hospitals, emergency room or as outpatients, or used on an as-needed basis, and in some cases these data were more complete than data from prescription registers and electronic health records. The size and diversity of the EU population was suitable for the study, and the methods used were considered scalable to other countries and languages.	 **Monitoring of pregnancy-related drug safety** Findings may encourage further research on use of new technologies for PV, as use of internet through smartphones is not currently the main communication channel. The validation and guidance developed for the use of self-reporting data collection methods increases the power and utility of evidence generated by benefit-risk monitoring, increasing knowledge of the effects of in-utero exposure to different medicines. More research into new technologies for PV may impact patient safety.

Methods and recommendations for improved signal detection (SD) The project developed new methods, and evaluated existing ones, for the detection of adverse reactions to licensed medicines (signal detection [SD]). Existing methods were improved based on data from electronic health records (EHR); SD techniques using clinical reports were evaluated. A comprehensive set of recommendations for improved SD practices was published, including guidance for future research.	 **Better post-market detection of adverse effects** The improvements made within the signal detection field provide PV professionals with methods to more accurately monitor for unexpected adverse effects of licensed medication. Implementation of these methods could therefore provide public health benefits through increased safety of clinical treatment and reduced the risk of harm to patients.
Methods for benefit-risk assessment Methods for use across all stages of benefit-risk assessment were developed and tested. These include processes for multi-source data collation, modelling techniques, and methods for graphical expression of the results for patients, healthcare providers, pharmaceutical companies and regulators. The PROTECT adverse drug reaction (PROTECT-ADR) is an online resource housing all adverse drug reaction listed in the Summary of Product Characteristics of all medicines authorised in the EU.	 **More effective benefit-risk monitoring and communication of results** More effective monitoring of the benefits and risks of licensed medicines increases drug safety and informs decision making of healthcare professionals and regulatory bodies. The improvements made to communication methods enhance these impacts, ensuring wide dissemination to stakeholders. The PROTECT-ADR saves time by reducing the number of times a signal validator needs to search for and consult a SmPC to identify whether an ADR is listed. The database neds to be continually maintained and updated to continue as an important resource-saving tool for the EMA and its stakeholders.

Infrastructure for further research

Table 183: Infrastructure for further research

Outcome	Socio-economic impact
Standards for PE studies A range of studies were carried out to develop and test methodological standards for the design, conduct and analysis of PE studies. Outputs included a review of methods to control for confounding (biasing/distortion of results) in PE studies, an evaluation of statistical methods used in multi-database studies, various protocols and guidelines and a publicly available inventory of drug consumption databases in Europe.	 **Knowledge base for improved post-market study of medicines** Project outputs provide PE researchers with new methods improve PE studies. This output may have an important impact on regulatory practice by establishing good practice in terms of planning, designing, conducting and analysing studies The inventory of drug consumption databases saves time by providing a resource to identify reliable and valid data sources.

Dissemination of information

The work of the project was presented to the scientific community through peer-reviewed journal articles and conference presentations (Table 184).

Table 184: Dissemination of information

Outcome	Socio-economic impact
Publications and conferences At the time of completion, project findings were reported in 97 publications, 38.1% of which were open access. Numerous presentations were made at international scientific meetings, and training materials were developed.	Publications had a normalised citation impact of 1.04, which suggests that the results of the project are easily accessible within the academic community. Presentations at scientific conferences and training materials further promoted the work of the project.

3.35.6 Conclusions of impacts

Enhanced benefit-risk assessment of licensed medicines

The PROTECT consortium developed and improved a wide range of methods for the of benefit-risk study of licensed medicines, with results ready to be implemented into PV and regulatory practice. Advancements were made across data collection, analysis and communication of results. Implementation of these outputs could provide long-term benefits to patients, ensuring clinical and regulatory decisions are informed by robust evidence on the relative benefits and risks of a treatment.

Methods for detection of unexpected adverse effects

The project generated new knowledge, methods and recommendations for the detection of adverse reactions caused by medicines in use in healthcare systems (signal detection). Improvements were made to signal detection methods based on data from a range of sources, and a comprehensive set of recommendations for good practice were made. More robust signal detection reduces the risk of adverse effects of marketed drugs going unnoticed and unaddressed, benefitting patients through increased drug safety. A pilot study in pregnant women suggested that PV data can be collected via self-reported methods, as an option in populations whose data healthcare providers may not have access to (for example pregnant women accessing non-prescription medication)

3.36 QuIC-ConCePT: Quantative imaging in cancer: connecting cellular process with therapy

09/2011 – 06/2018

3.36.1 Objectives of the project

Imaging biomarkers (IB) are biological features detectable in an image that are relevant to a disease state. In cancer, IBs within tumours are used for diagnosis, research and treatment. Despite this, only a small proportion of tumour pathologies can be visualised with current IBs. There is an unmet need for validated biomarkers that accurately measure aspects of tumour biology (tumour proliferation, apoptosis and necrosis).

The primary objective of the QuIC-ConCePT project was to validate IBs for use in Phase I clinical trials to measure the effects of candidate drugs on the proliferation, apoptosis and necrosis of tumours. The project aimed to introduce approaches for the development of novel IBs for tumour invasion and metastasis – pathological processes of increasing importance within oncology. It was hoped that in the long term this work would positively impact drug development.

3.36.2 Project coordinator and managing entity

Project Coordinator	European Organisation for Research and Treatment of Cancer
Managing entity	AstraZeneca AB

3.36.3 Participants

Table 185: Project participants

EFPIA companies	
Amgen	Glaxosmithkline Research and Development Ltd.
Astrazeneca AB	Merck Kommanditgesellschaft Auf Aktien
Eli Lilly And Company Limited	Pfizer Limited
F. Hoffmann-La Roche AG	Sanofi-Aventis Recherche & Developpement
Universities, research organizations, public bodies, non-profit groups	
Eidgenoessische Technische Hochschule Zuerich (Switzerland)	Stichting Maastricht Radiation Oncology Maastro Clinic (Netherlands)
Erasmus Universitair Medisch Centrum Rotterdam (Netherlands)	Stichting Vumc (Netherlands)

European Organisation for Research and Treatment of Cancer Aisbl (Belgium)	The Institute of Cancer Research: Royal Cancer Hospital (United Kingdom)
Imperial College of Science Technology and Medicine (United Kingdom)	The University of Manchester (United Kingdom)
Institut National De La Sante Et De La Recherche Medicale (France)	Universitair Ziekenhuis Antwerpen (Belgium)
King's College London (United Kingdom)	University of Cambridge (United Kingdom)
Stichting Katholieke Universiteit (Netherlands)	Westfaelische Wilhelms-Universitaet Muenster (Germany)
Small and medium-sized enterprises (SMEs)	
Keosys S.A.S. (France)	

3.36.4 Project inputs and funding

The QuIC-ConCePT project received funding of €7.0 million from IMI, from a total project cost of €16.2 million (Table 186).

Table 186: Funding received

Contributions	Financial support, €	% total funding
EU contribution	7,000,000	43.2%
EFPIA contribution	6,602,606	40.6%
IMI contribution	2,644,517	16.3%
Total funding	16,247,123	100.0%

3.36.5 Assessing the socio-economic impact of QuIC-ConCePT

Innovation

Table 187: Project innovation

Outcome	Socio-economic impact
Imaging biomarkers Four imaging biomarkers (IBs) were validated to measure cell death and necrosis, proliferation, apoptosis and metastasis in tumours of patients with liver and lung cancer. The IBs were based on PET, MRI and CT scanning techniques and were assessed for reproducibility, timing and dose response in multi-centre animal and human studies.	**Faster, safer drug development** The validated biomarkers provide researchers with an additional resource to predict the likely efficacy of cancer drugs during early development. This has the potential to reduce failure rates at clinical trial, increasing cost and time efficiency.
Radiomics approach to disease prediction The project contributed to a study involving radiomics, an image analysis technique based on scans from cancer patients. The study involved analysing CT scans and found that radiomics can be used to predict disease progression in individual patients, with potential applicability in clinical trials.	**Improved clinical trials and progress towards personalised cancer treatment** Further development of radiomics as a technique for prediction of cancer progression could result in its routine use in targeted clinical decision making, as well as its implementation in clinical trials of novel cancer treatments.

Infrastructure for further research

Table 188: Infrastructure for further research

Outcome	Socio-economic impact
Data sharing and imaging repository Sustainability plans were devised to make datasets generated by the QuIC-ConCePT project available via a data sharing policy. This includes an imaging repository containing >1200 MRI and 600 PET images from >860 tumours.	**Resources for enhanced biomarker research** The datasets and imaging repository expand opportunities for further biomarker research and reduce duplication of research efforts. This saves time and resources and accelerates further validation of biomarkers which could boost drug development within oncology.

Imaging biomarker roadmap in oncology Consortium experts contributed to an open access publication detailing a roadmap for IB development within oncology. In total, 14 key recommendations were made across a number of areas, including validation processes, cost-effectiveness, standardisation systems, and the requirement for multi-centre studies.	**More efficient biomarker development** The EU-led roadmap equipped project researchers with guidance to fulfil project objectives. It also provided clear guidance to future researchers for efficient, high quality development and validation of novel IBs. The open access nature of the article allows for wide dissemination of this knowledge.
Novel clinical protocols Three clinical protocols for lung and liver imaging techniques used in the multi-centre validation of imaging biomarkers were developed and validated. The protocols are publicly available online.	**Increased reproducibility of research** The clinical protocols facilitated consistent, standardised research during the project and helps future researchers replicate the results for further validation and implementation.

Dissemination of information

The work of the project was presented to the scientific community through peer-reviewed journal articles and conference presentations (Table 189).

Table 189: Dissemination of information

Outcome	Socio-economic impact
Publications and conferences At the time of completion, project findings were reported in 94 publications, 69.1% of which were open access. Presentations were made at scientific imaging meetings.	Publications had a normalised citation impact of 2.63, which suggests which suggests that the results of the project are easily accessible within the academic community

3.36.6 Conclusions of impacts

Use of biomarkers to monitor drug effectiveness

The QuIC-ConCePT project carried out numerous multi-centre animal and human studies resulting in the validation of novel imaging biomarkers for use in early stage cancer drug development. The biomarkers provide information on the effects of drug candidates on tumour biology, which may inform predictions of the drug candidates most likely to benefit patients. Radiomics field may contribute to future research in the personalised cancer medicines field.

Infrastructure for efficient imaging biomarker research

The project generated knowledge and infrastructure for further work, equipping European companies and institutions with resources to carry out further biomarker research. These resources include a detailed roadmap for imaging biomarkers, publicly-accessible clinical protocols, datasets and image collections available through data sharing agreements. These resources enhance the competitivity of Europe in oncology research.

3.37 RAPP-ID: Development of rapid point-of-care test platforms for infectious diseases

04/2011 – 09/2016

3.37.1 Objectives of the project

There is an unmet need for innovation in microbiology diagnostics. The aim of the RAPP-ID project was to develop technologies needed to speed up the development of diagnostic tests for patients with infectious diseases.

3.37.2 Project coordinator and managing entity

Project Coordinator	Janssen Pharmaceutica NV
Managing entity	Universiteit Antwerpen

3.37.3 Participants

Table 190: Project participants

EFPIA companies	
Glaxosmithkline Research And Development LTD	Merck Sharp & Dohme Corp, Whitehouse Station
Glaxosmithkline Vaccines SRL	Sanofi-Aventis Recherche & Developpement
Janssen Pharmaceutica Nv	
Universities, research organizations, public bodies, non-profit groups	
Cardiff University (United Kingdom)	Universite De Geneve (Switzerland)
Interuniversitair Micro-Electronica Centrum (Belgium)	Universiteit Antwerpen (Belgium)
Katholieke Universiteit Leuven (Belgium)	Universiteit Gent (Belgium)
Kungliga Tekniska Hoegskolan (Sweden)	Universiteit Twente (Netherlands)
Stockholms Universitet (Sweden)	University Of Cambridge (United Kingdom)
Small and medium-sized enterprises (SMEs)	

Lionex GMBH (Germany)

Q-Linea AB (Sweden)

Microfluidic Chipshop GMBH (Germany)

Third parties
Universitair Ziekenhuis Antwerpen (Belgium)

3.37.4 Project inputs and funding

The RAPP-ID project received funding of €7 million from IMI, from a total project cost of €16 million (Table 191).

Table 191: Funding received

Contributions	Financial support, €	% total funding
EU contribution	6,828,438	43%
EFPIA contribution	6,379,048	40%
IMI contribution	2,822,188	18%
Total funding	16,029,674	100.0%

3.37.5 Assessing the socio-economic impact of RAPP-ID

Innovation

Table 192: Project innovation

Outcome	Socio-economic impact
Development of Point-of-Care Test platforms for rapid detection of pathogens in respiratory tract infections RAPP-ID consortium aimed to develop Point-of-Care Test platforms (POCT) for rapid (hospital <2h, primary care <30min) detection of bacteria, mycobacteria, fungi and viruses, and antimicrobial resistance.	 **The project developed technologies to be applied in new diagnostic devices to facilitate the quick identification of respiratory tract infections pathogens** Reliable and quick diagnostic tests may improve clinical outcomes for patients with respiratory tract infections. This work may also encourage further research into diagnostic tests.

Development of a prototype breath sampler for influenza RAPP-ID developed a prototype breath sampler for influenza. Patients exhale into the instrument, which captures tiny particles which can be tested for the presence of pathogens.	**Ongoing research** Further research is needed before the test can be used in routine clinical practise. Uptake of the test may improve clinical outcomes for patients.
Development of a diagnostic test for VAP A prototype ventilator-associated pneumonia (VAP) test was developed which can isolate bacterial DNA from aspirates of patients with VAP.	**Ongoing research** This work may help to develop improve technology for diagnosing VAP.

Dissemination of Information

The work of the project was presented to the scientific community through peer-reviewed journal articles and conference presentations (Table 193).

Table 193: Dissemination of information

Outcome	Socio-economic impact
Publications and conference presentations At the time of its completion, the project had given rise to 41 published papers, 51% of which were open access. The consortium's work was presented in more than 20 scientific conferences and meetings.	RAPP-ID's papers had a normalised citation rate of 1.04 and ensured results were well disseminated for future use, with conference presentations further raising awareness within the scientific community.

3.37.6 Conclusion

Diagnostic tests were developed which may provide clinical benefits following further validation. The technologies developed during the project may facilitate future work in microbiology diagnostics.

3.38 SafeSciMET: European Modula Education and Training Programme in Safety Sciences for Medicines

01/2010 – 09/2016

3.38.1 Objectives of the project

Drug safety is an essential part of the drug development process ensuring that when new medicines reach patients they are safe for the patients and adverse drug reactions are kept to a minimum. However, the technologies, tools and information surrounding drug safety testing are evolving continually and it is challenging for safety scientists to be aware of all recent development s in their field. There is also a lack of training courses targeting established safety scientists. SafeSciMET provides education and training in Safety Sciences to safety scientists, or others working in drug discovery and development, who want to strengthen their professional area of expertise, including professionals at the start of their industry career.

The project aims to develop a new generation of safety specialists with strong competencies in integrative and translational medicines research and development. The programme also includes application of novel technologies in risk assessment. This will allow holistic and critical evaluations of the safety of drug candidates and new medicines by linking in vitro and in vivo data with patient data more effectively.

The objective of the project was to provide a comprehensive Modular Education and Training Program in Safety Sciences for Medicines (SafeSciMET) to fulfil the educational needs of pharmaceutical industry, regulatory authorities and academia.

3.38.2 Project coordinator and managing entity

Project Coordinator F. Hoffmann-La Roche AG

Managing entity Stichting VU

3.38.3 Participants

Table 194: Project participants

EFPIA companies	
Astrazeneca AB	Laboratorios Almirall S.A.
Bayer Pharma AG	Merck Kommanditgesellschaft Auf Aktien
Boehringer Ingelheim Internationalgmbh	Novartis Pharma AG
Eli Lilly And Company Limited	Novo Nordisk A/S
F. Hoffmann-La Roche AG	Orion Oyj

Glaxosmithkline Research And Development LTD	Sanofi-Aventis Recherche & Developpement
H. Lundbeck As	UCB Biopharma SPRL
Universities, research organizations, public bodies, non-profit groups	
Charite - Universitaetsmedizin Berlin (Germany)	Universitat Konstanz (Germany)
European Federation For Pharmaceutical Sciences, Järfälla (Sweden)	Universitat Wien (Austria)
Hospices Civils De Lyon (France)	Universite De Lorraine (France)
Karolinska Institutet (Sweden)	Universite Paris-Sud (France)
Kobenhavns Universitet (Denmark)	Universiteit Leiden (Netherlands)
Martin-Luther-Universitaet Halle-Wittenberg (Germany)	University Of Surrey (United Kingdom)
Stichting Lygature (Netherlands)	University Of Lisboa, Faculty Of Pharmacy (Faculdade De Farmácia Da Universidade De Lisboa) (Portugal)
Stichting Vu (Netherlands)	Uppsala Universitet (Sweden)
The University Of Liverpool (United Kingdom)	

3.38.4 Project inputs and funding

The SAFESCIMET project received funding of €2.4 million from IMI, from a total project cost of €6 million (Table 195).

Table 195: Funding received

Contributions	Financial support, €	% total funding
EU contribution	2,374,904	40%
EFPIA contribution	3,607,540	60%
IMI contribution	-	-
Total funding	5,982,444	100.0%

3.38.5 Assessing the socio-economic impact of SAFESCIMET

Table 196: Structuring the European research area

Outcome	Socio-economic impact
Establishment of a sustainable platform for the training of safety scientists The SafeSciMET consortium consists of 16 academic institutions for drug safety education and research and 14 industrial pharmaceutical companies working together to deliver the most up to date training available. Since 2017 the University of Konstanz is leading partner of the SafeSciMET education programme and has ensured the sustainability of the platform beyond the period of IMI funding	 **A cooperative European Advanced Master's Programme in Safety Sciences for Medicines**. Same master's level courses available and accessible for personal continuing professional development (CPD) among safety scientists. Reduced costs for drug discovery and development and accelerated innovation in the pharmaceutical industry. Reduction of adverse drug effects in the clinical research phases. Generally improved medicines safety evaluation, including in regulatory procedures

Dissemination of Information

The work of the project was presented to the scientific community through journal articles, conference presentations and training initiatives (Table 197).

Table 197: Dissemination of information

Outcome	Socio-economic impact
Publications and conference presentations At the time of completion, project findings were reported in four publications and were presented at international scientific conferences.	 Publications and conferences promoted the work of the project and ongoing research in Europe

Comprehensive Modular Education and Training Program in Safety Sciences for Medicines. Accredited Courses providing training for post-doctoral toxicology specialists in the EU. All courses use toxicology case studies provided by EFPIA partners.	**IMI's SafeSciMET project established an education and training programme for drug safety sciences in Europe.** More than 800 scientists have been trained through this new programme, improving toxicology research in the EU.

3.38.6 Conclusion

By bringing together top institutes for drug safety education as well as pharmaceutical industry leaders, IMI's SafeSciMET project established a comprehensive education and training programme in safety sciences for medicines in Europe.

Drug safety is an important part of the drug development process. Prior to the launch of IMI's SafeSciMET project in 2010, educational and training programmes in drug safety science in Europe were scarce. IMI's SafeSciMET project addressed this gap. The SafeSciMET courses are open to scientists from industry, academia and regulatory agencies, and include training on the safety, ethical, regulatory and societal aspects of drug discovery and development. About 800 students have been trained so far: about 40% of them came from the pharmaceutical industry, 35% from academia and 10% from regulatory offices, increasing knowledge of toxicology and drug development in Europe.

3.39 SAFE-T: Safer and Faster Evidence-based Translation

06/2009 – 06/2015

3.39.1 Objectives of the project

One of the key challenges in drug development is ensuring patient safety by early prediction of adverse events. The aim of the SAFE-T project was to address the lack of clinical tests to diagnose and monitor drug-induced injury of the kidney, liver and vascular system. Specific objectives of SAFE-T were to validate biomarker assays, create a database of clinical data, provide a biobank of the material collected for clinical qualification of biomarker candidates and obtain acceptance by regulatory authorities for the application of the biomarkers in clinical trials.

3.39.2 Project coordinator and managing entity

Project Coordinator	Novartis Pharma AG
Managing entity	NMI Natural and Medical Sciences Institute at the University of Tubingen

3.39.3 Participants

Table 198: Project participants

EFPIA companies	
Amgen	Glaxosmithkline Research And Development LTD
AstraZeneca AB	Laboratorios Almirall S.A.
Bayer Pharma AG	Novartis Pharma AG
Boehringer Ingelheim Internationalgmbh	Pfizer Limited
Eli Lilly And Company Limited	Sanofi-Aventis Recherche & Developpement
F. Hoffmann-La Roche AG	Takeda Development Centre Europe LTD
Universities, research organizations, public bodies, non-profit groups	
Assistance Publique Hopitaux De Paris (France)	The University Of Liverpool (United Kingdom)
Charite - Universitaetsmedizin Berlin (Germany)	Universidad De Malaga (Spain)

Consorci Institut Català De Ciències Cardiovasculars (Spain)	Universitaet Leipzig (Germany)
Naturwissenschaftliches Und Medizinisches Institut An Der Universitaet Tuebingen (Germany)	Universitaetsklinikum Aachen (Germany)
The Foundation For Medical Research Infrastructural Development And Health Services Next To The Medical Center Tel Aviv (Israel)	University College Dublin, National University Of Ireland (Ireland)
Small and medium-sized enterprises (SMEs)	
EKF Diagnostics Limited, Trinity Technology And Enterprise Centre (Ireland)	Firalis (France)
Edi Experimentelle Und Diagnostische Immunologie GMBH (Germany)	Interface Europe (Belgium)

3.39.4 Project inputs and funding

The SAFE-T project received funding of €14 million from IMI, from a total project cost of €36 million (Table 199).

Table 199: Funding received

Contributions	Financial support, €	% total funding
EU contribution	13,901,971	38%
EFPIA contribution	18,326,521	50%
IMI contribution	4,198,802	12%
Total funding	36,427,294	100.0%

3.39.5 Assessing the socio-economic impact of SAFE-T

Innovation

Table 200: Project innovation

Outcome	Socio-economic impact
Identification of biomarker candidates to assay drug-induced organ injuries during drug development SAFE-T addressed the current lack of clinical assays to monitor kidney, liver, and vascular drug-induced injury in humans by testing candidate biomarkers in human participants.	 **If successfully qualified, these safety biomarkers will facilitate drug development by predicting potential adverse effects early in drug development and minimising costs associated with high failure rates** Validation of biomarkers to monitor potential adverse events could provide the basis for new clinical risk management strategies. If successful, this work will support the safe clinical development of new medicines, provide cost savings for pharmaceutical companies.

Infrastructure for further research

Table 201: Infrastructure for further research

Outcome	Socio-economic impact
Implementation of a database for human safety biomarker profiles The TranSMART database is a summary of clinical and biomarker data collected during the SAFE-T project, including patients with a variety of conditions. TranSMART provides statistical tools for an easy cross-study data analysis.	 **All findings during the projects are collected in TranSMART** TranSMART is widely available across numerous organisations to increase research in the field.
Creation of biobank of human samples for qualification of additional safety biomarker candidates SAFE-T biobank took care of more than 30 sample shipments involving more than 60 different studies. Samples were prepared, properly labelled and stored.	 **Huge repository of biological samples of healthy volunteers and patients with different organ injury diseases** The repository contains a total of 48,447 samples from 11,454 different donors (healthy volunteers and patients with kidney, liver and vascular-related diseases) that are stored in more than 350,000 aliquots. The database can be used for future biomarker research.

Structuring the European research area

Table 202: Structuring the European research area

Outcome	Socio-economic impact
Submission of biomarker data to health authorities for regulatory approval. Following the joint scientific advice meetings that took place in April 2015 with the EMA and FDA, the consortium submitted the briefing book packages to support qualification (with limited Context of Use [CoU]) for vascular injury, and Letters of Support (LoS) for biomarkers of drug-induced kidney and liver injury, drug-induced vascular injury, renal tubular injury. Although regulatory approval has not yet been obtained, guidance and best practice papers have been developed in support of approval. **The FDA issues a Letter of Support for five new safety biological markers, opening the way for their clinical qualification in the future.**	 **Prediction of adverse events early in clinical development** If approved, the biomarker assays could be used throughout the drug development process, helping with early prediction of drug-related adverse events in clinical trials.

3.39.6 Dissemination of Information

The work of the project was presented to the scientific community through journal articles, conference presentations and publication of the scientific strategy of safety biomarkers (Table 203).

Table 203: Dissemination of information

Outcome	Socio-economic impact
Publications and conference presentations At the time of completion, project findings were reported in 20 publication, 25% of which were open access. The consortium's work was presented in more than 20 scientific conferences and meetings.	 Publications had a normalised citation rate of 1.27, which suggests that the results of the project are easily accessible within the academic community
Publication of scientific strategy for qualification of safety biomarkers SAFE-T achieved a scientific qualification plan for candidate biomarkers of drug induced organ toxicities.	 **IMI project SAFE-T has devised a simple strategy that is able to identify patients with early drug-induced liver injury before further damage has occurred.** The project created a reference guidance for generic scientific qualification strategy. The

The three organ toxicity work packages have been supported in close interaction with health authorities.	commission is waiting for the finalisation of the Letter Support to publish the guideline.

3.39.7 Conclusion

Improved tools for prediction, detection, and monitoring of drug-induced injuries to the kidney, liver and vascular system were developed during SAFE-T using patient biomarkers. This work may support the safe clinical development of new medicines. A scientific qualification plan for qualifying a candidate biomarker for drug-induced organ toxicities was also developed and the commission is waiting for the finalisation of the Letter of Support to publish the guideline.

3.40 StemBANCC: Stem cells for biological assays of novel drugs and predicitve toxicology

10/2012 – 03/2018

3.40.1 Objectives of the project

Tissue models that represent patient populations of interest are used in drug discovery research. *In vitro* disease modelling using stem cells offers the opportunity to study a range of diseases, however the use of stem cell-based models is associated with challenges such as lack of availability and poor characterisation.

The main aim of the StemBANCC project was to generate and characterise human induced pluripotent stem cell (iPSC) lines to study a range of chronic diseases and use them to test drug effectiveness and safety. The major disease groups of interest were peripheral neuropathies, neurodegenerative disorders, neurodysfunctional disorders, diabetes, and patients who had adverse responses to drugs.

3.40.2 Project coordinator and managing entity

Project Coordinator	F. HOFFMANN-LA ROCHE LTD
Managing entity	The Chancellor, Masters and Scholars of the University of Oxford

3.40.3 Participants

Table 204: Participants

EFPIA companies	
Abbvie Deutschland GMBH & Co Kg	Merck Kommanditgesellschaft Auf Aktien
AstraZeneca AB	Novo Nordisk A/S
Boehringer Ingelheim Internationalgmbh	Orion Oyj
Eli Lilly And Company Limited	Pfizer Limited, Sandwich
F. Hoffmann-La Roche AG	Sanofi-Aventis Recherche & Developpement
Janssen Pharmaceutica Nv	
Universities, research organizations, public bodies, non-profit groups	
Charite - Universitaetsmedizin Berlin (Germany)	The Hebrew University Of Jerusalem (Israel)

Helmholtz Zentrum Muenchen Deutsches Forschungszentrum Fuer Gesundheit Und Umwelt GMBH (Germany)	The University Of Birmingham (United Kingdom)
Institut National De L Environnement Et Des Risques Ineris (France)	The University Of Edinburgh (United Kingdom)
Institut National De La Sante Et De La Recherche Medicale (France)	Universitat Zu Lubeck (Germany)
King'S College London (United Kingdom)	Universite De Geneve (Switzerland)
Linkopings Universitet (Sweden)	Universite De Lausanne (Switzerland)
Medizinische Hochschule Hannover (Germany)	Universite De Technologie De Compiegne (France)
Medizinische Universitat Innsbruck (Austria)	University College London (United Kingdom)
Naturwissenschaftliches Und Medizinisches Institut An Der Universitaet Tuebingen (Germany)	University Of Newcastle Upon Tyne (United Kingdom)
Region Hovedstaden (Denmark)	University Of Cambridge (United Kingdom)
Tel Aviv University (Israel)	University Of Oxford (United Kingdom)
Small and medium-sized enterprises (SMEs)	
Concentris Research Management GmbH (Germany)	Univercell Biosolutions SAS (France)
Newcells Biotech Limited (United Kingdom)	
Third parties	
Universitatsklinikum Schleswig-Holstein (Germany)	

3.40.4 Project inputs and funding

The StemBANCC project received funding of €26 million from IMI, from a total project cost of €55 million (Table 205).

Table 205: Funding received

Contributions	Financial support, €	% total funding
EU contribution	26,000,000	47%
EFPIA contribution	20,761,386	38%
IMI contribution	8,249,094	15%
Total funding	55,010,480	100.0%

3.40.5 Assessing the socio-economic impact of StemBANCC

Infrastructure for further research

Table 206: Infrastructure for further research

Outcome	Socio-economic impact
Repository of iPSCs from a cohort of 500 patients A biobank was created of iPS cells from patients and healthy controls. Samples are linked to associated clinical data such as drug-induced adverse events.	**iPS for drug development** The repository now houses iPSCs to be used in drug development and further research across a number of disease areas.
Cell-based models for different disease One of the most important outcomes of StemBANCC was the reprogramming of stem cells lines for use by the scientific community in a range of disease areas. The cell lines can be expanded for rapid, on-demand distribution.	**Reprogrammable stem cell lines increase the number of diseases which can be modelled *in vitro*** These stem cell lines are ready to be used in research for the development of new treatments.
Developing differentiation protocols for cell lineages relevant to diseases Novel differentiation protocols have been developed and published. Differentiation protocols have been reproduced in multiple labs.	These protocols will encourage further use of stem cell models in drug development studies

Cellular phenotyping of stem cells from human subjects and identifying cellular pathophysiology or toxicology The project demonstrated that iPSC lines can recapitulate disease phenotypes and can be used in drug discovery programmes.	 **Promote and enhance drug discovery by encouraging academia and pharmaceutical companies to expand their drug studies using stem cells models in drug development programmes** Using iPSC lines in drug discovery allows researchers to model a range of disease and may minimise the use of animal models in later-stage pre-clinical testing of candidate treatments.
Establishing a single point of access database Creation of StemDB as the single point of access database. This database contains clinical data, cell line information and transcriptomic, proteomic and metabolomic data for available iPSC lines. All relevant data in StemDB was transferred to EBiSC and EBI.	 **All findings from the project including cell line information, clinical data and -omics experiments were collected in a database which is now part of the European Bank for Induced Pluripotent Stem Cells** Researchers in both academia and industry have access to scalable, cross-efficient and high-quality research tools to improve drug development research.

Dissemination of information

The work of the project was presented to the scientific community through journal articles, conference presentations and patient support group meetings (Table 207).

Table 207: Dissemination of information

Outcome	Socio-economic impact
Publications and conference presentations At the time of completion, project findings were reported in 100 published papers, 73.8% of which were open access. In addition, StemBANCC partners participated in conferences and research meetings as well as public talks and patient support groups to ensure the dissemination to the scientific community and general public.	 Publications had a normalised citation rate of 2.56, which suggests that the results of the project are easily accessible within the academic community.

3.40.6 Conclusions of impacts

The outputs of StemBANCC established resources, methods and tools to undertake disease modelling and drug discovery using human induced pluripotent stem cells

There is currently a reluctance by the pharmaceutical industry to invest in difficult-to-treat disorders. StemBANCC demonstrated that a low-risk approach to drug discovery may feasible by using iPSC lines. The work of StemBANCC has significantly contributed to establishing methods and platforms to de-risk drug discovery. Ultimately, the use of human cellular models will enable improvement in selection of compounds that are efficacious and have a reduced risk of toxicity. Although benefits of this work may take many years to materialise, the project has developed the foundations for this work to be translated into advances in drug discovery.

All cell line-related information is now available in a biobank, providing researches across academia and industry access to scalable, cross-efficient and consistent, high quality tools for new medicines development. All information from StemBANCC cell lines is available in the EBiSC database which can be accessed by researchers and provides a tool for new medicines development. In addition to research tools, protocols have been developed for generating iPSC lines to ensure continuation of their use in drug discovery research.

3.41 SUMMIT: Surrogate markers for micro- and macro- vascular hard endpoints for innovative diabetes tools

11/2009 – 10/2015

3.41.1 Objectives of the project

SUMMIT focused on the development of new biomarkers, imaging techniques and animal models that will make future pre-clinical and clinical trials more reliable and efficient, speeding up the development of new drugs for the treatment of diabetes. Diabetes is a lifelong disease that cannot be cured with currently available treatments, but only symptomatically treated. It is associated with chronic complications that impose an immense burden on patients. Novel means to prevent and treat these devastating diabetic complications are urgently needed. The aim of SUMMIT was to accelerate the development of such therapies.

Another aim of the project was to raise the profile of European researchers, enabling them to become globally recognised as leaders in the field.

3.41.2 Project coordinator and managing entity

Project Coordinator	Boehringer Ingelheim International GmbH
Managing entity	Lunds Universitet

3.41.3 Participants

Table 208: Project participants

EFPIA companies	
Astrazeneca AB	F. Hoffmann-La Roche AG
Boehringer Ingelheim Internationalgmbh	Pfizer Limited
Eli Lilly And Company Limited	Sanofi-Aventis Deutschland GMBH
Universities, research organizations, public bodies, non-profit groups	
Goeteborgs Universitet (Sweden)	Universita Cattolica Del Sacro Cuore (Italy)
Helmholtz Zentrum Muenchen Deutsches Forschungszentrum Fuer Gesundheit Und Umwelt GMBH (Germany)	Universita Degli Studi Di Firenze (Italy)
Istituto Di Ricerche Farmacologiche Mario Negri (Italy)	Universita Degli Studi Di Padova (Italy)

Itä-Suomen Yliopisto (Finland)	Universita Degli Studi Di Pavia (Italy)
Karolinska Institutet (Sweden)	Universita Di Pisa (Italy)
Lunds Universitet (Sweden)	University Of Dundee (United Kingdom)
Samfundet Folkhalsan I Svenska Finland Rf (Finland)	University Of Cambridge (United Kingdom)
Terveyden Ja Hyvinvoinnin Laitos (Finland)	University Of Oxford (United Kingdom)
The University Of Edinburgh (United Kingdom)	University Of Turku (Finland)
The University Of Exeter (United Kingdom)	
Small and medium-sized enterprises (SMEs)	
Biocomputing Platforms LTD Oy (Finland)	
Third parties	
Lunds Universitets Innovationssystem AB (Sweden)	

3.41.4 Project inputs and funding

The SUMMIT project received funding of €15 million from IMI, from a total project cost of €35 million (Table 209).

Table 209: Funding received

Financial support	Financial support, €	% total funding
EU contribution	14,654,559	42%
EFPIA contribution	15,252,050	44%
IMI contribution	4,905,472	14%
Total funding	34,812,081	100%

3.41.5 Assessing the socio-economic impact of SUMMIT

Innovation

Table 210: Project innovation

Outcome	Socio-economic impact
Novel genetic markers and soluble biomarkers to identify patients at high risk and differentiate between fast progressors and slow progressors These novel biomarkers have the potential to identify patients at high risk of diabetes complications and monitor of the complication progression and response to therapy.	**Use of markers as surrogate endpoints to shorten clinical trials by predicting progression** These markers can be used as surrogate endpoints in clinical trials. Thereby, shorten the long-lasting clinical trials to bring about earlier availability of new therapy to diabetic patients.
Novel animal models for micro and macrovascular complications to better replicate disease SUMMIT developed and characterised new diabetic mouse strains with altered insulin metabolism. Animal models exhibiting cardiovascular phenotypes were further characterised and validated for their use in related indications.	**SUMMIT covered an unmet need for animal models that could reproduce human vascular complications** These new animal models fulfil an unmet need for models that predict the development of diabetic micro and macrovascular complications. SUMMIT also reviewed more than 20 animal models and now research will benefit from a more careful selection of animal models depending on the question to answer.
Novel *in silico* methods for modelling and predicting diabetic complications An *in silico* model was developed to simulate the clinical complications in type 1 diabetes in the long term.	***In silico* models allow to test the effect of novel drugs in humans, when testing in real patients is not possible** *In silico* tools optimised to integrate accumulating omics knowledge into a clinical macro level and to test the effect of novel therapies on diabetic complications in patients were envisioned but not available.

Infrastructure for further research

Table 211: Infrastructure for further research

Outcome	Socio-economic impact
Development of a novel imaging technique for monitoring progression in atherosclerosis and retinopathy A method was developed to standardise Optical Coherence Tomography measurements in multi-centre trials and clinical practice. The method was based on the centre frequency shift of the ultrasound radio to measure plaque structure components of importance for plaque vulnerability.	 **New non-invasive technique to identify patients with atherosclerosis plaques and monitor response to interventions** This new method was validated through several clinical studies. This method is the first that measures the shift in ultrasound centre frequency to assess atherosclerosis plaque components. This method can be used to identify patients with plaque and monitor response to interventions using non-invasive techniques.

Structuring the European research area

Table 212: Structuring the European research area

Outcome	Socio-economic impact
Several spin-off companies have been created To prepare for effective commercial exploitation of the imaging technology, Mediscienta, was created and negotiate with other parties interested in imaging technologies. Two other commercial spin-offs (Biomaris, IT, and Pharmatics Ltd, UK, were created by former SUMMIT collaborators. Although not based on SUMMIT, the collaboration within SUMMIT provided training and helped to develop ideas and concepts.	 **Improving European competitiveness and wider societal benefits** The creation of spin-off companies improves European competitiveness in the pharmaceutical sector and also has wider societal benefits, such as creation of employment. Commercialisation through spin-off companies also ensures that the imaging techniques developed in SUMMIT are used effectively in further research.

Dissemination of Information

The work of the project was presented to the scientific community through peer-reviewed journal articles and conference presentations (Table 213).

Table 213: Dissemination of information

Outcome	Socio-economic impact
Publications and conference presentations At the time of completion, project findings were reported in 110 publications, 68% of which were open access.	Publications had a normalised citation rate of 1.42, which suggests that the results of the project are easily accessible within the academic community. Presentations at scientific conferences and training materials further promoted the work of the project.

3.41.6 Conclusions of impacts

Novel genetic markers and soluble biomarkers were developed to identify patients at high risk and differentiate between fast progressors and slow progressors. Using these markers as surrogate endpoints may allow clinical trials to be shortened, thereby resulting in new treatments becoming available more quickly for the patients who need them. An *in silico* model was also developed to predict diabetes complications when testing novel drugs, and animal models were reviewed to facilitate more appropriate selection.

A new non-invasive technique to monitor the response to interventions for treating atherosclerosis plaques was also developed during SUMMIT and validated through clinical trials. It is the first method that measures the shift in ultrasound center frequency to assess atherosclerosis plaque components and can be used to identify patients with plaques and monitor response to interventions using non-invasive techniques.

3.42 TRANSLOCATION: Molecular basis of the bacterial cell wall permeability

01/2013 – 06/2018

3.42.1 Objectives of the project

The TRANSLOCATION project was designed to address scientific and financial challenges associated with antibacterial drug discovery and development. TRANSLOCATION focused on bottlenecks originating during early stages of antibacterial drug discovery and on the challenge of sharing R&D data broadly to build future work.

TRANSLOCATION focused on understanding and overcoming the low permeability of the Gram-negative bacterial cell envelope, which can severely limit a drug's ability to reach its target. The objective was to increase the understanding of how small molecules (e.g. drugs) penetrate and are effluxed out of Gram-negative bacteria and to create and validate tools and assays that can be used to improve the design of new drugs to treat resistant Gram-negative infections. To facilitate data sharing, a repository of antibacterial data was created and population, as well as the framework to allow the analysis of those data to establish best practices for future antibacterial drug discovery efforts.

3.42.2 Project coordinator and managing entity

Project Coordinator	Glaxosmithkline Research And Development LTD
Managing entity	Jacobs University gGmbH

3.42.3 Participants

Table 214: Project participants

EFPIA companies	
Astrazeneca AB	Janssen Pharmaceutica Nv
Basilea Pharmaceutica International AG	Sanofi-Aventis Recherche & Developpement
Glaxosmithkline Research And Development LTD	
Universities, research organizations, public bodies, non-profit groups	
Assistance Publique Hopitaux De Paris (France)	Universitaetsklinikum Freiburg (Germany)
Centre National De La Recherche Scientifique Cnrs (France)	Universitat Basel (Switzerland)
Fraunhofer Gesellschaft Zur Foerderung Der Angewandten Forschung E.V. (Germany)	Universite D'Aix Marseille (France)

Fundacion Privada Instituto De Salud Global Barcelona (Spain)	Universite De Geneve (Switzerland)
Jacobs University Bremen Ggmbh (Germany)	University College Dublin, National University Of Ireland (Ireland)
Johann Wolfgang Goethe-Universitatfrankfurt (Germany)	Universita Degli Studi Di Cagliari (Italy)
Synchrotron Soleil Societe Civile (France)	University Of Newcastle Upon Tyne (United Kingdom)
The University Court Of The University Of St Andrews (United Kingdom)	
Small and medium-sized enterprises (SMEs)	
Gritsystems As (Denmark)	The Hyve BV (Netherlands)
Ionovation GmbH (Germany)	Yelen (France)
Nanion Technologies GMBH (Germany)	
Non-EFPIA companies	
Bruker Daltonik GMBH (Germany)	

3.42.4 Project inputs and funding

The TRANSLOCATION project received funding of €16 million from IMI, from a total project cost of €30 million (Table 215).

Table 215: Funding received

Financial support	Financial support, €	% total funding
EU contribution	15,984,203	54%
EFPIA contribution	8,135,833	27%
IMI contribution	5,634,118	19%
Total funding	29,754,154	

3.42.5 Assessing the socio-economic impact of TRANSLOCATION

Innovation

Table 216: Project innovation

Outcome	Socio-economic impact
Identification of novel bacterial uptake systems TRANSLOCATION created a new conjugate that can enter very effectively into *Pseudomonas aeruginosa*. This new system mimics the bacterium's own nutrient uptake pathways and acts as a ''Trojan Horse'', using the bacterium's own uptake to introduce the antibiotic into the bacterial cell.	 **New design for more effective drugs** The identification of this new conjugate and other interactions with the bacterial membrane could potentially be used to design more effective drugs. This information could serve as a starting point for new drug discovery efforts using these systems as an approach to improve penetration into Gram-negative bacteria.
Understanding the molecular mechanism for transit in and out of bacterial cells In collaboration with clinical teams, TRANSLOCATION identified and quantified the protein composition and distribution of bacterial membrane (*Acinetobacter baumannii* and *Pseudomonas aeruginosa*) during infection. These results provide a comparison of the proteins present (or absent) in the bacterial membrane in human infections and rodent model infections.	 **Assessment of the predictability of rodent infection models and the human clinical situation** The comparisons of proteins in human and rodent model infections can been used to assess how well rodent infection models can be applied to the human clinical situation.

Infrastructure for further research

Table 217: Infrastructure for further research

Outcome	Socio-economic impact
New tools and assays to study drug penetration into bacteria TRANSLOCATION solved new porin structures from different bacteria. Porins are structures from bacterial membrane that allow molecules to enter the bacteria. Analysing these structures allowed to develop and test a virtual tool in the form of a scoring function to predict the permeability of small molecules trough porins.	 **Prediction and prioritisation of molecules based on ability to penetrate bacteria** The tool can help to predict the ability of a molecule or drug to penetrate the bacterial membrane, saving time and money through reducing the need for bacterial models. The tool has a score function so molecules can be prioritised based on predictions of ability to permeate the bacterial membrane.

Creation and population of a database to share antibacterial R&D data A database was created to provide an infrastructure ready to host *in vitro* data of compounds with antibacterial activity.	**Creation of a comprehensive database to share antibacterial R&D data and historical know-how and data sets** This information can be used by experts to inform decision making around new antibacterial discovery projects.
New methods to study the impact of antibiotics physiochemical properties on their intracellular activity TRANSLOCATION developed concepts and methods to investigate the impact of drug influx and efflux, and the impact of antibiotic physicochemical properties on intracellular accumulation and activity. Combining spectrofluorimetry and spectrometry approaches, it is possible to quantify and visualise the intracellular accumulation in bacterial cells.	**New method to quantify antibiotic accumulation and real-time activity of antibiotics** This new method can help to quantify and correlate accumulation and real-teal time activity of antibiotics in bacterial cells. This tool can be used during for the development of new antibiotics.

Dissemination of Information

The work of the project was presented to the scientific community through peer-reviewed journal articles and conference presentations (Table 218).

Table 218: Dissemination of information

Outcome	Socio-economic impact
Publications and conference presentations At the time of completion, project findings were reported in 116 publications, 51% of which were open access. The consortium's work was presented in more than 200 scientific conferences and meetings around the world.	Publications had a normalised citation rate of 1.72, which suggests that the results of the project are easily accessible within the academic community. Presentations at scientific conferences and training materials further promoted the work of the project.

3.42.6 Conclusions of impacts

One of the key outcomes of TRANSLOCATION was the development of new techniques or assays to provide detailed information on the penetration of drugs into bacteria. These assays may be used to guide future efforts to discover Gram-negative antibiotics. The molecular basis of drug penetration into Gram-negative bacteria was also studied as part of the TRANSLOCATION project and results may assist in the selection of drug candidates based on their penetration properties. Novel bacterial nutrient uptake systems were also identified in the TRANSLOCATION project, which may allow a "Trojan Horse" approach to be taken for delivering drugs into Gram-negative bacteria.

3.43 U-BIOPRED: Unbiased biomarkers for the prediction of respiratory disease outcomes

10/2009 – 09/2015

3.43.1 Objectives of the project

Asthma is one of the most common chronic diseases. In most patients, symptoms are sufficiently controlled with currently available medicines. However, 3–5% of patients with severe asthma cannot be treated adequately with these medicine. There is an unmet medical need for new treatments for individuals with severe asthma. However, the development of new treatments is hampered by a lack of validated clinical and biological disease markers for severe asthma.

The aim of U-BIOPRED was to identify biomarker profiles comprised of various types of high-dimensional data to better categorise the distinct phenotypes for severe asthma. Ultimately, this may lead to improved prediction of therapeutic efficacy and therefore development of improved treatments for severe asthma.

3.43.2 Project coordinator and managing entity

Project Coordinator	Novartis Pharma AG
Managing entity	Academisch Medisch Centrum bij de Universiteit van Amesterdam

3.43.3 Participants

Table 219: Project participants

EFPIA companies	
Astrazeneca AB	Janssen Biologics BV
Amgen, Brussels, Belgium	Laboratorios Almirall S.A
Boehringer Ingelheim Internationalgmbh	Merck Sharp & Dohme Corp
Chiesi Farmaceutici S.P.A	Novartis Pharma AG
F. Hoffmann-La Roche AG	UCB Biopharma SPRL
Glaxosmithkline Research and Development LTD	
Universities, research organizations, public bodies, non-profit groups	
Academisch Medisch Centrum Bij De Universiteit Van Amsterdam (Netherlands)	Umeå University (Sweden)

Centre National De La Recherche Scientifique Cnrs (France)	Universita Cattolica Del Sacro Cuore (Italy)
Fraunhofer Gesellschaft Zur Foerderung Der Angewandten Forschung E.V (Germany)	Universita Degli Studi Di Catania (Italy)
Hvidovre Hospital (Denmark)	Universita Degli Studi Di Roma Tor Vergata (Italy)
Imperial College Of Science Technology And Medicine (United Kingdom)	Universitaet Bern (Switzerland)
International Primary Care Respiratory Group Lbg (United Kingdom)	Universite D'Aix Marseille (France)
Karolinska Institutet (Sweden)	Universiteit Gent (Belgium)
Kobenhavns Universitet (Denmark)	Universitetet I Bergen (Norway)
Semmelweis Egyetem (Hungary)	University Of Southampton (United Kingdom)
The University Of Manchester (United Kingdom)	Uniwersytet Jagiellonski (Poland)
The University Of Nottingham (United Kingdom)	

Small and medium-sized enterprises (SMEs)	
Aerocrine AB (Sweden)	Synairgen Research Ltd (United Kingdom)
Biosci Consulting Bvba (Belgium)	

Patient Organisations	
Asthma UK (United Kingdom)	Lega Ltaliana Anti Fumo (Italy)
European Lung Foundation (Switzerland)	Netherlands Asthma Foundation (Netherlands)
European Federation Of Asthma &Allergy Associations Ideell Forening (Belgium)	

Third parties	
AMC Medical Research BV (Netherlands)	Nottingham University Hospitals NHS Trust (United Kingdom)

Centre Hospitalier Regional De Mars Eille Assistance Publique-Hopitaux Marseille (France)

University Hospital Of South Manchester Foundation Trust (United Kingdom)

University Hospitals Southampton Nhs Foundation Trust (United Kingdom)

Non-EFPIA companies

Philips Electronics Nederland B.V. (Netherlands)

3.43.4 Project inputs and funding

The U-BIOPRED project received funding of €10 million from IMI, from a total project cost of €27 million (Table 220).

Table 220: Funding received

Financial support	Financial support, €	% total funding
EU contribution	9,935,501	37%
EFPIA contribution	14,574,652	54%
IMI contribution	2,415,549	9%
Total funding	26,925,702	

3.43.5 Assessing the socio-economic impact of U-BIOPRED

Infrastructure for further research

Table 221: Infrastructure for further research

Outcome	Socio-economic impact
Consensus and standardisation for severe asthma diagnosis U-BIOPRED consensus on the definition of severe asthma and the clinical algorithm for confirming diagnosis was published in 2011. This allowed the development of Standard Operating Procedures (SOPs) for the measurement of clinical parameters in clinical research.	 **Consensus leads to improved diagnosis and classification of patients in clinical research, facilitating the development of new treatments** Definitions and SOPs were aligned with those used in the US and subsequently became a standard for several projects. Generating consensus and global SOPs on diagnostic criteria, clinical phenotyping, and disease outcomes improves the basis for severe asthma research, ultimately facilitating the development of new treatments for more severe asthma cases.
Adult and paediatric cohorts for severe asthma Data and samples from 1,025 patients/controls (both adult and paediatric populations) were secured in the biobank and the TranSMART database.	 **Specific cohorts for severe asthma will facilitate clinical trials and, ultimately, new treatments** These cohorts of severe asthma patients will facilitate the clinical investigation of treatments for severe asthma.
Creation of high-quality biobanks SOPs were developed for ensuring the quality of biological samples and data from blood, sputum, bronchial brushes, and biopsies. The biobank was centralised and all procedures were conducted according to international recommendations.	 **Facilitation of research into new treatments for severe asthma** Biobanks may facilitate and improve the research into new treatment options for patients with severe asthma.
Experimental exacerbation Exacerbations are one of the main unresolved problems in severe asthma and are mostly primed by rhinovirus infection. During U-BIOPRED, the first good manufacturing practice stock of virus for use in viral challenge studies was developed and experimental rhinovirus infection was conducted based on strict SOPs as a model of exacerbation (mimic an asthma exacerbation in the lab).	 **Laboratory exacerbation using rhinovirus provides an important tool for future research** By mimicking asthma exacerbations using rhinovirus in laboratory conditions, researchers can identify new biomarkers and test new treatment options. This model therefore provides an important tool for further research

Pre-clinical models of severe asthma U-BIOPRED lined up the various pre-clinical models of severe asthma used in academia and pharmaceutical industry. By reviewing models and their SOPs, it was established that some of the current models do not match all aspects of severe asthma. However, improvements were made to these models, making them better tools for future research	**U-BIOPRED standardised new pre-clinical models of severe asthma** One of the main issues with was that current models did not match vital aspects of severe asthma, limiting their use in preclinical research. Improvements were made to several models in U-BIOPRED. For example, by adding influenza virus as an adjuvant a current pre-clinical mouse model was improved, providing a better tool for future research.
'Omics' platforms The main activity of U-BIOPRED was to detail the molecular profiles obtained from all biological samples collected during the project. Proteins, genes, and metabolites were studied and it was observed that those with mild-moderate asthma, healthy controls, and severe asthma expressed compounds differentially.	**Better selection of targets for severe asthma** This output has direct implications for selecting targets for phenotype-driven, novel treatments and thereby represents a core deliverable of the project, which may result in improved understanding of severe asthma profiles, potentially leading to the development of improved and more specific treatments.
Bioinformatics to discover severe asthma handprints A U-BIOPRED tool box was used to combine regular statistics and high-dimensional analysis, to connect raw data and eventual fingerprints and handprints. The TranSMART knowledge management system was used as starting point. The fingerprint and handprint analysis covered new ground in data sub-setting, feature filtering, omics-based clustering, and biomarker identification.	**Bioinformatic tools can be used for biomarker discovery for use in the clinical setting** These handprints can be used for biomarker discovery using the U-BIOPRED asthma map of mechanistic networks. This tool can be used in other studies to discover biomarkers and molecular handprints for severe asthma and contribute to further research.

Dissemination of Information

The work of the project was presented to the scientific community through peer-reviewed journal articles and conference presentations (Table 222).

Table 222: Dissemination of information

Outcome	Socio-economic impact
Publications and conference presentations At the time of completion, project findings were reported in 112 publications, 29.5% of which were open access. The consortium's work was presented in more than 80 scientific conferences and meetings around the world.	Publications had a normalised citation rate of 2.63, which suggests that the results of the project are easily accessible within the academic community. Presentations at scientific conferences and training materials further promoted the work of the project.

3.43.6 Conclusion

One of the main U-BIOPRED impacts has been better understanding and standardisation for severe asthma definitions, which leads to better classification of patients in clinical research and may improve the development of new treatments. Biobanks and bioinformatic tools (handprints) have also been developed as part of the U-BIOPRED project, which will facilitate further research into more personalised treatments for severe asthma. New tools to enhance further research have also developed, including such as new pre-clinical models and experimental exacerbation in humans.

3.44 WEB-RADR: Recognising Adverse Drug Reactions

09/2014 – 12/2017

3.44.1 Objectives of the project

There is rapid adoption of smartphones, and mobile apps for use in healthcare. WEB-RADR was conducted to develop a mobile reporting app for pharmacovigilance data and evaluate its utility both before making it available for adoption across Europe. Another aim of the project was to determine whether data collected via apps could add value to existing pharmacovigilance data collection methodologies and to develop policy recommendations.

3.44.2 Project coordinator and managing entity

Project Coordinator Novartis Pharma AG

Managing entity Medicines and Healthcare products Regulatory Agency (UK)

3.44.3 Participants

Table 223: Project participants

EFPIA companies	
Amgen	Janssen Pharmaceutica Nv
Astrazeneca AB	Novartis Pharma AG
Bayer Pharma AG	Sanofi-Aventis Recherche & Development
Glaxosmithkline Research And Development LTD	UCB Biopharma SPRL
Universities, research organizations, public bodies, non-profit groups	
Academisch Ziekenhuis Groningen (Netherlands)	Stiftelsen WHO Collaborating Centre For International Drug Monitoring (Sweden)
Agencija Za Lijekove I Medicinske Proizvode (Croatia)	The European Medicines Agency (United Kingdom)
Department of Health (United Kingdom)	The University Of Liverpool (United Kingdom)
Stichting Lareb, 'S (Netherlands)	University College London (United Kingdom)

Small and medium-sized enterprises (SMEs)	
Epidemico Limited (Ireland)	Srdc Yazilim Arastirma Ve Gelistirme Ve Danismanlik Ticaret Anonim Sirketi (Turkey)

Patient Organisations
Eurordis - European Organisation For Rare Diseases Association (France)

3.44.4 Project inputs and funding

The WEB-RADR project received funding of €2.3 million from IMI, from a total project cost of €6 million (Table 224).

Table 224: Funding received

Financial support	Financial support, €	% total funding
EU contribution	2,270,000	38.2%
EFPIA contribution	2,754,044	46.4%
IMI contribution	916,352	15.4%
Total funding	5,940,396	100.0%

3.44.5 Assessing the socio-economic impact of WEB-RADR

Infrastructure for further research

Table 225: Infrastructure for further research

Outcome	Socio-economic impact
Mobile app WEB-RADR developed and launched a mobile application, which allowed patients and healthcare professionals to reports suspected adverse events to medicines in real time. A proof of concept for electronic health record connectivity with the reporting app was also completed.	**Mobile app is a useful tool for patients and healthcare professionals to report adverse reactions** The WEB-RADR app empowered patients and healthcare professionals to report adverse reactions, and to provide users with accurate, timely and up-to-date safety information. The WEB-RADR team improved the mobile app user interface and backend systems to improve scalability and utilise more modern programming techniques. The app has been launched in some EU member states as well as non-European countries, including Burkina Faso and Zambia through collaboration with WHO.
WEB-RADR platform The WEB-RADR project's public private partnership has formed the foundation of the WEB-RADR platform; to allow WEB-RADR to provide services to the wider health network and for the technology to be sustainable.	**The platform extends the lifetime of project outcomes** By developing the WEB-RADR platform, the benefits extend beyond the lifetime of the project and provide the digital health community with clear models for interacting with regulators. WEB-RADR is positioned as the central hub of digital transactions for pharmacovigilance.

Structuring the European research area

Table 226: Structuring the European research area

Outcome	Socio-economic impact
Framework on the use of mobile devices, social media for pharmacovigilance, and ethical considerations WEB-RADR developed guidance and recommendations to be considered by the pharmaceutical industry and EU member states for the use of mobile devices and social media to capture pharmacovigilance information.	**Adoption of the regulatory framework recommendations makes the EU a leader in this area** The pragmatic nature of the recommendations made as part of WEB-RADR facilitates use of new technologies to detect safety issues,

	ultimately leading to improved patient health outcomes in the EU.

Dissemination of information

The work of the project was presented to the scientific community through workshops (Table 227).

Table 227: Dissemination of information

Outcome	Socio-economic impact
Workshops about social media Workshops were organised to discuss the use of mobile technologies and social media as new tools to generate evidence for the monitoring of medicine safety. The aim was to engage with consumers, patients, healthcare professionals, and regulatory authorities to discuss developments and to obtain input and feedback in order to maximise the utility and benefits of the project deliverables.	**Creation of a multi-disciplinary environment between different stakeholders to discuss new technologies as a tool for monitoring safety** These workshops allowed stakeholders from pharmaceutical industry and regulatory authorities to discuss the integration of new technologies for pharmacovigilance. Gathering inputs from stakeholders is the best way to improve and enhance the use of new technologies to improve pharmacovigilance.

3.44.6 Conclusions of impacts

Mobile app allows patients and healthcare professionals to report adverse reactions easily and to access to up-to-date safety information

One of the main achievements of the project has been the launch of mobile app for reporting of adverse reactions to medicines in several EU member states, as well as some non-EU countries. This app enables patients and healthcare professionals to report adverse events more easily than traditional methods and provides up-to-date safety information. The app also facilitates the recording and tracking of adverse events for the pharmaceutical industry and pharmacovigilance entities.

The WEB-RADR platform extends the project benefits beyond its lifetime, providing tools and guidance for the use of new technologies for tracking adverse reactions

The WEB-RADR public-private partnership has formed the foundation of the WEB-RADR platform. The platform includes models and recommendations for the interaction between the digital health community and regulators.

Framework on the use of mobile devices, social media for pharmacovigilance, and ethical considerations

In WEB-RADR, guidance and recommendations were developed to be considered by the pharmaceutical industry and EU member states for the use of mobile devices and social media to capture pharmacovigilance information. These recommendations will have an impact for future implementation of new technologies for pharmacovigilance within Europe.