Human Technopole

# ITALIA 2040

## PART 1

Executive Summary

# Human Technopole ITALY 2040

**Index of the Masterplan**

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The following **Acronyms** will be used in the document:

Besta: Istituto Neurologico Besta
CREA: Consiglio Ricerca in Agricoltura e l'Analisi dell'Economia Agraria
FEM: Fondazione Edmund Mach
Humanitas: Istituto Humanitas
IEO: Istituto Europeo di Oncologia
IIT: Istituto Italiano di Tecnologia
INGM: Istituto Nazionale Genetica Molecolare
INT: Istituto Nazionale Tumori
ISI: Institute for Scientific Interexchange (ISI-Foundation)
M. Negri: Istituto Farmacologico Mario Negri
OSR: Ospedale San Raffaele
PTP: Parco Tecnologico Padano

AD: Alzheimer's Disease
ALS: Amyotrophic Lateral Sclerosis
HT: Human Technopole
NHS: National Healthcare System
PD: Parkinson's Disease
PI: Principal Investigator
RL: Research Line

OGC: Onco Genomics Center (C1)
NGC: Neuro Genomics Center (C2)
AFNGC: Agri-Food and Nutrition Genomics Center (C3)
DSC: Data Science Center (C4)
CLSC: Computational Life Sciences Center (C5)
CADS: Center for Analysis, Decisions, and Society (C6)
CSMD: Center for Smart Materials and Devices (C7)

F1: Central Genomics Facility
F2: Imaging Facility
F3: Data Storage and High-Performance Computing Facility
F4: Common Shared Services Facility

## PART 1 - EXECUTIVE SUMMARY OF THE PROJECT

## 1. INTRODUCTION

Italy has one of the world's highest life expectancies (82.3 years in 2012 according to OECD Health Statistics 2014) and high nutrition standards. What accounts for this remarkable life expectancy and how it can be improved is still an open question. Health, aging, and quality of life are affected in a complex way by a combination of *intrinsic* factors, primarily related to each individual's genetics, and *extrinsic* factors, such as nutrition, lifestyle, and environment. A comprehensive approach to health and aging (hereafter referred to as ***Human Technologies***) does not yet exist, in part because this would require that cutting-edge technologies be integrated with high-profile basic and translational science in the critical areas of Medicine, Data Science, Nanotechnologies, and Nutrition.

Italy's challenge (namely *Italy 2040*) is to become a world leader in *Human Technologies* by embarking on an intensive cross-disciplinary project (Fig. 1) to synergistically develop fundamental and clinical genomics, nutrition, innovative algorithms for data analysis, multiscale methods in computational life sciences, and advanced technologies for food and diagnostics. To achieve this, we propose to create **a national cross-disciplinary research infrastructure named 'Human Technopole' (HT)** in Milan's EXPO site**. The Human Technopole's mission will be to develop personalized approaches, both medical and nutritional, focusing on cancer and neurodegenerative diseases. It will achieve this mission using genomics, the analysis of increasingly large data sets, and new diagnostics techniques.**

HT will pursue different major lines, including:

- the construction of a knowledge-based environment for the development of Genomic Sciences and the rapid and cost-effective translation of discoveries into patient benefits and industrial applications;
- the development and integration of state-of-the-art genomic technologies with advanced basic and translational research, big-data analyses and cutting-edge clinical care to tackle some of the most relevant threats to human health in ageing individuals, namely cancer and neurodegenerative diseases;
- developing healthier and safer food through integrative genomics and systems biology and by adopting new sustainable technologies for food production, conservation, and storage;
- implementing powerful methods for artificial intelligence and statistics to extract knowledge from data in order to facilitate an efficient Precision Medicine program;
- linking systems biology and network pharmacology using big data analysis and new predictive algorithms, and developing innovative multiscale approaches to computational biology, drug discovery, and health;
- processing the massive amounts of socioeconomic data available using high-performance computing and storage facilities so that innovative analytical solutions can be developed for public decision makers;
- developing new-concept fast, cheap, disposable devices for sensing, diagnostics, and high-throughput screening of biological samples (both patient and food samples);

The HT program's expected results will be:

- The creation of a large-scale international research infrastructure, located at Milan's EXPO site, to give continuity to the original idea of *feeding the planet* and to increase Italy's leadership in fields dealing with quality of life. The facility will involve about 1500 people and will include:
    - 30000 sqm of cross-disciplinary laboratories including 7 Centers and 4 Facilities;

    - Massive high-throughput genomic screening/sequencing;
    - Imaging dedicated to structural biology and proteomics;
    - Data storage and a high-performance computing center.
- The first large-scale national screening (carried out in a countrywide network of research hospitals) of:
    - cancer patients for treatment stratification;
    - patients with neurodegenerative diseases for genomic-based stratification;
    - healthy people for disease risk-assessment and prevention;
    - cancer patients for identification of new markers of sensitivity or resistance to innovative therapies.
- The recruitment of more than 1000 scientists (including about 100 principal investigators, researchers, technologists, postdocs etc.) exclusively *by international calls*, with a strong reverse brain-drain effect;
- The production of new scientific knowledge and new technologies for diagnostics and sustainability in the fields of health, nutrition, data analysis, computational life sciences, and nanotechnology;
- The development of predictive models that can be applied to large ensembles of data in a variety of domains, from health to other sectors of great public interest;
- The development of statistical, mathematical, and economic models that will support a new generation of data-aware public policies;
- The strengthening of public-private partnerships and industrial collaborations in fields of strong social impact and great economic relevance for the country, namely: public health, food and nutrition, data analytics, and diagnostics;
- A large-scale educational program (at PhD level) in the Human Technopole's research fields;
- A national outreach and dissemination program on science, health, and technology in collaboration with several national and international players .

The Human Technopole in Milan will trigger the development of a national precision medicine program in collaboration with the Istituto Superiore della Sanità (Ministry of Health) and with Regional Governments across the country.

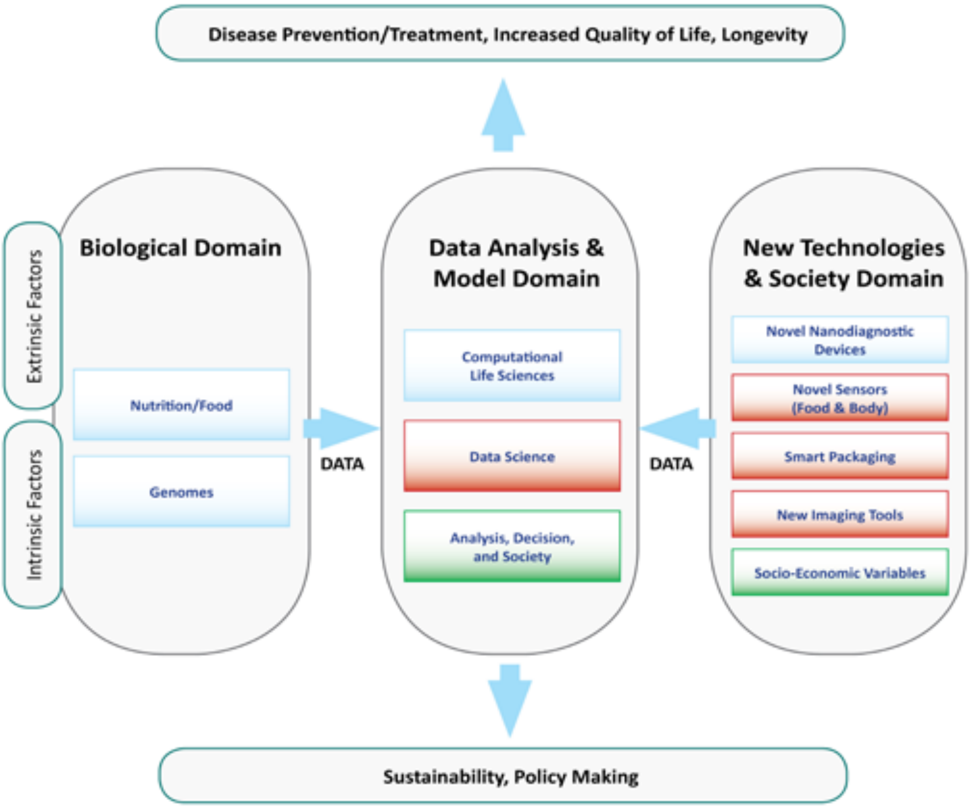



*Figure 1. Schematic representation of the project.*

**2. STATE OF THE ART**

Cancer and neurodegeneration are the most significant causes of death and detrimental aging in advanced societies. The WHO has calculated that, in 2030, 13 million people worldwide will die of cancer. In 2014, 366000 new cancer cases (1000 per day) were registered in Italy alone. In 2008, 2.45 million people were diagnosed with cancer and 1.23 million died from cancer in the 27 countries of the European Union (EU). In the EU, cancer costs reached €126 billion in 2009, with healthcare accounting for € 51 billion (40% of all cancer costs).

In addition, 35 million people worldwide suffer from a neurodegenerative disease. That number is likely to rise to 100 million in 2050. Disease progression is slow, resulting in a massive economic impact on society due to the costs of assistance and the disruptive consequences for families. The total cost for dementia care in Europe is €177 billion/year, with €80.8 billion spent on direct institutional care and €96.6 billion spent on informal care. In Italy, these costs are €4.8 and €15 billion, respectively (2008 data). Italy has one million patients with Alzheimer's disease (AD) and 200000 patients with Parkinson's disease (PD). AD, PD, Huntington's disease (HD), and amyotrophic lateral sclerosis (ALS) are all incurable. AD was recently recognized by the European Health Committee as a health policy priority.

Nutrition affects life expectancy and the quality of aging in advanced societies, with diet being an important contributor to both the development and the prevention of diseases. Aging and the rate of aging-associated diseases (cancer, diabetes, atherosclerosis, cardiomyopathies, autoimmune diseases, neurodegenerative diseases, respiratory diseases, and kidney diseases) are controlled by conserved genetic pathways, which are regulated by food intake and lifestyle. These factors influence several critical cellular functions by inducing changes in metabolism and gene expression. These pathways can be modulated pharmacologically or through the diet to increase longevity and reduce the incidence and severity of aging-associated diseases. The process should be monitored by specific (digital) genomic and epidemiological methodologies.

Understanding and exploiting the cross-correlations between nutrition, genetics, aging, and life expectancy would improve both healthcare and food technology, resulting in ***preventive nutrition*** and ***personalized medicine*** for citizens. This would positively impact the quality of life for future generations as well as the performance of the public health system. It would create new opportunities:

- *For science:* to take novel approaches in developing new technologies and in studying fundamental biological questions as well as new modelling and big data analytics methods;
- *For patients:* to improve risk assessment, diagnosis, prevention, and healthcare;
- *For the economy:* to pursue industrial development, particularly in the fields of food technology, models and software, diagnostics and therapies;
- *For public health:* to improve outcomes, to increase public expenditure efficiency, and to improve the population's quality of life and life expectancy;
- *For policy and decision makers:* to provide public decision makers with the analytical methods and predictive algorithms to better analyze, check, and predict complex socioeconomic scenarios, allowing them to make more informed decisions.

***Worldwide situation****:* The impact of genomics in healthcare has recently attracted attention in both the public and private sectors.

1. In 2004, the **Broad Institute** in Boston (US) was jointly launched by the Broad Foundation, MIT, and Harvard to study genomics and systems biology in correlation with various diseases (primarily cancer);
2. In late 2012, England launched the 100000 **Genomes Project**. Genomics England, a company wholly owned and funded by the Department of Health, was set up to deliver this flagship project, which will sequence 100000 whole genomes from patients by 2017;
3. The **National Institute of Health (NIH, US),** working with the Cancer Genome Initiative and the Wellcome Trust Sanger Institute's Cancer Genome Project (United Kingdom), has already sequenced thousands of cancer cell genomes;
4. In the US, the **Alzheimer's Disease Sequencing Project** has begun releasing data from the peripheral tissues of hundreds of patients;
5. **deCODE genetics** has gathered genotypic and medical data from more than half of Iceland's adult population to identify risk factors for several human diseases;
6. In 2015, Barack Obama launched the **Precision Medicine Initiative** to recruit a research cohort of one million or more volunteers in order to foster genomic data and scale up efforts to identify genomic drivers in cancer that can be used to develop new drugs;
7. **ELIXIR Centers Europe** is leading life science organizations in managing and safeguarding the massive amounts of data being generated every day by publicly funded research. It is a pan-European research infrastructure for biological information;
8. **Google Genomics** has been funded to provide IT infrastructures to store, process, explore, and share genomic data using Google's cloud infrastructure;
9. **Global Alliance for Genomics & Health (Precision Medicine)** has grouped research centers, hospitals, and pharmaceutical companies from 34 countries to facilitate and catalyze the sharing of genomic and clinical data in an effective, responsible, and interoperable manner;
10. In 2013, the Obama Administration launched an extended **Big Data R&D Initiative**, committing more than US$200 million in new funding through six agencies and departments to improve "our ability to extract knowledge and insights from large and complex collections of digital data";
11. **Oxford Parkinson's Disease Detection Dataset** is a Parkinson's Telemonitoring huge dataset run by artificial intelligence machine-learning voice recognition methods. It collects information on PD patients in real time and is the largest European repository of patient data produced using various brain imaging techniques;

12. In China, the **Bejing Genome Institute** has launched the 1000 Plant Genomes Initiative, inviting the most advanced institutions worldwide to collaborate in decoding all the major crops. It is exploring the potential of Genome Wide Association analysis to implement assisted breeding and breeding by design using cultivar resequencing and gene-to-trait association;
13. **Genome Canada** invests between $50 million and $100 million across public and private sectors each year to find new uses for genomics. It invests in large-scale science and technology to fuel innovation and to translate discoveries into applications, new technologies, societal impacts and solutions across key sectors of national importance (health, agriculture, forestry, fisheries & aquaculture, energy, mining, and the environment);
14. The Smithsonian Institute's **Global Genome Initiative (GGI)** is a collaborative effort to create a solid foundation for genomic research through a global network of biorepositories and research organizations. The GGI will preserve and study genomic diversity and increase access to genomic information from the key branches of the Tree of Life, expanding its contribution to the preservation and knowledge of life on our planet;
15. In Europe, the **JPI-ENPADASI** initiative in nutrigenomics and food science is a partnership to connect the major European Centers focused on nutrition, food, and health by establishing good practices and methods for data sharing and data integration at the EU level;
16. Worldwide, several Centers have started to combine methodological research, data-driven research, and domain-specific research in order to address important socioeconomic challenges in areas such as energy, finance, health delivery, epidemiology, economics, and management science. The Centers are: the **MIT Institute for Data, Systems, and Society**, the **Network Science Institute** at Northeastern University, the **Stern Center for Business Analytics** at New York University, the **Big Data Group** at Cambridge University, the **Alan Turing Center** in London, the **iLab at Carnegie Mellon University**, the **Center for Data Science and Public Policy** at University of Chicago, and the **Berlin Big Data Center**.

## 3. GENERAL DESCRIPTION

Within the international context outlined above, the Human Technopole seeks to:

*i)* create a large-scale scientific infrastructure and a collaborative public/private ecosystem at the EXPO site, adopting the highest quality standards to attract the best talent;

*ii)* develop an integrated approach to genomics, nutrition, diagnostics, and data analysis in order to prevent and treat those diseases which most greatly impact the healthcare system (namely, cancer and neurodegeneration);

*iii)* produce every year (in the early years) about 2000 genomic screenings of healthy individuals for disease risk-assessment and prevention, about 2000 genomic screenings of cancer patients for treatment stratification, about 1000 cancer patients for identification of new markers of sensitivity or resistance to innovative therapies, about 1000 genomic screenings of patients with neurodegenerative diseases, and about 1000 screenings of biomarkers for diagnostic purposes. After the start-up phase, these numbers will increase substantially thanks to the progressive involvement of research hospitals and universities in different regions (with a competitive target of 30000 genomes per year);

*iv)* develop new technologies to improve the fields of medicine and nutrition.

The Human Technopole's long-term goal is to make Italy a leading player in the use and development of Precision Medicine. Its novel and comprehensive approach will synergize medical science with the impact of Italian food and nutrition on human health and healthy aging.
*Italy 2040* is naturally a long-term vision and its progressive implementation will have a lasting impact on our society for the next 25 years and beyond. To fully implement this vision, strong synergy is required

between research institutions working in different fields. HT will thus create a network of collaborations with public and private research and clinical institutions in Italy and abroad. It will establish **joint research programs, joint laboratories**, and **outstations** in research hospitals and research entities orbiting around the Human Technopole program (Outstations are HT laboratories established outside the Expo Headquarter in relevant scientific/clinical hosting institutions which are operated with HT resources by HT scientists, based on a collaboration agreement with the hosting institution).
This is particularly important in view of the unprecedentedly broad effort required to create a unified national strategy by merging clinical studies, fundamental genomics, nanotechnology, data science, high-performance computing, and social analyses.

The Human Technopole will be a new legal entity to be incorporated at the beginning of 2017. The project will have a start-up phase of two years, with the target of:

1) Initiating the set-up of the main infrastructure;
2) Starting the collaborations network;
3) Starting the recruitment of senior scientific staff, exclusively by international calls;
4) Organizing the core of the HT administration offices.

During the start-up phase, IIT will be in charge of implementing the above items, supervised by a high-level Governmental Advisory Board. This masterplan presents the Human Technopole's scientific and organizational development in the first 7 years. Importantly, the masterplan forecasts are indicative and will need continuous updating as recruitment evolves, depending on the detailed scientific plans of the Principal Investigators hired.

**The Start-Up Phase**

The start-up phase's main targets are detailed below:

1. **To initiate the main infrastructure set-up, in part by renovating existing buildings at the EXPO site**;

The Human Technopole will begin with 7 main Centers and 3 large-scale Facilities (see Fig. 2) located at the EXPO site in Milan. **Centers** will have their primary infrastructure at the EXPO site, but may also have **Outstations** located outside the EXPO site according to specific interinstitutional agreements (e.g. in Research Hospitals).
Each Center may comprise one or more laboratories and will pursue several well-defined Research Lines (RL), as described in Part 2. Research Lines will be pursued autonomously by newly hired researchers in collaboration with Universities or other research institutions.
The 7 Centers and 3 Facilities located at the EXPO site will be (see Fig. 2):

**C1: Onco Genomics Center;**
**C2: Neuro Genomics Center;**
**C3: Agri Food and Nutrition Genomics Center;**
**C4: Data Science Center;**
**C5: Computational Life Sciences Center;**
**C6: Center for Analysis, Decisions, and Society;**
**C7: Center for Smart Materials and Devices.**

These will be supported by 3 main Scientific Facilities:

**F1: Central Genomics Facility;**
**F2: Imaging Facility;**
**F3: Data Storage and High-Performance Computing Facility;**

Laboratories and services of common interest will be grouped in a fourth Facility (F4: Common Shared Services Facility).

2. **To begin building the collaborations network, primarily with clinical partners**;

During the start-up phase, HT will rely on a collaborations network involving several institutions with complementary expertise (mostly in the Milan area), namely:

- Istituto Italiano di Tecnologia, Milan's three public universities (Politecnico, Università Statale, Università Bicocca);
- Istituto di Ricerche Farmacologiche M. Negri, Istituto Nazionale Genetica Molecolare, CREA (Consiglio Ricerca in Agricoltura ed Analisi Economia Agraria);
- A network of high-level Research Hospitals including: Istituto Europeo di Oncologia (IEO), Istituto Nazionale Tumori, Humanitas, Istituto Neurologico C. Besta, Ospedale Maggiore Policlinico, Ospedale Universitario San Gerardo - Milano Bicocca, Ospedale San Raffaele;
- The national supercomputer facility CINECA, the Institute for Scientific Interexchange (ISI-Foundation) - Torino; Fondazione Edmund Mach (FEM) – Trento;

For such a national long-term enterprise, these partners have been strategically chosen for their excellent skills in complementary fields. An additional factor is that they can supply high-quality PhD students (the Universities) and clinical data (the Research Hospitals). As the start-up phase progresses, additional Italian institutions will become involved via periodic calls and/or interinstitutional agreements for proposals to contribute to the Human Technopole's research plan. These instituations may include CNR, other Universities, research hospitals and companies country wide. Figure 2 exemplifies the collaborations network between the different Institutions participating in the Human Technopole's start-up phase.

Most Centers will have Outstations where a portion of the research and development will be conducted. The Onco Genomics Center and the Neuro Genomics Center will form a network of Outstations involving some of the most important Research Hospitals in both the Milan area and nationwide via the Istituto Superiore di Sanità. This network will ensure access to medical knowledge, biological samples, and clinical data as well as allowing proper data storage in a high-level unified national database and accelerating clinical trials.

Fundamental collaborations will be developed with Milan's three main public Universities. These collaborations will be based on joint activities and/or laboratories hosted within the Centers as well as outside the Centers. The core collaborations with the Statale di Milano will primarily deal with the Onco Genomics Center, the Neuro Genomics Center, and the Agri Food and Nutrition Genomics Center. The Center for Computational Life Sciences, the Center for Neuro Genomics, and the Center for Smart Materials and Devices will develop joint activities with Università Bicocca. The Center for Analysis, Decisions, and Society and the Center for Smart Materials and Devices will develop joint activities with Politecnico di Milano. The Data Storage and High-Performance Computing Facility will be located at the national supercomputer center in Bologna (CINECA), and will serve HT and the entire network of collaborating institutions.

Importantly, in addition to this team of core partners, other national and international public research entities have officially expressed interest in developing collaborations with HT. These includethe European Molecular Biology Laboratory (EMBL), INAIL (Istituto Nazionale per l'Assicurazione contro gli Infortuni sul Lavoro; the Italian National Work-Accident Insurance Company), the Istituto Superiore di Sanità, the ACC national network of IRCSS, and several Regional Governments (Lombardia, Emilia Romagna, Liguria, Umbria). Contacts with other Regions are already on going (Puglia, Lazio, Piemonte).

Finally, several private organizations have expressed interest in the Human Technopole. These organizations include: Assolombarda, several agro-food companies, IBM Research, ST Microelectronics, and several important charitable foundations such as Fondazione Cariplo, Compagnia San Paolo, Fondazione Don Gnocchi, Fondazione Feltrinelli, Fondazione Golinelli, Fondazione Veronesi, and Fondazione Altagamma.

Collaborations and joint initiatives with these entities will be crucial for creating an international public-private ecosystem at the EXPO site and for driving the Human Technopole's future development. They all will be discussed and developed during the start-up phase. A list of Letters of interest is enclosed in the Appendix 1 of this Part 1.

3. **To begin recruiting senior scientific staff (including Chief Scientist, Center Directors, and an initial core of Principal Investigators and Staff Researchers) exclusively by international calls;**

Recruitment at HT will be organized according to international standards and conducted exclusively via international calls, as described in Section 6. The start-up phase's first recruitment will be the Chief Scientist, an internationally acknowledged scientist to take charge of building the Human Technopole and implementing the Scientific Strategy. He/she should be recruited by an *ad hoc* search committee, through a confidential Expression of Interest procedure. The start-up phase's second recruitment action will be for Center Directors and Facility Directors. These hirings will be conducted through international calls (in a similar way to the IIT tenure track procedure). *Ad hoc* International Search Committees will be convened in different scientific areas to create shortlists and interview selected candidates. Once the Chief Scientist and the Directors of the Centers and Facilities are appointed, the scientific staff will be recruited. Tenure track researchers, staff researchers, technologists, and post docs will be recruited exclusively by international calls. PhD students will be recruited according to standard rules.

4. **To organize the core of the HT administration offices**;

During the start-up phase, an administrative core will be set up to ensure the HT initiative is correctly launched in accordance with the schedule for the initial fundamental activities, namely:

a. launch the calls for and recruitment of scientists (chief scientist, center coordinators, tenure track scientists, staff scientists, postdocs, technicians);
b. tenders and purchases;
c. infrastructure implementation;
d. website;
e. finances;
f. Institutional agreements/contracts/collaborations.

In the early stage, while the HT administration offices are still being put together, the above activities will be supported by IIT administrative staff from the following offices, temporarily located at HT:

- Human Resources and Organization and Research Organization Office (point a, f);
- Procurement and Purchasing Office (point b);
- Financial Planning and Control (all points);
- Technical Services and Facilities, Health and Safety, and Information and Communication Technology (point c);
- Communication and External Relations (point d);
- Administrative Management, Management Control Office (point e);
- Technology Transfer Office (point f).

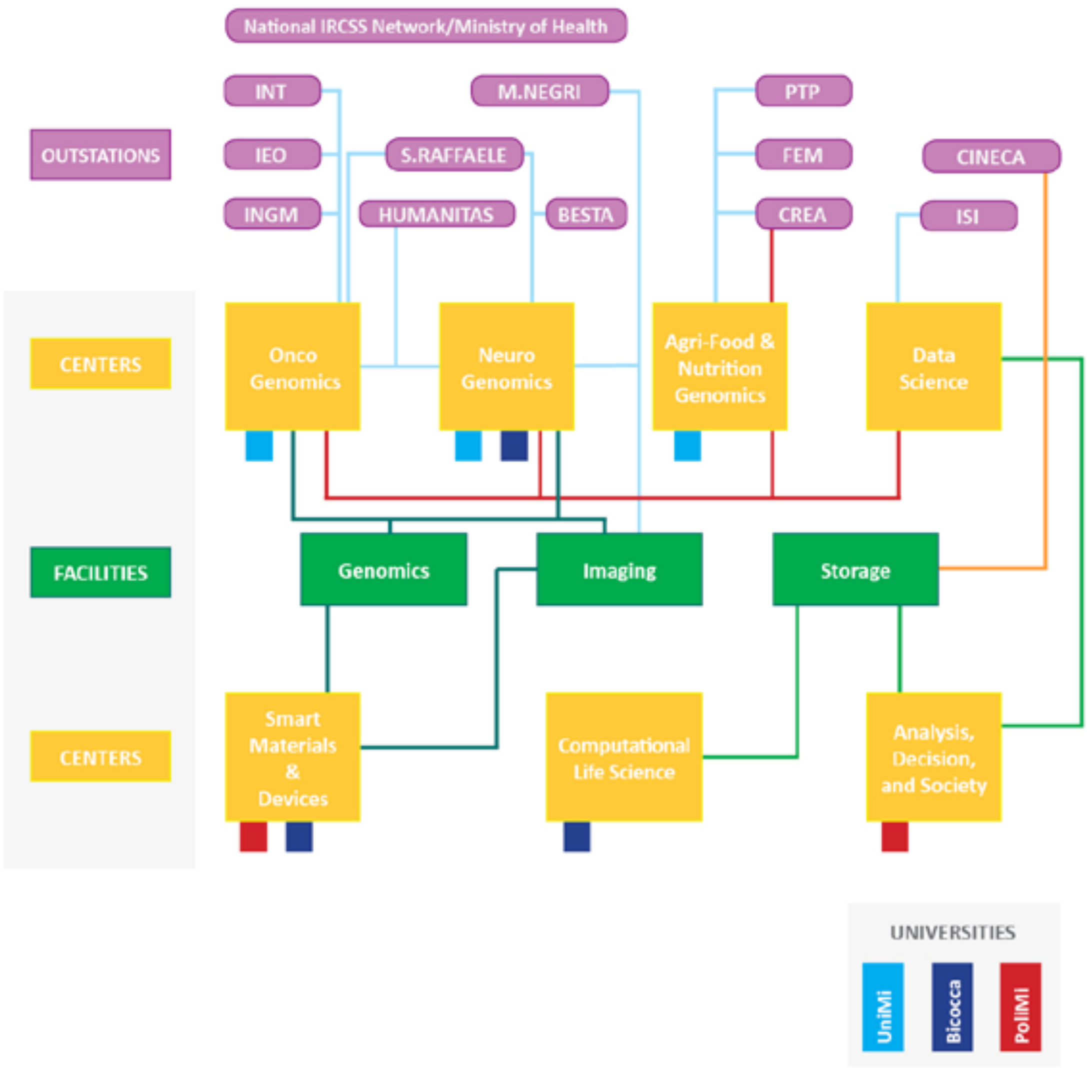



*Figure 2: Structure of the Human Technopole at the start-up. The Yellow boxes represent the Human Technopole's 7 Centers. Centers will conduct joint research activities with Milan's public Universities (Red bar: PoliMi, Light Blue bar: UniMi, Dark Blue bar: Bicocca) and with Institutions, where joint Outstations will be established outside the EXPO site (Purple boxes). All Centers will benefit from the shared Facilities for Genomics, Imaging, and Storage/HPC (Green boxes).*

The first assessment of the Human Technopole and the Centers is planned for the end of the start-up phase.
After the start-up phase, HT could develop other activities dedicated to young researchers and to scientific outreach and dissemination, namely:

**1) Seed Projects**

In addition to in-house research, the Human Technopole could open periodic **public calls for projects** dedicated to researchers around the country, bringing in new ideas and methods that are of interest for the Human Technopole program. These projects are intended to last for 2 years with funding mechanisms similar to those of junior research grants.

**2) Outreach and Dissemination**

A complete outreach and dissemination program associated with the Human Technopole's science and technology activities . This program should include the following initiatives:

- Digital and media dissemination of science (editorial agreements with national public TV network and with major newspapers);

- High school dissemination programs;
- Update courses for high school teachers;
- Partnerships with major national dissemination events to promote the Human Technopole's message (e.g. Festival della Scienza, Bergamo Scienza, and Repubblica delle Idee).

The Outreach and Dissemination program should be conducted in collaboration with major national editorial partners such as Fondazione Feltrinelli, Fondazione Golinelli, and Fondazione Altagamma.
Charities and patients' associations dedicated to cancer and neurodegenerative diseases will also be important partners in the dissemination and outreach campaign.

**3) HT PhD School**

A cross-disciplinary PhD course needs to be established, with courses and experimental projects focusing on the core scientific disciplines involved in the HT research program.

## 4. EXPECTED IMPACT, MILESTONES, AND PROJECT SCHEDULE

The basic ingredients of **Precision Medicine** and **Preventive Nutrition** are the big data analysis of the genetic profiles of large patient populations in correlation with the clinical, environmental, and lifestyle data of these populations. Together, they can reduce national health costs and improve quality of life. The Human Technopole will thus have a fundamental scientific focus as well as great technological potential in different contexts. Life scientists, clinicians, computer scientists, nanotech scientists, and data scientists will closely interact to achieve the shared goal of developing Precision Medicine approaches to cancer and neurodegenerative diseases. This will boost fundamental scientific knowledge and novel health-protecting strategies, including personalized prevention plans and treatments.
Data Science will allow us to merge Precision Medicine with data-based predictions, simulations, and scenario generations in order to provide decision makers and policy makers with new tools for developing rational strategies. We will develop novel algorithms to extract correlation patterns from large data sets. This will lead to more extensive information and, eventually, more profound knowledge of the mechanisms and processes of medicine and life science systems. By combining large-scale computational facilities, predictive modeling capabilities, and domain-specific competences and models, the HT will support significant innovation in analyzing socioeconomic systems.

*For patients:* the project proposes a brand-new modern approach to personalized therapy and prevention. It will provide a solid foundation for population screening and disease prevention. At the same time, it will optimize the decision-making process in therapy and decrease the current side-effects of several drugs and treatments for some of the greatest threats to human health.

*For the economy:* the project will provide Italy with a competitive advantage in reversing the brain drain, attracting industrial partners and investment (ICT, Food, Pharma and Biotech), and improving treatments in hospitals and clinics in terms of both clinical efficacy and cost containment. HT has the potential to create a favorable environment for start-ups: from software houses for analyzing genomic, clinical, and socioeconomic data to biotech companies producing tools, improved instruments, new drugs, and new diagnostics. Finally, the project will provide new ICT tools and predictive statistical methods for application in a variety of fields of great social importance (from health to public administration).

*For decision makers*: The Human Technopole's big data and information processing capabilities will provide a strengthened analytical background to support decision makers and policy makers in the following domains: *(i)* healthcare and welfare; *(ii)* science, technology, and industrial policy; *(iii)* analysis, management, prediction, and control of complex economic, social, and financial interactions; *(iv)* decisions and policies made by public and private institutions operating in complex domains.

The creation of the Human Technopole will follow a precise roadmap, based on the scientific plan described in Part 2. For the start-up phase (the first 2 years), the main objective will be to initiate the international recruiment of PIs and to build the main lab infrastructure, including laboratories, offices, and services (workshops, parking, warehouses etc.). The following Gantt (Fig. 3) displays the Human Technopole's tentative milestones for the first 4 years. Notably, this forecast may change depending on logistical issues, financial issues, and the recruitment schedule. Taking into account these caveats, we can safely assume that refurbishing the HT buildings will drive the time Gantt. The first heavy laboratories could be set up after approximately 24 months, with a steady state condition reached for the infrastructure after about 4 years. The growth in staff numbers (see 'headcount forecast' in section 7) is compatible with this logistical scenario. During the first 24 months, activities will be possible at some HT Outstations and, for equipment-light or computational research, at the EXPO site (shadowed lines in Fig. 3).

The following milestones are expected to be accomplished:

Year 2:

1. 50% of the infrastructure initiated or completed;
2. Outstations and collaboration network agreements completed;
3. Recruitment of directors completed;
4. Tender for laboratory instruments launched/completed.

Year 4:

1. Centers and Facilities completed;
2. Infrastructure completed;
3. Recruitment according to schedule (see section 6);
4. Fund raising activities started;
5. >5000 screening/year performed.

A more detailed Gantt with Milestones and Deliverables will be produced uring the first year together with the founding partners of the new legal entity "Human Technopole".

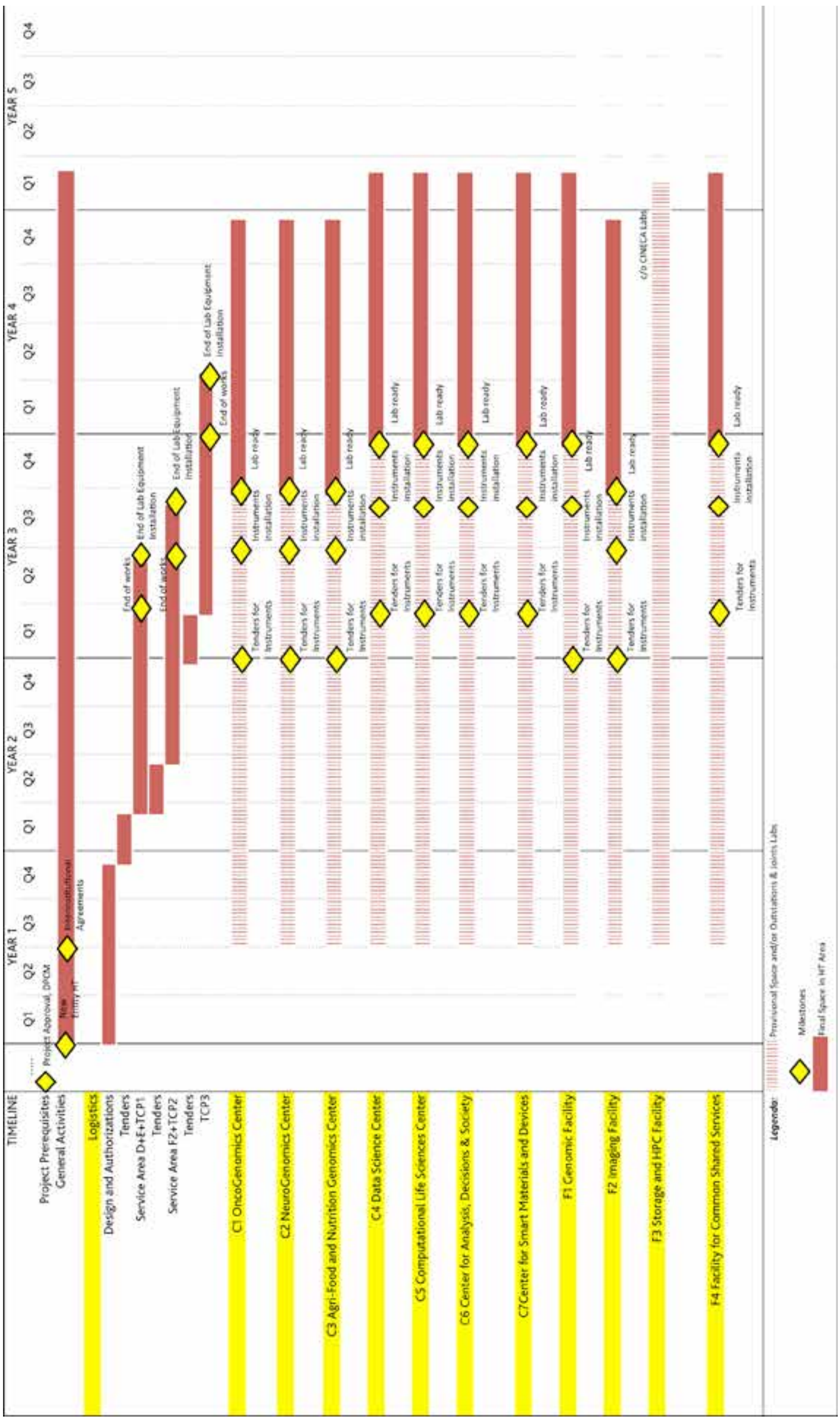



*Figure 3: Preliminary Gantt for the Human Technopole.*

## 5. INFRASTRUCTURE

The Human Technopole will consist of a facility **of approximately 30000 sqm,** including research laboratories, service labs, common areas, meeting and seminar rooms, and administration offices. This structure will host the 7 Centers, the 3 Facilities, common shared services (F4), and some of the Joint Laboratories with the Universities, as described above. The infrastructure's essential design must privilege functionality, safety, and energy saving. Important requisites are:

- About 3 MW power available;
- Continuity for at least 1 MW;
- Fast interconnection and ICT infrastructure;
- Antivibration platforms;
- EM-shielded areas.

Since the Human Technopole will attract national and international partners (universities, research centers, and companies), **additional logistics will be necessary to host teaching activities, Joint Laboratories and Outstations for external institutions, and Outreach Inititatives.** Finally, **space should be made available for start-ups and industrial laboratories**. At this stage, it is difficult to predict the needs and the timing of such collaborative initiatives. However, it is reasonable to start with a **buffer of available space in the range of 5000 sqm** to attract the first group of partner institutions. Further expansion can be postponed until after the start-up phase within the context of better defined and established project financing. **We envisage a final site comprising at least 35000 sqm of floorspace, where scientists, students, companies, and research teams will work together**.

A quick start-up for the Human Technopole can be achieved by refurbishing the preexisting infrastructures at the EXPO site.
Preliminary site inspections have revealed that several EXPO buildings located between the "Cardo" and the "Decumano" (the EXPO site's main streets) could be suitable for adaptation and refurbishment (Fig. 4).


*Figure 4: Areas, pavilions, and buildings which could be adapted for the Human Technopole.*

Figure 5 provides a detailed map of the area highlighted in Figure 4. The three so-called "Service Area" buildings (long orange structures in Fig. 5) each comprise two levels (4000 sqm plus basement) for a total useful area of about 12000 sqm. These buildings could be adapted with relatively little effort in about 24 months for a quick Human Technopole start-up. The three TCP buildings each have an area of 2000 sqm and are approximately 12 meters tall. Multiple-level structures could thus be designed for a total of

approximately 6000 sqm of floorspace for each building (3 levels, 4000 sqm for 2 levels), resulting in a maximum of 16000 sqm in about 36 months. Finally, new buildings could be constructed to produce more than 5000 sqm of floorspace.
We envisage laboratories on the ground floors (6000 sqm in the three TCP buildings, and 6000 sqm in the three Service Area buildings) and office spaces on the first floors of the 6 buildings. Assuming approximately 150 desks per floor plus common areas and services , we might consider 900 desks in the first 4 years. If a third level is built in each TCP, this would make additional office space available. Alternatively, additional office space could be provided by constructing a new building in the available area.


*Figure 5: Areas, pavilions, and buildings which could be adapted for the Human Technopole.*

Notably, while the available buildings are being refurbished in the early phase, a first allocation of offices and light laboratories (for about 250 people) could be provisionally located in the “Cascina Triulza” building (about 1250 sqm) and in the “Intesa-San Paolo Pavilion” (about 1900 sqm), which would be donated to HT by Banca Intesa-San Paolo. In addition, a portion of the scientific activity could begin at the Outstations and Joint Laboratories. This is consistent with the expected headcount growth (see section 6).

Before concluding this section, we would like to point out that the final decision about the HT location will be made at a later stage, in coordination with Arexpo Company, the owner of the areas and the buildings, within the masterplan of the entire Expo Area. In this frame Arexpo will also help to identify new areas (possibly near the HT buildings), for the location of new settlements of enterprises, services and companies whose activities are closely connected with the HT.

## 6. PEOPLE

Investigators operating at the Human Technopole will be:

- ***fulltime*** HT staff members, such as:
  - tenured scientists;
  - tenure track scientists;
  - researchers;
  - technologists;
  - postdocs;
- ***a few*** scientists with Joint Chair Positions between HT and Universities;
- ***a few*** scientists with Joint Positions between HT and other research institutions.

Associate members of HT would be

- university faculty/researchers (associate members);
- researchers from other research entities (associate members);
- researchers from industry;
- external collaborators;
- PhD students.

At steady state (i.e. after more than 7 years), the Human Technopole should involve approximately 1500 people (1000 staff + 500 PhD students). The staff distribution should follow the ratio shown in Table 1.

| | **P.I.**<br><br>(Directors and Tenure Track scientists) | **Researchers Technologists** | **Postdocs** | **PhD Students** | **Technicians** | **Administrative Staff** | **Support Staff**<br><br>(Patents, Projects Office, Tech Transfer, ICT, etc.) | **Total** |
|---|---|---|---|---|---|---|---|---|
| **Number** | 100 | 150 | 400 | 500 | 100 | 150 | 100 | 1500 |
| **Percentage** | 6.7% | 10% | 26.7% | 33.3% | 6.7% | 10% | 6.6% | 100% |

*Table 1: Forecast distribution of HT Human Resources at steady state (> 7 years).*

- The PI scientists with independent budgets and full scientific autonomy who coordinate Centers, Facilities, and/or Laboratories must be **full-time HT scientists**,. These scientists must be hired by international recruitment procedures. The positions can be Tenure Track or Tenured.
- Researchers and technologists are full time staff members acting as group leaders, staff scientists as well as facility scientists. They are hired by international selection, with time-limited contracts (typically 5 years);
- Post docs are recruited by standard international calls;
- PhD students in various disciplines will be enrolled through framework agreements with the Universities;
- Support staff will include experts in intellectual property and patents, technology transfer, technical office, scientific evaluation, research and project management, dissemination, outreach, and communication;
- Support, administrative, and technical staff will be recruited by open calls.

Salaries must follow European standards and will include a variable portion that depends on measurable results for **PIs, researchers/technologists, and managers** (i.e. MBO-Management by Objectives, evaluated by a Scientific Committee in the case of PIs). Details about the international recruiting system are given in Appendix 2.

Table 2 displays the planned growth of the Technopole's scientific and technical headcounts in the first 7 years, i.e. when steady state should be reached. These values are preliminary estimations and may vary during the recruitment process. However, they provide a reasonable indication of Technopole staff composition during the rump up phase. Note that Table 2 does not include: the associated researchers from the partner Universities and research institutions operating in the Joint Laboratories and the Seed Project Initiative.

| **Hiring Pgrm** | | | **Total** | | | | | |
|---|---|---|---|---|---|---|---|---|
| Totale | Year 1 | Year 2 | Year 3 | Year 4 | Year 5 | Year 6 | Year 7 | Total |
| Coordinators | 7 | - | - | - | - | - | - | 7 |
| Tenured / Tenure Track | 1 | 27 | 29 | 13 | 11 | 9 | 2 | 92 |
| Researchers | 2 | 22 | 32 | 24 | 11 | 11 | 1 | 103 |
| Technologists | - | 9 | 10 | 1 | 1 | 1 | - | 22 |
| PostDocs | 8 | 70 | 175 | 61 | 64 | 47 | 10 | 435 |
| Technicians | 3 | 30 | 33 | 16 | 15 | 15 | 4 | 116 |
| Subtotal - 1 | 21 | 158 | 279 | 115 | 102 | 83 | 17 | 775 |
| PhD Students | - | 75 | 139 | 100 | 63 | 48 | 14 | 439 |
| Subtotal - 2 | 21 | 233 | 418 | 215 | 165 | 131 | 31 | 1.214 |
| Admin & Support | 19 | 48 | 52 | 50 | 28 | 27 | 26 | 250 |
| **Total HT** | | | | | | | | **1.464** |

*Table 2: Human Technopole's staff headcount in the first 7 years (from Rump up phase to Steady State). The values do not include outreach and University staff operating at the Joint Laboratories).*

Table 2 assumes that each PI will form his/her own team within 24 months. The teams are standardized between 6 and 12 people (including PhD students, postdocs, technicians, and staff researchers) depending on the PI's seniority. According to this simplified model, the headcount should approach steady state after approximately 7 years, approaching **1500 headcounts** with the distribution shown in Fig.6**.**

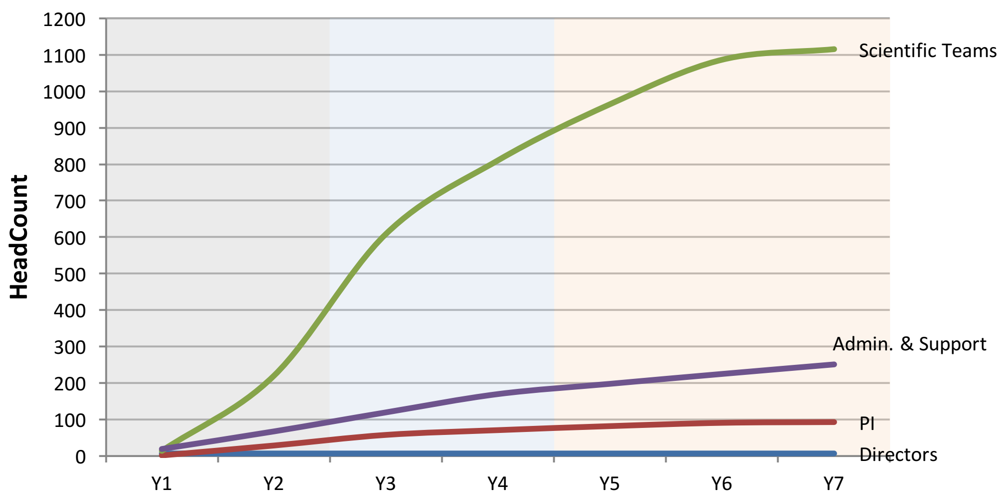
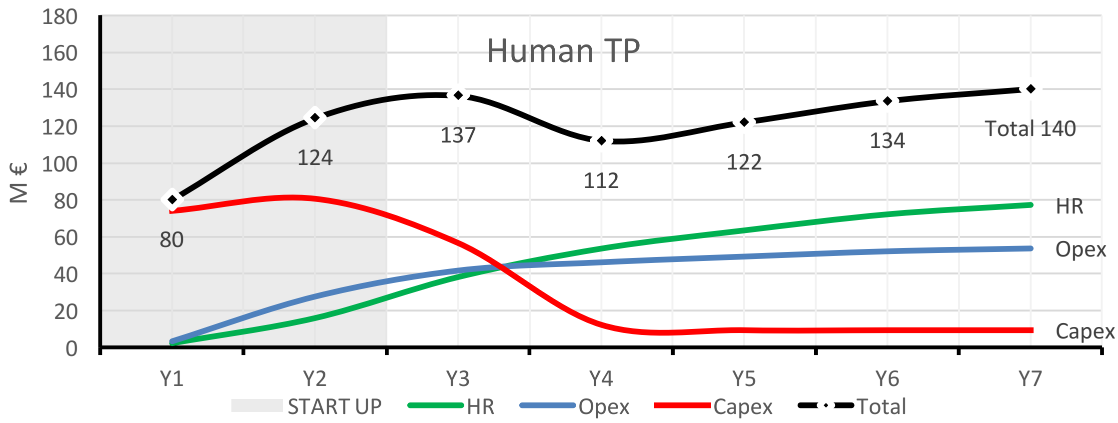



*Fig.6 Foreseen hiring rate of the Human Technopole approaching steady state.*

### 7. EXPECTED FINANCIAL NEEDS

**It must be pointed out that a dedicated long-term funding law is required to ensure the HT's long-term sustainability.** Based on the above forecast, Figure 7a displays the entire Human Technopole's financial needs in the first 7 years. Refurbishing and adapting the buildings are the most important items for the first two years. Staff and running cost expenditure are expected to grow continuously following international recruitment, overtaking capital expenditure in year 3. Approaching steady state, after year 7, the total financial need (including the Seed program) reaches about €140 million (44% of which dedicated to research running costs – CAPEX and OPEX- and about 56% to people). Figure 7b displays the headcount growth versus the financial need in the first 7 years. Steady state is approached after this period with a total budget of approximately €140 million/year and headcounts of 1464 units. At regime one can assume that the **average full cost per headcount stabilizes in the range of €95000 per year**.

**a)**




**b)**

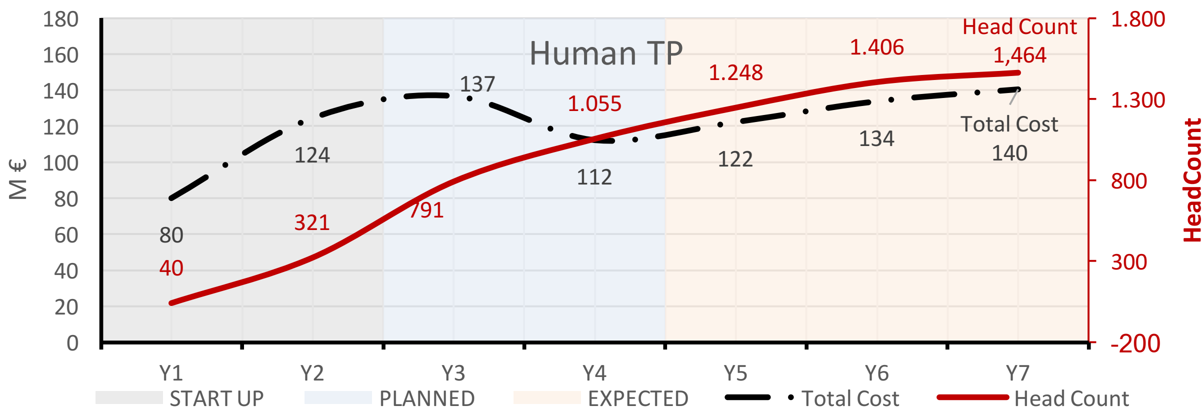



*Figure 7 Forecast of the HT costs (M€) and headcount growth during the first 7 years; a) green, blue, and red lines indicate personnel, operational expenditures (OPEX), and capital investment (CAPEX, laboratory equipment, adaption/refurbishment of buildings) respectively. The black line displays the total; b) the black and red lines indicate the total cost and the headcounts, respectively.*

Fund raising will be a primary target of HT. At steady state we envisage that HT will be able to raise up to 40% of its full cost. Competitive fund raising channels include Horizon 2020 calls, ERC and other individual awards, industrial grants and sponsored research agreements, charities. We also expect patent licensing and IP related revenues (e.g. royalties) to contribute to the global fund raising of HT. In addition to fund raising, indirect impact on GNP and social cost should be considered, such as start up creation, creation of new jobs, optimization of the public health system, etc.. The impact of the HT program on the health system, food and nutrition quality, predictive models for social needs and decision in the long term is indeed expected to be remarkable. Considering that in Italy the social cost of Cancer and Neurodegenerative diseases amounts to about 2% of the GNP (> 30 Billion Euro) per year, even a partial success of the precision medicine strategy would by far compensate the investment of the first 10 years of HT. A more detailed analysis of such forecast is provided in Appendix 3.

Human Technopole

ITALIA 2040