

## Making novel drugs safer for patients

**A growing number of medicines are based on biological molecules such as proteins and monoclonal antibodies. These novel drugs have resulted in new, more effective treatments for a number of serious conditions. Yet sometimes these medicines trigger a response from the patient's immune system, which can decrease the effectiveness of the drug or cause severe side effects. The aim of the IMI-funded ABIRISK project is to shed new light on the factors behind this immune response. The project, which represents the first concerted effort to solve this problem, will aid in the creation of new, safer biopharmaceuticals and also generate tools to determine how individual patients are likely to respond to them both in clinical trials and after release to the market.**

Biopharmaceuticals are drugs that are biological in origin (i.e. are made of proteins or DNA for example) and are manufactured using biotechnology. A number of biopharmaceuticals are already in use and have dramatically improved quality of life for patients with serious, hard to treat conditions such as multiple sclerosis, Crohn's disease, diabetes, rheumatoid arthritis, haemophilia A and some cancers. However, in some patients, biopharmaceuticals can trigger an immune reaction, a phenomenon known as immunogenicity. When this happens, the immune system produces antibodies (ADAs) that neutralise the drug, which can reduce the effectiveness of the biopharmaceutical. In some patients, the immune response causes side effects such as a rash, chest pains, or a fall in blood pressure. In the most severe cases, it can trigger anaphylactic shock and even prove fatal.

### Immunogenicity – the known unknowns

Diverse factors appear to be involved in immunogenicity. On the drug side, both the compound and the route and duration of administration seem to play a role, while on the patient side, the type of disease, age, genetic background and interactions with other medicines may be risk factors.

Therefore it is extremely hard to predict which biopharmaceuticals will have immunogenicity problems; although many tests exist, these are not always accurate. Furthermore, knowing which patients are at greatest risk of mounting an immune response to a given biopharmaceutical is extremely difficult.

### Reducing the risks

Even though immunogenicity continues to pose a problem in the development of new drugs, until now there has been no major effort to solve the problem.

Enter the ABIRISK project, which aims to give biopharmaceuticals a much-needed boost and represents the first concerted effort to tackle the immunogenicity problem by bringing together leading experts from hospitals, academia, industry, and small companies. The project will set up laboratory tests to probe the immunogenicity of several biopharmaceuticals that are already used on patients. The scientists will then match their test findings with the effect the drug actually has on patients. This will help the team to develop tools that are better at predicting immunogenicity during drug development.

Many pharmaceutical companies, academic institutions and patient registries have large amounts of data on biopharmaceuticals and patients' responses to them. In ABIRISK, these diverse databases

### ABIRISK at a glance

**Full project title:**

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

**Start date:** 01/03/2012**Duration:** 5 years**Total cost:** €34.9 million**Project coordinator:**

GlaxoSmithKline

**Managing entity:** INSERM**Project website:**

[www.abirisk.eu](http://www.abirisk.eu)

will be assembled into a single immunogenicity databank that will help researchers pinpoint the factors that influence a drug's immunogenicity and patients' risk of it. This will allow the researchers to generate tools that will accurately predict whether a patient will mount an immune response to a biopharmaceutical and how that immune response will affect the efficacy and safety of the drug.

### Safer, more effective drugs for patients

Immunogenicity means many patients today are denied the life-changing benefits of biopharmaceuticals. ABIRISK will ultimately result in a new generation of biopharmaceuticals with lower immunogenicity that can be safely and effectively used by more patients. In addition, the project will allow clinicians to determine which patients will respond best to which biopharmaceutical, thereby preventing patients from suffering the side effects of a drug that does not suit them.

For Europe's pharmaceutical industry, better tests will help companies identify the safest, most effective biopharmaceuticals and weed out those that pose a high immunogenicity risk earlier in the drug development process. This will save companies both time and money. Finally, by adding to our knowledge of the mechanisms behind immunogenicity, the project will help to improve regulatory guidelines for the approval of biopharmaceuticals.

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## Project Partners

### EFPIA member companies

- GlaxoSmithKline Research & Development Limited, Brentford, UK
- Bayer Pharma AG, Berlin, Germany
- IPSEN Innovation SAS, Paris, France
- Merck KGaA, Darmstadt, Germany
- Novartis Pharma AG, Basel, Switzerland
- Novo Nordisk A/S, Bagsværd, Denmark
- Pfizer Limited, Sandwich, UK
- Sanofi-Aventis Research and Development, Paris, France
- UCB Pharma SA, Brussels, Belgium

### Universities, research organisations, public bodies, non-profit groups

- Institut National de la Santé et de la Recherche Médicale (INSERM), Paris, France
- Academisch Medisch Centrum, Amsterdam, the Netherlands
- Academisch Ziekenhuis Leiden – Leids Universitair Medisch Centrum, Leiden, the Netherlands
- Centre National de la Recherche Scientifique, Paris, France
- Commissariat à l'Énergie Atomique et aux Énergies Alternatives, Paris, France
- DRK-Blutspendedienst Baden-Württemberg – Hessen gemeinnützige GmbH, Mannheim, Germany
- Fondazione per l'Istituto di Ricerca in Biomedicina, Bellinzona, Switzerland
- Fundació Institut de Recerca de L'hospital Universitari Vall D'hebron, Barcelona, Spain
- Groupe d'Études Thérapeutiques des Affections Inflammatoires du Tube Digestif, Paris, France
- Istituto Giannina Gaslini, Genova, Italy
- Johann Wolfgang Goethe Universität, Klinikum und Fachbereich Medizin, Frankfurt, Germany
- Karolinska Institutet, Stockholm, Sweden
- Klinikum rechts der Isar der Technischen Universität München, Munich, Germany
- Medizinische Universität Innsbruck, Innsbruck, Austria

- Paul-Ehrlich-Institut, Bundesinstitut für Impfstoffe und biomedizinische Arzneimittel, Langen, Germany
- Queen Mary and Westfield, University of London, London, UK
- Rambam Medical Center, Haifa, Israel
- Region Hovedstaden, Hillerød, Denmark
- Università di Firenze, Firenze, Italy
- Universitätsklinikum Bonn, Bonn, Germany
- Universitätsklinikum Düsseldorf, Düsseldorf, Germany
- University College London, London, UK
- University Hospital Basel, Basel, Switzerland
- Univerzita Karlova v Praze, Prague, Czech Republic

### Small and medium-sized enterprises (SMEs)

- ALTA Ricerca e Sviluppo in Biotecnologie Srlu, Siena, Italy
- Biomonitor A/S, Copenhagen, Denmark

### Financing

|                            |                      |
|----------------------------|----------------------|
| IMI funding                | €18.2 million        |
| EFPIA in kind contribution | €11.2 million        |
| Other contributions        | €5.5 million         |
| <b>Total project cost</b>  | <b>€34.9 million</b> |

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## Vaccine immunosafety: the next generation

**Since their discovery, vaccines have protected millions of people worldwide from a broad range of infectious diseases, making them one of the most effective public health interventions out. New and better vaccines are still urgently needed, yet their introduction is hampered by lengthy and expensive vaccine safety testing procedures. The aim of the IMI-funded BIOVACSAFE project is to develop cutting edge tools to speed up and improve the testing and monitoring of vaccine safety, both before and after release to the market. By bringing together Europe's top industrial and academic teams for the first time, the project will ultimately usher in a new generation of safer, more effective vaccines.**

Vaccines are widely acknowledged to be one of the cheapest and most efficient ways to combat infectious diseases in both developed and developing countries. With billions of doses of vaccines administered globally every year, vaccine safety is a top priority for pharmaceutical companies, regulators and the public alike. The problem is that testing and monitoring new vaccines for safety is a slow, cumbersome, and extremely expensive process; the development of a new vaccine costs millions of euros, and less than 1 vaccine in 10 makes it through clinical testing.

As companies add new components to vaccines to make them more effective, testing them for safety becomes even more challenging. And, while severe adverse reactions to vaccines are rare, predicting who is at risk of a severe reaction is extremely difficult; this problem will be further complicated by the ageing of the population and the growing burden of chronic conditions and diseases of the immune system.

### A new approach to vaccine safety

The BIOVACSAFE project will draw on the latest life science research findings to profile, in great detail, how individuals respond to the different components of vaccines at the cellular, genetic and molecular level. This will allow the project team to develop tools that can rapidly and accurately identify warning signs that a potential vaccine may be reactogenic. The tools could be employed early on in vaccine development, before vast amounts of time and money have been spent.

Meanwhile, the team will develop new ways to identify, classify and record adverse reactions to vaccines; this should also boost researchers' ability to pick up on problems early in vaccine development. Finally, the team will probe how natural illnesses and infections, particularly diseases of the immune system, interact with vaccines. By identifying these interactions, the team hopes to find ways of preventing them occurring in the first place. Finally, the team will create databases that can be used to store information on and explore reactions to vaccines.

### Towards the next generation of vaccines

By coming up with novel ways to identify and better understand the causes of adverse reactions to vaccines at all stages of development, BIOVACSAFE will accelerate the development and introduction of a new generation of safer, more effective vaccines to combat infectious diseases, cancer and chronic diseases. As well as speeding up vaccine development, the new, more accurate tools

### BIOVACSAFE at a glance

**Full project title:**  
Biomarkers for Enhanced  
Vaccine Immunotoxicity

**Start date:** 01/03/2012

**Duration:** 5 years

**Total cost:** €30.2 million

**Project coordinator &  
managing entity:**  
University of Surrey

**EFPIA coordinator:**  
Novartis

**Project website:**  
[www.biovacsafe.eu](http://www.biovacsafe.eu)



developed by BIOVACSAFE should help to boost public confidence in vaccine safety. Furthermore, because the project includes studies of populations in both developed and developing countries, its findings should be of global relevance.

## **An injection of health for Europe's vaccine development sector**

BIOVACSAFE brings together for the first time three of Europe's leading vaccine development and manufacture companies as well as top experts from academic institutions and small and medium-sized enterprises (SMEs). By sharing their expertise as well as access to data and patient groups, all project partners will see their knowledge base and their competitiveness grow. Crucially, by pooling their expertise, the BIOVACSAFE partners have a unique opportunity to make progress in this important area.

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## **Project Partners**

### **EFPIA member companies**

- Novartis Vaccines and Diagnostics, Siena, Italy
- GlaxoSmithKline Biologicals, Rixensart, Belgium
- Sanofi Pasteur, Lyon, France

### **Universities, research organisations, public bodies, non-profit groups**

- University of Surrey, Guildford, UK
- Chalmers University of Technology, Gothenburg, Sweden
- Charité Universitätsmedizin Berlin, Berlin, Germany
- Commissariat à l'énergie atomique et aux énergies alternatives, Paris, France
- Göteborgs universitet, Gothenburg, Sweden
- Health Protection Agency, London, UK
- Imperial College London of Science, Technology and Medicine, London, UK
- Liverpool School of Tropical Medicine, Liverpool, UK
- Max-Planck-Gesellschaft zur Förderung der Wissenschaften, Berlin, Germany
- Statens Serum Institut, Copenhagen, Denmark
- Università degli Studi di Siena, Siena, Italy
- Universiteit Gent, Ghent, Belgium
- Universiteit Utrecht, Utrecht, the Netherlands

### **Small and medium-sized enterprises (SMEs)**

- CDISC European Foundation, Woluwe-Saint Lambert, Belgium
- ImmunArray, Rehovot, Israel
- Islensk Erfdagreining ehf, Reykjavik, Iceland

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## **Financing**

|                            |               |
|----------------------------|---------------|
| IMI funding                | €17.4 million |
| EFPIA in kind contribution | €7.6 million  |
| Other contributions        | €5.2 million  |

**Total project cost €30.2 million**



Innovative Medicines Initiative

# DIRECT



## Diabetes treatment gets personal

**Type 2 diabetes patients are a diverse group; in some, the disease progresses rapidly, while in others it takes a slower course. Similarly, a treatment that works well in one patient may prove less effective in another. This has led researchers to acknowledge that there are actually a number of different subtypes of type 2 diabetes. The goal of the IMI-funded DIRECT project is to identify these subtypes and determine most appropriate treatments for them. The project brings together Europe's leading researchers from academia, healthcare, and the pharmaceutical industry.**

Some 285 million people worldwide have type 2 diabetes, and that figure is set to rise to 439 million by 2030. It arises when the body cannot make enough insulin (the hormone responsible for managing blood sugar levels), or when the body fails to respond to insulin. Although type 2 diabetes is a chronic, lifelong condition, it can be managed through a combination of medicines and lifestyle changes. If left unmanaged, patients' blood sugar levels become too high, triggering damage to the cardiovascular system, kidneys, eyes, and nerve endings.

Although there are a number of risk factors for type 2 diabetes (such as obesity), it is not always clear why some people develop the condition while others do not. Furthermore, the course of the disease and the effectiveness of different medicines vary from one patient to another. In other words, there are a number of different kinds of type 2 diabetes, and that is where the DIRECT project comes in.

### Variations on a theme

The focus of the DIRECT project is patient stratification, which involves identifying different subgroups of patients. The project will develop and validate tests to predict who will get diabetes, whose condition will deteriorate rapidly after diagnosis, and who will respond well or badly to certain drugs. The tests will then allow the DIRECT project to determine which existing drugs are effective for different varieties of type 2 diabetes.

DIRECT will gather large amounts of data as well as samples from people at risk of diabetes, people with diabetes, and people undergoing diabetes treatment. This will enable the project team to identify biomarkers (biological markers such as the level of a certain molecule in the blood) associated with different subtypes of type 2 diabetes and different rates of disease progression. These biomarkers will then be tested in prospective clinical trials, paving the way for their use as new diagnostic tests as well as in the creation of personalised therapies.

### DIRECT at a glance

**Full project title:**

Diabetes research on patient stratification

**Start date:** 01/01/2012

**Duration:** 5 years

**Total cost:** €43.1 million

**Project coordinator:**

Sanofi-Aventis Deutschland GmbH

**Managing entity:**

University of Dundee

**Project website:**

[www.direct-diabetes.org](http://www.direct-diabetes.org)

### Getting the right treatments to the right patients

The tests developed by DIRECT will ultimately usher in a new era of personalised medicine for diabetes patients. In practice, this means doctors will be able to diagnose their patients more accurately and tailor treatments to suit their own particular subtype of type 2 diabetes. In this way, patients will be able to manage their condition more effectively and hopefully avoid the complications associated with diabetes. Furthermore, patients who are at risk of diabetes could be identified and monitored.

## A boost for the drug development sector

The work carried out under the DIRECT project will substantially boost industry's understanding of the underlying causes of type 2 diabetes, helping it to develop tailored treatments that can be targeted to the right patients.

## Pieces of a pharma puzzle

The work carried out in DIRECT complements the efforts of IMI's other diabetes projects. IMIDIA ('Improving beta-cell function and identification of diagnostic biomarkers for treatment monitoring in diabetes') is studying the beta cells of the pancreas, which are responsible for producing insulin, with a view to developing a cure for diabetes. Meanwhile SUMMIT ('Surrogate markers for micro- and macro-vascular hard endpoints for innovative diabetes tools') is developing tools to identify the patients at greatest risk of developing complications relating to diabetes.

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## Project Partners

### EFPIA member companies

- Sanofi-Aventis Deutschland GmbH, Frankfurt am Main, Germany
- Eli Lilly and Company Ltd, Hampshire, UK
- Institut de Recherches Internationales Servier, Suresnes, France
- Novo Nordisk A/S, Bagsværd, Denmark

### Universities, research organisations, public bodies, non-profit groups

- University of Dundee, Dundee, UK
- Centre Hospitalier Regional et Universitaire de Lille, Lille, France
- Centre National de la Recherche Scientifique. Paris, France
- Consiglio Nazionale delle Ricerche, Rome, Italy
- Consorci Institut d'Investigacions Biomediques August Pi i Sunyer, Barcelona, Spain
- Eberhard Karls Universität Tübingen, Tübingen, Germany
- Helmholtz Zentrum München – Deutsches Forschungszentrum für Gesundheit und Umwelt GmbH, Neuherberg, Germany
- Imperial College of Science, Technology and Medicine, London, UK
- Kungliga Tekniska Högskolan, Stockholm, Sweden
- Leiden University Medical Center, Leiden, the Netherlands
- Lunds Universitet, Lund, Sweden
- Technical University of Denmark, Kgs. Lyngby, Denmark
- Universität Ulm, Ulm/Donau, Germany
- Université de Genève, Geneva, Switzerland
- University of Bath, Bath, UK
- University of Copenhagen, Copenhagen, Denmark
- University of Eastern Finland, Kuopio, Finland
- University of Exeter, Exeter, UK
- University of Newcastle upon Tyne, Newcastle upon Tyne, UK
- University of Oxford, Oxford, UK

- Vereniging voor christelijk hoger onderwijs, wetenschappelijk onderzoek en patiëntenzorg, Amsterdam, Netherlands

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## Financing

|                            |               |
|----------------------------|---------------|
| IMI funding                | €21.4 million |
| EFPIA in kind contribution | €16.5 million |
| Other contributions        | €5.2 million  |

**Total project cost €43.1 million**

## Towards new treatments for autism

**Around 1% of children are diagnosed with autism spectrum disorders (ASD), yet there are currently no drugs designed specifically to treat their main symptoms. Working to change this is the IMI-funded EU-AIMS project. The goal of EU-AIMS is to generate tools that will enhance our understanding of ASD, and ultimately pave the way for the development of new, safe and effective treatments for use in both children and adults. As well as dramatically improving quality of life, good treatments would help to cut the social and economic costs of ASD.**

ASD refers to a diverse group of development disorders that are characterised by difficulties in social interaction and communication, and the presence of unusual repetitive behaviours. It affects one child in 110, with boys at greater risk of developing ASD than girls. ASD is a lifelong condition, and for reasons which are not fully understood, the prevalence of ASD is rising.

The precise symptoms and their severity vary widely from one person to another; some are only mildly afflicted and can lead relatively independent lives, while others are severely disabled and require a lot of specialist care. Furthermore, while some individuals are intellectually impaired, others excel in areas like maths and music. Finally, to add to the complication, many people with ASD suffer from other conditions, such as seizures. This diversity of symptoms means that diagnosing ASD is far from easy, and in fact it was only formally recognised as a condition relatively recently.

### **An urgent need for effective treatments**

Today, there are no drugs designed specifically to treat ASD; instead, those affected are treated with medicines designed for other conditions. The good news is that recent research has shed new light on the neurobiology behind ASD and identified some genes that increase the risk of autism. The findings suggest that it may actually be possible to treat ASD, something that was once thought to be impossible.

### **EU-AIMS – aiming high**

EU-AIMS represents the first time that major pharmaceutical companies are joining forces, along with experts from academia, regulatory authorities and patient groups, to accelerate the development of innovative drugs to treat this complex disorder. In terms of both budget and scope, it is the largest initiative of its kind in the world.

EU-AIMS will generate new tools to study the biology behind ASD and test the efficacy of potential treatments. For example, the team will gather samples from people bearing certain mutations associated with ASD; this will pave the way for the generation of cell lines that can be used to test treatments. Elsewhere, the researchers will advance the use of brain scans as a tool to boost ASD drug discovery and also identify which people with ASD might respond best to a given drug.

The project will also create a pan-European network of clinical sites. As well as making it easier to run clinical trials, this network will create an interactive platform for those with ASD and professionals. Ultimately, the project aims to come up with methods and tools to develop effective treatments for ASD (in both children and adults) as well as tools to diagnose ASD and assess symptoms in the clinic.

### **EU-AIMS at a glance**

**Full project title:**

European Autism Interventions - a Multicentre Study for Developing New Medications

**Start date:** 01/04/2012**Duration:** 5 years**Total cost:** €35.9 million**Project coordinator:**

F. Hoffmann-la Roche

**Managing entity:**

King's College London

**Project website:**

[www.eu-aims.eu](http://www.eu-aims.eu)

## Relief for patients

Despite the lack of effective, dedicated ASD treatments, almost three quarters of children with ASD are on medication developed to tackle symptoms like tics, seizures, and hyperactivity. However, there is little evidence to suggest that the benefits outweigh the unpleasant side-effects of these drugs. Furthermore, little is known about what treatments are effective in adults. By paving the way for the development of new treatments, EU-AIMS is set to dramatically improve the quality of life of the growing numbers of people with ASD. In addition, EU-AIMS will help to cut the heavy economic and social costs of autism.

## Turning Europe into a hotspot for autism research

EU-AIMS brings together Europe's top ASD researchers from academia, the pharmaceutical industry, and patients' organisations. The partners have expertise in disciplines such as cell biology, behaviour, drug discovery, patient advocacy, clinical trials, genetics, psychiatry, brain imaging, and more.

By linking up these experts and creating a pan-European network for both people with ASD and professionals, EU-AIMS will place Europe firmly on the ASD research map and give Europe's pharmaceutical sector a competitive edge when it comes to getting novel ASD drugs to the market and the patient.

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## Project Partners

### EFPIA member companies

- F. Hoffmann-la Roche AG, Basel, Switzerland
- Eli Lilly and Company Ltd, Basingstoke, UK
- Institut de Recherches Servier, Suresnes, France
- Janssen Pharmaceutica NV, Beerse, Belgium
- Pfizer Ltd, Sandwich, UK
- Vifor SA, Villars-sur-Glâne, Switzerland

### Universities, research organisations, public bodies, non-profit groups

- King's College London, London, UK
- Birkbeck College, London, UK
- Central Institute of Mental Health, Mannheim, Germany
- Commissariat a l'Energie Atomique et aux Energies Alternatives, Paris, France
- European Molecular Biology Laboratory, Heidelberg, Germany
- Institute of Education, London, UK
- Institut Pasteur, Paris, France
- Karolinska Institutet, Stockholm, Sweden
- Max-Planck-Gesellschaft zur Förderung der Wissenschaften eV, Munich, Germany
- Stichting Katholieke Universiteit / Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands
- Universita Campus Bio Medico di Roma, Rome, Italy
- Universitair Medisch Centrum Utrecht, Utrecht, the Netherlands
- Universität Basel, Basel, Switzerland
- Universität Ulm, Ulm, Germany
- University of Cambridge, Cambridge, UK

### Patients' organisations

- Autism Speaks, Princeton, US

### Small and medium-sized enterprises (SMEs)

- GABO: millarium, Munich, Germany
- Islensk Erfdagreining ehf, Reykjavik, Iceland
- NeuroSearch A/S, Ballerup, Denmark

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## Financing

|                            |               |
|----------------------------|---------------|
| IMI funding                | €19.5 million |
| EFPIA in kind contribution | €7.9 million  |
| EFPIA US contribution      | €1.7 million  |
| Other contributions        | €6.8 million  |

**Total project cost €35.9 million**





Innovative Medicines Initiative

# EUPATI



## Turning patients into partners in therapeutic innovation

**Medicines research and development (R&D) is an increasingly complex process that remains a mystery for the majority of patients and the general public. Lifting the lid on the medical R&D process is the IMI-funded EUPATI project. EUPATI is a patient-led initiative that aims to develop the first European Patients' Academy on Therapeutic Innovation, with training courses, educational material, and an online public library that will empower patients to engage more effectively in the development and approval of new treatments and become true partners in pharmaceutical R&D.**

While patients are keen to have access to better and safer treatments, many find it hard to understand the benefits and risks of novel therapies. With demand for healthcare rising, and a growing emphasis on both the quality and sustainability of healthcare services, it is critical to address this major gap in public perception and knowledge.

There is therefore a proven need for information resources, designed specifically for patients and the public, on how medicines R&D and clinical trials are conducted. This should cover diverse aspects of pharmaceutical research and innovation, including translational research and personalised and predictive medicine, as well as the ways in which patients can support the research process and contribute to therapeutic breakthroughs. Well-informed patients are not only better placed to understand and make decisions about their treatments, but can also help to put patients' needs at the heart of drug development, for example by joining scientific, ethical and regulatory committees and getting involved in clinical trial design.

### Power to the patients

The Patients' Academy will produce comprehensive, scientifically reliable and user-friendly information for patients on the processes of medicines development. It will increase the capacity and ability of well-informed patients and patients' organisations to be effective advocates and advisors in medicines research.

The patient-led consortium, which includes patients' organisations, academic groups, non-governmental organisations (NGOs) and pharmaceutical companies, will generate educational resources in six key areas, namely the medicines development process; personalised medicine; drug safety and risk/benefit assessments; health economics and health technology assessment; clinical trials; and patients' roles and responsibilities in medicines development. Material will be developed in English, French, German, Italian, Polish, Russian, and Spanish.

Objectivity, transparency and independence are essential if EUPATI is to achieve its goals. The project's robust governance structure includes a multidisciplinary Project Advisory Board, a Regulatory Advisory Panel, and an Ethics Panel comprising renowned experts in bioethics, law, genetics, drug development, and patient advocacy, as well as representatives from regulatory authorities.

The project addresses three audiences. The 'Expert Level' will deliver a EUPATI Certificate Training Programme for patient experts, patient ambassadors and patient journalists. The accredited qualification will ensure that patients have the expertise and capacity to collaborate with all stakeholders involved in medicines R&D, wherever a strong patient voice is needed.

### EUPATI at a glance

**Full project title:**  
European Patients' Academy on Therapeutic Innovation

**Start date:** 01/02/2012

**Duration:** 5 years

**Total cost:** €10.1 million

**Project coordinator and managing entity:**  
European Patients' Forum (EPF)

**Project website:**  
[www.patientsacademy.eu](http://www.patientsacademy.eu)



Advocacy leaders from patients' organisations will be encouraged to access the 'Education Level' material in the EUPATI Toolbox. This will include a diverse range of cutting-edge resources such as e-learning courses, webinars, videos, slide shows for presentations, print material and face-to-face meetings.

Finally, all patients and the wider public will gain access to the EUPATI Internet Library, which will guide patients, including those with relatively low health literacy, through the complexities of the pharmaceutical R&D process.

### **Patients: industry's partners in drug development**

Involving patients in research can hugely benefit the drug development process; patients bring their own priorities and perspectives to the table and can offer fresh insights and challenge long-held beliefs, often resulting in entirely novel ideas and leading to better treatments for patients. Furthermore, greater patient involvement in R&D will boost the efficacy and safety of new treatments and raise public support for medical research.

### **Inducing a paradigm shift in patient involvement in medicines R&D**

The Patients' Academy is set to trigger a major rethink in the way patients and the public view the medicines development process and their own involvement in it. Armed with a deeper understanding of how the pharmaceutical sector works, patient experts and advocates will be empowered to work effectively with the relevant authorities, agencies, clinicians and industry to influence the drug development process for the benefit of patients.

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## **Project Partners**

### **Patients' organisations**

- European Patients' Forum (EPF), Luxembourg
- European AIDS Treatment Group (EATG), Düsseldorf, Germany
- European Genetic Alliances Network (EGAN), Brussels, Belgium
- European Organisation for Rare Diseases (EURORDIS), Paris, France

### **EFPIA member companies**

- Amgen Belgium SA/NV, Brussels, Belgium
- AstraZeneca AB, Södertälje, Sweden
- Bayer Pharma AG, Berlin, Germany
- Boehringer Ingelheim International GmbH, Ingelheim, Germany
- Chiesi Farmaceutici SpA, Parma, Italy
- Eli Lilly and Company Ltd, Basingstoke, UK
- F. Hoffmann-La Roche Ltd, Basel, Switzerland
- Farmaindustria, Madrid, Spain
- GlaxoSmithKline R&D Ltd, Middlesex, UK
- Janssen Pharmaceutica NV, Beerse, Belgium
- Laboratorios del Dr Esteve, SA, Barcelona, Spain
- Merck KGaA, Darmstadt, Germany
- Novartis Pharma AG, Basel, Switzerland
- Novo Nordisk A/S, Bagsvaerd, Denmark
- Sanofi Aventis R&D, Chilly-Mazarin, France
- UCB Pharma SA, Brussels, Belgium
- Verband forschender Arzneimittelhersteller eV, Berlin, Germany

### **Universities, research organisations, public bodies, non-profit groups**

- Biopeople / Copenhagen University, Denmark
- DIA Europe GmbH, Basel, Switzerland
- European Forum for Good Clinical Practice, Brussels, Belgium

- European Organisation for Research and Treatment of Cancer, Brussels, Belgium
- Hibernia College, Dublin, Ireland
- International Society for Pharmacoeconomics and Outcomes Research Inc., New Jersey, US
- Irish Platform for Patients' Organisations, Science and Industry, Rathmines, Ireland
- Nowgen / University of Manchester, Manchester, UK

### **Financing**

|                            |              |
|----------------------------|--------------|
| IMI funding                | €5.3 million |
| EFPIA in kind contribution | €4.8 million |

**Total project cost**                      **€10.1 million**

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## Drugs that are kinder to the liver

**Many medicines are harmful to the liver, and drug-induced liver injury (DILI) now ranks as the leading cause of liver failure and transplantation in western countries. However, predicting which drugs will prove toxic to the liver is extremely difficult, and often problems are not detected until a drug is already on the market. For the first time, the IMI project MIP-DILI brings together Europe's top industrial and academic experts in the field. Together, they will develop new tests that will help researchers detect potential liver toxicity issues much earlier in development, saving many patients from the trauma of liver failure.**

Clinicians and drug manufacturers recognise two kinds of DILI. Dose-dependent DILI is usually detected early on in drug development and, as the name suggests, the risk of an adverse reaction increases with the dosage. However, most DILIs are so-called idiosyncratic reactions. These cannot be predicted in experimental systems, occur only in certain patients, and are not dose dependent. Very often, idiosyncratic DILI problems are only picked up very late in drug development or even after regulatory approval. Over 1 000 approved drugs have been associated with idiosyncratic DILI; in most cases, around 1 in 10 000 patients are affected, although for some drugs the incidence of DILI is higher, at around 1 patient in 100. Estimates suggest that one in seven cases of liver failure are triggered by an adverse drug reaction, and DILI is now the leading cause of liver transplantation in many countries.

### A new look at liver toxicity

The goal of MIP-DILI is to dramatically improve the tools used to test for liver toxicity during drug development. The team aims to deepen our understanding of the science behind drug-induced liver injury, and use that knowledge to overcome the many drawbacks of the tests currently used.

A major focus will be on a systematic and evidence-based evaluation of both currently available and new laboratory test systems, including cultures of liver cells in one-dimensional and three dimensional configurations. The more complex models integrate different types of liver cells to form three-dimensional units that accurately mimic human liver physiology. The project will also develop models that take into account the natural differences between patients. This is important because factors such as certain genes, the liver's immune response, and viral infections have all been associated with an increased risk of DILI.

The project will seek to address the current lack of human liver cells available to researchers by using induced pluripotent stem cells (iPSCs, i.e. cells that have been altered so that they can turn into any kind of cell found in the body) generated from patients who are particularly sensitive to DILI.

Another strand of the project will develop computer models to unravel the complex, often inter-related mechanisms behind DILI. Finally, the team will assess how accurate the results of laboratory tests are at predicting actual outcomes in patients.

### MIP-DILI at a glance

**Full project title:**

Mechanism-Based  
Integrated Systems for the  
Prediction of Drug-Induced  
Liver Injury

**Start date:** 01/02/2012**Duration:** 5 years**Total cost:** €32.4 million**Project coordinator:**

AstraZeneca

**Managing entity:**

University of Liverpool

**Project website:**

[www.mip-dili.eu](http://www.mip-dili.eu)

## A leap forward for liver safety

Until now, the quest to develop better tests for DILI risk in potential drugs has been hampered by a lack of collaboration between industry and academia. By bringing together experts from these sectors in a single, coordinated effort, MIP-DILI promises to both advance our understanding of drug-induced liver injury and deliver tests to detect it early on in drug development.

Academic partners in the project will benefit from access to reference compounds, with known liver toxicity, that are held by pharmaceutical companies. For their part, pharmaceutical companies will gain a greater understanding of the complex science behind DILI.

The stakes are high; all too often, DILI and other toxicity problems are only identified extremely late in drug development, when vast amounts of time and money have been spent on a potential drug. According to a report from the Society for Medicines Research, just a 10% improvement in predicting failure before the start of clinical trials could cut the costs of drug development by upwards of €75 million.

## Safer treatments for patients

Although DILI is rare, when it happens, it is often extremely serious or even fatal for the patient concerned. Yet too many drugs that pose a risk of DILI still make it to the market, and DILI is a common reason for withdrawing drugs from the market. By helping researchers to detect DILI problems during drug research, before drugs are evaluated in clinical trials and approved for use, MIP-DILI will prevent considerable pain and suffering on the part of patients.

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## Project Partners

### EFPIA member companies

- AstraZeneca AB, Södertälje, Sweden
- Abbott GmbH & CoKG, Wiesbaden-Delkenheim, Germany
- Bristol Myers Squibb EMEA sarl, New York, US
- GlaxoSmithKline Research and Development Ltd, Middlesex, UK
- H. Lundbeck A/S, Valby, Denmark
- Institut de Recherches Internationales Servier, Suresnes, France
- Janssen Pharmaceutica NV, Beerse, Belgium
- Merck KGaA, Darmstadt, Germany
- Orion Corporation, Espoo, Finland
- Sanofi-Aventis Research and Development, Chilly-Mazarin, France
- UCB Pharma SA, Brussels, Belgium

### Universities, research organisations, public bodies, non-profit groups

- University of Liverpool, Liverpool, UK
- Albert-Ludwigs-University Freiburg, Freiburg, Germany
- Deutsches Krebsforschungszentrum, Heidelberg, Germany
- Karolinska Institutet, Stockholm, Sweden
- Universitätsklinikum Bonn, Bonn, Germany
- Université de Rennes 1, Rennes, France
- Universiteit Leiden, Leiden, the Netherlands
- Universiteit Utrecht, Utrecht, the Netherlands
- Vereniging voor christelijk hoger onderwijs, wetenschappelijk onderzoek en patiëntenzorg, Amsterdam, the Netherlands

### Small and medium-sized enterprises (SMEs)

- Cellartis AB, Gothenburg, Sweden
- CXR Biosciences Ltd., Dundee, UK
- Interface Europe, Brussels, Belgium
- KaLy-Cell, Illkirch, France
- Lhasa Ltd., Leeds, UK
- Solvo Biotechnology ZRT, Szeged, Hungary

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## Financing

|                            |               |
|----------------------------|---------------|
| IMI funding                | €15.3 million |
| EFPIA in kind contribution | €11.0 million |
| EFPIA US contribution      | €1.6 million  |
| Other contributions        | €4.5 million  |

**Total project cost €32.4 million**

## Hunting for a winning combination to tackle TB

**Tuberculosis (TB) infects over 9 million people worldwide every year and kills 1.7 million. Treatment takes several months, and many patients struggle to take their antibiotics properly, fuelling the rise of drug-resistant strains of the disease. However, putting together a new, shorter treatment regimen could take a quarter of a century using today's methods. The IMI-funded PreDiCT-TB project aims to speed up the search for new, more effective combinations of treatments to tackle the deadly disease. PreDiCT-TB is one of the world's only initiatives focused on tackling pre-clinical research barriers to the discovery and development of new TB drug combinations.**

TB is an airborne, infectious disease caused by the bacterium *Mycobacterium tuberculosis*. It usually affects the lungs, and symptoms include coughing, weight loss, night sweats, fever, and fatigue. Although it is both preventable and curable, it remains a leading cause of disease and death by infection, particularly in developing countries. TB treatment is tough; patients must take four antibiotics for at least six months. The length and complexity of this regimen mean that many patients do not take their treatment properly, or stop taking the drugs before the bacteria have been completely eradicated from the body. Thus poor compliance may well be driving a rise in multidrug-resistant (MDR) strains of TB that simply do not respond to the main first-line antibiotics. If the treatment regimen for standard TB is tough, the regimen for MDR TB is even tougher, taking upwards of two years and involving drugs that often cause severe side effects such as liver, skin and hearing problems. In addition, recent years have seen growing reports of extensively drug resistant (XDR) TB, which does not respond to a number of the core first and second line antibiotics.

There is therefore an urgent need to develop a more potent, yet patient-friendly, combination of drugs to tackle TB. However, very few new TB drugs have been developed in recent decades. Furthermore, to prevent TB from developing resistance, it must be treated with a combination of multiple drugs. Until now, new drug candidates were developed and added to the existing regimen one by one. As it takes at least six years to change one drug in the regimen by either substitution or addition, approving a new four-drug regimen through successive trials would take a quarter of a century.

Shortening this period is a top priority for the fight against TB, but current clinical trial methodologies make it very difficult to evaluate the optimal doses and combinations of drugs.

### PreDiCTing the best treatment regimens

We need a way to facilitate the complex decisions around which doses and combinations of new drugs should enter clinical trials, and that's where the PreDiCT-TB project will focus its combined resources.

PreDiCT-TB aims to develop an integrated set of laboratory-based models that will provide much-needed data to indicate the most appropriate doses and combinations of drugs for patients. In addition, the project will generate a comprehensive database of patient data from previous and on-going clinical trials for use as a reference for evaluating the performance of combination anti-TB drug regimens in these newly developed laboratory models.

Ultimately, they aim to enable researchers to be able to use the information generated by the novel models to design better clinical trials involving TB patients.

### PreDiCT-TB at a glance

**Full project title:**

Model-based preclinical development of anti-tuberculosis drug combinations

**Start date:** 01/05/2012**Duration:** 5 years**Total cost:** €28.6 million**Project coordinator:**

GlaxoSmithKline

**Managing entity:**

University of Liverpool

Therefore PreDiCT-TB brings together internationally-respected TB scientists and physicians with expertise in the biology, immunology and imaging of the disease, as well as those specialising in the behaviour of drugs in the body (pharmacokinetics), their interactions with one another (pharmacodynamics), and clinical trials.

### **A boost for TB patients**

Today's long, complex TB treatment regimen is simply not patient-friendly enough and potentially raises the risk of patients developing (and passing on to others) drug-resistant forms of the disease. By speeding up the development of better and shorter treatment regimens, PreDiCT-TB should dramatically increase the likelihood of patients completing the course of treatment successfully in future years.

### **New leads for the industry**

By assessing combinations of new candidate drugs and optimising clinical trial design, PreDiCT-TB is set to revolutionise the speed and effectiveness of drug discovery and development in the field of TB.

### **Making good on a promise**

Tackling TB is a high priority for governments worldwide; the international Stop TB Partnership has set the goal of eliminating TB as a global public health problem by 2050. The results of PreDiCT-TB are set to give a new impetus to efforts to deliver novel treatments against this deadly disease.

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## **Project Partners**

### **EFPIA member companies**

- GlaxoSmithKline Investigación y Desarrollo SL, Tres Cantos, Spain
- Sanofi-Aventis Research & Development, Chilly Mazarin, France
- Janssen Infectious Diseases – Diagnostics BVBA, Beerse, Belgium

### **Universities, research organisations, public bodies, non-profit groups**

- University of Liverpool, Liverpool, UK
- École Polytechnique Fédérale de Lausanne, Lausanne, Switzerland
- Erasmus University Medical Centre Rotterdam, Rotterdam, the Netherlands
- Health Protection Agency, London, UK
- Institut Pasteur, Paris, France
- Liverpool School of Tropical Medicine, Liverpool, UK
- Max Planck Gesellschaft zur Förderung der Wissenschaften E.V., Munich, Germany
- St George's University of London, London, UK
- Universidad Carlos III de Madrid, Madrid, Spain
- University College London, London, UK
- University of Leicester, Leicester, UK
- University of St Andrews, St Andrews, UK
- Uppsala universitet, Uppsala, Sweden

### **Patients' organisations**

- Vrije Universiteit Medisch Centrum, Amsterdam, the Netherlands

### **Small and medium-sized enterprises (SMEs)**

- Microsens Medtech Ltd, London, UK
- ZF-Screens BV, Leiden, the Netherlands

### **Financing**

|                            |               |
|----------------------------|---------------|
| IMI funding                | €14.8 million |
| EFPIA in kind contribution | €9.3 million  |
| Other contributions        | €4.5 million  |

**Total project cost €28.6 million**

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