

IHI 2022 In Focus

Annual Report Summary



Table of contents

Foreword	3
IHI's first year	4
IHI's calls	5
IHI's first calls - initial statistics	7
Administrative targets	9
Research highlights	10
Project dissemination	36
Key figures	41

Foreword

Looking back on the Innovative Health Initiative's first full year of operations, it is a good time to reflect on what a public-private partnership (PPP) is and what makes it successful.

What sets IMI and IHI apart is our ability to mobilise the very best people and organisations in Europe and bring them together in a neutral space where they can collaborate and share their expertise, resources and ideas. Thanks to this success, our projects have attracted players from outside Europe who recognise the benefits and power of collaboration, allowing our projects to become key focal points for international collaborations.

Many health challenges are global challenges, and as such need global responses, as illustrated by the COVID-19 pandemic. Our international partners help to disseminate the results of our projects far beyond Europe's shores. This increases our impact and showcases Europe as a leader in creating innovative, ambitious partnerships.

Looking to the future, we need to continue to mobilise the research community in Europe and beyond so that we remain a world-leading health PPP. Under IHI we look to go beyond the networks established under IMI, break down the silos between the different sectors in health and support innovative research partnerships that will deliver innovation into healthcare and benefit patients. With a partnership that spans diverse sectors, including the pharmaceutical, medical technology, biotechnology, digital health and vaccines industries, I am confident that we will achieve this.



Hugh Lavery
IHI Acting Executive Director

IHI's first year

IHI has had a busy first year!

We set up a suite of new governance bodies, who oversee our programme and define the strategic direction of IHI. The new Governing Board formally adopted the Strategic Research and Innovation Agenda (SRIA) for IHI as early as 20 January 2022, so we were ready to leap into action straight away!

We launched our first three calls for proposals during our first year, and we had a great response. **Our calls tackle a wide range of innovative areas in the field of health – from personalised oncology to next-generation imaging to hospital efficiency to rare diseases.** You can read about the topics that we've targeted as well as the details of our applicants and those who won the calls on [pages 7-8](#).

Our public-private partnership prides itself on being inclusive and addressing the concerns of the European citizen, which is why **we launched a platform where you can submit your idea for an IHI project for consideration.** You can see all of the ideas that are reviewed by our Science and Innovation Panel as well – these are experts from diverse sectors, disciplines and stakeholders who provide our Governing Board with advice relevant to research and innovation.

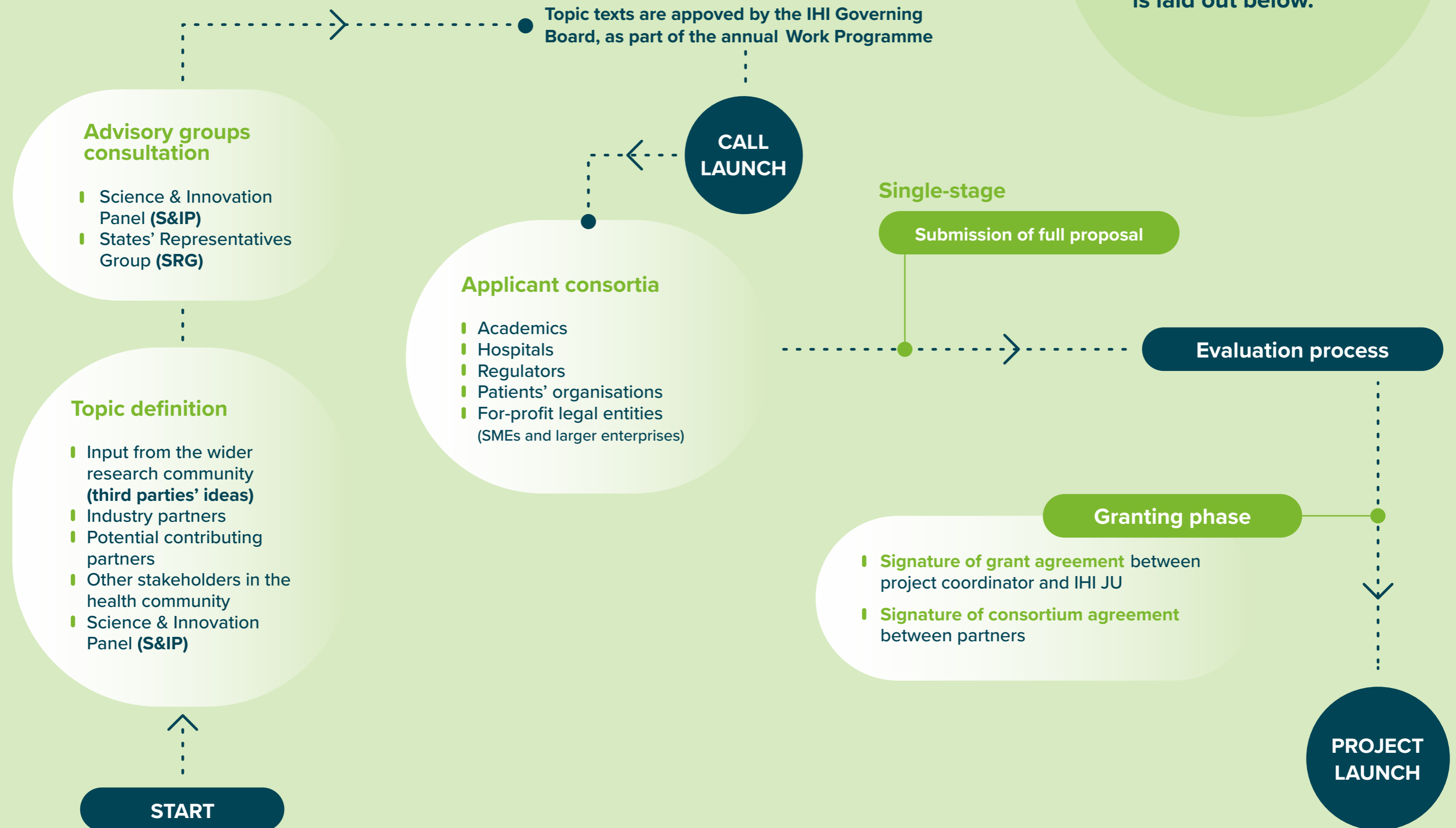
We ran a series of events to kick-start IHI with a bang. They included a high-level online event to introduce the Innovative Health Initiative Joint Undertaking which featured presentations from – amongst others – Jean-Eric Paquet, then Director-General of DG Research and Innovation of the European Commission, Bernt Bieber, President of COCIR, Serge Bernasconi, CEO of MedTech Europe, Claire Skentelbery, Director General of EuropaBio, Sibilia Quilici, Executive Director of Vaccines Europe, Nathalie Moll, Director General of the European Federation of Pharmaceutical Industries and Associations (EFPIA) and Maria da Graça Carvalho, Member of the European Parliament. We also organised dedicated webinars for each of IHI's calls for proposals as well as a hybrid kick-off brokerage event to help potential applicants find partners.

Although we are looking towards the future with IHI, our Innovative Medicines Initiative projects are continuing to deliver results. We've picked a selection to share with you in this brochure, available on [page 36](#).

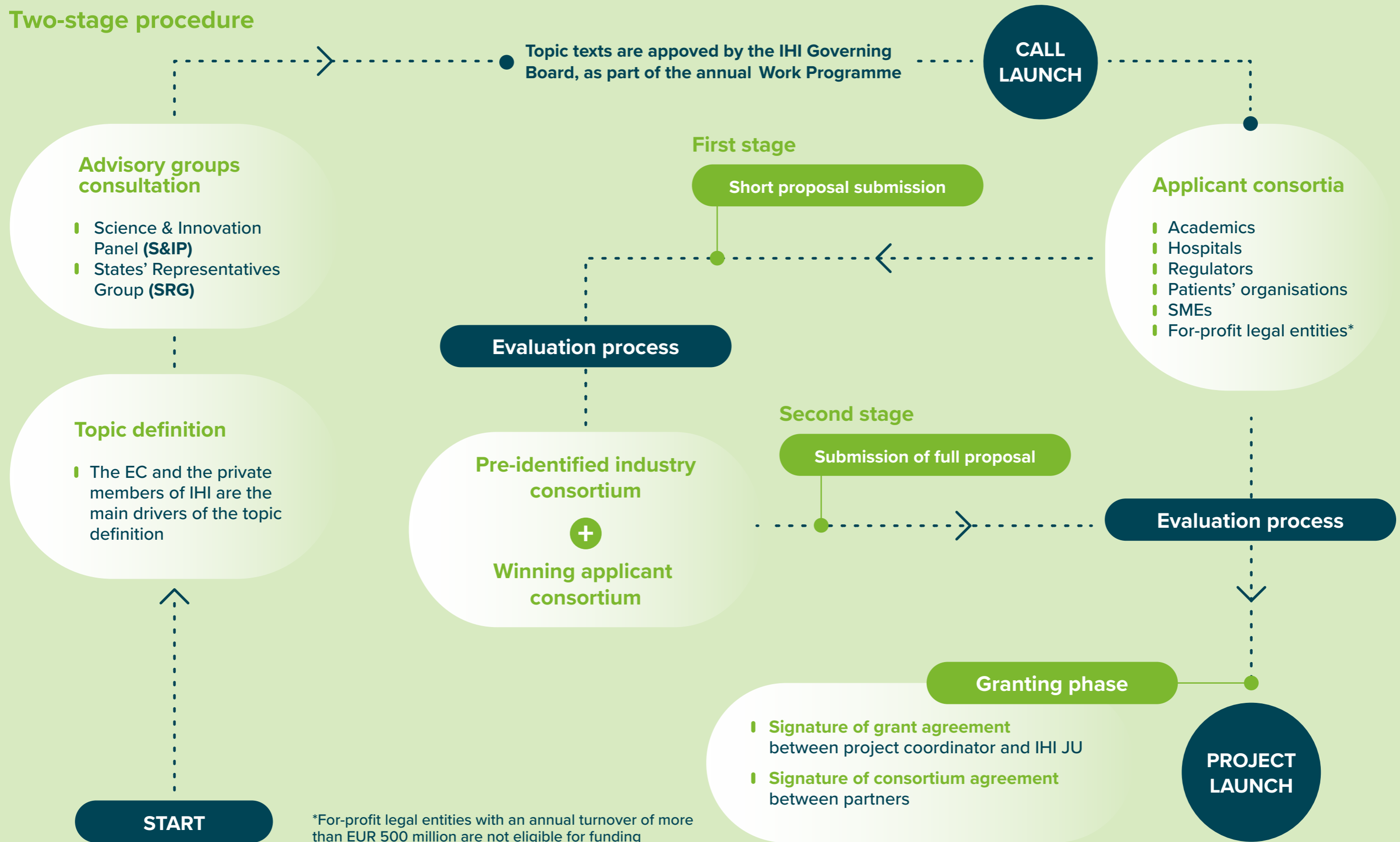
IHI's calls

Single-stage procedure

IHI launches two types of calls – single-stage and two-stage. The process for both is laid out below.



Two-stage procedure



IHI's first calls - initial statistics

In 2022, IHI launched its first three calls for proposals. IHI call 3 was still open for applications at the end of the year.

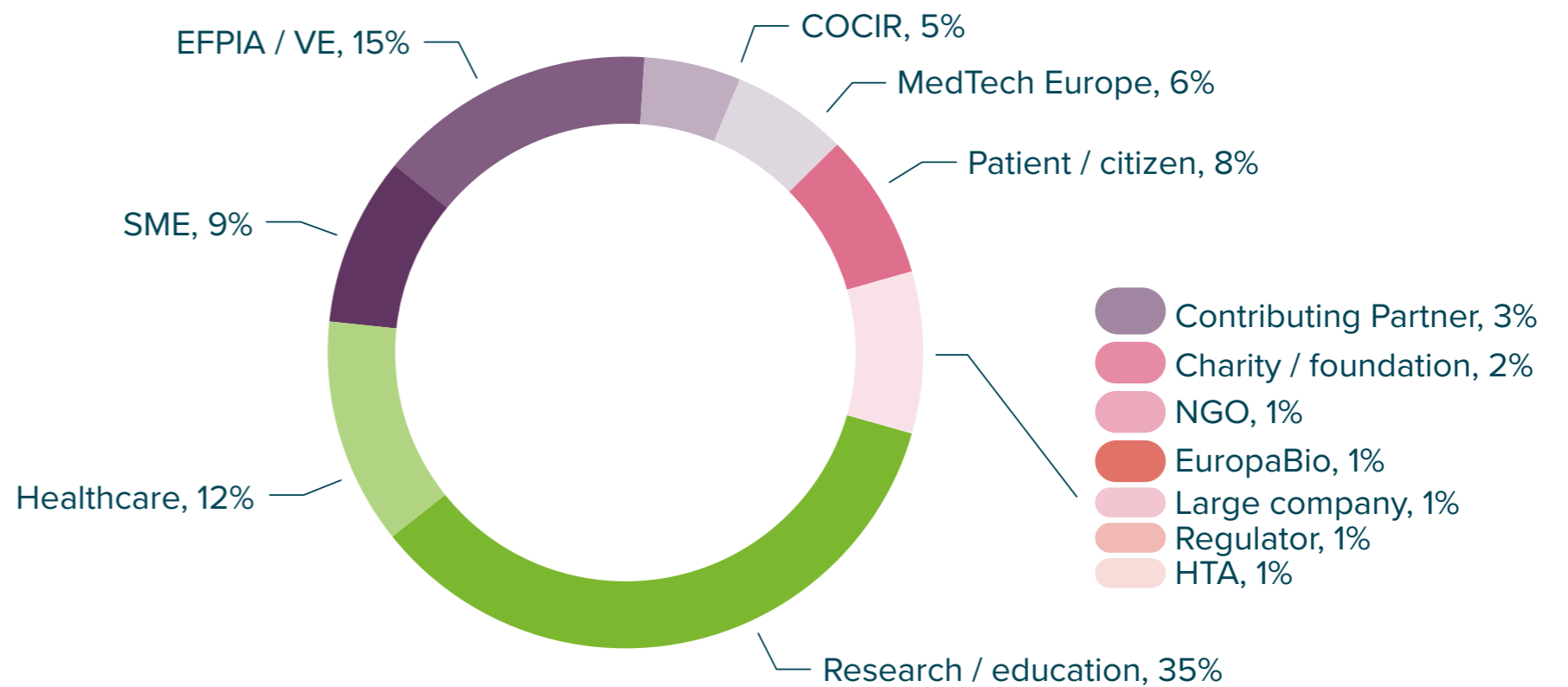
Call 1

IHI's first call was a **single-stage call that focused on four topics:**

- **Topic 1:** An innovative decision-support system for improved care pathways for patients with neurodegenerative diseases and comorbidities
- **Topic 2:** Next-generation imaging and image-guided diagnosis and therapy for cancer
- **Topic 3:** Personalised oncology: innovative people-centred, multi-modal therapies against cancer
- **Topic 4:** Access and integration of heterogeneous health data for improved healthcare in disease areas of high unmet public health need

18 proposals were submitted in response to this call for proposals: 5 each for topics 1-3, and 3 for topic 4.

IHI call 1 (single-stage): breakdown by organisation type of participants in selected proposals



Following an evaluation by independent experts, five proposals were selected for funding. The chart above shows the breakdown of participants in the selected proposals.

The chart clearly highlights IHI's industry partners by name while grouping other participants according to organisation type: large company, SME, healthcare, patient or citizen groups, charities or foundations, NGOs, regulators or health technology assessment organisations.

Call 2

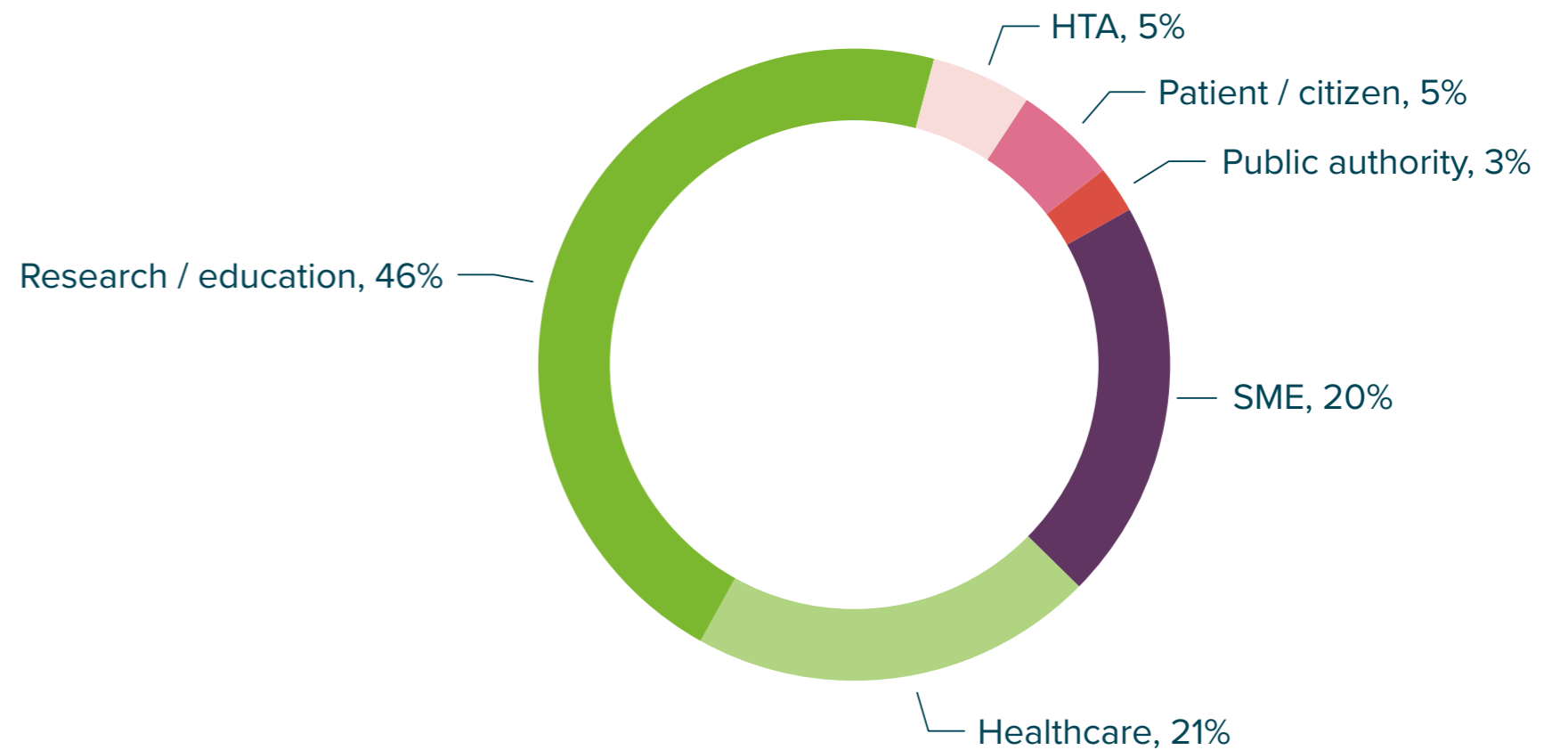
IHI's second call was launched in June 2022, and it was a **two-stage call with the following topics:**

- **Topic 1:** Cardiovascular diseases: improved prediction, prevention, diagnosis, and monitoring
- **Topic 2:** Setting up a harmonised methodology to promote the uptake of early feasibility studies for clinical and innovation excellence in the European Union

15 short proposals were submitted, 11 for topic 1 and 4 for topic 2.

The short proposals were evaluated by independent experts and the top-ranked consortium for each topic was invited to join up with the industry consortium identified in the call text and submit a full proposal.

IHI call 2 (two-stage): breakdown by organisation type of participants in selected proposals



This chart shows the participation structure of the two selected short proposals by organisation type: SME, healthcare, patient or citizen groups, research or education organisations, public authorities or health technology assessment organisations.

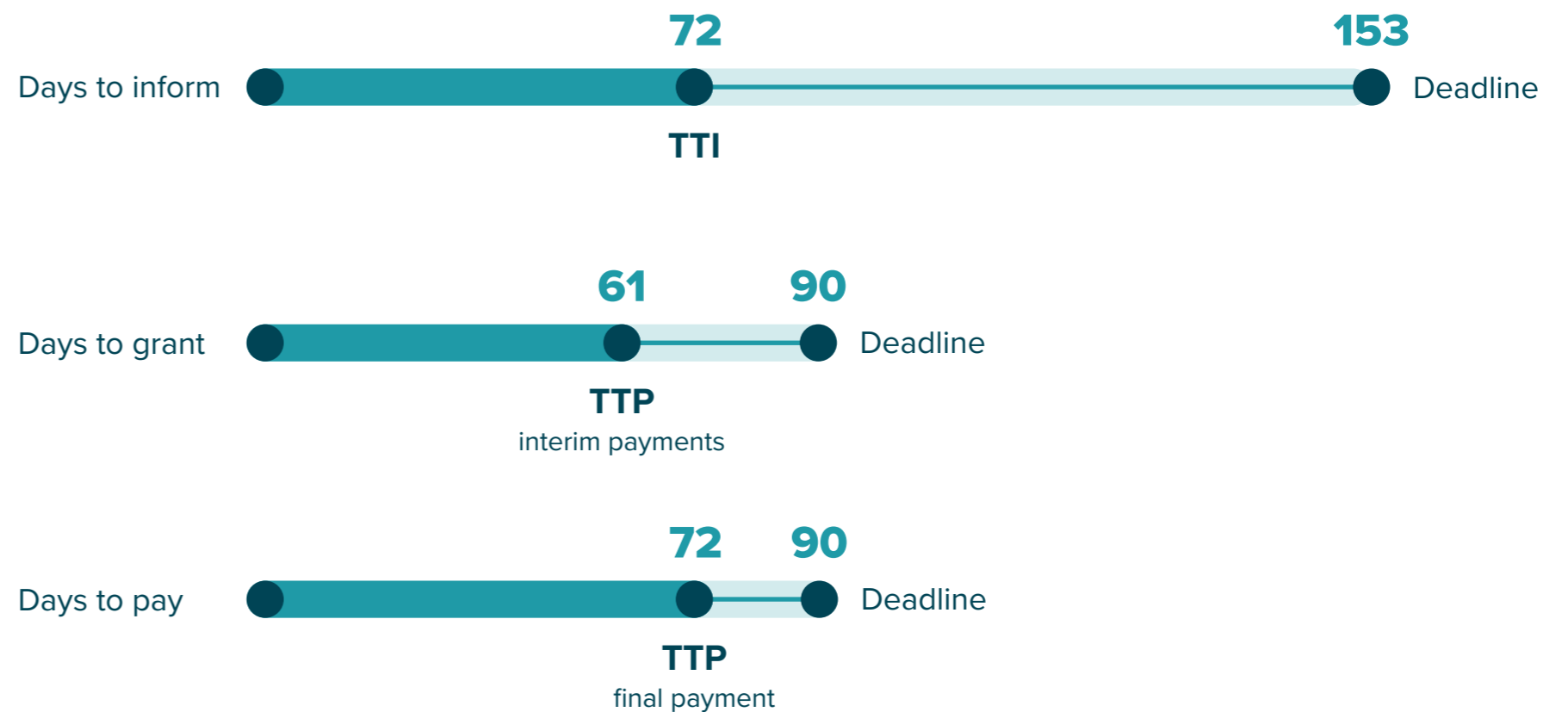
Industries appear to be under-represented because the pre-identified industry consortium members will join only in stage 2.

Administrative targets

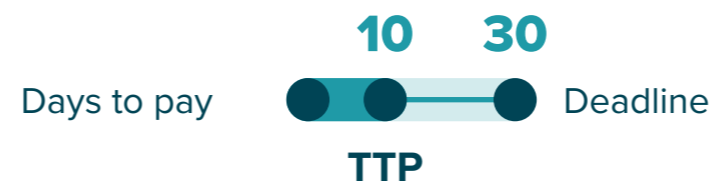
IHI has an excellent track record in terms of informing applicants and delivering payments on time.

The launch of IHI means that the Programme Office is now managing three programmes in parallel, with different sets of rules, as a number of projects launched under IM1 and IM2 are still ongoing.

Despite the challenges this entails, the office remained highly efficient, meeting all of its targets, and making payments to projects within the official deadlines.



The JU was also efficient in making administrative payments:



TTI: Time to inform applicants of evaluation results

TTP: Time to pay to project

Research highlights



IMI projects address diverse challenges in health research and innovation

From prevention to diagnosis to treatment, IMI projects drive innovation in healthcare. We leverage the skills of a range of scientific fields and bring various stakeholders together to address public health needs and strengthen the competitiveness of the European health industry.

Diabetes project results in prompt review of clinical trial outcomes

The **BEAt-DKD** project previously identified a number of different subtypes of type 2 diabetes.

Diabetes patients in one sub-group ('severe insulin-resistant diabetes') are particularly prone to kidney problems, a well-known complication in diabetes. The hope was that this new classification of type 2 diabetes would lead to the development of more personalised treatments for the disease.

BEAt-DKD partner Eli Lilly had a drug in development called tirzepatide, which can substantially increase insulin sensitivity. They also knew that other related drugs had slowed the progression of kidney disease in type 2 diabetes patients. The company therefore went back to the data gathered during the **SURPASS-4 clinical trial** which assessed the efficacy and safety of tirzepatide as a diabetes treatment.

They found that patients in the trial who received tirzepatide did better on measures of kidney function.

These new findings, which were published in The Lancet Diabetes and Endocrinology, could trigger a new clinical trial and eventually, lead to a new indication for the drug.

Putting the pharmaceutical sector on the path to a GREENER future

Active ingredients from medicines can get into the environment through a variety of routes, and once there they can prove harmful to wildlife and ecosystems.

The aim of **PREMIER** is to deliver a framework for assessing and characterising the environmental risks of active pharmaceutical ingredients (APIs).

Writing in the journal Environmental Science and Technology Letters, the **PREMIER** team sets out its '**GREENER**' concept for the discovery and development of medicines. As a starting point, the team highlights the close links between human and environmental health, noting that decision-making in drug discovery and development can be beneficial for both human and environmental health.

Among other things, the team highlights the importance of avoiding non-target effects, reducing environmental exposure to APIs (for example by using more targeted drug delivery methods), avoiding substances that don't break down in the environment, and mitigating risks as much as possible.

A vital resource for future drug discovery

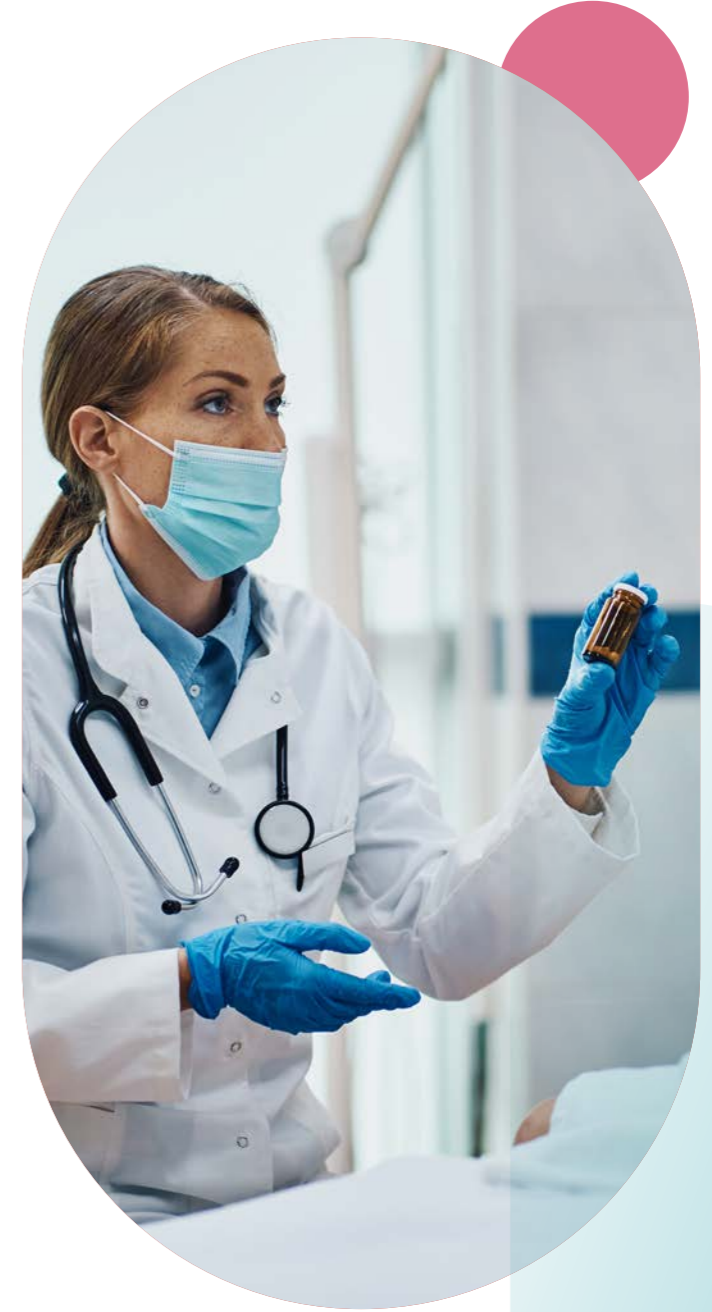
Transport proteins act as our cells' gatekeepers, controlling the flow of nutrients and other molecules (including drugs) into and out of the cell. With over 400 members, solute carriers (SLCs) represent the largest class of transport proteins. Yet, although they have been implicated in diseases ranging from Alzheimer's disease and amyotrophic lateral sclerosis (ALS) to schizophrenia, solute carriers have never been studied in depth.

IMI projects **RESOLUTE** and **RESOLUTION** are studying SLCs in unprecedented detail, delivering knowledge, resources, and tools to facilitate further research into, and drug discovery focusing on, these important proteins. Most importantly, the projects' outputs are freely available online, something that will boost their chances of having an impact.

For example, **RESOLUTE** has developed 25 assays to test the effect of different chemical compounds on individual SLC functions for future use in drug discovery by the pharmaceutical industry and SMEs.

These assays have been optimised and adapted to high throughput and medium throughput platforms for drug screening. The protocols and first results have been shared in the open-access repository [PubChem](#).

RESOLUTION has compiled publicly available data on genetic variation in SLC genes and their association with diseases which can be visualised in the [project's portal](#). An algorithm developed by the project allows the quantification and comparison of the variants across SLCs.



IMI research reveals how we can live healthier for longer

By 2050, experts predict that there will be half a million centenarians living in the EU. Europeans are living longer than ever before, and the age profile of society is rapidly developing. Although we have successfully managed to increase our lifespan, IHI and IMI are working on solutions that can improve our healthspan, meaning that not only will we live longer, but we will be healthier for longer.



RADAR-AD shows that subjective cognitive decline may be an early sign of Alzheimer's disease

The goal of the **RADAR-AD** project is to develop a digital platform that would draw on smartphone, wearable and home-based digital technologies to track subtle changes in the cognitive and functional abilities of people with Alzheimer's disease. **RADAR-AD** published a [research article](#) in the Journal of Alzheimer's Disease which showed that subjective cognitive decline might be a precursor of Alzheimer's Disease.

The study was the first to investigate brain connectivity using the high-density electroencephalography technique to explore network changes in subjective cognitive decline while performing various tasks.

In 2022, the project also successfully completed recruitment for a clinical study that will assess the feasibility of using remote monitoring technologies such as smartphones or wearable devices to assess function and cognition.

VITAL is tackling infectious diseases in the elderly

As people age, their immune systems become weaker, and they become more vulnerable to infectious diseases such as flu and COVID-19. Preventing these infections through a proper vaccination strategy is essential for promoting healthy ageing.

IMI project **VITAL** is delivering knowledge and resources to facilitate the design of vaccination strategies tailored to older people.

For example, they have developed an open-access, searchable online [catalogue](#) that offers users a rapid overview of existing data sources on infectious diseases that are known to affect ageing adults. The catalogue is interesting for pre-clinical drug development and for those interested in assessing the impact of specific infectious diseases.

Killing the superbugs: IMI tackles antimicrobial resistance to drugs

Antibiotic-resistant bacteria cause approximately 33 000 deaths in the EU and the annual treatment and social costs have been estimated at approximately 1.5 billion euros. An estimated 1.27 million deaths globally were caused by bacterial antibiotic resistance in 2019 alone. Continued research is needed in this area to identify solutions, as antibiotic resistance is on the rise.

COMBACTE continues the fight against antimicrobial resistance

The four **COMBACTE** projects – **COMBACTE-CARE**, **COMBACTE-CDI**, **COMBACTE-MAGNET** and **COMBACTE-NET**, are fighting antimicrobial resistance in various ways.

In 2022, **COMBACTE-CARE** was actively enrolling patients in the **REVISIT Phase 3 clinical trial**. This evaluates the drug combination of aztreonam-avibactam (ATM-AVI) for targeting carbapenem-resistant bacteria, which are amongst the most dangerous antibiotic-resistant bacteria.

COMBACTE-CDI targeted *Clostridium difficile* infections (a different type of antibiotic-resistant bacteria), which cause serious diarrheal infections and may result in colon cancer.

The project published the results of a Europe-wide study on the prevalence of *C. difficile* within potatoes and found that $\geq 10\%$ of all samples in 9/12 countries were contaminated.

This indicates that potatoes could potentially act as reservoirs for *C. difficile*. **COMBACTE-CDI** also published a study highlighting the burden that undiagnosed *C. difficile* places on healthcare systems.

COMBACTE-MAGNET aims to evaluate a new approach to prevent and treat life-threatening infections (often involving the lungs and airways, urinary tract, and intra-abdominal area) caused by Gram-negative bacteria. A study conducted in 2022 showed that there was a high prevalence (33.6%) of multidrug-resistant *Pseudomonas aeruginosa* in European ICUs. Another study carried out by the project showed that the gut can act as a reservoir for resistant *P. aeruginosa* before the pathogen moves to the lungs, and targeting the bacteria while it is in the gut may be an effective route to preventing lung infection. Results from the **EVADE study** carried out as part of **COMBACTE-MAGNET** showed that the human monoclonal antibody treatment tested was not effective against *P. aeruginosa* in mechanically ventilated patients in the intensive care unit (ICU).

COMBACTE-NET has built strong clinical, laboratory and research networks across Europe that enable more efficient clinical testing of novel antimicrobial drugs. It also carries out clinical trials. In 2022, the project enrolled 2 165 patients at risk of contracting hospital-acquired or ventilator-associated pneumonia (HAP/VAP) in ICUs into the **HONEST-PREPS study**. The goal of this study is to collect important data on HAP/VAP that will inform future diagnostic, preventative and therapeutic trials. The first patient was also enrolled on the **Phase 3 SAATELLITE-2 trial** which focuses on evaluating the safety and efficacy of a monoclonal antibody to prevent HAP caused by *Staphylococcus aureus* infections in intubated and ventilated patients. Prosthetic joint infections caused by *S. aureus* are one of the most complex infections a person can get, and results from another study showed that rates of treatment failure were high.

Eliciting solutions from stores of big data

Swathes of data exist today, but the problem is often sorting it into forms that are useable.

There are several IMI projects that focus on organising data into structures that will make it easier for researchers to access and new results will emerge.

BigData@Heart delivers a framework to boost the quality of research using real-world data

In a bid to address many of the quality, privacy, and transparency issues surrounding health data, the **BigData@Heart** project teamed up with the European Society of Cardiology (ESC) to develop 'pragmatic advice' on the use of structured healthcare data in clinical trials and observational research.

The goal was to deliver something that would be applicable across different disease areas and meet the needs and expectations of all stakeholders, including the general public.

The result, dubbed the **CODE-EHR framework**, aims to improve the quality of studies using structured healthcare data and provide confidence in the results of these studies for use in clinical decision-making. The framework is published via open-access papers in the *European Heart Journal*, the *British Medical Journal* (BMJ) and the *Lancet Digital Health*, and it was presented at the [ESC Congress](#).

The framework focuses on five key areas: dataset construction and linkage (to provide an understanding of how the data were identified and used); data fit for purpose (to ensure transparency on the coding systems used); disease outcomes and definitions (detailing how conditions and outcome events were defined); analysis (detailing how outcome events were analysed); and ethics and governance (covering processes for consent, privacy, and patient and public involvement).

For each area, the framework sets out both minimum and preferred standards and details the information that researchers should provide when writing up their study.

The consortium contacted the top journals in the field to ask them to join the initiative; four of them already added or agreed to include this checklist as a recommendation or requirement for new publications.

The EHDEN real world data portal is live!

The goal of **EHDEN** is to make the large-scale analysis of health data in Europe a reality. The project aims to do this by building a federated data network that allows access to the data of 100 million EU citizens standardised to a common data model. In 2022 the project published its **EHDEN real world data portal** which offers findable, standardised data at scale, designed to be a one-stop-shop with free access for the medical research community.

By the end of the year, it had 160 million patient records from 20 countries and will eventually include the complete **EHDEN** network of ~830 million patient records.

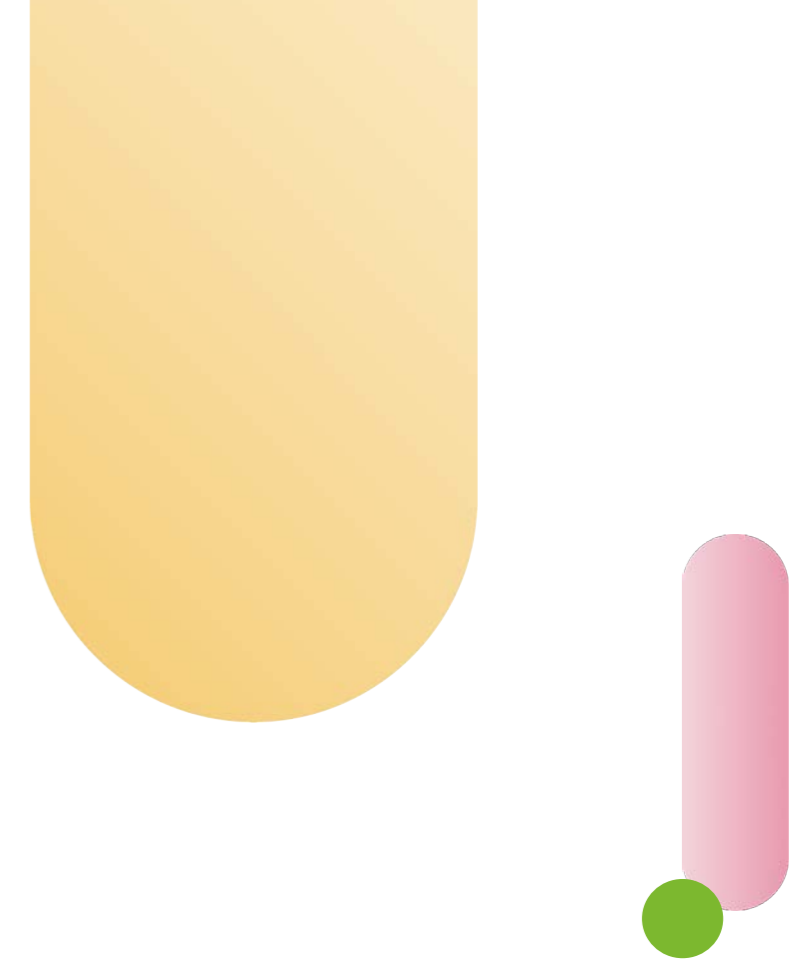
PharmaLedger applies blockchain technology to health challenges

In blockchain technology, data is decentralised, meaning it is stored across multiple servers. It is also immutable; this means data records (or 'blocks') cannot be changed or tampered with. Each new 'block' of data is connected to the previous one, creating the 'blockchain'. The blocks are connected by cryptography, making the system secure. Its most famous application is the Bitcoin currency, yet it could also revolutionise the way other sectors work. The goal of the **PharmaLedger** project was to deliver a blockchain-based platform for the healthcare sector.

By the end of the project, the consortium had created a digital trust ecosystem comprising organisations working together to implement blockchain technologies in healthcare. They had also developed a number of use cases demonstrating how blockchain could be used to tackle specific challenges in three domains: supply chain, health data, and clinical trials.

The most advanced use case is on electronic patient information (ePI) and shows how a simple app with a QR code reader could provide patients with the latest, regulatory-approved information on their medicines.

Although **PharmaLedger** has ended, the project's legacy lives on via the **PharmaLedger Association**, which was set up in 2022 and is building on the work started in the project.



New findings highlight the value of old data

In a demonstration of the longevity and long-term usefulness of resources generated by IMI projects, data from four IMI projects was used to shed new light on risk factors for type 2 diabetes.

In the new study, scientists analysed data from 7 000 individuals in 5 countries from four IMI projects – **SUMMIT, DIRECT, RHAPSODY** and **BEAt-DKD**. Their focus was a protein called follistatin, which is produced in many tissues and has been linked to metabolic diseases. The research revealed that people with high levels of follistatin in the blood have an increased risk of developing type 2 diabetes, independent of other known risk factors. The results are published in [Nature Communications](#). The team concludes that follistatin could be used as a target for treatments design to prevent type 2 diabetes.

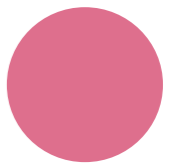
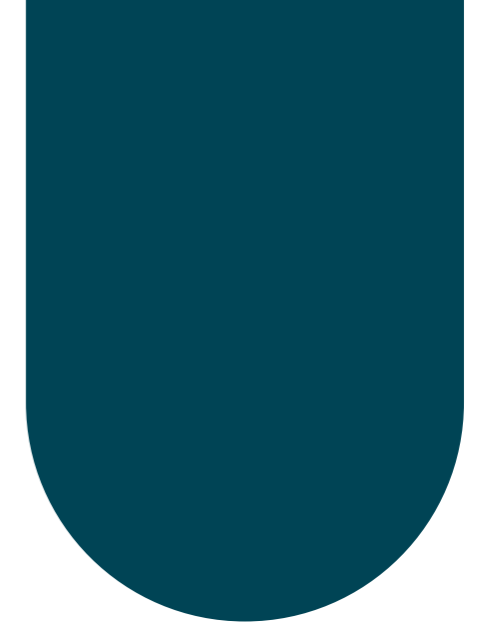
Another project which has used existing data to generate new insights is **BIOMAP**, which is probing the underlying causes of two common skin diseases that affect more than 300 million people worldwide: psoriasis and atopic dermatitis.

By analysing existing genetic datasets of people with psoriasis, they uncovered some previously unknown genetic factors that are associated with the onset of the disease. The results are published in [Human Genomics](#).

One thing that the data showed was that skin from a psoriatic lesion displayed genetic differences to healthy skin from the same person. Even more intriguingly, the genetic pattern looked different again when compared to the healthy skin of someone who didn't have psoriasis at all.

Another aspect of the study was the discovery of “bridge genes” (a group of genes that form connections between genes that are known to be associated with psoriasis) as well as breakdowns in connections within genetic networks. The findings could be used to identify new targets for drugs to treat psoriasis.

BIOMAP also continually updates a disease map that draws connections between the biomarkers of psoriasis severity, psoriatic arthritis and treatment responses.



Hunting out biomarkers to point to early disease onset

A biomarker is an indicator of a biological state, often used to point to early signs of disease. If a person presents with certain biomarkers, clinicians can make decisions to start treatments or decide to monitor individuals more closely. For many diseases, early diagnosis is associated with increased chances of survival so identifying accurate biomarkers can make a huge difference.

eTRANSAFE is on the hunt for biomarkers for liver toxicity

To date, no biomarkers for liver toxicity have been accepted by regulators, despite the fact that assessing potential drugs for liver toxicity remains a key challenge in drug development.

The eTRANSAFE project has set up a pipeline that explores possible biomarkers for liver problems and the consortium also developed a software tool to predict the chances of drug-induced liver injury in humans (published in the journal *Chemical Research in Toxicology*).

eTRANSAFE is also striving to reduce the number of animals used in *in vivo* toxicity studies by leveraging legacy data from historical controls.

To this end, eTRANSAFE launched a Virtual Control Group using more than 5 million historical data points, and EU and US regulators were approached regarding the qualification of the methodology.



LITMUS sheds light on identifiers of non-alcoholic fatty liver disease

About a quarter of all adults have some form of non-alcoholic fatty liver disease, which does not affect them, but a small minority – about one in a hundred of that quarter – develop non-alcoholic steatohepatitis (NASH), which is much more serious. Currently, surgical biopsies are the only way to identify people who will develop NASH.

LITMUS is looking for non-invasive biomarkers so that these procedures could be replaced by simple blood tests or scans.

New data was published in 2022 on several potential biomarkers in the journals *Hepatology*, *Science Translational Medicine* and *JHEP Reports*.

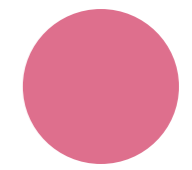
LITMUS also created a European NAFLD Registry and an associated biobank, which includes 13 483 event records from 8 984 individual patients supplemented by extra data and samples from 1 878 patients from EFPIA partners.

PRISM2's new clinical study protocol will validate biomarkers for social dysfunction

Currently, neurological disorders are diagnosed based on symptoms rather than causes of the disease. The **PRISM2** project focuses on social withdrawal, a common early symptom of many neurological disorders.

A new clinical study protocol finalised by **PRISM2** in 2022 will help to validate both digital and neurobiological biomarkers for social dysfunction in schizophrenia, Alzheimer's disease and major depressive disorder.

Four sites have started recruitment of patients for the trial, and 54 patients have signed up so far.



Fighting COVID-19 with innovative health research

IMI responded rapidly to the COVID-19 crisis by launching a specific call for proposals geared towards tackling the various challenges posed by the pandemic. €117 million was channelled into eight projects with 94 participating organisations.

CARE identifies the “core genetic signature” of recovering COVID-19 patients

The **CARE** project investigated a range of existing drugs to discover if there were any drugs that could be repurposed to tackle COVID-19.

In 2022, the project investigated whether there were genetic hallmarks in patients recovering from COVID-19. They successfully identified a “core genetic signature” in patients up to six months after infection, which was associated with a history of blood clotting and influencing blood coagulation and certain blood cell activation processes.

MAD-COV 2 strengthens arsenal against COVID-19

Scientists from IMI’s **MAD-COV 2** project showed that a low-dose combination of the antiviral remdesivir and a drug called APN01 (hrsACE2) can stop the SARS-CoV-2 virus which causes COVID-19 from multiplying in cells.

In 2022, the research was published in several peer-reviewed journals: Cell, Cell Metabolism, and eLife. The project also validated some newly identified host cell interactors, one of which had a dual role, and the findings are in preprint. Another discovery in 2022 was that the Omicron variant gained resistance against the natural antiviral interferon alpha, which was published in PNAS Nexus.



Leveraging digital technology to improve healthcare

Digital technology will have an important role in the healthcare of the future, giving patients more autonomy over their medication administration and health monitoring. Clinical trials can also be carried out remotely, far from official sites, by utilising digital devices. IMI projects are investigating how various digital technologies can be leveraged to improve our healthcare outcomes.

IDEA-FAST uses digital tools to evaluate sleep disturbance impact on patients

IDEA-FAST is investigating digital endpoints for fatigue and sleep disturbances that will indicate the impact of these symptoms on a patient, specifically patients with neurodegenerative diseases and inflammatory diseases.

The **IDEA-FAST** feasibility study was successfully concluded in 2022, and involved participants using several wearables and other devices to identify digital indications of fatigue and sleep disturbances.

It involved 146 patients with six different diseases: Parkinson's disease, rheumatoid arthritis, systemic lupus erythematosus, primary Sjögren's syndrome, inflammatory bowel disease and Huntington's disease.

Walk this way with MOBILISE-D

How we walk is an important indicator of health; a slow walking speed is associated with a greater risk of disease, cognitive decline, risk of falls and even earlier deaths. **MOBILISE-D** is developing a complex system that uses digital sensors to analyse people's gait, focusing on patients with conditions that affect mobility, like chronic obstructive pulmonary disease (COPD), Parkinson's disease, multiple sclerosis, hip fracture recovery and congestive heart failure.

In 2022, the project [published the protocol](#) of a study that demonstrated the clinical validity of their methodology of using digital sensors to evaluate mobility.

This is the first-ever systematic approach to evaluating mobility and will provide a model for future studies in digital health assessment.

Trials@Home leverages wearable tech to decentralise clinical trials

The goal of the **Trials@Home** project is to decentralise the clinical trial experience by enabling participants to monitor their health condition at home and submit the results virtually to the trial researchers.

Using digital technology and wearable devices, data can be uploaded automatically as the patient goes about his or her daily life.

Smartphones indicate worsening of depression with RADAR-CNS

The **RADAR-CNS** project aims to develop new ways of monitoring major depressive disorders, epilepsy and multiple sclerosis using wearable devices and smartphone technology.

Researchers from the project found that geolocation data from smartphones can be used to predict the worsening of depressive symptoms in people with major depressive disorder.

In a study published in the [JMIR Mental Health](#) journal, the analysis of geolocation data showed that participants who experienced a worsening of symptoms spent more time at home and less time in different locations.



Supporting clinical trials and medicine development for pregnant people and children

Pregnant and breastfeeding women have traditionally been excluded from clinical trials as a preventative measure to ensure that no harm would come to their children. However, women continue to fall sick while pregnant and breastfeeding and steps need to be taken to find out whether certain substances can be ingested by these women safely. Running clinical trials in children is also extremely challenging as there are a lot of rapidly changing factors – children grow quickly, often faster than the average lifespan of a clinical trial, for instance, and children react differently to various dosages of medication according to their age. IMI projects are cautiously investigating to what degree substances pass from mother to child and are building bridges between experts in children’s medicine to develop safer clinical trials for children.

Expert network works towards better drug development for children

Running clinical trials in children is challenging. There is no infrastructure across Europe capable of delivering high-quality clinical trials. Furthermore, as many children’s diseases are rare, finding enough patients to run a trial can prove difficult, and so major innovations are needed in the design of paediatric clinical trials. IMI project **connect4children** is working to address these challenges. One important project output is an advice service through which drug developers can easily access a wide array of important information directly from experts when designing clinical trials.

The idea is that drug developers can come to **c4c** asking for advice in relation to the treatment of a particular childhood disease that they are targeting. An advice group is quickly formed which the drug development company can then consult. The “experts” included not only clinicians, researchers, and methodology experts, but also parents and patients themselves.

The network, which is described in the journal Clinical and Translational Science, comprises over 20 expert groups involving more than 400 experts.

So far, some 40 advice requests have been received. The **c4c network** is now working to turn the pilot into a sustainable fee-for-service endeavour, which companies throughout Europe and beyond can benefit from.



ConcePTION builds the first Europe-wide breast milk biobank

The **ConcePTION** project is creating the first Europe-wide breast milk biobank (the European Breast Milk Collection) which will be used to find out more about the transfer of medicines (or medications) from mother to baby via breastmilk.

The first study involving the biobank included over 30 breastfeeding participants donating over 300 milk samples, with the goal of examining to what degree antihistamines (taken for allergies) pass into milk. In 2022, the **ConcePTION** team also developed an inventory of European data sources (e.g., healthcare databases, birth cohorts, disease registries, etc.) that can be used to evaluate perinatal and long-term childhood neurodevelopmental risks associated with in utero exposure to medication, published in PLoS ONE.

Conect4children and CDISC release user guide to facilitate paediatric medicines development

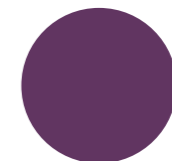
IMI project **conect4children** has teamed up with CDISC (the Clinical Data Interchange Standards Consortium) to produce a [Paediatrics User Guide](#).

The guide, which is freely available online, describes how to use CDISC standards to collect and structure data used in clinical trials to facilitate the aggregation of information, take advantage of big data and support data sharing.

Topics covered by the user guide include participant and participants' family information (e.g., medical conditions, reproductive, diet and nutrition, body system assessments), pregnancy and birth, and study conduct.

The guide shows how IMI projects, by collaborating with global standards development organisations like CDISC, can have an impact on research worldwide, and not just in Europe.

More importantly, it will boost the impact of data gathered during paediatric clinical trials and so help to advance research into diseases that affect children.



Respiratory diseases

Respiratory diseases accounted for almost 8% of all deaths in the EU in 2017, pre-pandemic. These airway diseases are prevalent across European citizens of all ages – in 2019, some 4.3 % of the EU population aged 15 years and over stated that they had some form of chronic lower respiratory disease (other than asthma) diagnosed by a medical doctor. Each year, influenza kills – there were 5 693 deaths of EU residents caused by influenza in 2020. IMI is investigating improved vaccines to tackle flu and RSV, as well as other respiratory diseases.

FLUCOP: a focus on flu vaccine efficacy

Every year, pharmaceutical companies develop vaccines designed specifically to combat the strains of flu that are most likely to be in circulation the following winter. However, accurately predicting how much protection a new vaccine would actually offer against emerging virus types is far from easy.

The **FLUCOP** project is delivering tools and knowledge to assess the efficacy of new vaccines more reliably.

For example, the haemagglutination inhibition (HAI) assay, which measures the levels of certain antibodies, has been used for decades to assess influenza immunity (caused by either vaccination or infection). However, HAI assay results from different laboratories can differ markedly. The **FLUCOP** team developed a protocol to improve the consistency of these tests and explored other factors that can influence the results of this vital assay, and published the results in the journal *mSPHERE*.

While most flu vaccination strategies focus on generating an immune response to the virus's haemagglutination surface protein, there is growing interest in the immune system's response to the virus's neuraminidase protein. **FLUCOP** set out to develop a reliable way of testing for this, and the results are published in *Frontiers in Immunology*. They note that their standard operating procedure for the assay, which has been validated and is provided as an annexe to the article, was 'precise, linear, robust within defined limits across multiple testing laboratories'.



DRIVE-ing the conversation on flu vaccine effectiveness

The **DRIVE** project set out to create a platform, bringing together diverse stakeholders, to study the effectiveness of different brands of flu vaccines in the EU over a five-year period.

Over the 5 flu seasons from 2017 to 2022, the project gathered data from more than 35 000 patients, approximately 60 variables and 13 influenza vaccines.

The **DRIVE** partners consider that this valuable database could be leveraged and further utilised for various reasons, such as research into the next generation of influenza vaccines, and as part of worldwide efforts to enhance global surveillance networks for respiratory viruses and associated diseases. The project therefore developed a framework for open access to research data, allowing the secondary use of the data generated since the 2018/19 season.

RESCEU highlights the scale of the RSV challenge

IMI project **RESCEU** is gathering information on the scale of RSV infection in Europe and its economic impacts so that we can improve how the disease is managed, treated, and (hopefully) prevented in the future.

Although mild for most people, the disease can be particularly dangerous for babies, small children and the elderly. In 2022, the project published research in The Lancet showing that in 2019, RSV was responsible for the deaths of 100 000 children under the age of 5 worldwide, meaning that 2% of deaths in young children were due to RSV. Currently, there is no approved vaccine for RSV for children, however, a number of vaccines are under development. The data gathered by **RESCEU** will help in the design of immunisation strategies so that they offer the best protection for those vulnerable to the disease.

A collaborative partnership for the respiratory research field

COVID-19 project **DRAGON** aims to use artificial intelligence (AI) and machine learning to develop a decision support system capable of delivering a more precise coronavirus diagnosis and more accurate predictions of patient outcomes.

Together with the **U-BIOPRED Alliance** (itself a legacy of IMI1 asthma project **U-BIOPRED**) and the Paediatric Asthma Alliance, **DRAGON** established Precision Medicine BioPharmaX. This collaborative partnership brings together different disciplines, stakeholders, initiatives, and disease domains such as asthma, chronic obstructive pulmonary disease (COPD), and COVID-19 to advance the concept of precision medicine. The new organisation will help to secure the sustainability of **DRAGON's** results.

Vaccines

Worldwide, immunisation prevents 3.5-5 million deaths per year, and we now have vaccines to prevent more than 20 life-threatening diseases. Vaccines are critical to the prevention and control of infectious disease outbreaks, as we saw during the COVID-19 pandemic and the Ebola epidemic. However, challenges persist in vaccine development and in finding new vaccines as new viruses emerge. IMI projects focus on rolling out new vaccines, such as those for Ebola, understanding and improving current vaccines, and improving vaccine manufacture.

VAC2VAC takes steps towards animal-free vaccine development

Every batch of human or animal vaccines that is manufactured must undergo a series of rigorous tests to ensure it meets certain standards for safety and potency. Today, many of these batch tests involve large numbers of laboratory animals. VAC2VAC aims to develop and validate alternative approaches to animal testing for vaccine development.

To this end, VAC2VAC developed and validated a new method for quantifying the amount of tetanus neurotoxin found in a bacterial medium in 2022.

That is important because testing the consistency of tetanus neurotoxin production by the bacteria that causes tetanus could help to ensure product quality in tetanus vaccine manufacturing. The findings are published in the peer-reviewed journal *Toxins*. The project has also published a [roadmap](#) for achieving meaningful change in regulatory policy through the replacement of *in vivo* (animal) methods with *in vitro* methods, which includes practical considerations and best practices for developing a strategy to encourage the adoption and implementation of non-animal methods by industry partners and regulatory agencies worldwide.

The VAC2VAC project also identified 12 monoclonal antibodies (mAbs) as being potentially important in the further development and validation of immunoassays for human diphtheria, tetanus, and acellular pertussis vaccines, and those mAbs are now available in purified form from the [National Institute for Biological Standards and Control in the UK](#).

VSV-EBOPLUS leverages big data to understand immune responses to an Ebola vaccine

The VSV-EBOPLUS project aims to use systems biology approaches to decipher the molecular and immune signatures of responses to the Eryebo vaccine (which tackles Ebola) in both adults and children.

In 2022, the project improved the BioFeatS tool, which is designed to sort through big data related to the vaccine.

The tool could be used in the future by thousands of laboratories that may need to analyse high-throughput datasets.

EBOVAC 3 tests Ebola vaccine suitability for infants

The IMI **EBOVAC** projects resulted in the development of an effective vaccine regimen against Ebola. In July 2020, the European Commission approved the vaccine regimen, and in 2021, the World Health Organization gave it prequalification status which was important to allow the vaccine regimen to be rolled out in Africa.

It was deployed in Rwanda and in the Democratic Republic of Congo (which faced the world's second-largest Ebola outbreak in 2018-2020) and to date, more than 260 000 people worldwide have received the first dose of the Ebola vaccine developed by the **EBOVAC** projects.

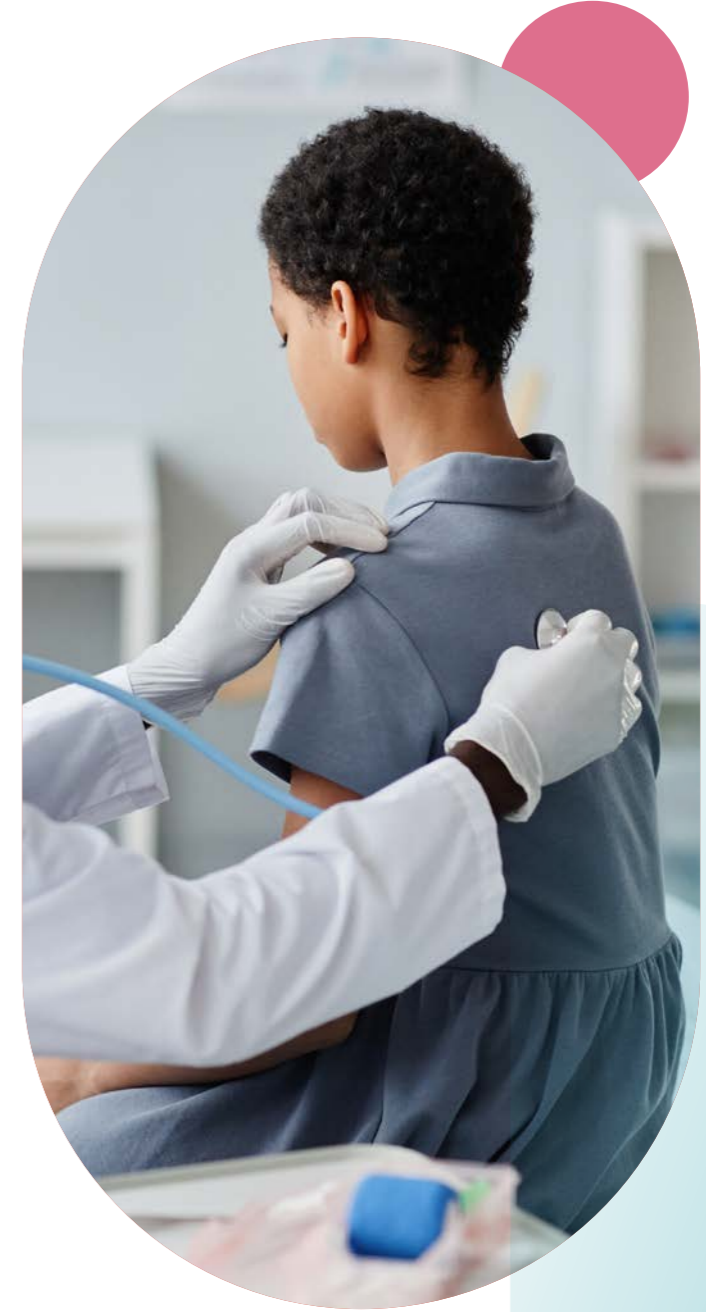
Conducting infant studies is also very important as infants are one of the most vulnerable populations affected by Ebola. In 2022 an **EBOVAC infant study** was being carried out – this is a Phase 2 study evaluating the efficacy and safety of the **EBOVAC vaccines** in infants aged 4-11 months.

PERISCOPE sniffs out whooping cough biomarkers

Vaccines have helped to cut cases of pertussis (whooping cough) worldwide. However, recent years have seen a rise in cases and the disease remains a leading cause of infant mortality around the world.

The **PERISCOPE** project is working to better understand how the currently available vaccines work, and to aid the development and licensing of the next generation of improved pertussis vaccines.

In 2022, an assay to measure cellular responses to pertussis in blood was qualified for deployment. Nasal sampling was established as a non-invasive diagnostic method and was assessed for use to measure immunity to pertussis. In 2022 a biomarker discovery platform was also established to investigate the immune system's response to pertussis.



Keeping the legacy alive

Maintaining resources and results once the funding period has finished is a challenge for most projects. A number of IMI projects have set up legacy organisations to ensure that the work started during the funding period can continue long into the future.

Non-profit set to continue IMI projects' ground-breaking diabetes work

Over the years, the **INNODIA** and **INNODIA HARVEST** projects have delivered a wealth of new knowledge on type 1 diabetes, as evidenced by numerous papers published in scientific journals. Crucially, they have also delivered a master protocol designed to facilitate and speed up the launch of clinical trials using drugs designed to arrest type 1 diabetes in those who have been diagnosed recently. Today, they are running four clinical trials of medicines designed to prevent and cure type 1 diabetes.

To ensure their legacy, the projects have established **INNODIA iVZW** (internationale vereniging zonder winst oogmerk / international non-profit association) and appointed a managing director.

At the core of **INNODIA iVZW's** work is the unique pan-European clinical trial infrastructure for type 1 diabetes that the projects have established.

Looking to the future, the organisation hopes to expand this infrastructure, especially to southern and eastern European countries which are currently underrepresented; provide expertise on smart clinical trial design; optimise the use of data and biosamples from people with, and at risk of, type 1 diabetes for biomarker analysis; and provide access to expert research and biomarker laboratories.

ENABLE-ing the early stages of antibiotic development

We urgently need new antibiotics, yet the early stages of antibiotic development are highly challenging as they require a diverse range of skills and expertise. **ENABLE** set up a successful drug discovery and development platform, and invited research groups to apply to use it for their antibiotic development programmes. In total, 23 programmes were accepted into the project, many of which reached key milestones in the drug development process.

The success of **ENABLE** prompted a group of institutes to set up the **ENABLE-2 Drug Development Platform** with funding from the Swedish government. Like **ENABLE**, **ENABLE-2** aims to move potential antibiotics through the early stages of drug development, with the hope that they will successfully 'graduate' to other initiatives that focus more on the later stages of development. A number of programmes have already been accepted into **ENABLE-2**, including one which had reached the 'lead' stage in the initial **ENABLE** project.

EQIPD for research quality

Poor quality data is an issue in many research fields – all too often, results carried out in one organisation cannot be replicated elsewhere, and it is not always clear why. In medical research, consequences include poor decision-making, resulting in higher failure rates and longer drug development times.

IMI project **EQIPD** developed the **EQIPD Quality System (EQIPD QS)**, which sets out a systematic approach to improving the quality of preclinical research data. **EQIPD** also developed a suite of tools and resources to further support researchers who want to follow best practices in this important field.

In 2022, the Guarantors of **EQIPD e.V. (GoEQIPD)** announced the formation of a registered association to provide the legal framework for future activities and ensure the preservation and further development of the legacy of the **EQIPD** project.

In addition to keeping the **EQIPD** resources up to date, **GoEQIPD** aims to oversee the **EQIPD** certification process and provide training to the research community on the generation of quality research.

GetReal Institute continues to grow

IMI projects **GetReal** and the **GetReal Initiative** developed new tools and resources to help advance the use of real-world evidence (RWE) in drug development and healthcare decision-making.

The **GetReal Institute** was set up in 2021 as a non-profit to promote the uptake of the tools and resources developed by the IMI projects and continue to advance the adoption of RWE in decision-making in Europe and beyond.

In 2022, the institute announced its 24 founding members, which include public, private, non-governmental and academic organisations, and announced the names of its first executive board members. The new institute also continued to offer a range of courses on RWE in medicine development as well as on structured benefit-risk assessments of medicinal products.



Showcasing synergies with other research programmes

A number of IMI projects have delivered results that were subsequently picked up by other projects, either within IMI or elsewhere, for further development.

European Lead Factory search uncovers potential COVID-19 treatment

The **European Lead Factory** boasts a collection of over half a million compounds and a state-of-the-art high-throughput screening centre that researchers can apply to use for their own drug discovery programmes. In the early months of the COVID-19 pandemic, the project launched a fast-track procedure to select projects focused on the new disease. They selected a proposal from the Pivot Park Screening Centre (PPSC) based in the Netherlands. The centre wanted to find compounds that would prevent the virus's spike protein from binding with the ACE2 receptor found in human throat and lung cells – the virus's main way of attack.

The search revealed over 40 compounds that represent a good starting point for further development, as they block the interaction of the virus with the ACE2 receptor without affecting the physiological function of the receptor.

The plan was to move to the next stage of drug discovery, dubbed the 'hit-to-lead' phase. This is done via the EU-funded **ISIDORE project**, which provides researchers with a portfolio of research services and resources to better prepare for future epidemic-prone pathogens.

Anti-TB drug booster highlights synergies between partnerships

Tuberculosis (TB) kills around 1.5 million people annually, making it one of the leading causes of death worldwide.

The aim of the **TRIC-TB** project is to advance the development of two molecules that could boost the infection-fighting ability of ethionamide, one of the main frontline drugs used to treat the disease.

In 2022, the project announced that it had successfully completed phase 1 clinical trials of one of the compounds, dubbed BVL-GSK098. The compound is now the subject of a phase 2a clinical trial being carried out via the **bEto-TB project**, which is funded by the European & Developing Countries Clinical Trials Partnership (**EDCTP2 programme**).

Studies highlight the potential of IMI-funded antibiotic

With antimicrobial resistance (AMR) on the rise, the hunt is on for a new class of antibiotics, i.e. one that works in a different way to existing antibiotics and so could prove lethal to bugs that are resistant to the antibiotics available today.

Enter Nosopharm, a French small and medium-sized enterprise (SME) which is on the verge of embarking on clinical trials of a new class of antibiotics that shows potential as a treatment for multi-drug resistant infections caused by bacteria defined as 'priority pathogens' by the World Health Organisation (WHO).

The new class of antibiotics is called odilorhabdins, and their early development was supported in part by the IMI project **ENABLE**, which set up a collaborative platform with the expertise and resources needed to advance the development of new antibiotics.

The work in **ENABLE** helped to refine and improve the odilorhabdins. More recently, their development has been further advanced in another IMI project, **GNA NOW**.

GNA NOW is running three antibiotic development programmes in parallel, and two are odilorhabdins – NOSO-502 and NOSO-2G.

In 2022, **GNA NOW** announced the successful completion of toxicology studies on NOSO-502 and this, combined with other results on the compound's efficacy in laboratory tests and other elements, has prompted Nosopharm to prepare an application to launch a phase 1 clinical trial. In a phase 1 trial, a drug is tested for the first time in a small group of human volunteers, with the goal of assessing its safety.



Regulatory impacts highlight PPP strength

Medicines development is necessarily a tightly regulated world, and so having an impact on the regulatory framework is a major achievement, and project outputs with regulatory approval of some kind are more likely to be taken up and used more widely in research and drug development. The key performance indicators for the IMI2 programme show that as of the end of 2022, IMI2 projects had reported 24 completed regulatory procedures (against a target of 10).

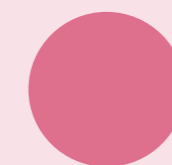
PREFER gets green light from EMA for patient preference work

Patient perspective is important in all medical research and particularly in drug development. The **PREFER** project set out to assess when and how patient preferences on benefits and risks should be incorporated into decisions on medicinal products. One of the project's core outputs is a framework for patient preference studies that covers purpose, objectives, how to design and conduct the studies, and how to interpret the results, as well as a document with points to consider when selecting the methods for carrying out a patient preference study.

In 2022, the European Medicines Agency (EMA) adopted a qualification opinion for the **PREFER** framework, endorsing it as a comprehensive reference document for planning and conducting patient preference studies (PPS).

The project published a report detailing its recommendations on when and how to best perform preferences studies and include patient preference in decision-making during the medical product life cycle. The recommendations are accompanied by an operational guidance document that consists of 9 templates for use in the development and execution of a patient preference study. The project also released a series of 16 webinars to further assist anyone who is interested in the development and execution of patient preference studies.

Finally, Working Group XI of the Council for International Organisations of Medical Sciences (CIOMS) encourages the use of the **PREFER** recommendations in its 2022 report on patient involvement in the development, regulation, and safe use of medicines.



NECESSITY's STAR shines bright

Primary Sjögren's Syndrome (pSS) is an autoimmune disease in which the immune system attacks cells in the body that secrete fluids, such as tear and salivary glands. Symptoms include itchy eyes, a dry mouth, joint and muscle pain, difficulty concentrating, and disabling fatigue. Although there are treatments to alleviate some symptoms of pSS, there is no cure. As different patients have different symptoms and respond differently to the treatments, it is very hard to assess the effectiveness of treatments. To address this, IMI project **NECESSITY** developed the Sjögren's Tool for Assessing Response (STAR) to improve the assessment of drug efficacy on all aspects of pSS.

Details of the STAR are published in [Annals of Rheumatic Diseases](#) and are freely available to the scientific community for analysis of completed and future trials.

Meanwhile, the EMA has reviewed the STAR and issued a [Letter of Support](#) for its use as a tool to improve the assessment of drug efficacy on all aspects of Sjögren's.

This recognition will facilitate the use of STAR in future academic- and industry-led clinical studies.

NECESSITY is further testing the STAR as a primary endpoint in its own trial, which will ultimately cover 300 randomised patients across 34 sites in 8 countries.

MACUSTAR study on common cause of blindness gets regulatory nod

People with age-related macular degeneration (AMD) gradually lose their central vision in both eyes. It is a leading cause of blindness, yet treatment options are extremely limited. Dry AMD, including the intermediate AMD (iAMD) stage, therefore represents a huge unmet need. One barrier to the development of new treatments is the lack of clinical endpoints capable of determining the effectiveness of treatments under development. Put simply, current tests do not detect all of the sight problems experienced by people with earlier stages of the disease (e.g., iAMD).

IMI project **MACUSTAR** was set up to develop and validate examinations that are capable of accurately detecting changes over time.

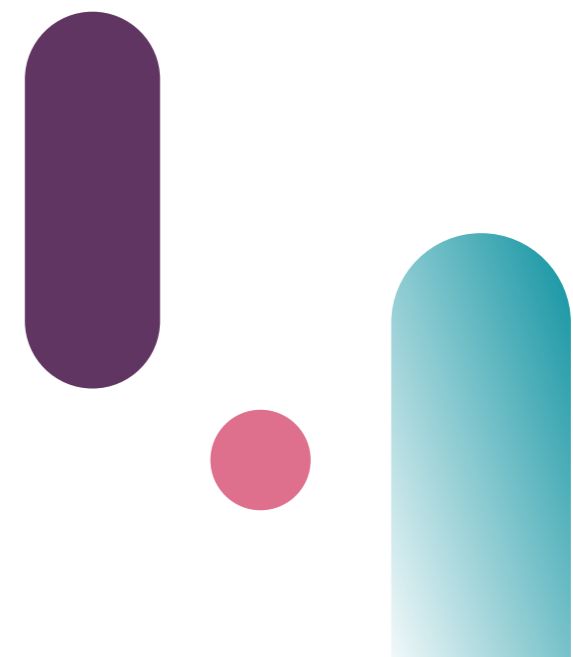
They have developed a suite of markers and measures that could be used to assess how well a potential treatment works.

Back in 2018, the European Medicines Agency (EMA) issued a first Letter of Support to **MACUSTAR** in which they endorsed the project's approach to developing and evaluating these measures. Since then, the project has completed its cross-sectional study, which assessed the ability of the measures to discriminate between patients with different stages of AMD.

The results of the cross-sectional study were promising, and EMA has now provided positive feedback on the results in a [second Letter of Support](#). In their statement, the EMA broadly supports the project's interpretation of the results and encourages the ongoing validation of the measures.

The project is still busy with the longitudinal study part of the project involving 700 people to assess the progression of AMD to late-stage AMD. Once the longitudinal data is captured, the project will again submit the results to the EMA for further scrutiny.

Regulatory feedback is important for projects like **MACUSTAR**, as this increases the likelihood of the project's biomarkers and endpoints being accepted for use in future interventional clinical trials for new AMD treatments. Ultimately, the project will therefore facilitate the development and testing of new treatments for AMD.



EHDEN data partners picked up by major EMA data network

In 2022, the EMA and the European Medicines Regulatory Network set up a coordination centre to provide timely and reliable evidence on the use, safety, and effectiveness of medicines, including vaccines, from real-world healthcare databases across the EU. Dubbed **DARWIN EU** (Data Analysis and Real World Interrogation Network) the centre is tasked with delivering real-world evidence from across Europe on diseases, populations, and the uses and performance of medicines. It is also an early flagship 'pathfinder' for the European Health Data Space.

Key to the success of **DARWIN EU** is the availability of data partners who can generate the real-world evidence needed for scientific evaluations and regulatory decision-making.

The first data partners were announced in 2022, and many are already data partners in the IMI project **EHDEN**, which is building a pan-European federated data network. **EHDEN** ensured the data partners' data was mapped to a common data model, and this in turn made those organisations suitable data partners for **DARWIN EU**.



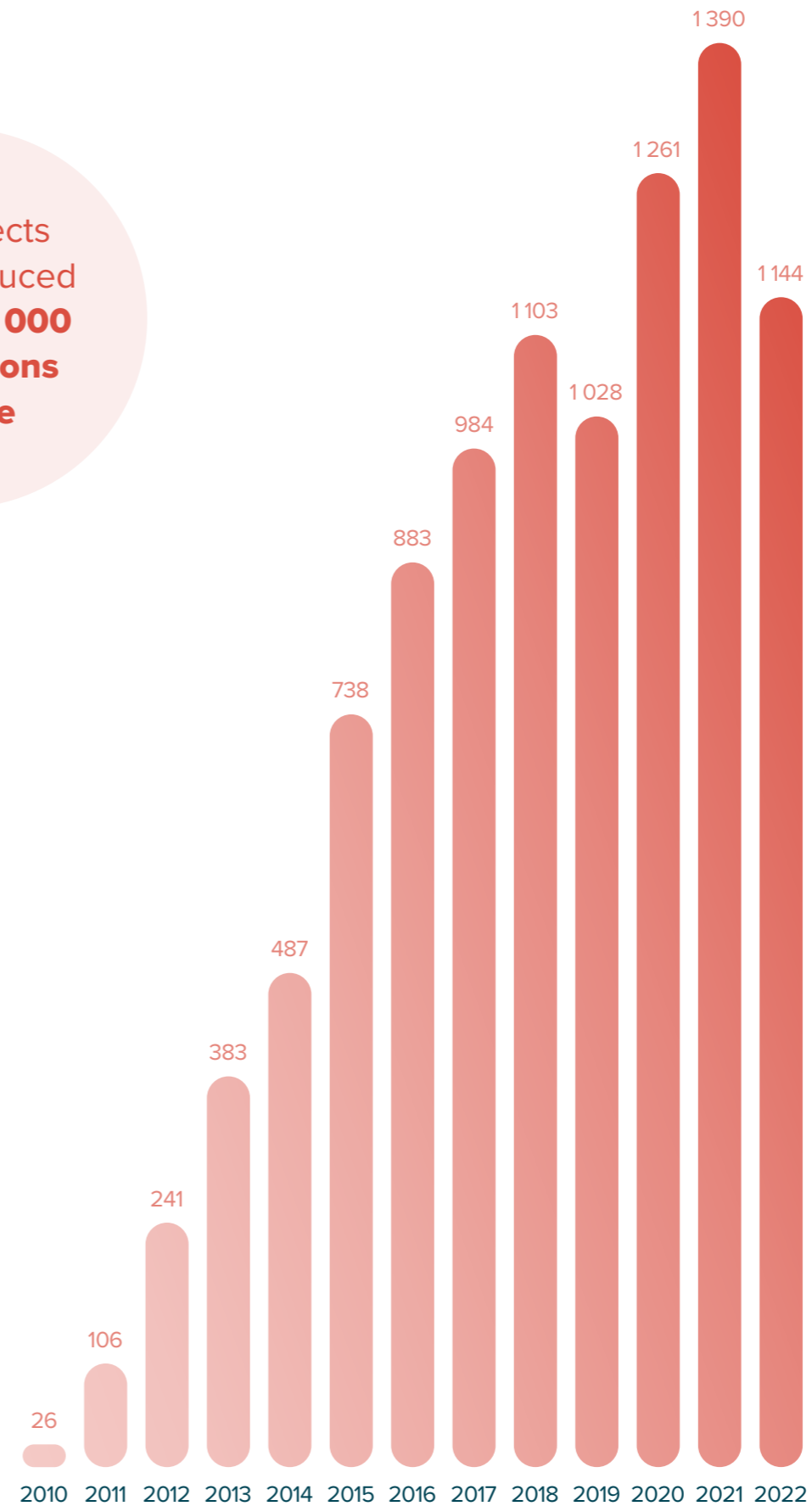
Project dissemination

IMI projects have produced almost 10 000 scientific papers, and their quality matches their quantity, with many papers achieving high citation rates. Peer-reviewed papers are the gold standard of the scientific world, and these figures show that **IMI-backed research is contributing significantly to expanding our knowledge base of innovative medicines and health.**

The figures are especially impressive because, prior to IMI's inception, concerns were raised by academic institutions that working with industry would hamper their ability to publish scientific papers on project results. IMI's high number of publications published in respected journals each year disproves that theory and shows that **research has advanced through collaborative efforts.**

In 2022 IMI projects generated 1 144 publications. In the past 5 years, IMI publications have surpassed the bar of 1 000 publications registered each year with an average of 1 185 publications per year.

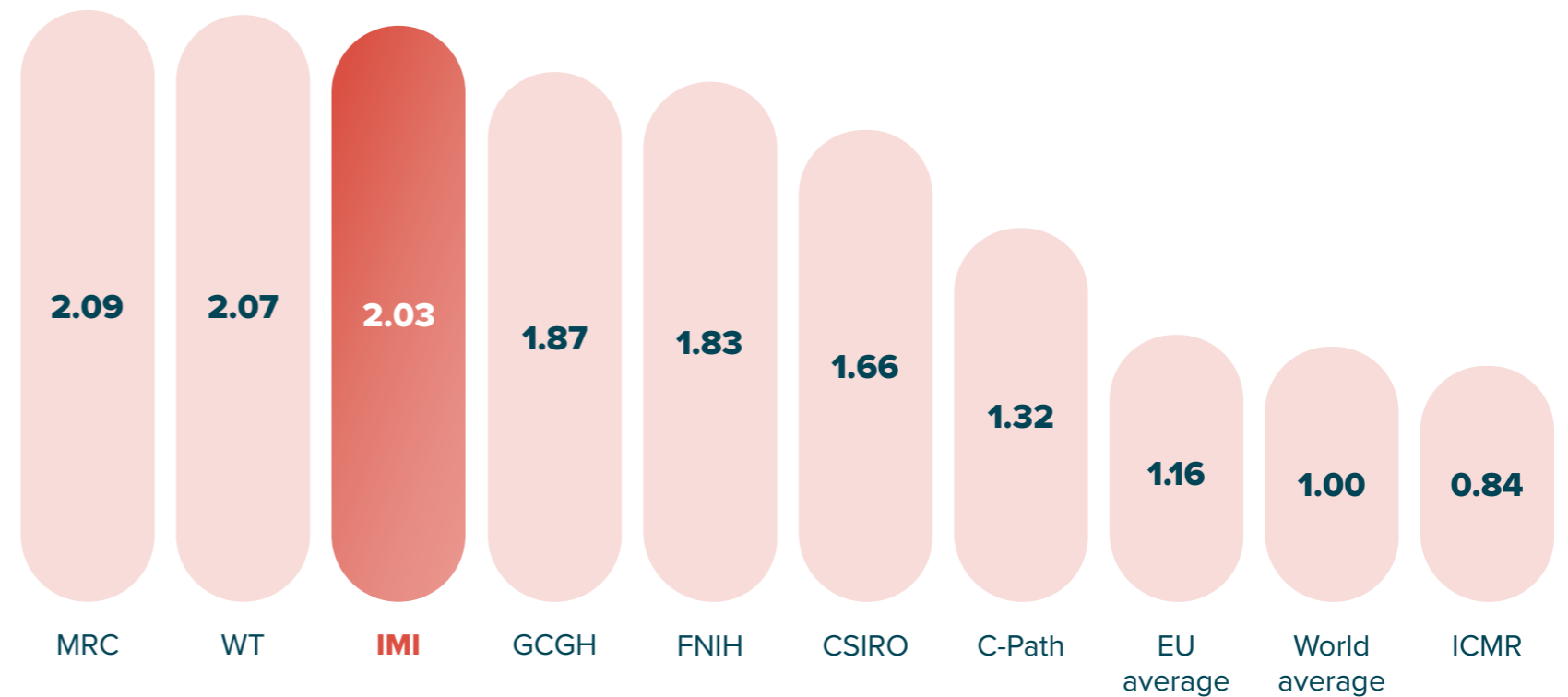
IMI projects have produced almost **10 000 publications to date**



Total number of publications 2010 to 2022 = 9 784

The citation impact of IMI research is higher than the EU and world averages

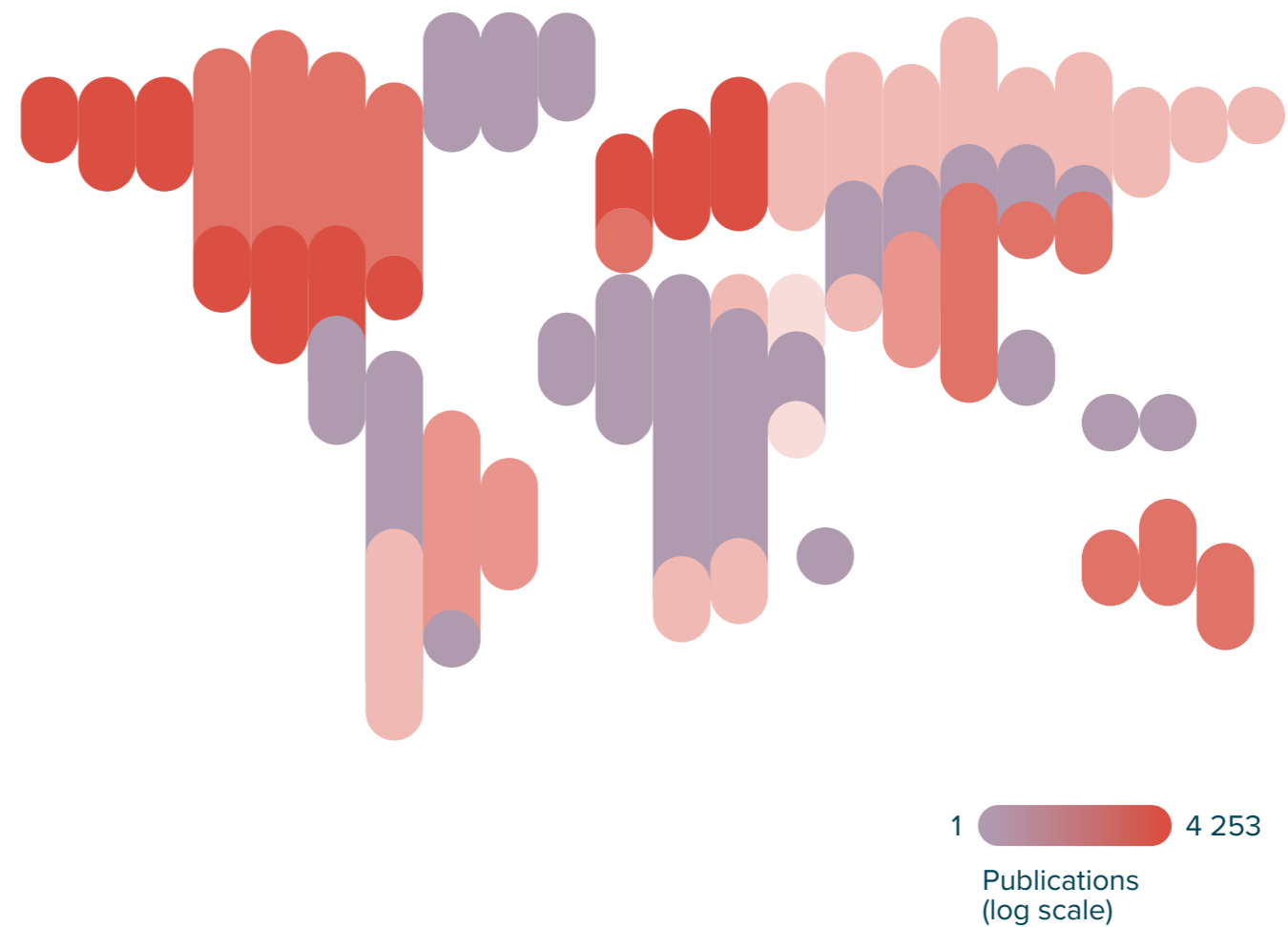
The citation impact of all IMI papers is 2.03, which is twice the world average (set as a baseline of 1) and a lot higher than the EU average (1.16). Furthermore, around a quarter (24.6%) of IMI project papers are highly cited, meaning the papers are in the world's top 10% of papers when ranked by number of citations (taking journal category and year of publication into account). IMI also compares favourably with similar organisations such as the Medical Research Council (MRC), the Wellcome Trust, and the Grand Challenges in Global Health (GCGH). This is similar to the result in previous years and shows that **IMI is maintaining a high standard even as its output increases.**



Citation Impact (Field Normalised)

Quick facts on IMI's publications

- ❑ **24.6% of papers from IMI projects are 'highly cited'**, meaning they are in the top 10% of papers by journal category and year of publication.
- ❑ **IMI projects have published in 1 681 journals to date**, and the average journal impact factor (JIF) for IMI research is 7.53.
- ❑ **IMI's 2022 papers had a larger impact (2.10) than IMI's 2021 papers (1.98)** as measured by the field-normalised citation impact, which demonstrates increasing research impact.
- ❑ **Journals with a particularly high impact factor that have published IMI research** include the Lancet (and other Lancet Journals e.g., Lancet Respiratory Medicine and Lancet Microbe), New England Journal of Medicine, Journal of the American Medical Association (JAMA), Nature (and other Nature journals e.g., Nature Molecular Cell Biology, Nature Reviews Drug Discovery, Nature Immunology, Nature Medicine), and the British Medical Journal (BMJ).
- ❑ **The internationally collaborative nature of IMI is reflected in the authorship of the papers**, with over half of papers recording authors from more than one country.



The scale shows countries having from 1 publication to 4 253 publications (the UK being at the top end with 4 253 publications).

IMI research is highly collaborative

Two-thirds (67%) of all IMI project papers were published by **co-authors working in different sectors.**

Single-sector
33% of all papers



Cross-sector
67% of all papers

The majority (86%) of IMI project papers involved **collaboration between different institutions.**

Single-institution
14% of all papers



Cross-institution
86% of all papers

More than half (65%) of all IMI project papers involved **international collaboration.**

Domestic
35% of all papers



International
65% of all papers

Hot publications in 2022

Hot publications are those that received enough citations to place in the top 0.1% of papers in their research field.

Remdesivir, Molnupiravir and Nirmatrelvir remain active against SARS-CoV-2 Omicron and other variants of concern

Remdesivir, Molnupiravir, and Nirmatrelvir are antivirals that were used during the pandemic to help prevent patients with mild to moderate COVID-19 symptoms from progressing to severe forms of the disease. **Under the CARE project, the impact of these antivirals against the Omicron variant and other variants of concern was assessed, and the main finding was that these treatments remained effective.**

Citation: Vangeel, Laura *et al.* (2022) *Remdesivir, Molnupiravir and Nirmatrelvir remain active against SARS-CoV-2 Omicron and other variants of concern*, *Antiviral Research* 198: n/a

Mapping genomic loci implicates genes and synaptic biology in schizophrenia

In a two-stage study that involved assessing the genomes of almost eighty thousand individuals, **this paper found commonalities at 287 different points on the gene chromosomes.** Schizophrenia is 60-80% heritable, and the work identified 120 genes (106 of which were protein-coding) that were likely to underpin associations at some of those loci.

Citation: Trubetskoy, Vassily *et al.* (2022) *Mapping genomic loci implicates genes and synaptic biology in schizophrenia*, *Nature* 604: 502

Amelioration of Alzheimer's disease pathology by mitophagy inducers identified via machine learning and a cross-species workflow

Alzheimer's disease has been linked to an impairment in the removal mechanisms of old and dysfunctional mitochondria from the cell. **The DRAGON project used machine learning to find and describe those molecules that induce the removal of dysfunctional mitochondria, and successfully identified 18 small molecules, two of which were powerful inducers.** The paper's findings suggested that the memory loss that is characteristic of Alzheimer's is driven by faulty mitochondrial removal.

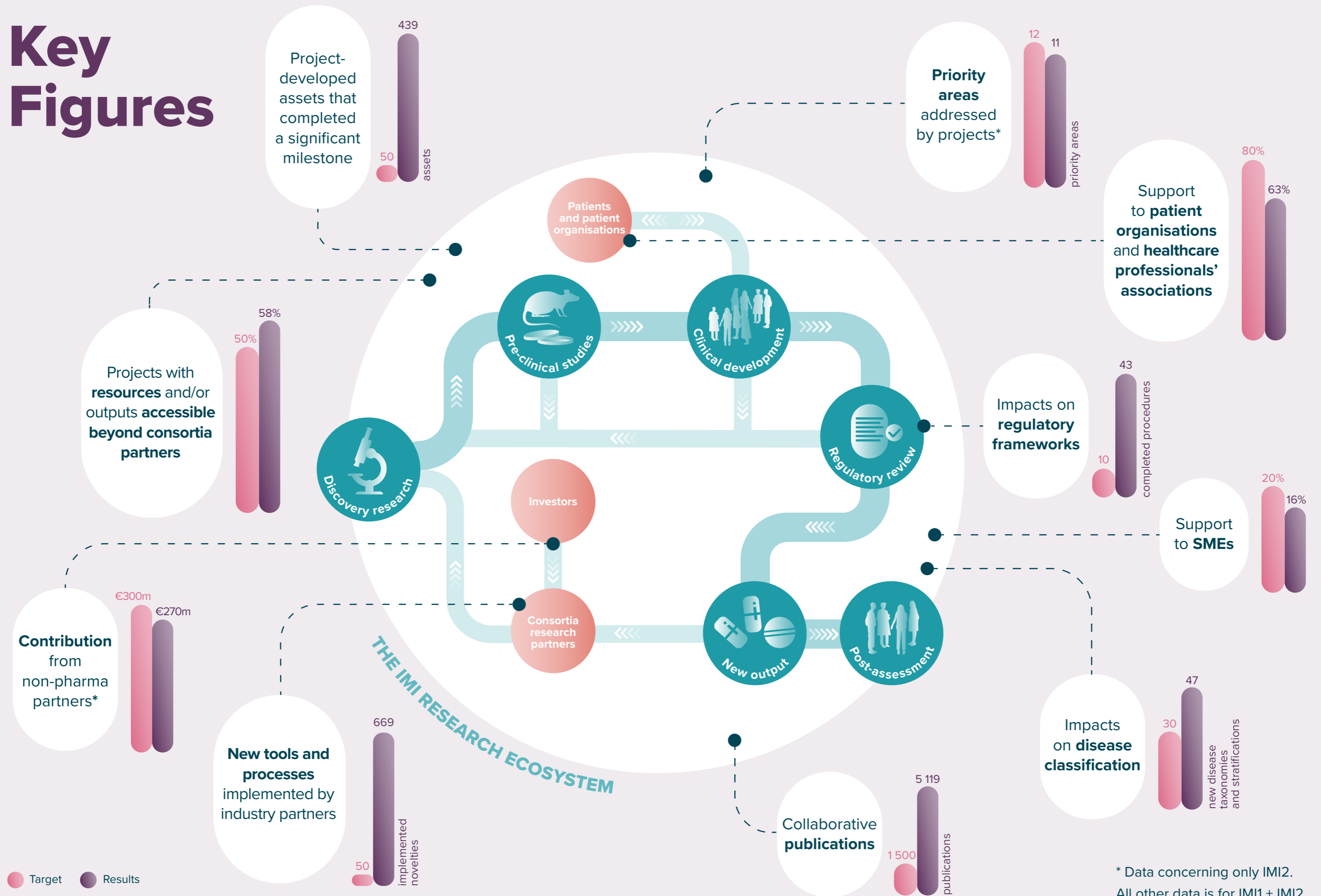
Citation: Xie, Chenglong *et al.* (2022) *Amelioration of Alzheimer's disease pathology by mitophagy inducers identified via machine learning and a cross-species workflow*, *Nature Biomedical Engineering* 6:76

Second Revision of the International Staging System (R2-ISS) for Overall Survival in Multiple Myeloma: A European Myeloma Network (EMN) Report Within the HARMONY Project

Multiple myeloma (MM) is a disease that can have a range of outcomes and has survival rates ranging from few months to more than a decade. **In 2015, the Revised International Staging System (R-ISS) was introduced to develop a robust prognostic system on the basis of widely available biomarkers and is now considered a standard risk stratification model for patients with newly diagnosed multiple myeloma (NDMM).** The R2-ISS system was developed by the IMI-funded HARMONY project to improve the stratification of patients further. Compared with the original R-ISS, the R2-ISS can be easily updated with new factors as they emerge.

Citation: D'Agostino, Mattia *et al.* (2022) *Second Revision of the International Staging System (R2-ISS) for Overall Survival in Multiple Myeloma: A European Myeloma Network (EMN) Report Within the HARMONY Project*, *Journal of Clinical Oncology* 40: 3406.

Key Figures



* Data concerning only IMI2. All other data is for IMI1 + IMI2.

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