ANNEX 1

EU4Health Programme (EU4H)

Description of the action (DoA)

Part A
Part B

Version 1.0
15 April 2021

IMPORTANT NOTICE

What is the Description of the Action (DoA)?

The Description of the Action (DoA) is the Annex of the Grant Agreement which contains the details of how the project will be carried out. For EU framework partnerships for grants (FPAs) this Annex is called Action Plan.

It consists of 2 parts, which must be generated from the submitted proposal:

- Part A contains structured tables with project information
- Part B is a narrative description on the work to be carried out.

Part A is generated by the IT system. It is based on the information which you enter into the Portal Grant Preparation screens.

Part B (+ annexes) must be uploaded on the Grant Preparation Documents screen.

⚠ Make sure that Part B is synchronised with the information entered into the screens. Make sure that any changes are agreed with us.

DESCRIPTION OF THE ACTION (PART B)

Part B of the Description of the Action (DoA) must be uploaded on the Portal Grant Preparation Documents screen.

COVER PAGE

Part B of the Application Form must be downloaded from the Portal Submission System, completed and then assembled and re-uploaded as PDF in the system.

***Note:** Please read carefully the conditions set out in the Call document (for open calls: published on the Portal). Pay particular attention to the award criteria; they explain how the application will be evaluated.*

PROJECT	
Project name:	Building the EU Cancer and Health Genomics platform
Project acronym:	CAN.HEAL
Coordinator contact:	Marc Van den Bulcke (Sciensano)

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PROJECT SUMMARY

Project summary

Genomics plays an emerging role in clinical and public health research. Cancer is strongly driven by genomic modifications, and wide-profiling of these modifications with new technological approaches has become a major asset for (early) diagnosis, prognosis and therapy in regard to personalised medicine. The CAN.HEAL consortium recognises that prevention, diagnosis and treatment should be approached in a concerted way for optimal benefit of patients and citizens. In the clinical arm in our project, responding to the 'Cancer Diagnostic and Treatment for All', we focus on applying 'next generation sequencing' technology and identify implementation paths to extend the application of genetic profiling of patients and tumour cells in a way that EU Cancer Centres 1°) could take advantage of national initiatives to structure omics use in patient care to allow harmonized data interpretation and facilitated treatment decisions, 2°) could better share their data allowing to apply the same or similar diagnostic and therapeutic approaches to patients with comparable cancer profiles across the EU, thus improving equity, and 3°) take up the molecular tumour profiling biomarkers that estimate cancer predisposition to allow better counselling of family members regarding cancer risk. In the arm on 'Genomics for Public Health', the application of novel insights on estimating cancer risks in healthy populations by polygenic risk score analysis within population-wide interventions as well as strategies of remote genetic counselling and telegenetics will be further developed. Current genetic screening interventions such as the non-invasive prenatal testing (NIPT) for trisomy can be direct sources for incidental findings on cancer status of the mother while also attention is given to implementing genomic profiling in paediatric cancers. Finally, we wish to set the framework for integrating and aligning the Genome of Europe biobanking initiative into public health genomics for cancer. We will further deepen the ethical and legal consents towards access to medical information and develop training tools on oncogenomics at large. Capacity building exercises will be performed in several countries. We will build on distinct use cases towards developing an integrated approach to improve access of individuals and cancer patients and survivors to prevention, diagnosis and treatment of cancer through personalised medicine.

1. RELEVANCE

1.1 Background and general objectives

Background and general objectives

Describe the background and rationale of the project.

How is the project relevant to the scope of the call? How does the project address the general objectives of the call? What is the project's contribution to the priorities of the call?

Genomics plays an emerging role in clinical and public health research. Cancer is strongly driven by genomic modifications, and wide-profiling of these modifications with new technological approaches has become a major asset for (early) diagnosis, prognosis and therapy in regard to personalised medicine. (Horizon Scanning in Cancer Genomics: How Advances in Genomic Medicine Will Change Cancer Care Over the Next Decade. *Curr Genet Med Rep 9, 37–46, 2021*) Today, the detection of molecular biomarkers in liquid or tumour biopsies, is very often based on some form of **Next Generation Sequencing (NGS)** that allows the detection of different types of alterations with a potential clinical utility. The application of these approaches while guaranteeing a sustainable and a high standard of performance should be accessible to all cancer patients in need, and will be a key objective of this project by upscaling available innovation (e.g. the EC Horizon 2020 Pre-commercial procurement project oncNGS) and national initiatives.

Just like precision medicine, the aim of precision public health is to provide the right intervention to the right *population* at the right time, with the goal of improving health for all. (The impact of genomics on precision public health: beyond the pandemic. *Genome Med 13, 67, 2021*) Applications of genomic information in public health are non-invasive prenatal screening (NIPT), genomic tests for childhood and

rare disorders, genetic predisposition to adverse drug effects (pharmacogenomics) and use of polygenic risk scores (PRS) in disease detection and prevention. Examples of each of these are integrated in this project and will open new perspectives to personalised risk assessment and targeted cancer prevention. Indeed, the impact of public health programs in accelerating the identification of individuals with hereditary cancers in populations (e.g., Lynch syndrome, hereditary breast and ovarian cancer) are examples in the cancer domain that are integrated in this project. This so-called cascade screening involves the identification of people at risk in health systems and through testing relatives of affected individuals, an aspect that will be addressed in this project.

A major hurdle to apply human genomic information for improving population health is the uptake of evidence-based interventions and the potential for widening existing health disparities. Implementation science is thus needed to identify the most effective methods and strategies for integrating the use of genomic applications in population health. Partnerships between healthcare organizations and public health programs can help bridge the implementation gap and reduce health disparities. Addressing this gap is one of the major targets of the EBCP and the MoC of the European Commission and co-creating the necessary integration structure in this proposal and scaling up the '1+ Million Genome Initiative' to translate outcomes into implementable public health measures are aims of this project. More generally, public health and cancer genomics take into account the combination of information/data obtained from genes and environmental, behavioral, and social determinants. Indeed, cancer has known environmental, social, and behavioral risk factors (e.g., smoking, physical activity, diet, etc.) hence it is important to evaluate the benefits, harms and costs of the use of human genomic information in the prevention and control of cancer. Applying genomic tools in practice will as a consequence require a multidisciplinary research collaboration that includes healthcare professionals, molecular biologists, bioinformaticians, epidemiologists, IT specialists, sociologists, philosophers, communication scientists, health services researchers as well as patient advocates. Experts in all these domains are represented in this project.

Consortium response to scope of the call

The CAN.HEAL consortium recognises that many synergies between the two subtopics are possible and necessary for the optimal benefit of patients and citizens and has decided to respond to both topics in a concerted way towards a so-called *Medical and Public Health Cancer Genomics Platform*. Within this consortium, we are bringing together partners with extensive experience in public health and cancer genomics who are involved in ongoing national and international initiatives.

In the clinical arm, covering the 'Cancer Diagnostic and Treatment for All', we will focus on applying 'NGS' technology (e.g. comprehensive genomic profiling, WGS, liquid biopsy) in clinical settings and identifying paths (e.g. combined somatic and germline screening, data sharing platforms, molecular tumour boards (MTB), ability to match actionable drivers to effective drugs) to extend the application of genetic profiling of patients and tumour cells in a way that Cancer Centres 1°) could take advantage of national initiatives to structure omics use in patient care to come to harmonized data interpretation and facilitated treatment decisions, 2°) could better share their data allowing to apply the same or similar diagnostic and therapeutic approaches, to patients with comparable cancer profiles across the EU, and 3°) take up the molecular tumour profiling biomarkers that estimate cancer predisposition to allow better counselling of family members regarding cancer risk.

In the arm on 'Genomics for Public Health', the application of novel insights on estimating cancer risks in healthy populations by polygenic risk score analysis within population-wide interventions as well as strategies of remote genetic counselling and telegenetics will be further developed. Current genetic screening interventions such as the NIPT testing for trisomy can be direct sources for incidental findings on cancer status of the mother, of vital importance not only for her but also for the child and other relatives. Implementing genomic profiling in paediatric cancers and the concurrent counselling is another element addressed in this context. Finally, we wish to set the framework for integrating and aligning the 1+MG Genome of Europe reference genomes initiative within both arms of this proposal.

In both arms, we have identified several ongoing activities as use cases that can provide evidence or valuable tools for developing the Medical and Public Health Cancer Genomics platform and pave the way for implementation at broader scale. A methodology for evidence-based implementation will be developed taking into account principles of inequality and HTA. We will also provide recommendations for an ethical-legal framework not only for health research applications but also for applying the platform within a medical healthcare context to the benefit of patients/citizens. Additionally, a training and education package of various stakeholder groups (patients, healthcare professionals and laymen) will be integrated.

Knowledge transfer exercises are being foreseen between a limited number of countries with different healthcare system organisations (federated/centralized, large/small territory/population, high/lower GNI).

CAN.HEAL responds in this way to all elements that are covered in both the 'Cancer Diagnostic and Treatment for All' and the 'Genomics for Public Health' initiative and is established with a perspective to develop methodology and tools that can help Member States improve access of individuals and cancer patients and survivors to prevention, diagnosis and treatment of cancer through personalised medicine.

1.2 Needs analysis and specific objectives

Needs analysis and specific objectives

Describe how the objectives of the project are based on a sound needs analysis in line with the specific objectives of the call. What issue/challenge/gap does the project aim to address?

The objectives should be clear, measureable, realistic and achievable within the duration of the project. For each objective, define appropriate indicators for measuring achievement (including a unit of measurement, baseline value and target value).

The consortium fully recognizes that international multi-centric collaboration is key to large-scale high quality, viable prevention, diagnosis and treatment of cancer, but is currently not the case (Issue 1). The consortium is strongly convinced that better integration and alignment of clinical and population-based interventions at EU level is essential in fulfilling the ambitions set by the European Commission both in the *Europe's Beating Cancer* plan as well as in the *Mission on Cancer* (Issue 2). For this, the Consortium wishes to develop the framework for building a novel healthcare paradigm for cancer patients and citizens within a lifespan health-continuum integrating environmental, medical and biophysical elements (Issue 3).

In line with the objectives set in this call, the consortium will focus on integration and alignment of clinical and population-based interventions that are depending on genomics information obtained through massive parallel genome sequencing of DNA/RNA (including NGS panels, exome & whole genome sequencing, amongst others).

Harmonization and standardization of the results obtained by complex genomic profiling is essential for obtaining and achieving strong impact from international multi-centric collaboration efforts (Challenge 1), while secure sharing and analysing of outcomes of such efforts is a major necessity (Challenge 2). Lack of understanding of genomics by patients, citizens, healthcare professionals and policymakers is still very prominent and should be addressed to implement innovative approaches effectively (Challenge 3). Finally, throughout life, all individuals should have the right and opportunity to be fully informed on where and how their genomics data are being applied, be it for the sake of their own health, their relatives or the society at large (e.g. in research) (Challenge 4).

Needs that were identified by the consortium as major gaps and should be addressed in this project are:

- Conceptualize the lifespan paradigm for cancer patients and citizens, integrating environmental, medical and biophysical elements with focus on prevention, diagnosis and treatment.
- Develop an operational framework for individuals to be fully informed on where and how their genomics data are being applied within such lifespan paradigm following on clear ethical and legal guidelines.
- Setting standards for complex genomics profiling for diagnostics and therapeutics and data-sharing within international multi-centric collaboration efforts (both clinical and public health.)
- Provide protocols to allign prevention, diagnosis and treatment within a lifespan approach.
- Develop a literacy package for different target groups, including patients, their relatives and citizens, as well training packages for health professionals at various levels.

Based on the needs analysis, the following specific objectives were identified:

Specific Objective **1**	Develop the lifespan approach for prevention, diagnosis and treatment (PDT)
Key Process Indicator(s)	Target Measure of success
Integrated clinical utility concept – Medical & Public Health Genomic (M&PHG) aspects – in Molecular Tumour Board (MTB) framework	At least one integrated Molecular Tumour Board concept
Key Output Indicator(s)	Target Measure of success

Decision support tools for M&PHG aspects (MTB)	Application of MTB in at least one use case
Outcome/Impact Indicator(s)	Target Measure of success
Logical framework for the M&PHG MTB	Proof of concept of application of the integrated MTB

Specific Objective **2**	Develop tools and procedures to establish integration or alignment of clinical and population-based interventions that are dependent on genomics data obtained through massive parallel genome analysis of DNA/RNA
Key Process Indicator(s)	Target Measure of success
Molecular tools for integrated M&PHG analyses	At least one molecular tool for M&PHG
Key Output Indicator(s)	Target Measure of success
Analysis applying molecular tools for integrated M&PHG analyses	Application of one molecular tool for M&PHG use in at least one use case
Outcome/Impact Indicator(s)	Target Measure of success
Proof of concept molecular tools for integrated M&PHG analyses	Proof of concept of one molecular tool for M&PHG use in at least one use case

Specific Objective **3**	Provide specific education and training for health workers to advance their understanding of genomics in cancer care and control
Key Process Indicator(s)	Target Measure of success
Development of a training & education package on integrated M&PHG analyses for PDT based on qualified existing resources	Beta-version of training & education package
Key Output Indicator(s)	Target Measure of success
Providing a training & education package for integrated M&PHG analyses for PDT	Piloting the training & education package in at least 5 participating Member States
Outcome/Impact Indicator(s)	Target Measure of success
An online training & education package for integrated M&PHG analyses for PDT	Operational online training & education package for PDT in at least 3 participating Member States

Specific Objective **4**	Support Member States to organise health services to implement the PDT-lifespan approach by developing guidelines and recommendations to better determine who to test for what, when and where.
Key Process Indicator(s)	Target Measure of success
Stakeholder surveys, focus groups on needs, gaps, challenges in integrated M&PHG analyses for PDT	Perform surveys, focus groups in at least 3 Member States
Key Output Indicator(s)	Target Measure of success
Conceptual framework for capacity building on knowledge transfer in integrated M&PHG analyses for PDT	Endorsement by the conceptual framework by at least 75% of partners
Providing data governance recommendations informed by legal and ethics analysis and citizen/patient perspectives.	5 participating Member States have consents in place allowing data access through the 1+MG Initiative.
Outcome/Impact Indicator(s)	Target Measure of success
Protocol on capacity building on knowledge transfer in integrated Medical & PHG analyses for PDT	Endorsement of the protocol by 75% of partners

1.3 Complementarity with other actions and innovation — European added value

Complementarity with other actions and innovation

Explain how the project builds on the results of past activities carried out in the field and describe its innovative aspects. Explain how the activities are complementary to other activities carried out by other organisations.

Illustrate the European dimension of the activities: trans-national dimension of the project; impact/interest for a number of EU countries; possibility to use the results in other countries, potential to develop mutual trust/cross-border cooperation among EU countries, etc.

Which countries will benefit from the project (directly and indirectly)? Where will the activities take place?

A. Past and ongoing activities within the Consortium in the policy field of genomics in cancer prevention and care

1. Joint Actions (JA) on Cancer

JA EPAAC: Relevant outputs: National Cancer Plans especially the European Guide on Quality National Cancer Control Programmes.

JA Cancon: Relevant outputs: *European Guide on Quality Improvement in Comprehensive Cancer Control* and 5 policy papers.

JA on Rare Cancers: Relevant outputs: 10 recommendations of the Rare Cancer Agenda 2030.

JA iPAAC: Relevant outputs: *Roadmap on Implementation and Sustainability of Cancer Control Actions*, which will support Member States in implementation of iPAAC and Cancon recommendations.

2. Multiple national and international initiatives integrating genomics into the healthcare system, either at the clinical or public health level

- **Belgium:** Introduction of NGS into routine oncolologic care, routine NIPT testing
- **Estonia:** Introduction the polygenic risk score into some health care services from 2023
- **France:** '2025 French Genomic Medicine Initiative' and Introduction of NGS into routine oncologic care. CINECA: Common Infrastructure for National Cohorts in Europe, Canada, and Africa (www.cineca-project.eu/partners); Easi-Genomics: European Advanced InfraStructure for Innovative Genomics (www.easi-genomics.eu/about); EQA in molecular biology including NGS for haematological malignancies (GBMHM).
- **Germany:** IMI-funded CANCER-ID (2015-2019); ELBS on Liquid Biopsy/NGS (www.elbs.eu); Public Private Partnership for Big Data in Hematology (HARMONY, www.harmony-alliance.eu/)
- **Greece:** Hellenic Precision Medicine in Oncology (https://oncopmnet.gr/?page_id=2921&lang=en)
- **Italy**: Gersom trial; ACC working group on MTB for national procedure harmonization, national guidelines released (www.alleanzacontroilcancro.it/wp-content/uploads/2021/03/Linee-guida.pdfACC); Creation of a national database for analysis and interpretation of clinical and genomic data (Health Big Data project, www.alleanzacontroilcancro.it/en/progetti/health-big-data/)
- **Latvia:** NGS analysis of all paediatric cancer cases; Latvian National biobank for PRS analysis
- **The Netherlands:** routine NIPT testing; COIN: ctDNA on the road to implementation in the Netherlands (cfdna.nl/coin-2021-new/); Integrating targeted genetic tests in routine care; Clinical trials in inclusion of polygenic risk scores in clinical care; (Genetic) Risk-based entry into population screening guidelines.
- **Poland:** Introduction of NGS into routine oncolologic care (in CCC for selected cancers)
- **Portugal:** National Strategy for Genomic Medicine (PT_MedGen), the Genome of Portugal initiative, 1+Million Genomes initiative
- **Spain:** Translating NGS data into the clinical routine of some blood cancers for a better integral evaluation and treatment decision-making (PETHEMA ALL 2019; UMBRELLA project 2021).

B: Complementarity of project with parallel ongoing or soon to start EC initiatives

Several parallel ongoing or soon to be started EC initiatives will be aligned with the activities in this project:

- EU4H-2021-JA-03: Direct grants to Member States' authorities: network of Comprehensive Cancer Centres: Preparatory activities on creation of National Comprehensive Cancer Centres and EU Networking (lead: INT, Italy)
- EU4H-2021-JA-04: Direct grants to Member States' authorities: network of Comprehensive Cancer Centres: Establishment of new EU Network of Expertise on Cancers and Cancer Conditions (lead: NIJZ, Slo)
- EU4H-2021-JA-05: Direct grants to Member States' authorities: strengthening eHealth, integrating telemedicine and remote monitoring in health and care systems for cancer prevention and care (lead: Sciensano, Be)

- JA Towards the European Health Data Space (TehDAS): https://tehdas.eu/
- CSA unCAN (lead: INSERM, Fr)
- CSA PHIRI (lead: Sciensano, Be)
- CSA Healthy Cloud (lead IACS, Sp)
- CSA B1MG (lead: Elixir)
- 1+Million Genomes Initiative (coordinator DG-Connect)
- AG Genomics Dataspace (to be submitted)
- JRC 'Knowledge Centre on Cancer'
- JRC ECIBC & ECICC
- ICPerMed Secretariat Coordination and Support Action (Horizon 2020)
- HEcoPerMed CSA "Healthcare- and pharma-economics in support of the International Consortium for Personalised Medicine – ICPerMed" (Horizon 2020)
- PERMIT CSA – Personalised Medicine Trials Coordinated by ECRIN (Horizon 2020)

CAN.HEAL aims particularly to develop a trans-national collaboration which may impact/interest all EU countries, but at first focuses on the 17 partner Member States. To develop the possibility to use the results in other countries and to develop mutual trust/cross-border cooperation among EU, four exercises are planned to transfer knowledge between Member States with different healthcare system organisations (federated/centralized, large/small territory/population, high/lower GNI).

2. QUALITY

2.1 Concept and methodology

Concept and methodology

Outline the approach and methodology behind the project. Explain why they are the most suitable for achieving the project's objectives.

Overall concept: integration/alignment of clinical/medical care and public health in cancer

CAN.HEAL aims to address the challenges put forward in the call through integration and alignment of genomics application in medical clinical care and public health interventions to the benefit of cancer patients, their relatives and the population at large. Diagnosis and treatment of cancer has made already substantial advances thanks to the integration of NGS linked to precision clinical management of patients. However, as recently addressed by the WHO, 40% of cancers are preventable and can be linked to one or more of the major risk factors for cancer (smoking, diet, alcohol, physical activity, sun, infections (HPV)). Moreover, the burden of genetic susceptibility is underestimated; current large-scale sequencing studies detect cancer-predisposing variants in ~10% of patients with cancer, especially in children. In this context, progress in our knowledge of preventable causes of cancer will require large population-based studies and biorepositories, coupled with appropriate cancer genomics studies both on healthy and sick people. Indeed, it is becoming apparent that studying the genomic profile of tumours can help to identify cancers at an earlier and more treatable stage using screening or other early detection approaches on pre-diagnostic bio-specimens. Indeed, one may consider that cancer patients that are treated in the hospitals, were a priori part of and represent the individuals at (high/medium) risk in the healthy population. The consortium is fully recognizing that the successful outcome will depend on broad international collaboration and will provide the framework for such initiative in the EU.

General approach:

To foster practical needs of developing the medical and public health cancer genomics platform, we have identified in both the clinical and the public health arm, several ongoing activities at the partner institutes of the Consortium that can serve as use cases. All use cases aim at addressing the application of genomics for providing better care for cancer patients and their relatives and better control for healthy citizens. The use cases will provide a basic level of evidence for the application of genomics within their respective domain. A (limited) number of additional analyses can be performed in the use cases within the context of this project, taking into account the novel mutual perspective of integrating clinical and public health. Based on these experiences, a set of recommendations, guidelines and good practices will be prepared to support the establishment of the platform and implementation of use cases to other partners will be explored.

From two arms to an integrated medical and public health cancer genomics platform

As requested in the call, the project addresses both the clinical and the public health side to improve access of individuals, cancer patients and survivors to prevention, diagnosis and treatment of cancer through personalised medicine. The core of the project consists of 7 technical WPs driven by several use cases. Below we describe in short the aims per WP, how they will reach the medical/public health alignment or integration goal and how the ongoing activities in the use cases contribute to this endeavour.

Note that WP7 on "**Prevention and early detection"** should be considered as a bridging WP within the lifespan cancer continuum concept but for the sake of logical flow from the patient view, we opted to include it in the clinical arm.

Methodology in the public health arm (co-coordinator lead: MHH-Ger)

WP4: Genome of Europe (lead: Erasmus MC, NL): Use cases: Belgium, The Netherlands, Estonia

WP4 aims to deliver three main outputs. 1) By a survey across consortium members, we will create an inventory of existing genetic datasets that can be used to validate genetic risk prediction tools in specific populations (e.g. in an EU country where this has not been done). Local validation efforts will be used as templates to feed the questions that must be asked in the survey. The overview of datasets will be published within the consortium. 2) For populations where validation of genetic profiling is requested, but no genetic dataset is available, samples can be genotyped to create novel genetic datasets. Biomaterial or DNA will be sent to Erasmus MC (NL), can be biobanked there, and additional genetic data will be collected. Data will be processed using existing standardized and accredited procedures and returned to the owner consortium members. 3) Validation of genetic risk profiles will be performed using existing tools and scripts (e.g. Canrisk, R-scripts for PRS calculation and analysis) and analyses will be planned jointly by WP4/5/6. Members of WP4 are engaged in the Genome of Europe (GoE) consortium and will connect between both efforts when this is appropriate. Specific request for information from GoE will be collected during the recurring consortium meetings and conveyed to the respective experts in GoE, or vice-versa.

WP5: Polygenic Risk Scores (PRS) and Decision Support Tools (lead: Tartu Univ, Est): Use cases: Breast, prostate, colorectal cancer and melanoma.

The main goal of WP5 is to develop recommendations for a genomic risk assessment report for physicians and genetic counsellors that they could use in selecting treatment options for the cancer patient and for genetic counselling in general. To that purpose, PRS and also protective loci of the most common cancers will be researched, an inventory of decision support systems (DSSs) will be created and recommendations for establishing large scale population-based early intervention programs for the prevention of various cancers will be developed.

Analysis of PRS of the most common cancers will be based on the data from large GWAS studies. In each population, individuals' genetic variants can be used to calculate PRS to determine personal increased/decreased risk for many common diseases such as cancer. Here the data from the GoE project will be essential. Sequencing technologies have also provided insight into the genetic factors that are protective against disease, providing the potential to develop genomically anchored inventions that assist in maintaining health. DSSs are AI-based programs that analyse data within electronic health records to provide prompts and reminders to assist healthcare providers in implementing evidence-based clinical guidelines at the point of care. The usage and availability of DSSs is increasing, however, there may be differences in how particular DSSs are developed, the information they include, the decisions they recommend, and how they are used in practice. The objective will be to provide recommendations about this process by piloting through existing precision medicine initiatives at the national level as a use case of real-world data.

In the clinical care of patients with cancer predisposition, the genetic counselling of the index patient (person with very high risk of cancer) and their family members is important to support diagnosis, prevent cancer diseases and clarify therapeutic implications. Genetic diagnostics without qualified medical genetic counselling results in a high rate of misinterpretation of test results, inaccurate clinical management as well as a lack of education of first-grade family members and, subsequently, in a negative psychosocial outcome. Thus, the implementation of remote genetic counselling and telegenetics is highly needed to reduce these obstacles and provide access to clinical genetics and genetic counselling services for patients and health care providers. The objective is to establish strategies for the implementation of telegenetics and remote genetic counselling in Europe to personalize public health care.

WP6: Building Clinical utility (lead: KUL, Be): Use cases: cancers in pregnancy (CIP), paediatric leukaemia, cancer risk stratification

Clinical utility generally refers to the utility or usefulness of a finding, practice or technology for clinical or medical purposes. WP6 will provide a map of clinical utility evidences for cancer and chart measures of evaluation. To demonstrate clinical utility of Public Health Genomics (PHG), we will pilot and evaluate clinical

utility for 3 use cases. Each case targets a specific patient population with an unmet need. These use cases will lead to >information about monogenic and polygenic oncogenes and actionability, as well as PRS-linked data in a single comprehensive platform, unique in its kind and sharing information will assist in establishing its clinical utility.

Use case 1: cancers in pregnancy (CIP)
Incidental cancer detection during pregnancy may improve early intervention and may result in better outcomes. A new EU wide NIPT network will determine and implement the parameters to classify a NIPT test as suggestive of cancer and define clinical utility measures. A centralized second reading of suspicious NIPT will be performed in the reference centres. The goal is to define and facilitate the clinical implementation of guidelines for the downstream clinical management of these candidate CIP patients. Via collaboration with the International Network on Cancer Infertility and Pregnancy (INCIP) we aim to follow-up children born to pregnant cancer patients.

Use case 2: Paediatric leukaemia
We will establish criteria for family-based genetic testing in childhood leukaemia, and identify patients and their families suited for inclusion. This implies addressing ethical issues regarding consenting and genetic analysis. By gathering genetic data on index patients and their families, we aim to identify family-based monogenic or polygenic alterations causative for paediatric Acute Lymphoblastic Leukaemia (ALL). In cooperation with the clinical study groups, clinical implications of these results on diagnosis, prognosis and prevention will be assessed.

Use case 3: Cancer risk stratification
PRS resulting from genetic data of Hereditary Breast and Ovarian Cancer syndrome genes and SNPs in carrier and non-carrier breast cancer families will be incorporated in the current risk stratification, allowing comparison of risk stratification with and without PRS. In cooperation with the collaborators, shared data will be translated into improved personalised risk stratification with implications for clinical follow-up of the patients. We aim to extend experience and knowledge about PRS to other breast cancer families and to other cancer types.

Methodology in the clinical/medical arm (co-coordinator lead: ACC, It)

WP7: Prevention and early detection (lead: ACC, It): Use cases: GERSOM, oncNGS, EO-LUNG

WP7 will build a common EU vision on how to tackle cancer as early as possible during the clinical history. We will address a Damocle's sword (minimal residual disease) hanging on the heads of patients and their families. Patients (n=40) with lung, breast and other highly prevalent cancers will be enrolled in clinical trials in the adjuvant setting, e.g. when treatment has curative intents, and tools are needed for selective therapy intensification in high-risk patients. Families may also be at risk when cancer is a manifestation of heredofamilial predisposition. We will simultaneously search for germ line (inherited) and somatic (acquired) alterations in leukocytes and tumour tissue. Since both types of alterations are also released in blood plasma, we will test circulating nucleic acids (liquid biopsy). We will adopt both newly designed targeted NGS panels and highly personalised liquid biopsy. We will encompass from primary to tertiary prevention in the earliest applicable settings. We will determine the best strategy for execution, integration, annotation (a dedicated task will explore bioinformatics tools), harmonization, and reporting. We will address HTA and ELSI in collaboration with WP3, WP10, WP11 and WP12.

WP8: Diagnosis and treatment decision via MTB (lead: IC, Fr): Use case: Carcinoma of Unknown Primary and ultra-rare cancers

Non-standardized variant interpretation and multiple simultaneous alterations in the tumour genome are issues that contribute to inconsistency and inequity in treatment decisions. With the increasing number of targeted therapies approved in the same indication in oncology, and with the increasing complexity of tumour profiles, molecular screening programs have been further implemented in clinical routine to facilitate the access to matched therapies via the organisation of Molecular Tumour Boards (MTBs). MTBs have been implemented in several cancer centres worldwide and include different specialists (medical oncologists, haematologists, pathologists, geneticists, medical biologists, computational biologists, pharmacists and radiologists) involved in tumour profiling, molecular alterations' interpretation and treatment decision. However, it can differ widely across MTBs, since no standard procedures, quality requirements or guidelines have been published to date. Standard guidelines and harmonization are still needed.

The aim of this WP is to:

- Define MTB structures and functioning across the different countries with a focus on national initiatives.
- Provide guidelines for optimized sample and data workflow strategies used in MTBs (starting from the patient and tumor sampling, to techniques for molecular profiling, interpretation and reporting).

- Define impact and challenges of omics implementation on patient treatment including access to clinical trials and genetic counselling.

All tasks will cover solid and haematological tumours. Carcinoma of Unknown Primary and ultra-rare cancers will be used as models to identify the impact of high throughput sequencing of tumour samples (including NGS, WGS and RNAseq) on both diagnosis and treatment decision. The data accumulated within the consortium will be key for future clinical trials and research exploitation. The integration of clinical and molecular data will be useful to provide standardized guidelines for molecular interpretation that utilize reproducible bioinformatics pipelines (including machine learning approaches) to support treatment decision (WP9, WP10 & WP11).

WP9: Treatment and Follow-up (Lead: Jessa Hosp, Be): Use case: Belgian Precision initiative and BALLETT study

WP9 will build on explorative tasks of WP8 as well as on the Belgian Precision oncology initiative. Comprehensive Genomic Profiling (CGP) of solid tumours is performed using the TSO500 platform (Illumina), that covers 523 cancer genes and all types of genomic alterations and by the BALLETT consortium of 9 Belgian NGS labs in a fully standardized way, both for wet lab and bio-informatics. Targeted treatment recommendations based on the CGP results are done by the Belgian national MTB. Data for up to 1000 patients generated in real world will be collected and analysed. Endpoints are the number of 'targetable' variants with their clinical significance (strong, potential, unknown, none), number of patients receiving the targeted therapy (approved, in medical need program, in clinical trial or off-label) and clinical value based on the PFS ratio. The tools used to present the CGP and clinical data to the MTB are based on the online eCRF and a Shiny app that will be optimized in a close collaboration with WP10 that aims towards a true decision support tool. A publicly available database of genomic variants will be established in the cBioPortal platform, preferentially as part of a general EU CAN.HEAL cohort. Microcosting of CGP in a real world diagnostic setting will be done to advise WP3. For the capacity building task, it will be explored to what extent NGS/CGP and a similar CGP+MTB approach can be adopted in other countries (Poland, Spain, Greece, Malta and Serbia). An inventory of the NGS situation in these countries will be established using surveys, site visits and focal group discussions. Gaps, challenges and barriers will be identified, as well as the resources needed to implement CGP+MTB in a broad way, both in terms of indications and geographically. The resulting report will also include recommendations for next steps.

WP10: Oncology Decision Support Tools (Lead: SC, Be): Use cases: cBioPortal, DIGICORE, oncNGS, HARMONY, BALLETT, GERSOM, EOLUNG

The main objective of this WP is to optimise and harmonise tools for data integration (genomic and clinical data) and decision support (MTB and treatment) to scale up and standardise cancer diagnosis and treatment (EU-oncDST concept). This will be reached by mapping and defining available platforms and tools for genomic and clinical data integration with longitudinal follow-up, decision support of the MTB and the standardized precision oncology and haemato-oncology treatment choices. There will be interaction with WP5 to align and integrate the PRS and DSS. Interaction with the other clinical WPs will support the concept regarding integration process, structuring and standardisation of required data, MTB structure, guiding treatment decisions. Together with the use cases, we will be able to develop and optimise tools and come to a common protocol. In a next phase, capacity building will be explored in the consortium and pilot studies will be set up.

Methodology in the transversal WP activities

Next to the three standard WPs for Coordination (WP1), Communication, dissemination & outreach (WP2) and Evaluation (WP3), we have included 4 transversal WPs that cover general issues to be addressed when considering to develop the medicine and public health cancer genomics platform. All four WPs will interact with the technical WPs in the respective arms and with all the use cases therein. All WPs focus their outputs towards establishing recommendations and guidelines that will ultimately be summarized and synthesized by WP14 into the framework for a medical and public health cancer genomics platform.

WP11: NGS including liquid biopsy (lead: UKE, Ger | CERTH, Gr)

This WP will focus on implementing NGS-based and liquid biopsy assays in clinical practice. To this end, we will first develop a salient set of qualitative and quantitative metrics for the assessment of NGS data, starting from the quality of the input material to sequencing and data analysis. Next, a framework for phenotypic and clinical data from patients will be developed to make genetic data useful in clinical settings. This framework will constitute a Centralized Online Repository of SOPs internal to the consortium, as a knowledge hub. Another framework will be developed that facilitates interoperability across the national genomic, clinical and phenotypic data aligned with EOSC standards and guidelines, including FAIR principles. It will include coordination efforts across ongoing initiatives (e.g. ELIXIR Federated Human Data, EOSC-Life, EUCANCan, EJP RD), and re-use existing research infrastructure capacities from the EOSC. More particularly, we will

investigate how phenotypic data can be captured across Europe in order to show the added value of linking additional, more detailed phenotypic and clinical data to genomic data

Available liquid biopsy assays will be validated for subsequent introduction into clinical practice. Based on our expertise gained in the previous EU IMI network CANCER-ID and its current successor consortium ELBS (www. elbs.eu), we will perform experimental quality assurance (QA) studies (e.g., development of external quality standards and ring experiments for technical assay validation) using tests of EU technical readiness level 4 or higher, assessing key liquid biomarker analytes. All assays will be tested for solid tumours and hematologic malignancies in ring trials involving 5 different laboratories from within the consortium. Assays for three different tumor markers will be investigated, these include cell-free DNA (cfDNA), circulating tumor cells (CTCs), and cell-free microRNAs (cfmiRNA). cfDNA assays will include targeted NGS, ddPCR, and UltraSeek; CTC assays will include CellSearch and Parsortix; cfmiRNA will include PCR, microarrays, and NGS. Finally, a framework for the establishment of a permanent organization for the maintenance of a recurrent liquid biopsy QA program and certification will be created.

WP12: Law, ethics and citizen engagement (ELSI) (lead: UNILU, Lux)

With a move towards routine genomic sequencing in healthcare and prevention contexts, there will be important opportunities to re-use this data beyond the individual context, e.g., for research, to develop clinical decision support tools, or to directly inform clinical interpretation for other patients. Realising these opportunities will require not only appropriate infrastructure but also appropriate data governance to ensure respect for data protection law and ethical principles. The emerging European legislation, governance and infrastructure for enabling re-use of health data will also have important applications for cancer genomics. Citizen and patient involvement is also essential to successfully integrating genomics into clinical care and public health. The methodology will be to review data protection legislation (and case law), data governance legislation, professional and ethics guidelines, and associated literature in order to define key legal and ethical requirements that must be respected for cancer genomics. We will build on the findings of other projects including the 1+ Million Genomes Project use cases in the cancer context as well as legal and ethical requirements for genomic data sharing. We will also collect a sample of existing consent forms from clinical partners to identify current best practises. In terms of citizen and patient perspectives, we will build on recommendations made by the following completed and ongoing citizen/patient forums, interpreted for application in the cancer genomics context: JA IPAAC (finished), JA TEHDAS (in progress), and JA JANE (to start in 2022). An annual WP workshop will be used to identify areas for further inspection of citizen/patient perspectives on data governance by ongoing citizen engagement initiatives, including the WP2 Stakeholder Engagement events and white paper.

WP13: Training and Education (Lead: ISS, It)

Building on existing resources in the consortium and in European projects and infrastructures in the field of oncogenomics and precision medicine in public health, WP13 aims at laying the groundwork for a training platform that will address the multiple challenges and training needs and literacy of healthcare professionals, patients, and the general public. WP13 will produce deliverables in three main domains: 1) basic e-learning modules on oncogenomics addressed to healthcare professionals 2) advanced e-learning modules addressed to healthcare professionals involved in Molecular Tumour Board (MTB) 3) educational modules for patients and the general public. The general vision is to focus on quality certified initiatives that can be shared at the European level to promote harmonised capacity building, preferably in e-learning mode to be more easily scaled and expandable to cater for increasingly wider scopes of knowledge themes. To increase utility and impact for professionals, effort will be put in certification processes according to national/European CME standards and in translations into local languages, wherever useful. Methodology for task 1 includes a rigorous process to define the core curriculum for physicians (General Practitioners and other specialties) on knowledge, attitudes and practical abilities about oncogenomics based on literature review and a Delphi survey by an expert international panel (https://link.springer.com/article/10.1007/s13187-021-01956-w). In task 2, particular effort will be made towards aligning the identified gaps to the framework of actors in the EOSC ecosystem (roles and skills), as defined in the Digital skills for FAIR and open science report. By matching the expected roles of the target MTB members (medical oncologists, hematologists, pathologists, geneticists, medical biologists, computational biologists, pharmacists, radiologists, nurses) to the framework of actors in the EOSC ecosystem, we will ensure that their specific skills are clearly captured. Relevant European infrastructures and associations (such as ELIXIR, EATRIS, EHA, ESMO) will be the privileged sources to map the existing advanced training resources. In task 3, literature review and collection of the existing recommendations implemented so far in Europe will be used to identify both educational needs and best practices, and develop engaging educational content targeted at patients and the general public, including videos and brochures to be disseminated across the EU in various languages. Intersectoral focus groups involving the target audience (general public, patients), patient organisations, and healthcare professionals will be established, both at the national and at the European level, to get further insight. Media communication professionals will be involved to create a framework to convey key educational content on oncogenomics.

WP14: HCS Implementation (Lead: UCSC, It)

The main objective of WP14 is to develop recommendations to support public health authorities in implementing personalised approaches in cancer prevention, diagnosis and treatment in the EU healthcare systems. WP14 will build up also on the results of other WPs (mainly WP3, WP6, WP10 and WP12). Evidence and mapping analysis conducted in the other WPS will be synthetized to have a full understanding of the latest research advancements in personalised approaches in terms of effectiveness and clinical utility of current approaches (WP6), new technology (WP10) and data protection issues (WP12). The synthesis of mapping exercises will lead to the identification of key success factors, gaps and challenges related to the adoption of personalised approaches and their potential to be scaled up (Task 14.1). A platform aimed at aggregating and sharing data, evidence and outcomes emerged in the project will be designed to ensure that the evidence and knowledge base built up by the project becomes available for healthcare professionals, policy makers citizens and patients in EU Member States (Task 14.2). Moreover, an optimal Cancer Care Model (Task 14.3) focused on a given clinical pathway will be defined and will include all the key components that should be adopted in the European context to ensure the better sustainable care to patients, also according to the results of WP3 (Task 14.3). In collaboration with WP3, a value-based assessment digital tool will be developed capable of combining patient-centred medicine and personalised medicine by considering e.g. genomic profile, PREMs and PROMs, safety, (clinical) benefits, sustainability, well-being. The assessment will be focused on the perspective of patients, HTA and care workers, respectively. A digital platform to longitudinally collect data in the different case study sites will be designed applying suitable and user friendly tools to encounter the patients' expectations and enhance their participation. Training courses targeted to the users from the different sites will be designed and performed, also to deal with the ethical and privacy issues.

The WP14 Tasks focus their outputs towards establishing recommendations for the adoption of personalised approaches into EU health system that will be developed following a co-creation approach ensured by a strong stakeholder engagement done in collaboration with WP2 (Task 14.4). The recommendations will be developed after a Delphi consultation with Key Stakeholders (in collaboration with WP2) and public discussion with the main institutional health bodies (Health Ministries, National Health Institutes, Cancer Centers…).

2.2 Consortium set-up

Consortium cooperation and division of roles (if applicable)

Describe the participants (Beneficiaries, Affiliated Entities and Associated Partners, if any) and explain how they will work together to implement the project. How will they bring together the necessary expertise? How will they complement each other?

In what way does each of the participants contribute to the project? Show that each has a valid role and adequate resources to fulfil that role.

***Note:** When building your consortium you should think of organisations that can help you reach objectives and solve problems.*

Our proposal is supported by a large consortium of 42 institutes in 17 countries. The institutes represent 17 medical hospitals (of which 12 are Comprehensive Cancer Centres), 15 universities/research institutes, 6 public health institutes, 4 patient and stakeholder organisations and one representative of the Ministries of Public Health. Below, we have listed all partners in the Consortium, indicated the WP leads in bold, and indicated for each partner their specific expertise and their implication in the activities in the AG:

Country	Organisation	Role (lead/WP participation)	Expertise
BE	SC	Lead WP1, WP10; Partner in WP2 & 3	Cancer policy, Joint Actions, NGS implementation
BE	Jessa Hosp	Lead WP9; Partner in WP6 & 10	NGS reference lab for (haemato-)oncology, NIPT sequencing; Comprehensive Genomic Profiling

BE	IJB	Partner in WP8 & 9	Comprehensive Cancer Centre, MTB structures, NGS analysis, PRECISION BELGIUM initiative.
BE	KUL	Lead WP6; Partner in WP4, 5 & 11	Molecular diagnostics, systems medicine, genetic epidemiology, precision medicine, NGS, NIPT
BE	UGent	Partner in WP1, 4 & 5	Epidemiology, genetics, personalised medicine
BE	ULiège	Partner in WP4 & 5	Systems genetics; biostatistics, AI for precision medicine
BE	DIGICORE (Affiliated entities: INT, IFO)	Partner in WP10 & 13	Real-world evidence, development of digital tools, data standardization, training
CZ	IHBT	Partner in WP6, 8 & 11	Translational research on blood cancers
DK	AU	Partner in WP11	Development and utilization of NGS technologies in translational LB cancer research
EE	Tartu-UN	Lead WP5	NGS implementation for early detection and prevention, population-based biobank
FR	HCL	Partner in WP8	NGS in haematological malignancies
FR	INSERM	Partner in WP2, 4, 8, 10,12 & 13	Implementation and coordination of the '2025 French Genomic Medicine Initiative'
FR	IC	WP8 lead and partner in WP2, 5, 6, 7, 9, 10, 11 & 13	Comprehensive Cancer Center, early clinical trials, MTB structures, NGS in clinical use, oncogenetics.
DE	Charité	Partner in WP7 & 8	CCC, early clinical trials, comprehensive NGS programs in solid and haematologic malignancies
DE	MHH-Ger	Co-Lead WP1, Partner in WP5 & 6	CCC, reference lab for paediatric cancer, comprehensive somatic/germline NGS and cytogenetic analysis, genetic counselling
DE	EKUT	Partner in WP4, 5, 7, 10 & 11	CCC, MTB, DST, Molecular Diagnostics, NGS (WES, RNA-seq), PRS, liquid biopsy, counselling.
DE	UKE/ELBS	Lead WP11	Liquid biopsy (Cancer ID, ELBS consortium), single cell genomic analysis
DE	UKSH/ELBS (Affiliated entity: UzL)	Partner in WP8 & 11	University cancer centre, personalised cancer treatment, predictive biomarkers
GR	CERTH	Lead WP11; partner in WP9 & 13	Precision oncology, cancer policies, NGS diagnostics, patient empowerment in care
GR	ELLOK	Partner in WP11, 13 & all WPs	National Cancer Patient Organization, cancer policy, capacity building of cancer patient organizations, patient empowerment

IT	ACC (Affiliated entities: IEO, HSR, IFO, FGP)	Co-lead clinical, lead WP7 and partner in WP3, 8 & 10	Translational and clinical research, national CCPs, NGS panel development and validation, MTB implementation
IT	ISS	Lead WP13	Medical research, control, training and consultation in public health protection
IT	UCSC	Lead WP14; Partner in WP2 & 6	Personalised Medicine, Health Policy research, Genetic Epidemiology, Public Health
LV	LBMC-LV	Partner in WP4, 5, 6 & 11	Population genetics, biobanking, paediatric cancer, NGS technologies, bioinformatics
LU	UNILU	Lead WP12	Data privacy and research ethics, genomic data sharing, ELSI, GDPR
MT	MFH	Partner in WP 8, 9, 13, 14	Cancer policy, national cancer services provision, CGP & MTB implementation
NL	RIVM	Partner in WP14	Policy advice, prevention and control response, information to professionals and general public.
NL	NKI-AVL	Partner in WP3, 9 & 11	HTA, molecular diagnostics, NGS implementation, data stewardship
NL	Erasmus MC	Lead WP4; partner in WP5 & 6.	Population genetics, genotyping techniques, polygenic risk scores, Genome of Europe project
PL	MUW	Partner in WP7, 8 & 9	NGS panels implementation in clinical diagnostics, translational research, oncogenetics
PL	MSCI	Partner in WP8 & 10	Precision oncology, early drug development, decision support sytem, rare cancer
PT	INSA	Partner in WP6 & 13	National institute of Public health, public health genomics, pharmacogenomics
CS	OIV	Partner in WP 8, 9 & 11	CCC, translational and clinical cancer research . Molecular diagnostics, NGS implementation
SI	IOL	Partner in WP6 & 13	Cancer genetics, public health and epidemiology, NGS implementation
SP	FISABIO	Partner in WP3	Promote, encourage and develop scientific-technical, health and biomedical research
SP	ICO	Partner in WP7, 8, 13	Multicenter organization for cancer prevention, treatment & research; NGS analyses, MTB
SP	IBSAL-IECSCYL	Partner in WP5, 8, 10, 11 & 13	Basic/translational biomedical research on blood cancer (NGS; pharmacogenomics; big data/AI)
SP	AQUAS	Lead WP3, Partner in WP1, 2, 9 & 14	Unmet Needs assessment, value-based pre-commercial procurement, demand-driven innovations

SI	EAPM	WP2 and all WPs	Multistakeholder Organisation representing different stakeholders at the EU and MS level,
BE	ECPC	WP2 and all WPs	European Patient organization representative

2.3 Project teams, staff and experts

Project teams and staff

Describe the project teams and how they will work together to implement the project.

List the staff included in the project budget (budget category A) by function/profile (e.g. project manager (PM), senior expert (SE)/, junior expert (JE), trainers/teachers, technical personnel (TP), administrative personnel (AP) etc. — use the same profiles as in the detailed budget table, if any) and describe briefly their tasks. Provide CVs of all key actors (if required).

Name and function	Organisation	Role/tasks/professional profile and expertise
M. Van den Bulcke, PM	SC	Manages the overall content of the AG as Scientific Coordinator, CV attached
E. Van Valckenborgh, SE	SC	Project management and scientific support, CV attached
TBH, PM	SC	Coordination support management
S. Tabakkalt, AP	SC	General project management support
L. Lahousse, SE	UGent	Scientific support, CV attached
M. Saiselet, SE	IJB	Scientific support, NGS, precision Belgium initiative, MTB
P. Aftimos, SE	IJB	Scientific support, NGS analysis, precision Belgium initiative, MTB, CV attached
B. Maes, PM	Jessa Hosp	Clinical pathologist, expert in molecular precision oncology, manages the overall content of WP9, CV attached
TBH, SE	Jessa Hosp	Scientific co-worker, analyses data generated within WP9, linking NGS data
G. Froyen, SE	Jessa Hosp	Molecular biologist, expert in NGS and in the biological classification of genomic alterations, CV attached
B. Cruys, SE	Jessa Hosp	Molecular biologist and bio-informatician, CV attached
G. Ciliberto, SE	DIGICORE	Scientific support, CV attached
S. Di Cosimo, SE	DIGICORE	Scientific support, CV attached
C. Lombardo, SE	DIGICORE	Manages the day-to-day participation, the administrative procedure, participation to the dissemination activities, CV

R. Plesoianu, AP	DIGICORE	Support to the administrative procedures
K. Van Steen, PM	KUL/ULiège	Manager of the overall content of the WP, co-manager of use case 'PRS', CV attached
J. Vermeesch, SE	KUL	Expert in genomics and liquid biopsies, CV attached
L. Lenaerts, SE	KUL	Manager use case 'cancer in pregnancy', CV attached
M. Belickova, PM	IHBT	Manages the overall content project within WP, CV attached
M. D. Merkerova, SE	IHBT	Scientific support, CV attached
H. Votavova, SE	IHBT	Scientific support, CV attached
C. L. Andersen, SE	AU	Managing head of unit, Scientific support, CV attached
M. H. Rasmussen, SE	AU	Scientific support, CV attached
TBH, SE	AU	Liquid biopsy Scientist who will execute the tasks in WP11
A. Metspalu, SE	Tartu-UN	Lead of WP5: PRS and decision support tools, CV attached
J. Vilo, SE	Tartu-UN	Scientific support, CV attached
M. Vaht, SE	Tartu-UN	Scientific support, CV attached
P. Sujobert, SE	HCL	Scientific support, haematological malignancies
M. Kamal, PM	IC	Senior expert in Precision medicine projects and MTB, CV
C. Le Tourneau, SE	IC	Senior scientific and Medical expert in precision medicine, CV
D. Stoppa Lyonnet, SE	IC	Senior scientific and Medical expert in Oncogenetics, CV
C. Colas, SE	IC	Senior scientific and medical expert specialized in Oncogenetics, CV attached
F. Nowak, SE	Inserm/Aviesan	Scientific support, expertise in implementation of national genomic medicine projects, CV attached
I. Amado, JE	Inserm/Aviesan	Scientific support, expertise in implementation of national genomic medicine projects, CV attached
E. Génin, SE	Inserm/ Aviesan	Scientific support, Expertise in population genetics and genetic epidemiology, statistical genetics, CV attached

A. Cambon-Thomsen, SE	CNRS/Aviesan	Scientific and ethical support. Expertise in public health, biobanks, open science, bioethics, research ethics, CV attached
L. Bullinger, SE	Charité	Senior expert managing the contribution of Charité to the respective WPs in which the partner is involved, CV attached
O. Blau, SE	Charité	Scientific support
E. Fräßdorf, AP	Charité	Project management support
K. Pantel, SE	ELBS / UKE	Coordinator, CV attached
C. Koch, PM	ELBS	Project manager
S. Joosse, SE	UKE	Senior expert, statistical and bioinformatic analysis, CV
A. Bergmann, SE	MHH-Ger	Manages the overall content of the WP as managing head of unit, CV attached
T. Ripperger, SE	MHH-Ger	Scientific support, CV attached
M. Schrappe, SE	UKSH	Scientific support, CV attached
To be Hired, JE	MHH-Ger	Biochemist/Molecular Biologist who will execute the tasks of WP5
J. Tecklenburg, SE	MHH-Ger	Scientific support, CV attached
To be hired, SE	MHH-Ger	Physician or Public Health Scientist to execute WP6 tasks
N. von Bubnoff, SE	UKSH/ELBS	Senior expert, CV attached
O. Riess, SE	EKUT	Director of the Institute of Medical Genetics and Applied Genomics, CV attached
S. Ossowski, SE	EKUT	Scientific support, CV attached
C. Schroeder, SE	EKUT	Medical Coordinator Centre for Personalised Cancer Prevention Tübingen, CV attached
TBH, JE	EKUT	Building clinical utility, reporting and documentation of actionable findings in whole genome/exome sequencing
TBH, SE	EKUT	Standardization and ring trials of cancer and liquid biopsy
K. Stamatopoulos, SE	CERTH	Haematological malignancies, Precision Oncology, immunogenetics, CV attached
A. Chatzidimitriou, SE	CERTH	Scientific support, diagnostics, Precision Oncology, immunogenetics, CV attached

F. Psomopoulos, SE	CERTH	Scientific support, Bioinformatician, CV attached
E. Minga, JE	CERTH	Scientific support, electrical engineer; software engineering, data engineering, CV attached
M. Theodoridou, SE	ELLOK	Senior Expert, CV attached
A. Kaparakis, PM	ELLOK	Project Manager, CV attached
M. Nomikou, AP	ELLOK	Administrative personnel
D. Horgan, PM	EAPM	WP Co-Lead, manages the overall content of the WP2 as Executive director of EAPM, CV attached
J. Leprouze, SE	EAPM	Senior Communication Officer, CV attached
A. Gelemanović, SE	EAPM	NGS & PHG Stakeholder Engagement , CV attached
M. Kozarić, AP	EAPM	Events & Logistics, CV attached
P. Giacomini, SE	ACC (IFO)	WP7 coordinator, wet lab and liquid biopsy, CV attached
M Genuardi, SE	ACC (FPG)	Geneticist, genetic predisposition to cancer, CV attached
L. Mazzarella, SE	ACC (IEO)	Medical oncologist, CV attached
G. Tonon, SE	ACC (HSR)	Bioinformatician, functional genomics of cancer, CV attached
R. De Angelis, PM	ISS	Manages the overall content of the WP as managing head of unit, CV attached
E. Stellacci, SE	ISS	Scientific support, CV attached
S. Venanzi, AP	ISS	Project management support
A. De Nicolo, SE	ISS (Nom. Exp.) and ACC	Scientific support, physician scientist, cancer genetics and experimental cancer biology, CV attached
S. Boccia, SE	UCSC	Lead of WP14, CV attached
R. Pastorino, SE	UCSC	Project Manager of WP14, CV attached
A. G. De Belvis, SE	UCSC	Senior Expert of Healthcare Systems and Policies, CV attached
C. Angioletti, JE	UCSC	Junior Expert of Health Economics, CV attached
V. Rovite, PM	LBMC-LV	General management, CV attached

R. Peculis, SE	LBMC-LV	Scientific support, bioinformatics and statistical analysis, CV attached
O Rogoza, TP	LBMC-LV	Bioinformatics and statistical analysis, data preparation and quality control
A. Thorogood, JE	UNILU	Manages the overall content of the WP, CV attached
R. Becker, SE	UNILU	Scientific support, CV attached
To be hired, JE	UNILU	Expert in law and ethics who will execute the tasks in WP12
M. Dalmas, SE	MFH	Project Lead for MFH, Dept. for Policy in Health, CV attached
S. Baldacchino, SE	MFH	Senior expert/Scientific Support. Dept of Pathology, Mater Dei Hospital, CV attached
J. Scerri, SE	MFH	Senior expert/Scientific Support. Dept of Pathology, Mater Dei Hospital
V. Buhagiar, AP	MFH	Administrative support. Dept. for Programme Implementation
A. Uitterlinden, SE	Erasmus MC	Manages the overall content of the WP as managing head of unit, CV attached
J. van Rooij, SE	Erasmus MC	Manages and executes the tasks of the WP, CV attached
To be hired, JE	Erasmus MC	Execute the tasks of the WP
R. Fijneman, SE	NKI-AVL	Scientific support, CV attached
M. Bierkens, JE	NKI-AVL	Coordinating cBioPortal activities
V. Retèl, SE	NKI-AVL	Head Health Technology Assessment department, CV attached
I. van Klink, JE	RIVM	Junior researcher / expert, CV attached
T. Stoklosa, SE	MUW	Expertise in NGS panels implementation in clinical diagnostics, in translational research and oncogenetics, CV attached
To be hired, JE	MUW	Participation in WP8 and WP9
I. Lugowska, SE	MSCI	Partner representative in WP8 and 10, CV attached
M. Rosinska, SE	MSCI	Scientific support, CV attached
A. Janowska, JE	MSCI	Scientific support

A. M. Vicente, SE	INSA	Senior researcher in Biomedical Sciences and Public Health Genomics, CV attached
M. L. Cardoso, SE	INSA	PhD in Pharmaceutical Sciences, Senior Pharmacist Expert in Genetics and Pharmacogenomics, CV attached
M. Popovic, SE	IOV	Gynae-oncologist; main contact person for site, CV attached
T. Ivkovic- Kapicl, SE	IOV	Professor of Pathology, CV attached
M. Krajc, SE, PM	IOL	Head of Cancer Genetics Clinic, clinical geneticist and public health specialist, CV attached
A. Blatnik, SE	IOL	MD. Consultant in clinical genetics
K. Strojnik, JE	IOL	PhD, MD. Consultant in clinical genetics and medical oncology
U. Kuhar, TP/AP	IOL	Department for research and education (ERID), project's financial officer
A. Molina-Barceló, SE	FISABIO	Scientific support. Ensure the inclusion of equity perspective across the entire project. CV attached
M. Pinto- Carbó, PM	FISABIO	Scientific support in the inclusion of the equity perspective across the entire project. CV attached
P. Romeo-Cervera, JE	FISABIO	Scientific support in the inclusion of the equity perspective across the entire project
J. M. Hernández Rivas, SE	IBSAL-IECSCYL	Scientific coordination by managing and distributing the work within the organisation, CV attached
M. R. Benito Sánchez, SE	IBSAL-IECSCYL	Scientific support, CV attached
M. Abáigar Alvarado, JE	IBSAL-IECSCYL	Scientific support, CV attached
I. Serramito Gómez, JE	IBSAL-IECSCYL	Scientific support, CV attached
E. Nadal Alforja, SE	ICO	Head of Section of Thoracic, Head & Neck and Brain Tumors. Manages the overall content of the WP, CV attached
J. Bosch, SE	ICO	Scientific support for WP8. CV attached
E. Carcereny, SE	ICO	Scientific support for WP8.
To be hired, JE	ICO	Scientific support for Pilot study, scientific and administrative support for WP7, WP8, WP13
R. Maspons, SE	AQuAS	Provide advice for the evaluation and the needs for the integration in the health system, CV attached

R. Alessandrello, SE	AQuAS	Provide advice on the valued-based innovation adoption, CV attached
M. Sanchis, PM	AQuAS	Support in the management of the overall of the WP3 and interactions with other WP's, CV attached
TBH, PM	AQuAS	Manages the overall of the WP3 and interactions with other WPs

Outside resources (subcontracting, seconded staff, etc) *If you do not have all skills/resources in-house, describe how you intend to get them (contributions of members, partner organisations, subcontracting, etc.).* *If there is subcontracting, please also complete the table in section 4.*
YES, see section 4
Experts (if applicable) *Explain if **national** and/or **international experts** will be nominated by national authorities to support the project implementation. Describe the specific professional and technical expertise and experience of each proposed expert and their contribution to the project implementation. Provide CVs (if required).* *Minimum requirements:* • *Qualification: A level of education which corresponds to a Bachelor's degree.* • *Professional experience: At least 4 years of proven experience in XXX* • *Other skills: ability to work in English (minimum B2 level)*
NONE

2.4 Consortium management and decision-making

Consortium management and decision-making (if applicable) *Explain the management structures and decision-making mechanisms within the consortium. Describe how decisions will be taken and how regular and effective communication will be ensured. Describe methods to ensure planning and control.* ***Note:** The concept (including organisational structure and decision-making mechanisms) must be adapted to the complexity and scale of the project.*
As we decided to respond to both the clinical and public health arm in a single proposal, the general coordination of the project by SC (Be) will be supported by two co-leads, one for the clinical arm (ACC, It) and one for the public health arm (MHH, Ger). **The governance structure of the project will entail the following roles and 2 bodies:** **The Action Coordinator (AC)** ensures appropriate contact between the consortium and the EC services and will oversee liaison with other EC actions and initiatives in the field. The AC chairs meetings of the Steering Committee and the Leadership Council (see below). The AC is supported by two co-leads and a Project Management Team in charge of daily management of the Action. The **Co-leads (CoL)** are responsible for managing the activities endorsed by the technical WPs in the respective arms on clinical and public health issues. They will take up the daily management of the activities in their arm and will closely interact with the AC. All WPs have a **WP Lead,** responsible for steering the implementation of their respective WP tasks in accordance to the objectives of this proposal. WP Leads coordinate the work in close cooperation with WP task leads. Each WP shall be represented by at least one member in meetings. Quality and risk management mechanisms are put in place in close collaboration with WP1 (Coordination) and WP3 (Evaluation).

The Leadership Council (LC) is responsible for aligning and coordinating the ongoing work across all WPs through a continuous assessment of inputs and emerging results. It is composed of all WP leaders and co-leaders and is chaired by the Coordinator. The LC will meet once a month by teleconference.

The Steering Committee (SCo) is chaired by the AC and is composed of all partners. The SCo monitors the overall activities and progress of the project and is the body where all partners together define the strategic directions of the initiatives. The SCo meets on a quarterly basis (every 3 months) by teleconference and twice face-to-face in year 1, and once in year 2.

2.5 Project management, quality assurance and monitoring and evaluation strategy

Project management, quality assurance and monitoring and evaluation strategy

Describe the measures planned to ensure that the project implementation is of high quality and completed in time.

Describe the methods to ensure good quality, monitoring, planning and control.

Describe the evaluation methods and indicators (quantitative and qualitative) to monitor and verify the outreach and coverage of the activities and results (including unit of measurement, baseline and target values). The indicators proposed to measure progress should be relevant, realistic and measurable.

MONITORING AND EVALUATION of ACTIVITIES:

The process of the AG will be monitored through output indicators, qualitative risk assessment of the WP leads and participant satisfaction measures. The outputs of the AG are defined primarily by the deliverables and intermediary outputs (in form of milestones). Timeliness of achieving the milestones and deliverables will be assessed. The indicators will measure progress towards each deliverable and milestone. In order to identify risks and opportunities we will seek qualitative input from WP leaders in the form of short interview or email commentary. The AG participants' satisfaction will be evaluated in terms of satisfaction with the quality of communication, internal procedures, partner website and shared space, and the satisfaction with the project events.

Specific action-level indicators defined for the two sub-topics for reporting purposes are:

Sub-topic (a) - 'Cancer Diagnostic and Treatment for All' project

- Number and type of available 'next generation sequencing' technology proposed for application of personalised cancer diagnosis and treatments.

- Number of cancer centres, which are skilled and are offering 'next generation sequencing' technology for application of personalised cancer diagnosis and treatment.

- Member States and Regions that have a capacity to offer 'next generation sequencing' technology for application of personalised cancer diagnosis and treatment.

- Number of patients who have benefitted from 'next generation sequencing' technology for personalised cancer diagnosis and treatment.

Sub-topic (b) - 'Genomic for Public Health' project

- Number and type of implementable public health measures to identify individual genetic profiles, indicating susceptibility of individuals to develop a certain type of cancer.

- Number of cancer centres, which are skilled and routinely offering approaches and measures to identify individual genetic profiles, indicating susceptibility of individuals to develop a certain type of cancer.

- Member States and Regions that have the capacity to offer approaches and measures to identify individual genetic profiles, indicating susceptibility of individuals to develop a certain type of cancer.

- Number of patients who have benefitted from approaches and measures to identify individual genetic profiles, indicating susceptibility of individuals to develop a certain type of cancer.

The effect of the AG is defined by producing guidelines, recommendations and the platform which will be relevant and feasible to support Member States promoting the wider roll-out of the initiatives in the field of oncology, including prevention and care. Based on these inputs the progress briefs will be prepared, focusing on the process indicators (output) and risk identification. The impacts of the AG will be assessed in a Final Stakeholder Survey and inputs of the Final Conference. The Final Stakeholder Survey will be performed at the end of AG among partners and stakeholder engaged in the AG, including policy

makers, coordinating centers for national cancer strategies, payers, medical associations, industry, patient organizations.

PILOT INTEGRATION EVALUATION:

The evaluation of pilot integration within the development of the platform will incorporate three aspects: feasibility, levelling inequalities and cost-effectiveness. Although the aim of the pilot evaluation in the AG is not to evaluate any specific solution, but rather to identify challenges and opportunities for genomics application in cancer prevention and care in different European settings, it is still useful to use a validation structure including the areas of clinical effectiveness and safety (evaluated in the clinical trials) socio-cultural, ethical and legal aspects, patient perspectives and organisational aspects.

Transferability assessment in terms of feasibility of application in the Member States, scalability, and cross-border application will also be assessed. In particular, quantitative assessment will be used to collate lessons learnt from the perspective of the patients and service providers. Evaluation also includes SWOT analysis of the technical and implementation aspects as well as framework cost-effectiveness analysis in view of future implementation in Europe. This task will contribute to the development of a pilot evaluation framework including guidelines and tools for the data collection. It is envisaged that the guidelines and tools will feed into an integrated toolkit for sites piloting integrating/aligning clinical and public health interventions. However, it should be also possible to use it in case of pilots focusing on either arm separately.

2.6 Cost effectiveness and financial management

Cost effectiveness and financial management

Describe the measures adopted to ensure that the proposed results and objectives will be achieved in the most cost-effective way.

Indicate the arrangements adopted for the financial management of the project and, in particular, how the financial resources will be allocated and managed within the consortium.

⚠ *Do NOT compare and justify the costs of each work package, but summarize briefly why your budget is cost effective.*

The financial management of the AG will be undertaken by the Project Management Team, with dedicated support from Sciensano's Finance department. The Finance Department of Sciensano has extensive experience with large scale national and European projects (ie. JA iPAAC (WP Lead), CSA-PHIRI (Coordinator), JA InfACT (Coordinator), JA BridgeHealth (Coordinator), the Horizon 2020 PCP project oncNGS (Coordinator).

The Financial Officer is well acquainted with the rules and regulations of the funding mechanism and has several years of experience in management of EC project and partner budgets. Dedicated project management software will be used for the purposes of the specific projects we are coordinating. We will be requiring all partners to fill in timesheets and retain their financial documents (invoices, salary slips, proof of travel costs, etc.) for justification and eventual check. In order to monitor expenditure, we will require partners to submit a financial progress report every six months.

Teleconferences between the Project Management Team and the financial officers of the partner institutions will be organised around key financial reporting milestones, such as the interim and final reports. Additionally, each SCo meeting with all partners will have at least one agenda point dedicated to financial management. Financial reporting will also be covered in the partnership consortium agreement.

2.7 Risk management

Critical risks and risk management strategy

Describe critical risks, uncertainties or difficulties related to the implementation of your project, and your measures/strategy for addressing them.

Indicate for each risk (in the description) the impact and the likelihood that the risk will materialise (high, medium, low), even after taking into account the mitigating measures.

Note: *Uncertainties and unexpected events occur in all organisations, even if very well-run. The risk analysis will help you to predict issues that could delay or hinder project activities. A good risk management strategy is essential for good project management.*

Risk No	Description	Work package No	Proposed risk-mitigation measures
1	**Delays in obtaining the ethical board approval for pilots:** Likelihood: moderate / high; Impact: High	WP4, 5, 6, 7, 8, 9, 10, 11	Select already approved running projects, as indicated by the partners
3	**Restrictive data protection procedures at pilot sites/countries:** Likelihood: moderate; Impact: low	WP4, 5, 6, 7, 8, 9, 10, 11	A common strategy for data analysis allowing for data privacy restrictions at cBioPortal is developed
4	**Lack of pilot outcomes data standardization**: Likelihood: low; Impact: moderate	WP4, 5, 6, 7, 8, 9, 10, 11	Proper comparable data, including development of common data collection framework based on standardized formats.
6	**Recruitment and stakeholders Engagement:** Likelihood: low; Impact: moderate	All WP	Country-specific and EU-wide stakeholder engagement activities are embedded within WP2 with dedicated person months for local dissemination.
9	**Delays in meeting AG reporting and output deadlines** Likelihood: low; Impact: moderate	All WP	Strict PM is installed with various partners
10	**COVID-19 pandemic and lockdown policies:** Likelihood: moderate; Impact: high	WP1	Organization of virtual meetings and use of digital material and web trainings

3. IMPACT

3.1 Impact and ambition

Impact and ambition — Progress beyond the state-of-the-art

Define the short, medium and long-term effects of the project.

Who are the target groups? How will the target groups benefit concretely from the project and what would change for them?

Does the project aim to trigger change/innovation? If so, describe them and the degree of ambition (progress beyond the status quo/state-of-the-art).

The proposal directly supports activities in two Flagships of the EBCP: **Flagship 6 on '**The new 'Cancer Diagnostic and Treatment for All' initiative and **Flagship 7** on 'Genomic for Public Health'. As indicated above, the Consortium strongly supports the integration and/or alignment of activities in either flagship towards optimal cancer burden reduction within a cancer lifespan continuum paradigm.

Short-term effects of the project will be to raise awareness in the community on the need of building such cancer lifespan continuum and provide a new conceptual health paradigm for cancer prevention, diagnosis and treatment. The concept will build on ongoing activities at the partner institutes/regions/countries, previous experience from past initiatives (e.g. JAs on Cancer, the ECIBC, ECICC, …) and maximize interaction with the various parallel initiatives that touch on the content of the concept and should be integrated herein (e.g.

the Networks of expertise, the CCC networks, the JRC Knowledge Centre on Cancer, the ERN's, the EHDS, etc.).

In a next phase, covering the **medium-range effects**, efforts will be made to define how the new paradigm can fit and be integrated into the healthcare systems of the member states. Large capacity building and knowledge transfer initiatives will be needed for this, which will be piloted to a limited extent in this proposal to allow providing guidance for upcoming activities.

In the **long-term**, the cancer PDT-lifespan approach is to be structurally aligned or integrated into the healthcare systems of the member states, preferentially including an overarching support mechanism at the EC level. Such new paradigm introduction is a long-term process and will have major impacts on all aspects of how we see health and healthcare in our European community. This proposal already will start building towards creating such support structure by establishing an expert group from the consortium teams (also open for additional members) on the cancer lifespan cancer health paradigm in all its dimensions (technical, medical, public health, ethical, legal, social, HTA, regulatory, data registration, patient, citizen, policy maker, organisational , …).

The **target population** of this proposal in principle includes all stakeholders directly or indirectly concerned in creating the cancer lifespan concept: cancer healthcare professionals & researchers, cancer patients, citizens and cancer healthcare policy makers. Each of the target groups will **benefit** in a different way from the results of this proposal: patients and citizens will receive more effective clinical support, healthcare professionals will gain a broader view on the cancer of their patient or the risk of the citizen, policy makers will be provided recommendations to develop their system in a more integrated way with a final aim to most-effectively lower the cancer burden of the population and increase quality of life. In the next phases, the target population will expand to include the health community at large and also go beyond the healthcare policy makers.

The project aims to develop an **innovative** approach in tackling cancer by developing a cancer lifespan continuum paradigm for prevention, diagnosis and treatment. In itself, this new paradigm will impose a new view on cancer which the partners will explore in the use-cases. Their experience will provide guidelines and recommendations for further fine-tuning and/or research towards an evidence-based cancer lifespan continuum. To fully develop the latter, we recognize that other fields of expertise and the industry should become closely involved in the follow-up of this project. Indeed, as it is anticipated that many new applications, tools, infrastructures, technologies and networks are to be developed at various levels (digital, molecular, logistic,…), we will have to integrate harmonized clinical, molecular and environmental data, statistics, engineering, production and commercial expertise in the next steps. Optimally, private-public partnerships at EU level should be envisaged for these developments which also may invoke **innovative** legal, financial, political instruments to be developed in parallel.

3.2 Communication, dissemination and visibility

Communication, dissemination and visibility of funding

Describe the communication and dissemination activities which are planned in order to promote the activities/results and maximise the impact (to whom, which format, how many, etc.). Clarify how you will reach the target groups, relevant stakeholders, policymakers and the general public and explain the choice of the dissemination channels.

Describe how the visibility of EU funding will be ensured.

This AG considers the communication and dissemination activities as a continuing component of this process and a shared responsibility, strategically planned to perfuse throughout the whole duration of the project. WP2 aims to ensure a high visibility and impact for the activities and its results to policy makers, competent authorities and experts, and the society, both at national and European level.

To achieve this goal, the following two specific objectives have been formulated:

1: The Dissemination and Communication plan will specify the overall dissemination strategy and the definition of the lines of communication for society, as well as the lines of dissemination for stakeholders. This plan will be developed at the first three months of the project and reviewed after concluding the stakeholder analysis.

The communication activities will take place in the following order:

a) Dissemination and communication planning;
b) Visual identity creation;

c) Project website and Social Media accounts creation;
d) Stakeholder and policymaker mapping and analysis;
e) Dissemination and communication of the different WP activities and of the project results.
f) Final conference organisation.

As the research and results involve relevant information from several EU Member States, reports for communication and dissemination will be produced in both English and the national language of the participating Member States as far as possible.

2: The visibility of EU funding will be ensured by:

a) Linking up to EU priorities in the communication activities
b) Using the EU emblem correctly and prominently
c) Using accurate information; involving the EU when communicating

3.3 Sustainability and continuation

Sustainability, long-term impact and continuation

Describe the follow-up of the project after the EU funding ends. How will the project impact be ensured and sustained?

What will need to be done? Which parts of the project should be continued or maintained? How will this be achieved? Which resources will be necessary to continue the project? How will the results be used?

Are there any possible synergies/complementarities with other (EU funded) activities that can build on the project results?

As already mentioned, CAN.HEAL directly supports activities in two Flagships of the EBCP: **Flagship 6** on **'**Cancer Diagnostics and Treatment for All' initiative and **Flagship 7** on 'Genomics for Public Health'.

In CAN.HEAL we develop a concept to integrate and/or align activities in both flagships towards optimal cancer burden reduction within a cancer lifespan continuum paradigm. Considering our aim to develop a new paradigm, all elements that have been assessed and further developed within this project are essential to be maintained and transferred to the healthcare systems.

To achieve integration/alignment of the new paradigm, maximal interaction and synergy with other parallel EC initiatives, where MS representatives are included, will be established – especially collaboration with the JAs on Networks and Comprehensive Cancer Centres, the EHDS initiatives and the 1+Million Genomes initiative. In this way, co-creation processes can be launched which should increase the chances for successful continuation and uptake of the outcomes of this process. Participation with MS is a critical element in bringing this innovation to patients and citizens and will require major investments or re-allocation of funding at the member state level. Such impacts should be addressed along the further development of the paradigm preferentially in collaboration with organisations such as the ECB, the OECD,… and in concert with other EC funding mechanisms (such as the structural funds).

However, the project output can directly feed into numerous initiatives of the EBCP and the Mission on Cancer which could provide resources and funding for the continuation of follow-up steps of the CAN.HEAL activities:

- **UNCAN.eu**: CAN.HEAL partners are represented in the CSA and bring in the cancer lifespan continuum paradigm as an essential element
- **'Inter-specialty training programme'**: CAN.HEAL will directly interact with these initiatives and supply the effort with the validated experience from the project
- **Repurposing** of existing medicines: CAN.HEAL partners will align in this concept and support building evidence for these molecules within the cancer lifespan PDT continuum paradigm
- **Health Technology Assessment** regulation: support for the effectiveness demonstration for a cancer lifespan continuum paradigm will be seeked at EUNeHTA):
- **Partnership on Personalised Medicine** - 2023: CAN.HEAL partners will directly participate with these initiatives and bring in the cancer lifespan continuum paradigm as a working element
- Develop a **Roadmap towards precision prevention** – 2023-2025 and the '**Genomic for Public Health'** project– 2021-2025: Can.Heal cancer lifespan continuum paradigm can become the framework for the roadmap and project
- **High-Performance Computing** to rapidly test existing molecules and new drug combinations – 2023-2025: CAN.HEAL outcomes will provide pathways for new insights in potential drug developement and seek collaboration with this project(s)

- CAN.HEAL partners wish to work on development of **personalised cancer treatments** through tailored support and new digital platforms – 2021-2027.
- CAN.HEAL partners wish support collaborative projects on cancer diagnostics and treatment using **High-Performance Computing and AI** – 2021-2027.
- CAN.HEAL recommendations on ethical and legal data governance will inform the development of the 1+ Million Genomes project frameworks.

As CAN.HEAL partners are well represented in most of these initiatives and would be valuable partners in most of the others, the continuation of the outcomes of the project can be truly guaranteed. Moreover, all CAN.HEAL partners are committed to continue to work together in upcoming initiatives, notwithstanding the possibility for other partners to join the consortium.

4. WORK PLAN, WORK PACKAGES, TIMING AND SUBCONTRACTING

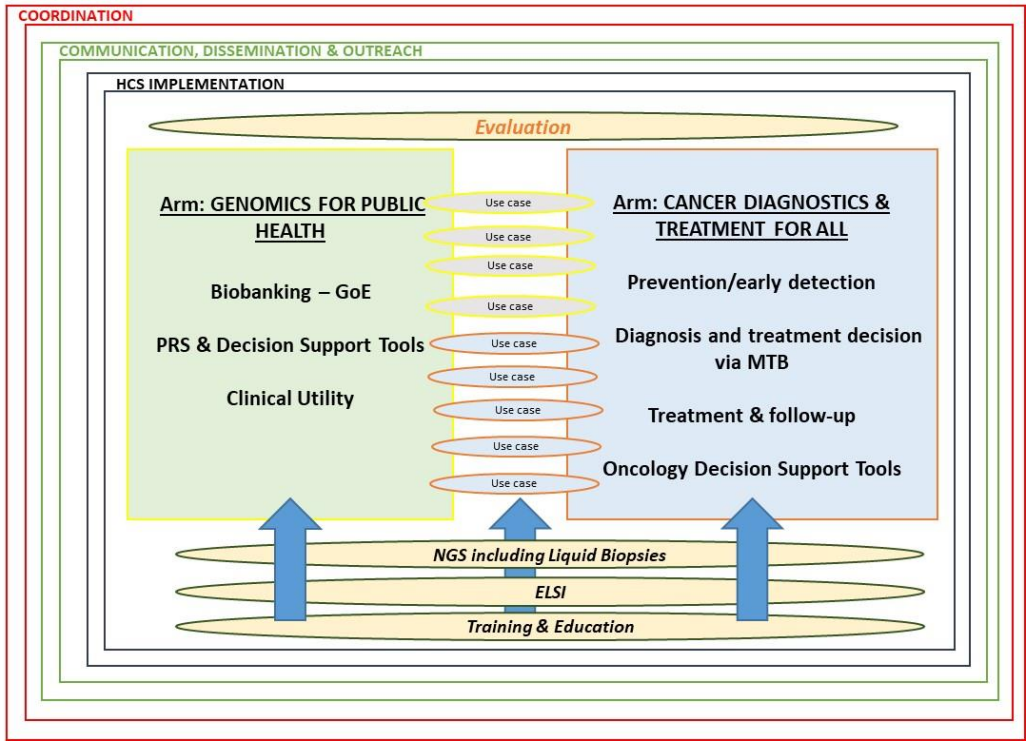
4.1 Work plan

Work plan

Provide a brief description of the overall structure of the work plan (list of work packages or graphical presentation (Pert chart or similar)).

Overall structure of the proposal

WP1	Coordination
WP2	Communication, Dissemination and outreach
WP3	Evaluation
	ARM: GENOMICS FOR PUBLIC HEALTH
WP4	Biobanking - Genome of Europe
WP5	Polygenic Risk Scores and Decision support Tools
WP6	Building clinical utility
	ARM: CANCER DIAGNOSTICS AND TREATMENT FOR ALL
WP7	Prevention/early detection
WP8	Diagnosis and treatment decision via MTB
WP9	Treatment and follow-up
WP10	Oncology decision support tools
WP11	NGS including liquid biopsy
WP12	ELSI (Law, Ethics and Citizen Engagement)
WP13	Education & training
WP14	HCS Implementation



4.2 Work packages and activities

WORK PACKAGES
This section concerns a detailed description of the project activities. *Group your activities into work packages. **A work package means a major sub-division of the project**. For each work package, enter an objective (expected outcome) and list the activities, milestones and deliverables that belong to it. The grouping should be logical and guided by identifiable outputs.* *Projects should normally have a minimum of 2 work packages. WP1 should cover the management and coordination activities (meetings, coordination, project monitoring and evaluation, financial management, progress reports, etc) and all the activities which are cross-cutting and therefore difficult to assign to another specific work package (do not try splitting these activities across different work packages). WP2 and further WPs should be used for the other project activities. You can create as many work packages as needed by copying WP1.* *For very simple projects, it is possible to use a single work package for the entire project (WP1 with the project acronym as WP name).Work packages covering financial support to third parties (⚠ only allowed if authorised in the Call document) must describe the conditions for implementing the support (for grants: max amounts per third party; criteria for calculating the exact amounts, types of activity that qualify (closed list), persons/categories of persons to be supported and criteria and procedures for giving support; for prizes: eligibility and award criteria, amount of the prize and payment arrangements).* ⚠ *Enter each activity/milestone/output/outcome/deliverable only once (under one work package).*

Work Package 1: Project management and coordination			
Ensure consistence with the detailed budget table (if applicable).			
Duration:	M1 – M24	**Lead Beneficiary:**	SC
Objectives *List the specific objectives to which this work package is linked.*			
▪ To set up, manage and implement the project and consortium management ▪ To set up, manage and implement the scientific and collaborative coordination (interaction within the consortium and with other EU initiatives) ▪ To set up, manage and implement a financial management and reporting			
Activities (what, how, where) and division of work			

Provide a concise overview of the work (planned tasks). Be specific and give a short name and number for each task.

*Show who is participating in each task: Coordinator (COO), Beneficiaries (BEN), Affiliated Entities (AE), Associated Partners (AP), indicating **in bold** the task leader. Add information on other participants' involvement in the project e.g. subcontractors, in-kind contributions.*

Note:

In-kind contributions: In-kind contributions for free are cost-neutral, i.e. cannot be declared as cost. Please indicate the in-kind contributions that are provided in the context of this work package.

The Coordinator remains fully responsible for the coordination tasks, even if they are delegated to someone else. Coordinator tasks cannot be subcontracted.

If there is subcontracting, please also complete the table below.

Task No (continuous numbering linked to WP)	Task Name	Description	Participants		In-kind Contributions and Subcontracting (Yes/No and which)
			Name	Role (COO, BEN, AE, AP, OTHER)	
T1.1	General project and consortium management	Setting-up and managing the governance structure (see 2.4); daily management of the Action, including administrative, organisational and financial issues; preparing and managing Grant Agreement, preparing docs for reporting, planning and managing consortium meetings.	**SC**	COO	Yes, 20% in-kind
T1.2	Scientific and collaborative coordination	Aligning and coordinating the ongoing work across all WPs through a continuous assessment of inputs and emerging results via a variety of methods. Monitor the overall progress of the AG. Coordination and integration with other closely-related projects.	**SC**, ACC and MHH-Ger Support by all partners	COO, BEN	Yes, 20% in-kind
T.1.3	Install an ad hoc project expert group on precision medicine and health	Evaluation of the clinical use of germline and somatic mutations, polygenic risk scores for precision medicine and health.	**MHH-Ger, ACC** & all other partners	BEN	Yes, 20% in-kind
T1.4	Financial management	Monitor and submission of financial expenditure (six-monthly reports, yearly and final)	**SC** and all other partners	COO, BEN	Yes, 20% in-kind
Milestones and deliverables (outputs/outcomes)					

Milestones *are control points in the project that help to chart progress. Use them only for major outputs in complicated projects. Otherwise leave the section on milestones empty.*

Means of verification are how you intend to prove that a milestone has been reached. If appropriate, you can also refer to indicators.

Deliverables *are project outputs which are submitted to show project progress (any format). Refer only to major outputs. Do not include minor sub-items, internal working papers, meeting minutes, etc. Limit the number of deliverables to max 10-15 for the entire project. You may be asked to further reduce the number during grant preparation.*

For deliverables such as meetings, events, seminars, trainings, workshops, webinars, conferences, etc., enter each deliverable separately and provide the following in the 'Description' field: invitation, agenda, signed presence list, target group, number of estimated participants, duration of the event, report of the event, training material package, presentations, evaluation report, feedback questionnaire.

For deliverables such as manuals, toolkits, guides, reports, leaflets, brochures, training materials etc., add in the 'Description' field: format (electronic or printed), language(s), approximate number of pages and estimated number of copies of publications (if any).

For each deliverable you will have to indicate a due month by when you commit to upload it in the Portal. The due month of the deliverable cannot be outside the duration of the work package and must be in line with the timeline provided below. Month 1 marks the start of the project and all deadlines should be related to this starting date.

The labels used mean:

Public — fully open (⚠ automatically posted online on the Project Results platforms)

Sensitive — limited under the conditions of the Grant Agreement

EU classified — RESTREINT-UE/EU-RESTRICTED, CONFIDENTIEL-UE/EU-CONFIDENTIAL, SECRET-UE/EU-SECRET under Decision 2015/444.

Milestone No (continuous numbering not linked to WP)	Milestone Name	Work Package No	Lead Beneficiary	Description	Due Date (month number)	Means of Verification
MS1	Kick-off meeting	WP1	SC	First meeting with all partners of the consortium	M1	Minutes of meeting
MS2	Mid-term meeting	WP1	SC	Meeting with all partners of the consortium	M12	Minutes of meeting
MS3	Final meeting	WP1	SC	Final meeting with all partners	M24	Minutes of meeting
MS4	Expert group	WP1	ACC, MHH-Ger	Establishment of an expert group on precision medicine and health	M6	Member list / Minutes of initiation meeting

Deliverable No (continuous numbering linked to WP)	Deliverable Name	Work Package No	Lead Beneficiary	Type	Dissemination Level	Due Date (month number)	Description (including format and language)
D1.1	Kick-off meeting	WP1	SC	R — report	PU — Public	M3	Mid-term technical and fin. report, pdf, English
D1.2	Final meeting	WP1	SC	R — report	PU — Public	M24	Mid-term technical and fin. report, pdf, English

Work Package 2: Communication, dissemination and outreach

Subtitle: Translational Stakeholder Policy Platform for Communication, Outreach and Dissemination

Ensure consistence with the detailed budget table (if applicable).

Duration:	M1 – M24	**Lead Beneficiary:**	EAPM & ECPC

Objectives

List the specific objectives to which this work package is linked.

O2.1: Create a Stakeholder Coordination Framework (SCF) to engage and align a broad range of stakeholders to facilitate bringing NGS and Public Health Genomics (PHG) in healthcare systems at MS and EU level.

O2.2: Support the **creation of a cross-European framework for stakeholders to align national and international efforts** on best practices in terms of governance frameworks, to support this implementation of NGS and PHG into healthcare systems.

O2.3: To ensure effective **communication and dissemination**.

Using this framework, WP will:

O2.4: In collaboration with the **two project pillars** drive a process to allow framework to implement NGS and PHG into healthcare systems to ensure early diagnosis

O2.5: Provide **operational feedback from stakeholders to the other WPs, based on the wider needs of the community.**

O2.6: Ensure **effective external communication and dissemination** of key findings.

Activities (what, how, where) and division of work

Task No (continuous numbering linked to WP)	Task Name	Description	Participants		In-kind Contributions and Subcontracting (Yes/No and which)
			Name	Role	
T2.1	Creating a Stakeholder Coordination Framework and terms of reference documents (Top down/Bottom Up) – Communication plan	Drafting a terms of reference paper to support stakeholder engagement and alignment	**EAPM** Support by all other partners	BEN	Yes – 20% in-kind
T2.2	Develop project website & Logo	External facing website to showcase and provide a platform for the public and external stakeholder			
T2.3	Organise a series of events to support engagement with Stakeholders	Two external events to engage with a broader group of stakeholders as well as policy makers			
T2.4	Develop a policy white paper to bring NGS and public Health genomics into healthcare systems	Policy paper that will provide recommendation of how stakeholders can facilitate bringing NGS and PHG into healthcare systems			
T2.5	Communication Material	Quarterly newsletter issued to promote the project, twitter page			

Milestones and deliverables (outputs/outcomes).

Milestone No (continuous numbering not linked to WP)	Milestone Name	Work Package No	Lead Beneficiary	Description	Due Date (month number)	Means of Verification
MS2.1	Stakeholder Coordination Group	WP2	EAPM	Setting up the Stakeholder framework, and putting this into operation and terms of reference documents	M4-M24	Members constitued, Document

MS2.2	Website & Logo	WP2	EAPM	Website and logo created		M3	Website/Logo
MS2.3	Bi-annual events	WP2	EAPM	Events for consortium/stakeholders		M10, M20	Report of event & agenda
MS2.4	Policy white paper	WP2	EAPM	Policy Paper to provide a framework to allow for multi-stakeholder input to support the adoption of NGS & PHD		M16	Paper Developed
MS2.5	Communication material	WP2	EAPM	Newsletters, press release and content for the website		M2-M24	Newsletter, press release
MS2.6	Communication & Dissemination plan to support the dissemination	WP2	EAPM	Plan developed and operational throughout the different WPs.		M6	Plan developed and finalised
Deliverable No (continuous numbering linked to WP)	Deliverable Name	Work Package No	Lead Beneficiary	Type	Dissemination Level	Due Date (month number)	Description (including format and language)
D2.1	Communication & Dissemination plan	WP2	EAPM/ECPC	Plan developed and implemented	Public	M6	Plan developed and finalised
D2.2	Website/Logo	WP2	EAPM	Website created & operational/update and logo	Public	M3	Website/Logo
D2.3	2 stakeholder events	WP2	EAPM/ECPC	Events Organised	Public	M10, M20	Report of event & agenda
D2.4	Policy white paper	WP2	EAPM/ECPC	White paper prepared	Public	M16	Paper Developed
D2.5	Communication material	2	EAPM/ECPC	Newsletter, press releases, content for website	Public	M2- M24	Newsletter, press release

Work Package 3: Evaluation			
Ensure consistence with the detailed budget table (if applicable).			
Duration:	M1 – M24	**Lead Beneficiary:**	AQuAS
Objectives *List the specific objectives to which this work package is linked.*			
O3.1 to assure and evaluate that the CAN.HEAL project is implemented as planned and that it accomplishes the objectives defined. O3.2 to assure that the produced knowledge and outcomes meet high quality standards, are appropriately disseminated and communicated and have a relevant impact on the 'Genomics for Public Health' and 'Cancer diagnosis and treatment for all' EU wide, as a way to ensure the sustainability of the project and its outcomes after its execution. O3.3 to provide with guidelines and tools for the evaluation to ensure equity, accessibility and scalability of value-based innovation adoption in personalised medicine to improve access to individuals and cancer patients to prevention, diagnosis and treatment programmes.			
Activities (what, how, where) and division of work			

Task No (continuous numbering linked to WP)	Task Name	Description	Participants		In-kind Contributions and Subcontracting (Yes/No and which)
			Name	Role	
T3.1	Development of Evaluation Plan (the quality of outputs and outcomes; involvement of different stakeholders; achievement objectives)	Create a tool (questionnaires, check-list and working groups) for a systematic and continuous monitoring of processes, outputs, outcomes and context.	**AQuAS**, WP leaders and SC	BEN COO (SC)	No
T3.2	Equity mainstreaming	Map existing guidelines and tools, as well as, best practices for mainstreaming equity in cancer prevention and control programmes and policies. A specific guide and related tools will be internally developed and promoted to support and monitor	**FISABIO**, WP leaders	BEN	No

		the entire project in addressing equity and gender sensitive-approach.			
T3.3	Development of dynamic and multidimensional impact assessment-(DMIA)-tool (incl. foresight scenarios & sustainable implementation scenario's)	Map existing initiatives, expertise and requirements for reimbursement and implementation of NGS tools. Construct an infrastructure to enable actual data input, according to the "living" reviews performed for COVID-19. Develop and promote a DMIA tool, (examples of tools that could be included for performing HTAs, (cost-) effectiveness, budget impact, value based healthcare). The tool will be pilot tested in cooperation with the Organisation of European Cancer Institutes, working group health economics, by using 10% of the budget for this specific task.	**NKI-AVL**, WP leaders	BEN	No
T3.4	Development of innovation adoption and integration assessment framework for the evaluation of the NGS programmes	Initial mapping of existing unmet need assessment, business case definition, value-based procurement and demand-driven innovation assessment frameworks. Co-creation of guidelines and recommendations for the evaluation of the NGS programmes and use cases therein to: 1) support and monitor the project in addressing a sustainable impact of the demand-driven innovation and a scalable adoption of the innovation and 2) ensure a good integration into the health systems at country and EU level.	**AQuAS**, WP leaders FISABIO NKI-AVL	BEN	Yes, 20% in-kind

Milestones and deliverables (outputs/outcomes)

Milestone No (continuous numbering not linked to WP)	Milestone Name	Work Package No	Lead Beneficiary	Description	Due Date (month number)	Means of Verification

MS1	Evaluation Plan Dissemination	WP3	AQuAS	Evaluation plan and tools disseminated and promoted through WPs leaders.		M8	Evaluation plan and tool sent and promoted through WP Leaders
MS2	Equity Guide Dissemination	WP3	FISABIO	Equity Guide disseminated and promoted through WPs leaders.		M8	Guide sent and promoted through WP leaders
MS3	DMIA tool	WP3	NKI-AVL	Development of a DMIA tool		M24	Tool sent and promoted through the WP leaders
Deliverable No (continuous numbering linked to WP)	Deliverable Name	Work Package No	Lead Beneficiary	Type	Dissemination Level	Due Date (month number)	Description (including format and language)
D3.1	Evaluation Plan and assessment tool	WP3	AQuAS	R — Document	SEN — Sensitive	M8	Contains all information for ensuring the succesful performance of the WP (incl tools) - Electronic, English
D3.2	Equity Guide	WP3	FISABIO	R — Document	SEN — Sensitive	M8	Contains all information and tools to address health inequalities in the context of the project - Electronic, English
D3.3	DMIA tool	WP3	NKI-AVL	Open access file & document	PU — Public	M24	Contains information for the use of the tool. Electronic, English
D3.4	Evaluation Guide-Report	WP3	AQUAS	R — Document	PU — Public	M24	Contains information for the multidimensional impact assessment, equity and gender equality, adoption of innovation in the CAN.HEAL project. - Electronic, English

Work Package 4: Biobanking - Genome of Europe			
Duration:	M1 - M24	**Lead Beneficiary:**	Erasmus MC

Objectives

- Create biobanks and (germline) genetic datasets for cancer patient cohorts
- Validate (germline) cancer genetic risk profiles in patient cohorts
- Integrate with results and guidelines from the million genomes of Europe effort (MG+)

Activities (what, how, where) and division of work

Task No	Task Name	Description	Participants		In-kind Contributions and Subcontracting (Yes/No and which)
			Name	Role	
T4.1	Create biobanks and genetic datasets	Coordinate with consortium members and determine where patient cohorts must be biobanked and/or genotyped for genetic profiling. Collect genetic data in the two-year period where possible.	**Erasmus MC**, KUL, LBMC-LV, NKI-AVL, MFH, CERTH, ELLOK, UGent, INSERM, EKUT	BEN	Yes – 20% in-kind
T4.2	Validate genetic profiles	Validation of genetic risk profiles in collaboration with WP5 and WP6. Investigate novel developments in PRS predictions, such as protective effects or personalised predictions.	**Erasmus MC, Tartu-UN**, **ULiege/KUL**, EKUT, INSERM, CERTH, LBMC-LV	BEN	Yes – 20% in-kind
T4.3	Integrate with 1 million genomes (1MG) efforts	Integrate genetic data collected from patients with 1MG collected reference data. Includes the comparison of genetic profiles, local population reference datasets and joint analyses.	**Erasmus MC, Tartu-UN, LBMC-LV**, INSERM	BEN	Yes – 20% in-kind

Milestones and deliverables (outputs/outcomes)							
Milestone No	Milestone Name	Work Package No	Lead Beneficiary	Description		Due Date (month number)	Means of Verification
MS1	Genetic overview	WP4	Erasmus MC	Overview of genetic or biobanking sets in consortium is created		M3	Overview circulated among consortium
MS2	Novel datasets	WP4	Erasmus MC	Novel genetic datasets to be used by consortium are generated		M12	Datasets announced and data returned within consortium
MS3	Genetic profiles	WP4/5/6	Erasmus MC, Tartu-UN, KUL	Genetic profiles are validated in existing + novel genetic datasets (if feasible)		M20	Results of genetic profile validation
Deliverable No	Deliverable Name	Work Package No	Lead Beneficiary	Type	Dissemination Level	Due Date (month number)	Description (including format and language)
D1.1	Biobanking and genotyping	WP4	Erasmus MC	R — Document, report	SEN — Sensitive	M3	List of cohorts to be biobanked/genotyped
D1.2	Genotyping data	WP4	Erasmus MC	R — Document, report	SEN — Sensitive	M12	Any datasets needed to be generated for the project
D1.3	Validation of genetic profiles	WP4 WP5/WP6	Tartu-UN/Erasmus MC/KUL	R — Document, report	PU — Public	M24	Local validation of any genetic profiles required

Work Package 5: Polygenic Risk Scores and Decision support tools			
Ensure consistence with the detailed budget table (if applicable).			
Duration:	M1 – M24	**Lead Beneficiary:**	Tartu-UN

Objectives

List the specific objectives to which this work package is linked.

1. Study the portability of PRS across the EU for breast and prostate cancer and investigate the concept of adding liquid biopsy (LB) based NGS analysis for the very high PRS individuals in order to increase the precision of personalised prevention in population-based early cancer detection and prevention (LB with WP11).

2. Study the AI-based decision support systems (DSS) using genetic and environmental data to predict disease before symptoms and investigate the concept of protective genes in case of the cancer phenotypes (With WP4).

3. Study the telegenetic applications, possible outcomes and quality criteria for remote genetic counselling on families and also on population scale.

Activities (what, how, where) and division of work

Task No	Task Name	Description	Participants		In-kind Contributions and Subcontracting (Yes/No and which)
			Name	Role	
T5.1	Analysis of the portability of PRS of most common cancers (breast, prostate, colorectal, melanoma)	Study the portability of PRS across the EU based on data from large GWAS studies	**Tartu-UN**, LBMC-LV, Erasmus MC, ULiège	BEN	No
T5.2	Inventory of DSSs for cancer treatment and prevention in research and clinical practice and investigate the concept of protective genes in estimation of PRS	Providing a state-of-the-art overview on the use of DSSs and evidence-based recommendations for minimizing risk in DSS design, implementation, evaluation, and maintenance.	**Tartu-UN**, Erasmus MC, LBMC-LV, UGent, ULiège	BEN	No
T5.3	Developing recommendations and population screening guidelines for identifying people with high cancer risk and for large scale population-based early intervention programs which include LB in certain cases	Investigating the applications of LB together with next-generation sequencing (NGS)	**Tartu-UN**, UKE, LBMC-LV, IBSAL-IECSCYL	BEN	No
T5.4	Collecting regulations and best practices of population-based genetic counselling and remote telegenetic genetic	Establishing strategies for the implementation of telegenetics and remote genetic counselling in Europe to personalize public health care	**MHH-Ger**	BEN	No

	counselling in EU						

Milestones and deliverables (outputs/outcomes)

Milestone No	Milestone Name	Work Package No	Lead Beneficiary	Description	Due Date (month number)	Means of Verification
MS1	Portability of the PRS and DSS	WP5	Tartu-UN	Data is collected for the analysis	M12	Report
MS2	Collecting regulations and best practices of population-based genetic counselling	WP5	MHH-Ger	Data is collected for subsequent analysis	M12	Report

Deliverable No	Deliverable Name	Work Package No	Lead Beneficiary	Type	Dissemination Level	Due Date (month number)	Description (including format and language)
D5.1	Inventory of the portability of the PRS across the EU and inventory of protective genomic loci in cancer.	WP5 Cooperation with WP4	Tartu-UN	R — Document, report	PU — Public; SEN — Sensitive; R-UE/EU-R — EU Classified ; C-UE/EU-C — EU Classified	M24	Portability of the PRS tested and its predictive ability validated in local cohort, in different biobanks in collaboration with Erasmus MC. Analysis of genomic and health data in biobanks in respect of protective genes.
D5.2	Inventory of the DSS and recommendations for establishing large scale population-based early intervention programs for the prevention of cancers utilizing NGS and LB	WP5 Cooperation with WP4, WP11	Tartu-UN	R — Document, report	PU — Public	M24	Analysis of the augmentation of PRS with LB in case of cancer and recommendations for experimental testing of this approach.

D5.3	Description of regulations in remote genetic counselling in EU	WP5, Cooperation with WP2, 3, 5, 7, 8, 9, 12, 13	MHH-Ger	R — Document, report	Public	M1- M9	Collecting regulations and delivery opportunities of genetic counselling and remote genetic counselling in participating EU countries/ Overview article
D5.4	Regulations and recommendations in remote genetic counselling, access to telegenetics/remote genetic counselling	WP5, Cooperation with WP2, 3, 5, 7, 8, 9, 12, 13, 14	MHH-Ger	R — Document, report	Public	M10-M20	Recommendations (feeds into D5.3)
D5.5	Quality criteria for different telemedical platforms	WP5, Cooperation with WP2, 3, 5, 7, 8, 9, 12, 13, 14	MHH-Ger	R — Document, report	Public	M18-M24	Recommendations (feeds into D5.3)

Work Package 6: Building clinical utility			
Ensure consistence with the detailed budget table (if applicable).			
Duration:	M1 – M24	**Lead Beneficiary:**	KUL
Objectives *List the specific objectives to which this work package is linked.*			
(1) Map clinical utility evidences and chart measures of evaluation; (2) Set up a network and reference centers to aid identification of cancers during pregnancy using non-invasive prenatal testing (NIPT); (2) Identify monogenic and polygenic genetic alterations in pediatric leukemia patients and their family members to better understand the cause of paediatric leukemia; (3) Improve familial cancer risk prediction in the population by evaluating the impact of incorporation of PRS in the current standardized risk stratification.			

Activities (what, how, where) and division of work					
Task No (continuous numbering linked to WP)	Task Name	Description	Participants		In-kind Contributions and Subcontracting (Yes/No and which)
			Name	Role	
T6.1	PHG based clinical utility	Catalogue and define evidences of the clinical utility field for cancer and associated evaluation measures (incl. aspects of health economics and PRS directed towards early/inherited cancer)	**KUL**, EAPM, UCSC, Erasmus MC, OIL, INSA	BEN	Yes – 20% in-kind
T6.2	Use case: cancers in pregnancy (CIP)	Design and facilitate the implementation of guidelines for the downstream clinical management of candidate CIP patients. AIMS: Create a network of NIPT centres/ reference centres; Define parameters to classify a NIPT test as suggestive of cancer and identification of patients and their families (include information on clinical utility measurements); Centralized validation of suspicious NIPT in reference centre; Roll out guidelines for downstream clinical management of NIPT results suspicious of cancer; On the road to translation by assessing performance characteristics. [Prospective task: follow-up children born to pregnant cancer patients]	**KUL**, UCSC, ELBS, Jessa Hosp	BEN	Yes – 20% in-kind
T6.3	Use case: Paediatric cancer	Identify ALL patients and their families that meet criteria, and ethically share clinical information; Perform genetic and bioinformatics analyses; Ensure accessibility of data for participating partners; On the road to translation regarding clinical implications on diagnostics, prognostics, and preventive or treatment implications [Prospective Task. Extend experience and knowledge to other entities of childhood cancer]	KUL, ULiège, **MHH-Ger**, Erasmus MC, LBMC-LV	BEN	Yes – 20% in-kind
T6.4	Use case: Cancer risk stratification	Evaluate the impact of incorporation of PRS in current standardized risk stratification; Perform genetic analyses of predefined HBOC genes and SNPs in carrier and non-carrier breast cancer families; Bioinformatics analyses and PRS incorporation; Ensure accessibility of data for participating partners; On the road to translation of	**KUL**, Erasmus MC, LBMC-LV, IHBT, EKUT, IC	BEN	Yes – 20% in-kind

		results. Demonstrate clinical utility of PRS in cancer risk assessment by individualized counselling and follow-up [Prospective Task: Extend to other breast cancer families and to other cancer types; Demonstrate clinical utility of measurable residual disease (MRD) by NGS in acute myeloid leukemia and incorporated to into routine practice]			
T6.5	Monogenic/polygenic disease risk genes and their actionability as part of an information platform on genomics-driven cancer risk factors for clinical utility	Collect all information about monogenic oncogenes, actionability, therapeutic potential. Demonstrate the utility of polygenic risk profiling to identify groups of individuals who could benefit from the knowledge of their probabilistic susceptibility to disease (with WP4-5).	**KUL**, MHH-Ger, ERN, Gentauris, OIL, Erasmus MC, Tartu-UN, EKUT	BEN	Yes – 20% in-kind

Milestones and deliverables (outputs/outcomes)

Milestone No (continuous numbering not linked to WP)	Milestone Name	Work Package No	Lead Beneficiary	Description	Due Date (month number)	Means of Verification
MS1	Map clinical utility evidences and chart measures of evaluation	WP6	KUL	Inventory and assessment of clinical utility measurements focused on the WP's use cases cancer	M12	Inventory
MS2	Use case: detection of cancers in pregnancy (CIP)	WP6	KUL	EU based reference network fully operational; Defined parameters to classify a NIPT test as suggestive of cancer; Guidelines for downstream management of NIPT results suspicious of cancer developed	M4, 6 & 24	Public via website, report, position paper
MS3	Use case: Paediatric cancer	WP6	MHH-Ger	Identification of family-based monogenic or polygenic alterations in paediatric ALL;Clinical implications for diagnostics, prognostics, and preventive or treatment implications.	M16 & 24	Report, position paper

MS4	Use case: Cancer Risk Stratification	WP6	KUL	Identification PRS and new risk stratification in HBOC; Demonstrate clinical utility of PRS in cancer risk assessment.		M20 & 24	Report, position paper
MS5	Information platform on genomics-driven cancer risk factors for clinical utility	WP6	KUL	Collect all information about monogenic oncogenes, actionability, therapeutic potential. Demonstrate the utility of polygenic risk profiling to identify groups of individuals who could benefit from the knowledge of their probabilistic susceptibility to disease		M24	Online platform
Deliverable No (continuous numbering linked to WP)	Deliverable Name	Work Package No	Lead Beneficiary	Type	Dissemination Level	Due Date (month number)	Description (including format and language)
D6.1	PHG based clinical utility map of evidences and models for cancer,	WP6	KUL	R — Document	PU — Public	M24	Overview article/ Guidelines
D6.2	Ealuation criteria of use case cancers in pregnancy screening	WP6	KUL	R — Document, report	PU — Public	M24	Recommendations
D6.3	Platform integrating information on actionable monogenic and polygenic cancers, with clinical utility in childhood cancers and familial cancers	WP6	MHH-Ger, KUL	R — Document, report	PU — Public	M24	Recommendations; Central EU based information point about actionable cancer predisposition

Work Package 7: Prevention/early detection

Ensure consistence with the detailed budget table (if applicable).			
Duration:	M1 – M24	**Lead Beneficiary:**	ACC

Objectives

List the specific objectives to which this work package is linked.

- To apply wet lab tools for early cancer detection (simultaneous NGS testing of germ line (GER) and somatic (SOM) DNAs)
- To run clinical pilots with selected wet lab tools

Activities (what, how, where) and division of work

Task No (continuous numbering linked to WP)	Task Name	Description	Participants		In-kind Contributions and Subcontracting (Yes/No and which)
			Name	Role	
T7.1	NGS platforms: integrating germ line and somatic DNA testing in early cancer diagnostics	**Tumor tissues and leukocytes:** GERSOM (164 somatic-actionable genes, 120 cancer-predisposing genes, 180 driver genes,141 pharmacogenomics-relevant SNPs). **ctDNA:** OncNGS (>300 genes: GER + SOM + mutation burden surrogates). TILB (≥5 SNVs/patient). Technical deployment; NGS testing platforms open to all other WP7 partners.	**ACC,** CERTH, Charité, IC, ICO, INSERM, KUL, MUW, NKI-AVL, EKUT, IOV	BEN	Yes – 20% in-kind
T7.2	Pilots: trials in early cancer (adjuvant setting)	Recruitment of patients in the ongoing GERSOM (ACC: breast and colorectal) and EOLUNG (ICO: lung) study designs (n=20 each); Develop Standard Operating Procedures (SOP) for biospecimen collection, and investigate possibilities to upscale pilot studies to all partners (capacity building).	**ICO,** ACC, CERTH, Charité, IC, INSERM, KUL, MUW, NKI-AVL, EKUT, IOV	BEN	Yes – 20% in-kind

T7.3	Evaluation: Health Technology assessment, social and economic implications, patient benefit.	Explore/identify suitable platforms and tools (e.g. cBioPortal, oncNGS,…) to achieve the best possible integration of T7.1 and T7.2 outputs. Share experience with and provide a one-stop harmonized solution to record monogenic actionable alterations, multi-omic integration, standard recommendation, and risk assessment (individual patients and families) to obtain cost-effective patient benefit.	**NKI-AVL,** ACC, CERTH, Charité, IC, ICO, INSERM, KUL, MUW, EKUT, IOV	BEN	Yes – 20% in-kind

Milestones and deliverables (outputs/outcomes)

Milestone No	Milestone Name	Work Package No	Lead Beneficiary	Description	Due Date (month number)	Means of Verification
MS1	NGS platform testing complete	WP7	ACC	Testing of 5 patients with each of the three techniques (GERSOM, OncNGS and TILB).	M6	Raw data shared among the partners
MS2	Completion of pilot studies	WP7	ICO	Recruitment complete, biospecimens collected, shipped and tested for all 40 patients.	M16	NGS data available and uploaded on the selected platform
MS3	Annotation	WP7	NKI-AVL	Annotation of T7.1 and T7.2 data on the selected database platform(s).	M20	Platform basic functions functional with all datasets.

Deliverable No	Deliverable Name	Work Package No	Lead Beneficiary	Type	Dissemination Level	Due Date (month number)	Description (including format and language)
D7.1	NGS testing data	WP7	ACC	R — Document, report	PU — Public	M18	40 evaluable patients tested, raw and curated NGS data. Link with ELBS (WP11) to address technical NGS issues.

D7.2	Integration of NGS and clinical data	WP7	ICO	R — Document, report	PU — Public	M20	NGS data available in the framework of clinical information.
D7.3	HTA	WP7	NKI-AVL	R — Document, report	PU — Public	M22	Data transfer to WP3 for HTA evaluation.

Work Package 8: Diagnosis and Treatment decision via MTB

Ensure consistence with the detailed budget table (if applicable).

Duration:	M1 – M24	**Lead Beneficiary:**	IC

Objectives

List the specific objectives to which this work package is linked.

- Define MTB structures and functioning across the different countries with a focus on national initiatives.
- Provide guidelines for optimized sample and data workflow strategies used in MTBs (starting from the patient and tumor sampling, to the techniques used for molecular profiling, and to the interpretation and reporting of the clinical relevance of identified molecular alterations).
- Define impact and challenges of the omics implementation on patient treatment including access to clinical trials and genetic counselling.

Activities (what, how, where) and division of work

Task No (continuous numbering linked to WP)	Task Name	Description	Participants		In-kind Contributions and Subcontracting (Yes/No and which)
			Name	Role	
T8.1	Molecular Tumor board Organisations	Describe the different organizations of MTB across countries and institutions of the	**IC,** CERTH, ACC, HCL, Charité, ICO,	BEN	Yes – 20% in-kind

		consortium; Describe applied NGS panel types and patient selection criteria for genomic screening per country.	IHBT, IOV, UCCSH, MSCI		
T8.2	National initiative programs for genome wide tumor characterization	Identify national initiatives (WGS) and MTBs with focus on the French initiative and Belgian Precision program aiming to provide country-wide access for cancer patients to diagnosis and treatment.	**IC**, INSERM**,** IBSAL-IECSCYL, MUW, ACC, HCL, Charité, ICO, IJB, MSCI	BEN	Yes – 20% in-kind
T8.3	Molecular interpretation and bioinformatics for clinically relevant molecular alterations and clinical decision	Provide standardized guidelines for molecular interpretation that utilize reproducible bioinformatics pipelines (including machine learning approaches).	**CERTH,** IBSAL-IECSCYL, MUW, ICO, IC, ACC, HCL, Charité, ICO, IHBT, IJB, IOV, UCCSH, MSCI	BEN	Yes – 20% in-kind
T8.4	MTB endpoints - Use case: Carcinoma of unknown primary (CUP)	Describe the different experience on drug and clinical trial access, management of MTB endpoints across institutions/countries. Aims to: identify the impact of high throughput NGS of tumour samples (WGS/RNAseq) on diagnosis and treatment decision using CUP and rare cancers as model; list EU initiatives with CUP as model and beyond workflow experiences; integrate different clinical and molecular data available within the consortium for future clinical trials and research exploitation	**IC,** MUW, ACC, HCL, Charité, ICO, IJB	BEN	Yes – 20% in-kind

Milestones and deliverables (outputs/outcomes)

Milestone No (continuous numbering not linked to WP)	Milestone Name	Work Package No	Lead Beneficiary	Description	Due Date (month number)	Means of Verification
MS1	EU initiatives and databases (CUP-other rare cancer)	WP8	IC	List EU initiatives and databases for CUP and other rare cancer	M24	Document with list

Deliverable No (continuous numbering linked to WP)	Deliverable Name	Work Package No	Lead Beneficiary	Type	Dissemination Level	Due Date (month number)	Description (including format and language)
D8.1	Local MTB organizations	WP8	IC	R — Document, report	PU — Public, R-UE/EU-R — EU Classified	M12	Description of the different organizations of MTB, applied NGS panel types, and patient selection criteria across Europe. PDF, English
D8.2	Genomic national initiatives	WP8	IC	R — Document, report	PU — Public, R-UE/EU-R — EU Classified	M12	List and description of national initiatives for genome wide tumor characterization. PDF, English
D8.3	Standardized guidelines	WP8	ACC	R — Document, report	PU — Public, R-UE/EU-R — EU Classified	M19	Standardized guidelines for molecular interpretation. PDF, English
D8.4a	Number of patients oriented towards personalised treatment	WP8	ICO	R — Document, report	PU — Public, R-UE/EU-R — EU Classified	M24	Overview of the number of patients oriented towards personalised treatment. PDF, English
D8.4b	Impact of WGS on patients care	WP8	IC	R — Document, report	PU — Public, R-UE/EU-R — EU Classified	M24	Results of studies describing the impact of WGS on patient care. PDF, English

Work Package 9: Treatment and follow-up

Ensure consistence with the detailed budget table (if applicable).

Duration:	M1 – M24	**Lead Beneficiary:**	Jessa Hosp

Objectives

List the specific objectives to which this work package is linked.

- To evaluate the clinical value of CGP in “real-world” practice for offering more therapeutic options to cancer patients and a broader access to precision oncology.
- To implement a fully standardized CGP wet-lab performance, data analysis, clinical interpretation, therapy recommendation and reporting among NGS labs of the EU.
- To describe and quantify the uptake of innovative treatments and the inclusion in clinical trials recommended by a national or international MTB guided by the CGP.
- To work in a multi-stakeholder approach to attract more innovative treatments and clinical trials to countries of the EU.

Activities (what, how, where) and division of work

Task No (continuous numbering linked to WP)	Task Name	Description	Participants		In-kind Contributions and Subcontracting (Yes/No and which)
			Name	Role	
T.9.1	National Precision oncology initiatives	Data on up to 1000 patients will be collected. Subtask 1: CGP implementation, standardization and “real world” execution Subtask 2: Precision oncology therapy choices in “real world” Subtask 3: Quantification of access to innovative drugs guided by CGP+MTB results (eg. standard-of-care, by inclusion in clinical trials or medical need programs or by off-label use) Subtask 4: Follow-up of precision oncology treatment outcomes Subtask 5: microcosting of CGP and provide info to WP3 (HTA) Use case: establishing a NGS laboratory consortium covering all Belgium geographically and a national MTB assuring access to CGP and CGP based standardized treatment recommendations for all Belgian citizens	**Jessa Hosp** IJB	BEN BEN	Yes – 20% in-kind

T.9.2	CGP variant database	Establishment of a publicly available database of genomic variants in cancer including the quantification of the clinical significance (strong, potential, unknown or no clinical significance) Use case: Data of T.9.1 upload in a cBioPortal cohort and embed in CAN.HEAL module of cBioPortal (bridge to relevant other WPs)	**Jessa Hosp** CERTH	BEN BEN	Yes – 20% in-kind
T.9.3	Virtual MTB tools	Optimize tools used to integrate CGP results and clinical data, to support the working of the MTB and the standardized precision oncology treatment choices Share experience with and provide advice to WP10: Decision support tools Use case: Practical organisation of a national MTB in Belgium	**Jessa Hosp** IJB, IC	BEN BEN	Yes – 20% in-kind
T9.4	Capacity building Precision initiative - CGP+MTB EU expansion	Transpose the concept to other EU countries and investigate feasibility of implementation Use case: Greece, Spain (Catalunya), Malta, Serbia, Poland, Italy	**Jessa Hosp** CERTH, ICO, MFH, IOV, MUW, IC, ACC	BEN BEN	Yes – 20% in-kind

Milestones and deliverables (outputs/outcomes)

Milestone No (continuous numbering not linked to WP)	Milestone Name	Work Package No	Lead Beneficiary	Description	Due Date (month number)	Means of Verification
MS1	Preliminary data analysis CGP+MTB	WP9	Jessa Hosp	Mid-term analysis of the endpoints of T.9.1	M12	Report
MS2	Capacity building methodology	WP9	Jessa Hosp	Consensus on the methodology of T.9.4	M12	Protocol including surveys, work plan and timeline

Deliverable No	Deliverable Name	Work Package No	Lead Beneficiary	Type	Dissemination Level	Due Date	Description (including format and language)
D9.1	National Precision initiatives	WP9	Jessa Hosp	R — Document, report	PU — Public	M24	Results of national precision oncology initiatives. Electronic, English, 20 pages

							Online database
D9.2	Capacity building	WP9	Jessa Hosp	R — Document, report	PU — Public	M24	Overview and results of the capacity building activities. Electronic, English, 20 pages

Work Package 10: Oncology decision support tools			
Ensure consistence with the detailed budget table (if applicable).			
Duration:	M1 – M24	**Lead Beneficiary:**	SC

Objectives

List the specific objectives to which this work package is linked.

- Map and define tools for clinical and genomic data integration and decision support for the Molecular Tumour Board and treatment decision
- Harmonisation and optimization data integration and decision support tools
- Integration of data from national initiatives to scale up and to standardise
- Pilot deployment and usability evaluation of the Decision Support Tool

Activities (what, how, where) and division of work

Task No (continuous numbering linked to WP)	Task Name	Description	Participants		In-kind Contributions and Subcontracting (Yes/No and which)
			Name	Role (COO, BEN, AE, AP, OTHER)	

T10.1	Mapping, describing, and identifying the gaps of current decision support tools (DST) used in nation-wide covered initiatives	Summary of available platforms and tools for genomic and clinical data integration with longitudinal follow-up, decision support of the MTB and the standardized precision oncology and haemato-oncology treatment choices. Interact with WP6 (PRS and DST)	**SC** DIGICORE, Jessa Hosp, IC, ACC, CERTH, INSERM, IBSAL-IECSCYL, KUL, MFH, MSCI	COO BEN	Yes, 20% in-kind
T10.2	Harmonization/interoperability national DST	Interaction with WP7, 8, 9 to support the concept regarding integration process, structuring and standardisation of required data, MTB structure, treatment decisions; Develop or optimise tools based on the guidelines. Use cases: cBioPortal, Digicore, oncNGS, HARMONY, BALLETT, GERSOM, EOLUNG			
T10.3	Capacity building in EU for DST in (hemato-)oncology and pilot application	Develop transfer modalities of standardized DST to other countries.			

Milestones and deliverables (outputs/outcomes).

Milestone No (continuous numbering not linked to WP)	Milestone Name	Work Package No	Lead Beneficiary	Description	Due Date (month number)	Means of Verification
MS1	MAP-DST	WP10 (WP6)	SC	Description of current DST in partner countries	M12	Document with description mapping
MS2	CapBuild-DST	WP10 (WP7, WP8, WP9)	SC	Identify at least 2 partner countries for DST transfer	M24	Protocol document

Deliverable No (continuous numbering linked to WP)	Deliverable Name	Work Package No	Lead Beneficiary	Type	Dissemination Level	Due Date (month number)	Description (including format and language)
D10.1	EU-oncDST	WP10	SC	R — Document, report	PU — Public	M12	Report with the concept, pdf, English

D10.2	Protocol-oncDST	WP10	SC	R — Document, report	PU — Public	M24	Protocol, pdf, English

Work Package 11: NGS including Liquid Biopsy (LB)			
Ensure consistence with the detailed budget table (if applicable).			
Duration:	M1 – M24	**Lead Beneficiary:**	UKE/ELBS & CERTH

Objectives

List the specific objectives to which this work package is linked.

- Establish a quality management system for NGS-based clinical assays
- Standardize assay-reporting outcomes to facilitate data harmonization across the EU
- Develop recommendations, guidelines, and best practices to move the clinical implementation of NGS technologies forward
- Perform Experimental Quality assurance (QA) studies based on expertise from ELBS consortium (www.elbs.eu)

Activities (what, how, where) and division of work

Task No (continuous numbering linked to WP)	Task Name	Description	Participants		In-kind Contributions and Subcontracting (Yes/No and which)
			Name	Role	
T11.1	Horizontal NGS themes	Subtasks: **Standards and quality metrics** for NGS: develop a salient set of qualitative and quantitative metrics for the assessment of NGS data; **Phenotypic and clinical metadata framework**: develop a framework for phenotypic and clinical data from patients in order to make genetic data useful in clinical settings; **Best practices in sharing and linking phenotypic and genomic data**: develop a framework that facilitates interoperability across the national genomic, clinical and phenotypic data	**CERTH,** ELBS (UKE**,** AU**,** NKI-AVL**,** UCCSH), ELLOK, LBMC-IV, IOV, IHBT, IBSAL-IECSCYL	BEN	Yes, 20% in-kind

T11.2	Technical validation of liquid biopsy assays	Perform experimental quality assurance (QA) studies (e.g. development of external quality standards and ring experiments for technical assay validation) for solid tumors and hematologic malignancies. Create a framework for the establishment of a permanent organization for maintenance of a recurrent liquid biopsy QA program and certification. Subtasks: Technical **ctDNA** based assay validation; **cfmiRNA** based liquid biopsy assays including multiplex PCR, arrays, and NGS; **Circulating tumor cell (CTC)** based liquid biopsy assays	**ELBS, UKE,** AU**,** NKI-AVL**,** UCCSH**,** IOV, ACC	BEN	Subtasks 1 and 3 may expect in-kind contribution from Agena, Menarini and Angle

Milestones and deliverables (outputs/outcomes).

Milestone No (continuous numbering not linked to WP)	Milestone Name	Work Package No	Lead Beneficiary	Description	Due Date (month number)	Means of Verification
MS1 (Task 11.1)	Resource catalogue	WP11	CERTH	An initial catalogue of relevant resources	M6	Live document is made available as an internal list
MS2 (Task 11.1)	Prototype repository of SOPs	WP11	CERTH	First prototype of the Centralized Online Repository	M18	Outlining the functionality of the repository
MS3 (Task 11.1)	Standard recommendations	WP11	CERTH	Set standards for the consortium	M24	Live document is made available as an internal list
MS4 (task 11.2)	Preparation	WP11	ELBS	Site deployment and training of instruments and existing technologies,	M6	Live document
MS5 (task 11.2)	Ring trials	WP11	ELBS	Execution of ring trials to test standards and protocol feasibility	M18	Live document is made available as an internal list
MS6 (task 11.2)	Recommendations	WP11	ELBS	Write recommendations based on analysis of ring trials	M24	Publication of document

Deliverable No (continuous numbering linked to WP)	Deliverable Name	Work Package No	Lead Beneficiary	Type	Dissemination Level	Due Date (month number)	Description (including format and language)

D1 (Task 11.1)	Data exchange SOP	WP11	CERTH	R — Document	PU — Public	24	SOPs for clinical, image and omics data exchange
D2 (Task 11.2)	Liquid biopsy guidelines	WP11	ELBS	R — Document	PU — Public	24	Preparation of written guidelines for LB assays.

Work Package 12: Law, Ethics and Citizen Engagement (ELSI)

Ensure consistence with the detailed budget table (if applicable).

Duration:	M1 - M24	**Lead Beneficiary:**	UNILU

Objectives

List the specific objectives to which this work package is linked.

- Developing legal, ethical and trust frameworks for clinical and public health cancer genomics.

Activities (what, how, where) and division of work

Task No	Task Name	Description	Participants		In-kind Contributions and Subcontracting (Yes/No and which)
			Name	Role	
T12.1	Legal and Ethical Requirements and Data Governance	Develop ethical and legal data governance for cancer genomics. A key aspect will be to clearly define the purpose(s) for which data will be processed, which may include integrated screening and treatment, reporting of incidental findings to sequenced individuals and their families, as well as data sharing and secondary use for research, care of other patients (“clinical data sharing”), and public policy purposes.	**UNILU** SC	BEN COO	Yes – in-kind; No - subcontracts.

T12.2	Citizen/Patient Perspectives on Data Governance	Ensure the appropriate integration of citizen and patient perspectives specifically on matters of ethical governance of genomic data in clinical and public health contexts related to cancer.	**SC** UNILU	COO BEN	Yes – in-kind; No - subcontracts.

Milestones and deliverables (outputs/outcomes).

Milestone No (continuous numbering not linked to WP)	Milestone Name	Work Package No	Lead Beneficiary	Description	Due Date (month number)	Means of Verification
MS1	ELSI Workshop	WP12	SC	To identify areas for further inspection of citizen/patient perspectives on data governance	M12	Workshop report

Deliverable No (continuous numbering linked to WP)	Deliverable Name	Work Package No	Lead Beneficiary	Type	Dissemination Level	Due Date (month number)	Description (including format and language)
D12.1	Ethical and legal compliance recommendations for data governance	WP12	UNILU	R — Document, report	PU — Public	M24	Privacy, security, and access governance recommendations for genomic data sharing in screening/treatment contexts. (Word, English)
D12.2	Citizen/patient engagement recommendations for data governance	WP12	SC	R — Document, report	PU — Public	M24	Recommendations on criteria or processes for engaging citizens and patients on ethical aspects of genomic data sharing, and how to integrate the results of such engagement into data governance.

Work Package 13: Training & Education

Ensure consistence with the detailed budget table (if applicable).			
Duration:	M1 – M24	**Lead Beneficiary:**	ISS

Objectives

List the specific objectives to which this work package is linked.

- Develop models for training and educational interventions on oncogenomics addressed to health professionals, patients and the general public
- Provide specific education and training for health workers to advance the implementation of genetic testing in oncology
- Promote harmonised and certified European training pathways on oncogenomics for health professionals involved in Molecular Tumour Boards (MTB)

Activities (what, how, where) and division of work.

Task No	Task Name	Description	Participants		In-kind Contributions and Subcontracting (Yes/No and which)
			Name	Role	
T13.1	Basic e-learning on oncogenomics for health professionals	The aim is to disseminate on a wider scale in EU the iPAAC JA pilot e-learning on Oncogenomics Specific sub-tasks are: 1.1 Finalisation of the pilot iPAAC e-learning module 1.2 Translation of the module into local languages (at least two: IT, SP) 1.3 CME certification 1.4 Capacity building in piloting countries: Italy, Spain, Malta, Greece, Portugal, France	**ISS** ICO, INSA, MFH, CERTH, ELLOK, IC, IBSAL-IECSCYL, INSERM, DIGICORE	BEN	Yes/Subcontracting
T13.2	Advanced courses addressed to health professionals	Taking input from the thematic WPs and target communities, develop learning pathways addressing the multidisciplinary educational needs of the health professionals involved in (MTB). Specific sub-tasks are:	**CERTH** ACC, IBSAL-IECSCYL, IC,	BEN	Yes, 20% in-kind

		2.1 Gap analysis (challenges and training needs). 2.2 Collection of existing and development of new training materials from European infrastructures and Associations (ELIXIR, EATRIS, EHA, ESMO). Topic specific learning pathways will be developed through targeted workshops, leveraging knowledge and experience from the network of consortium experts. 2.3 Demonstration and delivery of the training repository. Deliver an open repository of FAIR training materials, accessible online will be delivered. Pilot sites: Greece, Italy, Germany, Spain	ICO, DIGICORE, ISS, INSERM		
T13.3	Training and literacy initiatives addressed to patients and general public	Identify and improve the public's and patients' literacy levels on broad concepts about genetics and oncogenomics, by deriving a communication framework, co-creating and disseminating materials through a variety of channels. Organise for both public and patients, a literature review and intersectoral focus groups to identify key educational needs and best communication means. Prepare creative and engaging educational contents and disseminate through on-line channels and public events. Develop a framework with recommendations for assessing the impact of educational content on literacy and attitudes of the public/patients. Pilot sites: 5-6 pilot partner countries, with an approximate geographical distribution across all EU regions, and in the national language.	**ELLOK/INSA** CERTH, OIL, MFH, ACC, ISS, IC, INSERM, DIGICORE	BEN	Yes/Subcontracting

Milestones and deliverables (outputs/outcomes).

Milestone No	Milestone Name	Work Package No	Lead Beneficiary	Description	Due Date (month number)	Means of Verification
MS1	Task 1 e-learning module finalisation	WP13	ISS	Task1 e-learning module finalised	M6	Application for CME credits English version

MS2	T1 e-learning module delivery	WP13	ISS	Basic e-learning module on-line in participating countries (English or local languages)		M18	web links to access Task 1 e-learning module
MS3	T2 thematic workshops	WP13	CERTH	Thematic workshops for the preparation of training materials achieved		M12	Report on the materials produced
MS4	T2 learning pathways	WP13	CERTH	Successful completion of demonstrator workshops/webinar(s)		M18	List of delivered workshops
MS5	T3 Literature and literacy review	WP13	ELLOK	Successful completion of the literature review		M6	Report on the review of literature
MS6	T3 Focus Groups	WP13	ELLOK/INSA	Successful completion of the focus groups foreseen in tasks 3.1 and 3.2		M12	Report on the results of the focus groups
MS7	T3 Educ. material	WP13	ELLOK/INSA	Educational materials for tasks 3.1&2		M18	Educational materials
Deliverable No (continuous numbering linked to WP)	Deliverable Name	Work Package No	Lead Beneficiary	Type	Dissemination Level	Due Date (month number)	Description (including format and language)
D13.1	Basic E-learning module on Oncogenomics	WP13	ISS	R — Document, report	PU - Public	M20	Basic e-learning module on Oncogenomics addressed to Health professional. Module's materials (Eng, Ita, Sp, Fr)
D13.2	Open on-line repository of advanced training modules on Oncogenomics	WP13	CERTH	R — Document, report	PU - Public	M24	An open repository of FAIR training material, accessible online; link to training material collection; English

D13.3	Educational materials with dissemination plan	WP13	ELLOK/INSA	R – Document report with reference to on-line resources	PU - Public	M24	Development and dissemination plan for material on oncogenomics to the public, patients and their families
D13.4	Framework for the evaluation	WP13	ELLOK/INSA	R – Document report	PU - Public	M24	Framework for the evaluation of the materials to patients/general public

Work Package 14: Healthcare system implementation

Ensure consistence with the detailed budget table (if applicable).

Duration:	M3 – M24	**Lead Beneficiary:**	UCSC

Objectives

List the specific objectives to which this work package is linked.

- To have a full understanding of the research advancements and of the effectiveness, the clinical utility, key success factors and gaps of current personalised approaches and their potential to be scaled up
- To support Public health authorities with a coordinated, harmonised and comprehensive research strengthening their capacity in implementing personalised and sustainable approaches.

Activities (what, how, where) and division of work

Task No	Task Name	Description	Participants		In-kind Contributions and Subcontracting (Yes/No and which)
			Name	Role	
T14.1	Synthesis of mapping exercises and identification of key success factors and gaps of current personalised approaches	Synthetize evidence and mapping analysis conducted in WP6, WP10 and WP12.	UCSC, INSERM	BEN	Yes, 20% in-kind

T14.2	Set-up of the Medical and Public Health Cancer Genomics Platform	To design the concept of a platform aimed at aggregating and sharing data, evidence and outcomes emerged in the project, including documentation of ongoing initiatives.	UCSC, INSERM	BEN	Yes, 20% in-kind
T14.3	A modelling tool for forecasting impact of an optimal Cancer Care Model	Starting from the results of the analysis conducted in the other WPs, an optimal Cancer Care Model focused on a given clinical pathway (e.g. breast cancer) will be defined.	UCSC, INSERM	BEN	Yes, 20% in-kind
T14.4	Recommendations development towards effective and sustainable implementation	Recommendations for the adoption of Personalised approaches into EU health system will be developed following a co-creation approach ensured by a strong stakeholder engagement done in collaboration with WP2.	UCSC, RIVM, INSERM	BEN	Yes, 20% in-kind

Milestones and deliverables (outputs/outcomes).

Milestone No (continuous numbering not linked to WP)	Milestone Name	Work Package No	Lead Beneficiary	Description	Due Date (month number)	Means of Verification
MS1	Release of the recommendations	WP14	UCSC	Release of the Recommendations for adopting innovative, sustainable and high-quality personalised approaches in the EU health system	M24	Specific deliverable submitted

Deliverable No	Deliverable Name	Work Package No	Lead Beneficiary	Type	Dissemination Level	Due Date (month number)	Description (including format and language)
D1.1	Report on Mapping results	WP14	UCSC	R – report	PU - Public	M17	Report about the synthesis of mapping exercises and identification of key success factors and gaps of current personalised approaches

D1.2	Final version of the Recommendations	WP14	UCSC	R – report	PU - Public	M24	Release of the final version of the recommendations

RIVM has a formal collaboration (2021-2024) with NIVEL, NI within the EUHealthSupport consortium which helps the EC DG-Santé on punctual issues raised by the Europe's Beating Cancer Plan.

4.3 Timetable

Timetable (projects up to 2 years)

Fill in cells in beige to show the duration of activities. Repeat lines/columns as necessary.

Note: *Use the project month numbers instead of calendar months. Month 1 marks always the start of the project. In the timeline you should indicate the timing of each activity per WP.*

ACTIVITY	MONTHS																							
	M 1	M 2	M 3	M 4	M 5	M 6	M 7	M 8	M 9	M 10	M 11	M 12	M 13	M 14	M 15	M 16	M 17	M 18	M 19	M 20	M 21	M 22	M 23	M 24
Task 1.1: Management																								
Task 1.2: Coordination																								
Task 1.3: Expert group																								
Task 1.4: Financial man.																								
Task 2.1: Stakeholder FW																								
Task 2.2: Website/logo																								
Task 2.3: Events																								
Task 2.4: Policy White paper																								

Task 2.5: Communication	
Task 3.1: Evaluation Plan	
Task 3.2: Equity	
Task 3.3: DMIA tool	
Task 3.4: Framework	
Task 4.1: Biobanks	
Task 4.2: Validation PRS	
Task 4.3: Integration 1MG	
Task 5.1/5.2/5.3/5.4: PRS and DSS	
Task 6.1: Clinical utility (CU)	
Task 6.2/6.3/6.4: Use cases CU	
Task 6.5: CU platform	
Task 7.1: NGS platforms	
Task 7.2: Pilots	
Task 7.3: Evaluation	
Task 8.1: MTB organisation	
Task 8.2: Genomic initiatives	

Task 8.3: Variant interpretation																								
Task 8.4: MTB endpoints																								
Task 9.1: Precision oncology																								
Task 9.2: CGP variant database																								
Task 9.3: Virtual MTB tools																								
Task 9.4: Capacity building																								
Task 10.1: Map DST																								
Task 10.2: Harmonisation DST																								
Task 10.3: Capacity building																								
Task 11.1: Horizontal NGS themes																								
Task 11.2: Liquid biopsy	**PREPARATION**						**EXECUTION**												**DATA ANALYSES**					
Task 12.1 – 12.2: ELSI																								
Task 13.1.1: Final. e-learning																								
Task 13.1.2: Translation																								
Task 13.1.3: CME certification																								
Task 13.1.4: Capacity building																								
Task 13.2.1: Gap analysis training																								

Task 13.2.2: Training materials																								
Task 13.2.3: Repository																								
Task 13.3: Literacy																								
Task 14.1: Synthesis mapping																								
Task 14.2: M&PH GEN platform																								
Task 14.3: Modelling tool																								
Task 14.4: Recommendations																								

4.4 Subcontracting

Subcontracting

Give details on subcontracted project tasks (if any) and explain the reasons why (as opposed to direct implementation by the Beneficiaries/Affiliated Entities).

Subcontracting — Subcontracting means the implementation of 'action tasks', i.e. specific tasks which are part of the EU grant and are described in Annex 1 of the Grant Agreement.

***Note:** Subcontracting concerns the outsourcing of a part of the project to a party outside the consortium. It is not simply about purchasing goods or services. We normally expect that the participants have sufficient operational capacity to implement the project activities themselves. Subcontracting should therefore be exceptional.*

Include only subcontracts that comply with the rules (i.e. best value for money and no conflict of interest; no subcontracting of coordinator tasks).

Work Package No	Subcontract No (continuous numbering linked to WP)	Subcontract Name (subcontracted action tasks)	Description (including task number and BEN to which it is linked)	Estimated Costs (EUR)	Justification (why is subcontracting necessary?)	Best-Value-for-Money (how do you intend to ensure it?)
WP13	S13.1	expert WP13 activities	ISS Tasks: T13.1 and T3.2	10,000	expert supervision of training modules	direct awarding on the basis of proven expertise

WP13	S13.2	academic T13.1	ISS Tasks: T13.1	5,000	e-learning module pharmacogenomics	direct awarding on the basis of proven expertise
WP11	S11.1	Health-RI	NKI-AVL	50,000	cBioPortal services	direct awarding on the basis of proven expertise
Other issues: *If subcontracting for the project goes beyond 30% of the total eligible costs, give specific reasons.*			Insert text			

5. OTHER

5.1 Ethics

Ethics *If the Call document contains a section on ethics, describe ethics issues that may arise during the project implementation and the measures you intend to take to solve/avoid them.*
Not applicable.

5.2 Security

Security *If the Call document contains a section on security, describe security issues that may arise during the project implementation and the measures you intend to take to solve/avoid them.* *Indicate if there is need for EU classification of information (Decision 2015/444) or any other specific security measures.*
Not applicable.

6. DECLARATIONS

Higher funding rate (if applicable)	**YES/NO**
Do you fulfil the conditions set out in the Call document for a higher funding rate? If YES, explain and provide details.	**YES**
17 MS REPRESENTED AND MORE THAN FOUR BELOW 90% OF EU AVERAGE GNP	

Double funding	
Information concerning other EU grants for this project ⚠ *Please note that there is a strict prohibition of double funding from the EU budget (except under EU Synergies actions).*	**YES/NO**
We confirm that to our best knowledge neither the project as a whole nor any parts of it have benefitted from any other EU grant *(including EU funding managed by authorities in EU Member States or other funding bodies, e.g. Erasmus, EU Regional Funds, EU Agricultural Funds, European Investment Bank, etc)*. If NO, explain and provide details.	YES
We confirm that to our best knowledge neither the project as a whole nor any parts of it are (nor will be) submitted for any other EU grant *(including EU funding managed by authorities in EU Member States or other funding bodies, e.g. Erasmus, EU Regional Funds, EU Agricultural Funds, European Investment Bank, etc)*. If NO, explain and provide details.	YES

Financial support to third parties (if applicable) *If in your project the maximum amount per third party will be more than the threshold amount set in the Call document, justify and explain why the higher amount is necessary in order to fulfil your project's objectives.*

Not applicable

ANNEXES

LIST OF ANNEXES

Standard
Detailed budget table (annex 1 to Part B) — *mandatory*
CVs (annex 2 to Part B) — *mandatory, if required in the Call documents*

LIST OF PREVIOUS PROJECTS

List of previous projects *Please provide a list of your previous projects for the last 4 years.*					
Participant	Project Reference No and Title, Funding programme	Period (start and end date)	Role (COO, BEN, AE, OTHER)	Amount (EUR)	Website (if any)
[name]					
[name]					

HISTORY OF CHANGES		
VERSION	PUBLICATION DATE	CHANGE
	02.09.2022	2.6 Cost effectiveness and financial management: Change: “We will be requiring all partners to fill in timesheets and upload their financial documents (invoices, salary slips, proof of travel costs, etc.) to the system, as already been used by Sciensano for managing other EC projects.” To: We will be requiring all partners to fill in timesheets and retain their financial documents (invoices, salary slips, proof of travel costs, etc.) for justification and eventual check.
	02.09.2022	Lygature is not participating in the Can.Heal project, due to the financial requirements of the grant. They are not able to cover the 20% in-kind contribution. 2.2 Consortium set-up: Lyg is removed from the table. 2.3 Project teams, staff and experts: I. Custers and R. Azevedo are removed from the table.
	02.09.2022	Affiliated entities for Digicore (INT, IFO), UKSH (UzL), ACC (IEO, HSR, IFO, FGP) are added in table page 15-17 (Consortium set-up)
	02.09.2022	The beneficiary in the project is the organization Universitätsklinikum Schleswig-Holstein. The correct short name is UKSH, not UCCSH. Short name UCCSH is changed to UKSH at 2.2 Consortium set-up and 2.3 Project teams, staff and experts.

	02.09.2022	2.3 Project teams, staff and experts: ACC (IRE) is changed to ACC (IFO) for P. Giacomini
	14.10.2022	4.4 Subcontracting: The subcontracting costs (50,000) for WP11 are added for cBioPortal services.
	20.10.2022	2.5 Project management, quality assurance and monitoring and evaluation strategy: Specific action-level indicators defined for the two sub-topics for reporting purposes are added.
	03.11.2022	WP1: Deliverables changed (in yellow) WP8 & WP9: Description of delivrables provided (in yellow)
	18.11.2022	Type of deliverables were revised. Datasets and pilots were changed to reports (in yellow)