

HEAL ITALIA

Health **E**xtended **A**lliance for **I**nnovative **T**herapies,
Advanced **L**ab-research, and **I**ntegrated **A**pproaches
of Precision Medicine

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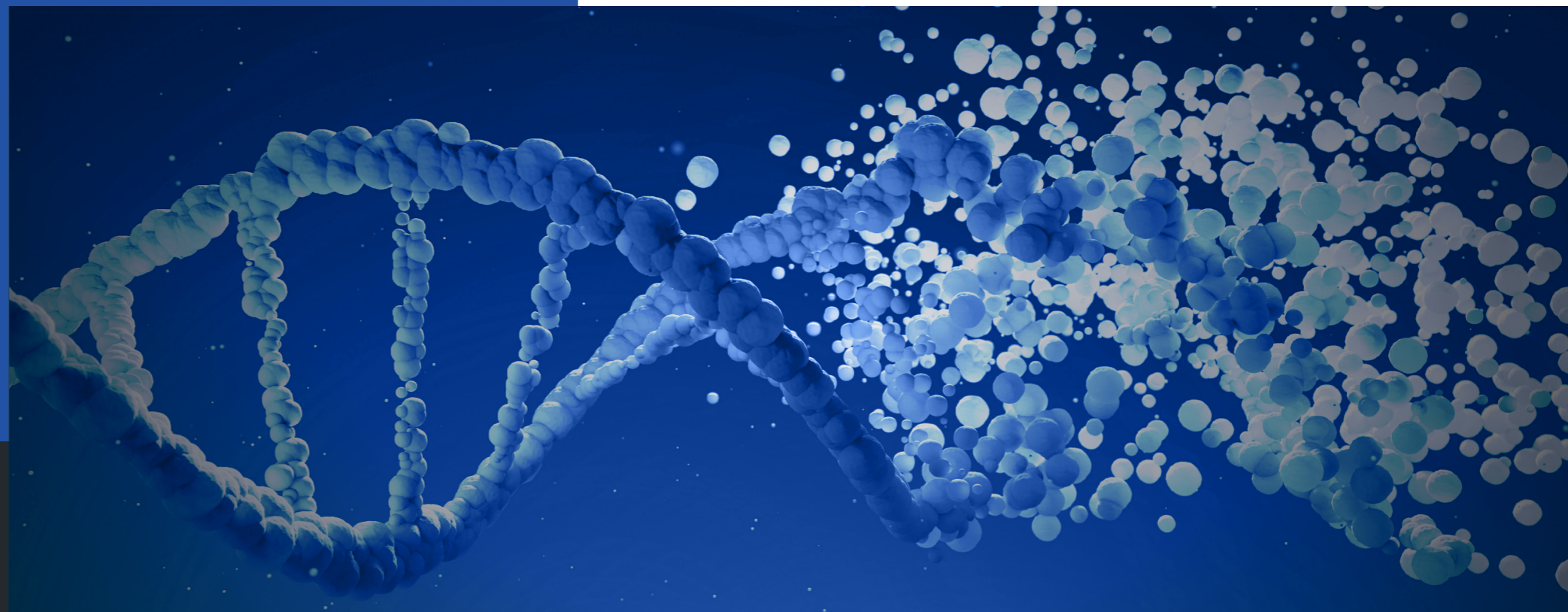
ABOUT HEAL ITALIA

HEAL Italia represents the first Italian Foundation that coordinates a qualified multidisciplinary network of Universities, IRCCS and Companies, scientists, technologists and young researchers who share knowledge, research and innovative technologies in order to bring our National Health System into the contemporary era of Medicine of Precision through new methods, new services and above all an important network of clinical data to support translational research for advanced diagnoses and therapies in the fight against cancer and cardiovascular, metabolic and rare diseases.

Heal Italia foundation is the first national supply chain dedicated to research and innovation in the field of Precision Medicine. The initiative is part of one of the 14 extended partnerships envisaged by the Pnrr in the context of Mission 4 Component 2 'From Research to Business', with the aim of investing in innovation poles to strengthen research chains at national level and promote their participation in European and global strategic value chains.

The Heal Italia (Health Extended Alliance for Innovative Therapies, Advanced Lab-research, and Integrated Approaches of Precision Medicine) project was presented by the University of Palermo, as the proponent, together with 11 other universities, the Istituto Superiore di Healthcare, five Scientific Research and Treatment Institutes, six companies and a research foundation, and represents the first national network of scientists, technologists and young researchers who develop knowledge and innovative technologies in order to bring the National Health System into the era of Precision Medicine through new methods, new services and a network of clinical data to support translational research for advanced diagnoses and therapies in the fight against cancer and cardiovascular, metabolic and rare diseases.

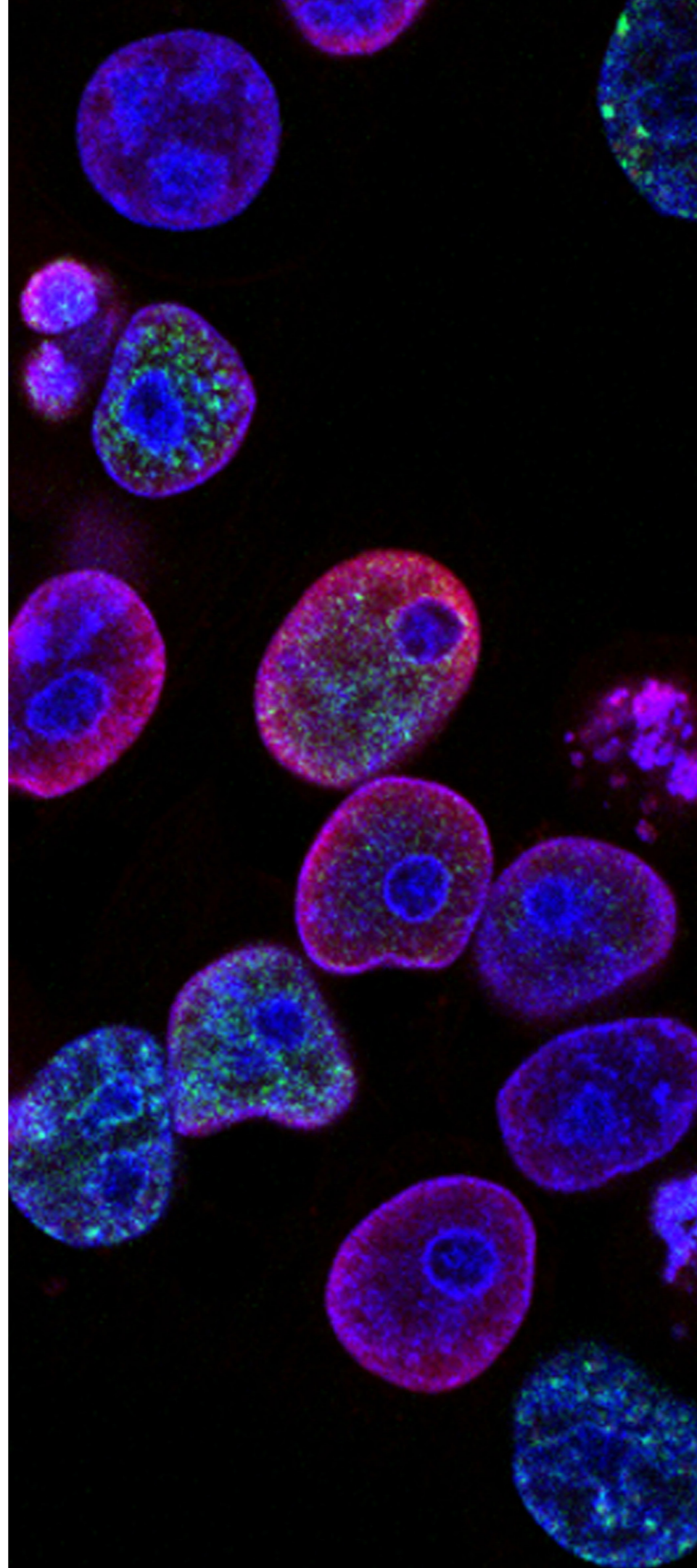
Overall, the research team is made up of 350 researchers belonging to the project partners and will be further strengthened with the recruitment of more than one hundred new researchers and the training of over one hundred PhD students.



OUR VISION

The HEAL ITALIA Program is conceived with an interdisciplinary holistic vision, which combines fundamental and translational research with technology transfer, leveraging the capabilities of key players in the academic, clinical and private sectors. With a One Health approach, HEAL ITALIA coordinates a team made up of 350 researchers from 25 public and private institutions divided into multi-regional and multidisciplinary groups and 8 inter-regional networks covering all areas of interest in the fight against cancer (from research on omics sciences, to new technologies for early diagnosis, the repositioning of drugs, new protocols for primary, secondary and tertiary prevention, new clinical protocols for radiotherapy treatments, etc.) with the participation of more established scientists operating for the first time within the same mother-network. The goal is not research per se but to bring solutions and innovative therapies to the patient's bedside and allow the citizen to discover the pathology as soon as possible and treat it in the best possible way and offer the health system solutions that are useful for the daily management of services (early diagnoses also through the reduction of waiting lists, territorial services that continuously support the taking charge of the patient. The definition of the factors that determine the development and progression of distinct diseases in individual patients is allowing Precision Medicine to progressively reach a variety of clinical settings that combine precision diagnostics with targeted therapies. Applied to all medical disciplines, this approach allows the NHS to generate safer and more effective individual approaches in areas such as, for example, precision surgery and precision radiotherapy.

HEAL ITALIA wants to consolidate and innovate the results achieved in oncology and govern further emerging contexts, promoting basic research that generates approaches to prevention, screening, risk stratification, early diagnosis and personalized precision therapies for the recently defined disease phenotypes. The originality of the project is based on the analysis of prospective observational cohort studies (started since 2005) of a large normal and healthy population that is slowly progressing towards distinct diseases, to perform a large multiomic screening in order to identify relevant factors for the progression, or protection, against specific diseases. Understanding the molecular mechanisms underlying these factors will allow their use as biomarkers, patient stratification, preventive approaches and will form the basis for the development of innovative drugs and therefore for therapeutic intervention. To realize this



vision, HEAL ITALIA has been ambitiously organized into 8 thematic biomedical research spokes generating a workflow from data acquisition and model development, to precision diagnostics, innovative therapies and prevention strategies, to finally generate a clinical tool based on new devices and technologies. The strongly interconnected spokes are directing their results towards various pathologies, such as cancer, cardiovascular, metabolic and rare diseases, with the long-term vision of satisfying the right of every person to receive effective health services in a homogeneous way, personalized and sustainable, respecting privacy and data protection, for the benefit of the entire community.

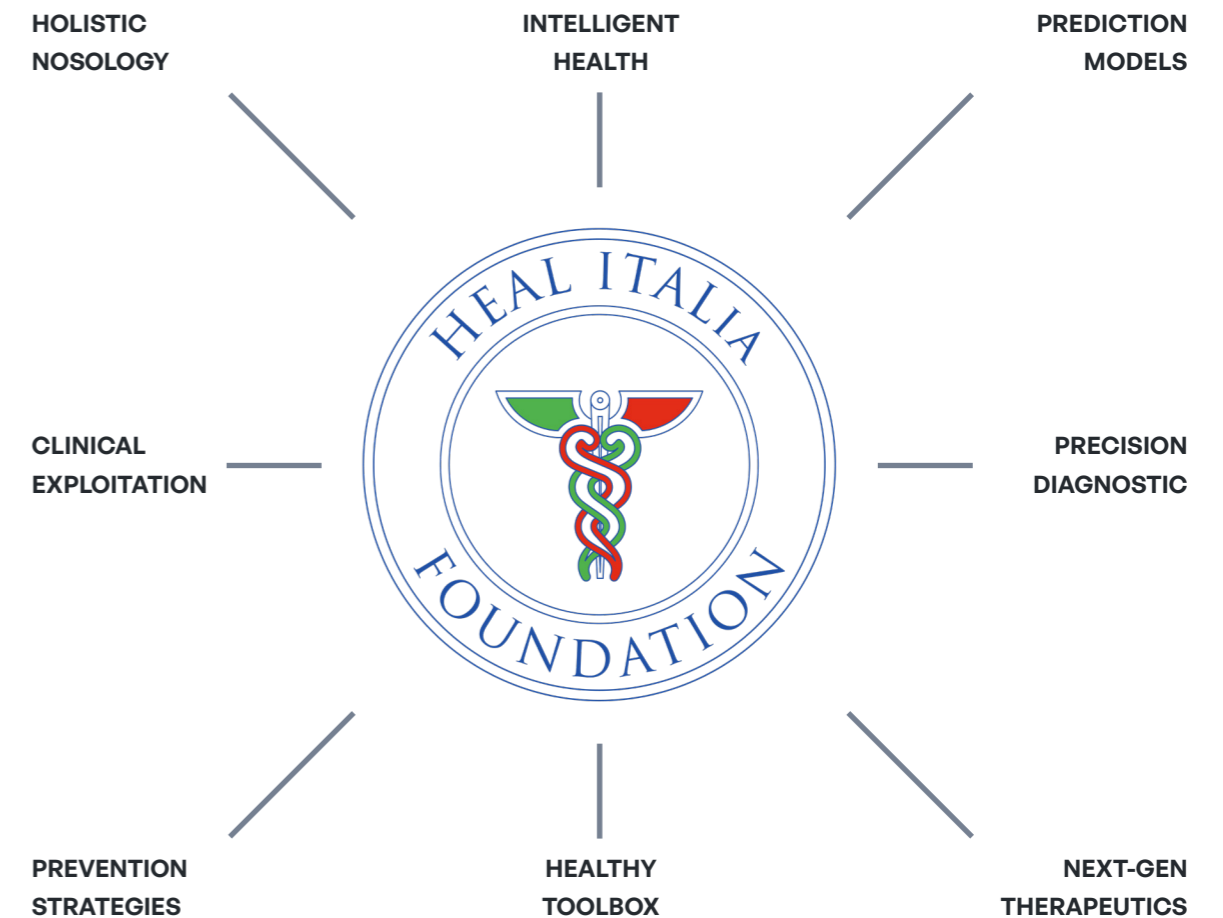
Complex diseases, including monogenic diseases (rare diseases), polygenic diseases (cardiovascular and metabolic diseases) and cancer are the leading causes of mortality worldwide, for which the incidence and mortality rate are estimated to increase in next decades. The complexity and etiopathogenetic and prognostic heterogeneity of pathologies make it imperative to apply precision medicine, which addresses individualized pathways for diagnosis and treatment, in order to obtain an optimal clinical result. Therefore, it is crucial to study the molecular mechanisms that link these diseases together, identifying potentially prognostic and pathogenic disease biomarkers to develop innovative strategies for personalized measures of prevention, prediction, diagnosis, monitoring and for precision therapeutic planning, for individuals at risk of developing and affected by these disorders.

Our network project aims to identify and reduce inequalities (extremely large between Northern and Southern Italy), developing an interregional collaboration roadmap to define evidence-based pathways that are easily usable in clinical practice. The overall goal of the project is to provide new, cost-effective, evidence-based predictive and non-invasive diagnostic pathways for faster, earlier, more accurate, accessible and cost-effective prediction, detection and monitoring of monogenic diseases (rare), polygenic (cardiovascular and metabolic) and cancer, as well as to identify innovative and effective therapeutic approaches. The project aims to build permanent thematic networks functional to research in the field of precision medicine:

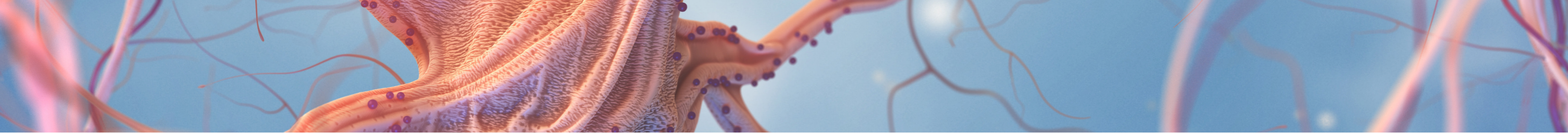
TARGET AREAS

- a nationally controlled system of biobanks able to process the material and the dataset in a homogeneous way, including the collection of diagnostic images according to standardized protocols, and to allow the realization of prospective studies for the identification of prognostic biomarkers, the screening of off-label drugs and disease risk prevention. off-label drug screening and disease risk prevention. Within the system, omics technologies such as metabolomics, lipidomics and proteomics will be developed which, together with the application of systems biology, will allow the definition of prognostic and therapeutic profiles for precision medicine;
- open and competitive access to cell factories and high-quality preclinical research infrastructures to support and evaluate the quality of the activities of precision medicine scientists;
- construction of a platform with a common computer language that can facilitate access to clinical practice to the genetic information obtained in the context of characterizing the profile of individual patients.
- realization of the process of transferring the results deriving from translational scientific and technological research to the markets.

These networks will last over time and therefore, at the end of the three-year investment period, the results of the HEAL ITALIA program will have an impact on society in all sectors (academic, clinical, entrepreneurial, national health system) involved in its implementation which will lead to networks system above. The specific objectives of the project are divided into distinct branches, highly interconnected both at a technical and translational level, which aim at all the pathologies investigated.



TARGET AREAS	SKILLS AND TRAINING FACILITY
<p>New Omic Technologies</p>	<ul style="list-style-type: none"> -Big Data and HPC for Genomics -Design of clinical trials in patients with different types of cancer -Genomics and Artificial Intelligence -Genetics, Genomics and Bioinformatics -New Omic Technologies for the study of Chronic pathologies and transfer into clinical practice

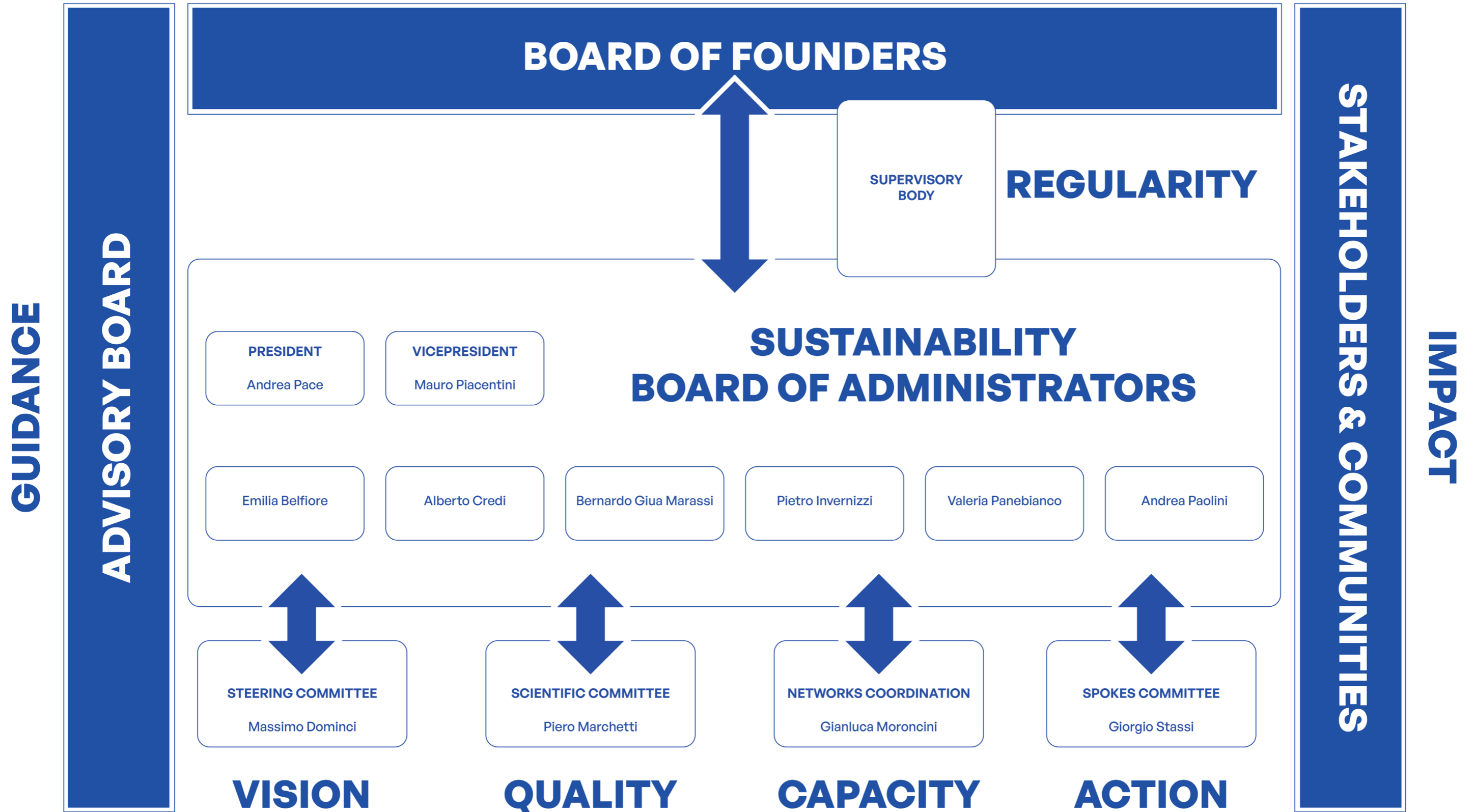


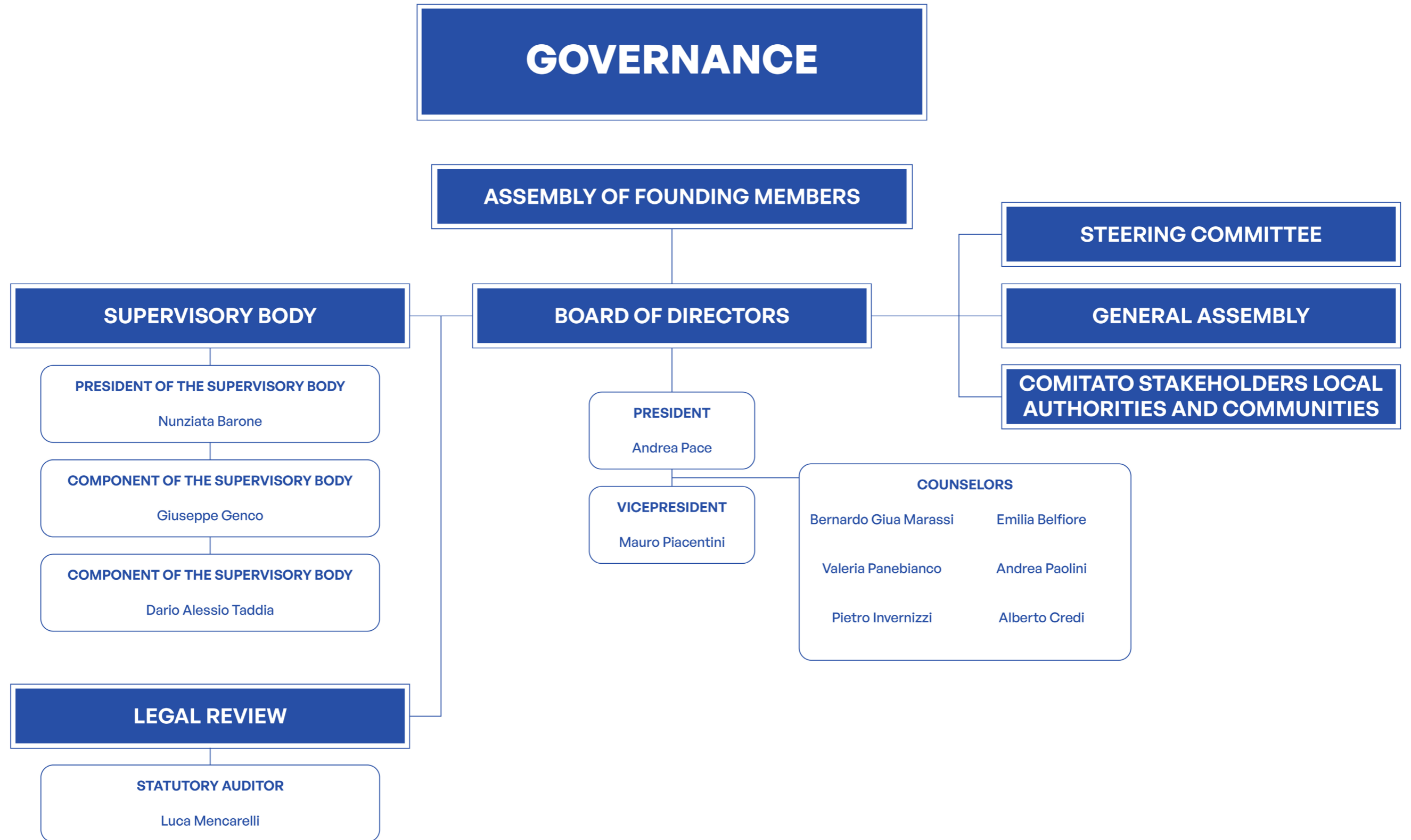
Digital Health Big Data, Analytics, Supercalculation for Precision Medicine	<ul style="list-style-type: none">-Data management and development of advanced methods, algorithms and machine learning approaches integrating healthcare big data for precision medicine.-Data platform and functional analysis for learning of the swarm, a decentralized machine learning approach for further accelerate the introduction of precision medicine in the clinic.-Development of new and innovative computational models and frameworks multipurpose artificial intelligence tools, compatible with the data and integrating multi-level data (biological, imaging and clinical data) for precision medicine to predict disease diagnosis, regulate cellular functions and fate through both proteolytic and non-proteolytic actions and by influencing the response of the individual patient.
Virtual and augmented reality	Simulate clinical procedures, infrastructure and device management
Robotics 4.0.	<ul style="list-style-type: none">-Progettazione di tecniche di IA per la realtà aumentata in chirurgia robotica-Dispositivi dedicati alla terapia attraverso la chirurgia di precisione: sviluppo di materiali e strumentazione di imaging avanzata, nonché soluzioni software e hardware per la robotica, il tutto nell'ottica di una chirurgia minimamente invasiva più efficiente e incentrata sul paziente.
Translational medicine	Methods and processes for technology transfer in the clinical field thanks to the HEAL ITALIA Network.

Innovative therapies	<ul style="list-style-type: none">-Design and management of computational platforms for drugs and innovative therapeutic approaches for precision medicine.-Development of materials and instrumentation for precision therapy: Development of new scaffolds, implants and nanostructures for regenerative medicine; fabrication and validation of prototypes for flash radiotherapy, a revolutionary new technique for treating cancer.-Development of therapeutic devices characterized by materials of nanometric dimensions: through the whole chain that goes from rational design to synthesis, characterization and validation in preclinical models.-Development of intelligent drug delivery systems and responsive nanotherapeutic agents to target diseases ranging from cancer to rare diseases. In this context, a standardized approach to health technology assessment will guide the introduction of such technologies into clinical practice.
Management and Business Intelligence for Precision Medicine	<p>Design, coordination and management of complex projects in the Life Sciences field using PNRR, PON, PNC, SIE Funds 2021/2027 tools.</p> <p>Design of advanced training courses for new skills in the field of precision medicine aimed at:</p> <ul style="list-style-type: none">-New researchers recruited-Students and PhD students-Doctors and health personnel-Professionals, Managers-Healthcare companies-PMI-Technology Transfer Centers

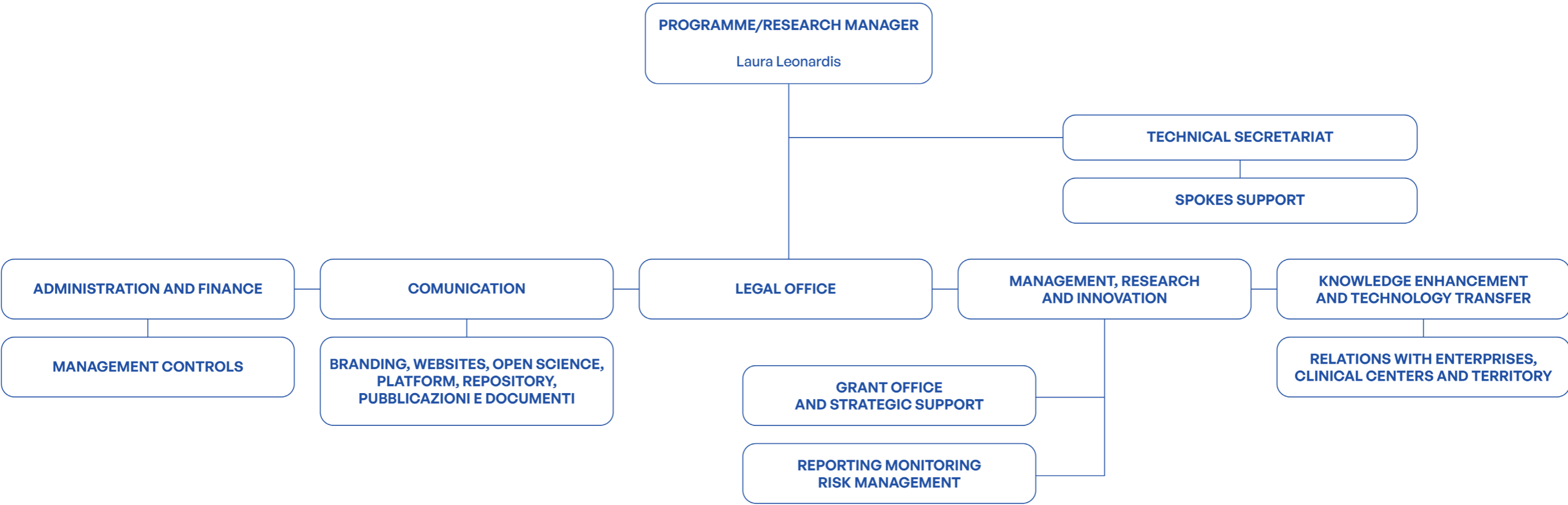
ORGANIZATION CHART

DECISION

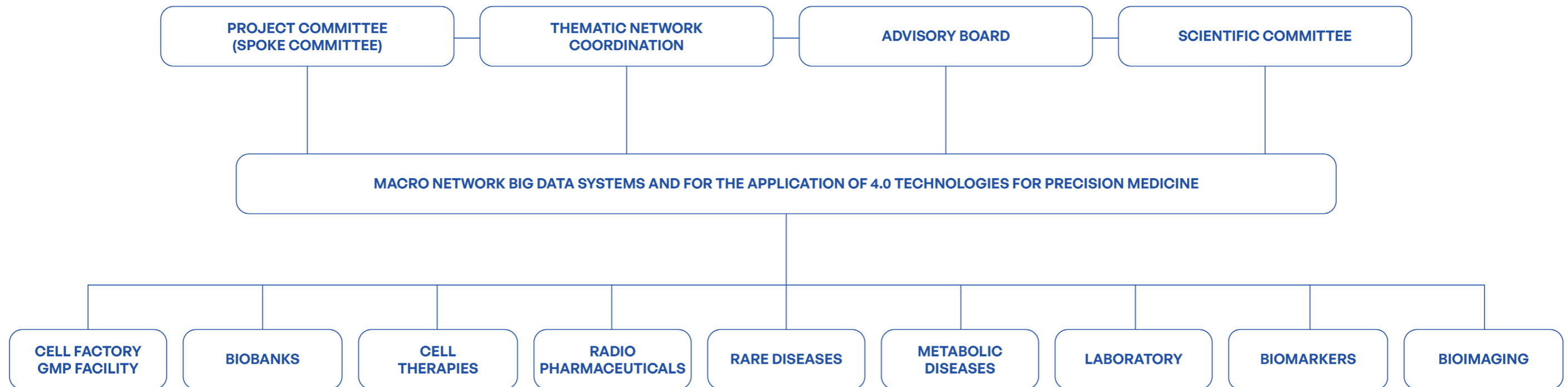




OPERATIONAL MANAGEMENT



SCIENTIFIC ACTIVITY



A DIFFUSE NATIONAL PARTNERSHIP

25 INTERSECTORAL ENTITIES



UNIROMA 2



UNICT



UNICA



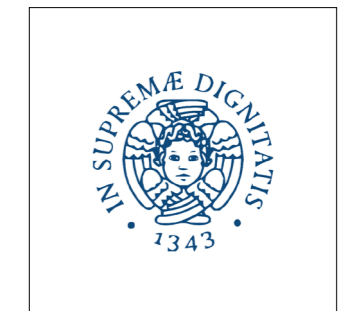
UNIPA



UNIFG



UNIMORE



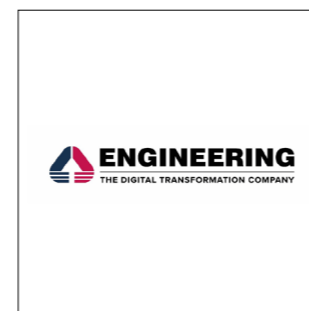
UNIFI



UNIBO



CONSORZIO BI-REX



ENGINEERING SPA



UNIVR



UNIMB



UNIVPM



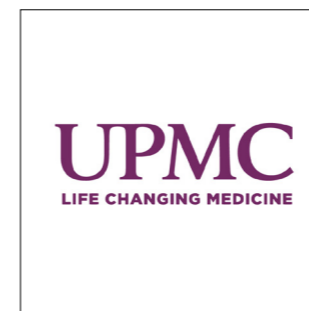
TOSCANA LIFE SCIENCES



AOSP S. ORSOLA BO



CRO AVIANO



UPCM



MARIO NEGRI



SANOFI



IFO



ISS



IOM



NEUROMED



UNIROMA 1



SIT

SPOKE 1
OMICS



1. HOLISTIC NOSOLOGY

From patients to molecules and back: mapping the omic landscape of clinical to molecular environment, to identify, classify, and refine the phenotypes of multifactorial diseases;

GENERAL OBJECTIVE: Mapping the omics landscape of clinical to molecular environment, Spoke 1 will define the molecular markers predictors of adverse or protective events underlying the molecular mechanisms of multifactorial diseases, which will offer potential novel therapeutic targets and clusters of prognostic factors.

Referent: Prof. Gennaro Melino

Leader Institution: University of Rome Tor Vergata

SPOKE 2
DATA



2. INTELLIGENT HEALTH

Health Data Science: Data management and development of advanced methods, algorithms, and machine learning approaches integrating health big data;

GENERAL OBJECTIVE: Through an efficient data management and development of advanced methods, algorithms, and machine learning approaches integrating health big data, Spoke 2 will establish a model of a collaborative data and analysis platform in full compliance with the Italian privacy legislation for enabling the processing of predictive computer models on large volumes of digital heterogeneous data, opening new avenues for modern healthcare and personalized medicine.

Referent: Prof. Stefano Diciotti

Leader Institution: Alma Mater Studiorum University of Bologna

SPOKE 3
MODELS



3. PREDICTION MODELS

Advanced prediction models for prognosis and therapeutic response based on comprehensive data treatment;

GENERAL OBJECTIVE: Spoke 3 will develop advanced computational and animal models recapitulating the complex evolution of a cell even following an action of an external agent including compounds and radiation, which will support clinical decisions for the management of patients affected by monogenic and polygenic diseases including those dependent from specific mutations, and cancer, thus avoiding radiation toxicity to resistant patients and reducing the treatment costs.

Referent: Prof. Giorgio Stassi

Leader Institution: University of Palermo

SPOKE 4
DIAGNOSIS



4. PRECISION DIAGNOSTICS

Precision medicine integrating clinic and imaging biomarkers for a high precise in space and time diagnosis;

GENERAL OBJECTIVE: Implementing the computational tools in the clinical practice supported by the integrated analysis of digital data including bioimaging, omics and data derived from medical devices, performed using computational tools (AI and network medicine), Spoke 4 will deliver new, cost-effective, evidence-based, predictive risk-based and non-invasive diagnostic pathways for faster, earlier, more precise, accessible, and affordable early detection and screening of mono- and polygenic diseases and cancer.

Referent: Prof. Andrea Isidori

Leader Institution: Sapienza University of Rome

SPOKE 5
THERAPY



5. NEXT-GEN THERAPEUTICS

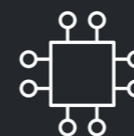
From silico to bedside: design and validation of innovative tailored and personalized therapeutic strategies;

GENERAL OBJECTIVE: Validating new targets and therapeutic effectors, determining the cellular and molecular targets and completing the analysis in pre-clinical settings, spoke 5 will define the drug candidate and drug action mechanisms at the cellular and molecular level, establishing reproducible and quick pipelines for the preclinical validation of innovative therapies against monogenic, polygenic diseases and cancer.

Referent: Prof.ssa Francesca Granucci

Leader Institution: University of Milano-Bicocca

SPOKE 6
DEVICES



6. HEALTHY TOOLBOX

Development of innovative devices for precision diagnosis and personalized therapy;

GENERAL OBJECTIVE: Spoke 6 will develop a technological toolbox of devices for applications both in precision diagnostics including biosensors, electronic and optical devices, integrated with microfluidics, and therapy such as robotic systems and development of nanotherapeutic agents for minimally invasive treatment, design and fabrication of strategies to selectively direct a drug towards a specific organ or tissue or cellular system, and to obtain the release/maintenance of the therapeutic agent at the target site for an extended period.

Referent: Proff. Massimo Dominici and Augusto Carlo Bortolotti

Leader Institution: University of Modena and Reggio Emilia

SPOKE 7
PREVENTION



7. PREVENTION STRATEGIES

Integrated and gender medicine approaches for prevention strategies based on environmental, lifestyle and clinical biometric data;

GENERAL OBJECTIVE: Spoke 7 aims at predicting more accurately which prevention strategies/interventions for a particular disease will work in which groups of people and will assist in establishing public health recommendations for specific subgroups based on phenotype, genotype and the exposome. The proposed research aims at identifying determinants of the individual risk to develop diseases with a high impact on the health status of a population, such as cardiovascular, cancer, or endocrine-metabolic diseases.

Referent: Prof. Gianluca Moroncini

Leader Institution: Politechnic University of Marche

SPOKE 8
CLINICAL



8. CLINICAL EXPLOITATION

Clinical validation and implementation of innovative predictive, preventive, diagnostic and therapeutic precision medicine approaches, based on established or emerging molecular and clinical phenotyping and AI-driven decision-making protocols.

GENERAL OBJECTIVE: This spoke aims on the clinical validation and implementation of precision medicine approaches, mainly based on data currently available in the participating centers or being generated by the applicants in this Spoke, and with readiness to exchange and apply emerging knowledge by interactions with all other Spokes.

Referent: Proff. Piero Marchetti e Chiara Cremolini

Leader Institution: University of Pisa

1 NATIONAL PHD PROGRAM WITH ADDITIONAL UNIVERSITIES AND PARTNERS

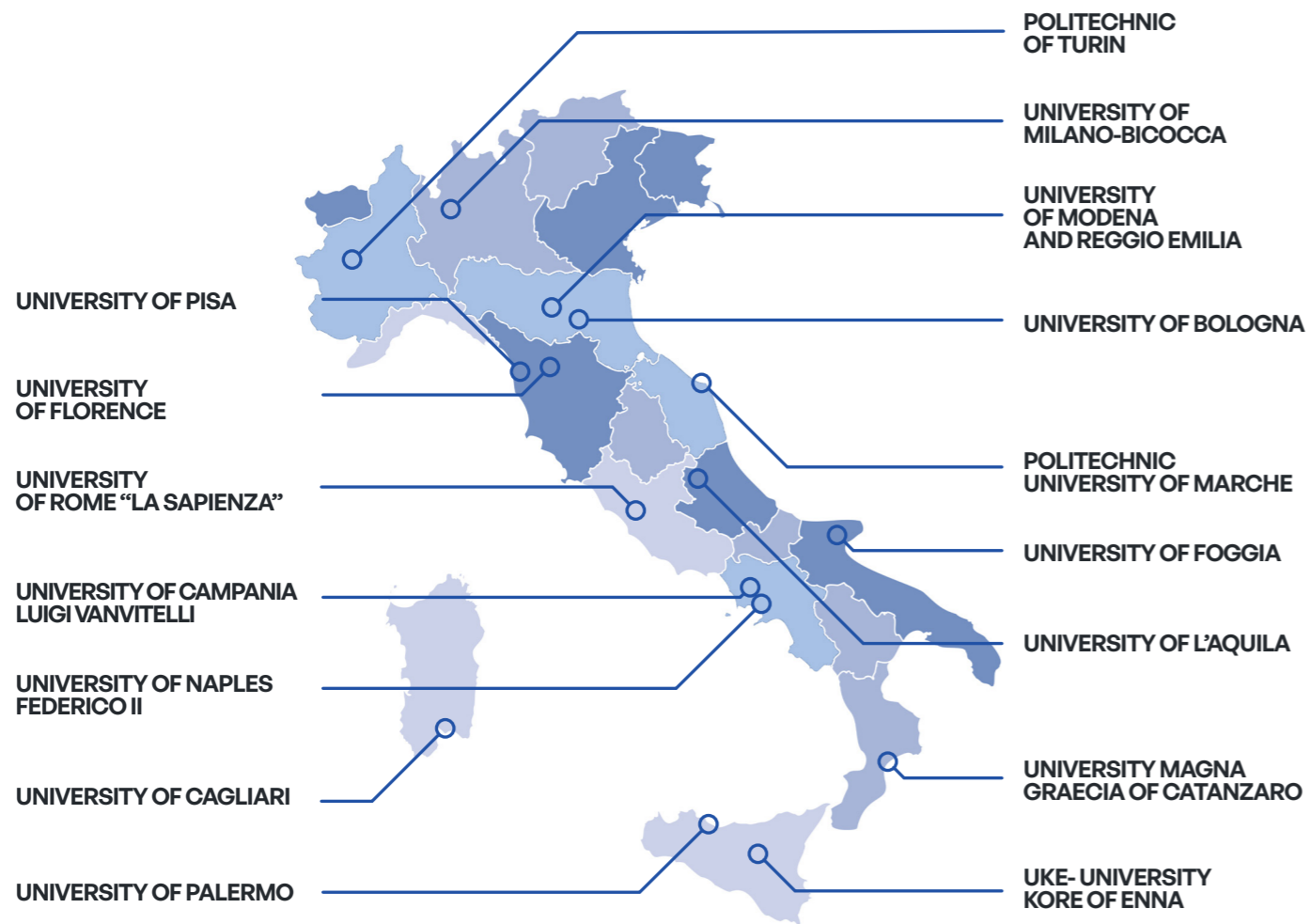
48 FUNDED SCHOLARSHIPS

23 OPERATIVE SITES

57 NATIONAL TEACHERS

10 INTERNATIONAL EXPERTS

16 UNIVERSITIES INVOLVED IN NATIONAL PHD



ENDING

The purpose of the Foundation is the promotion and implementation of scientific and technological research, the development of innovation and the valorisation, also of a socio-economic nature, of the results of its activities in the field of life sciences with particular reference to advanced research in the field of diagnostics and innovative therapies with integrated approaches of translational and precision medicine, including the related applications in every disciplinary area, as well as the realization of the Research and Innovation Program "HEAL ITALIA - Health Extended Alliance for Innovative Therapies, Advanced Lab-research, and Integrated Approaches of Precision Medicine". In this context, the Foundation acts as an implementing body for the implementation of the Research and Innovation Program and provides - pursuant to art. 4 paragraph 6 of the Notice - to the implementation of the Extended Partnership through a governance structure compatible with the requirements of the Notice and formed by the Hub, the Spokes and the subjects affiliated to the Spokes.

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