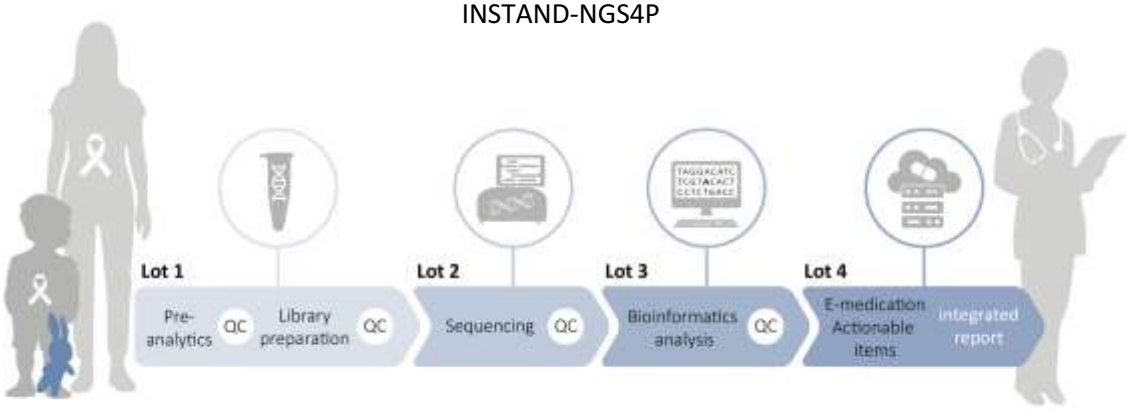
Co-funded by the European Union
Grant Agreement n°874719

INtegrated and STANDardized NGS workflows FOR Personalized therapy

INSTAND-NGS4P



INSTAND-NGS4P is an EU-funded Pre-Commercial Procurement (PCP) project for improving cancer patient's benefit from Next Generation Sequencing (NGS) by developing an integrated and standardized NGS workflow. For this, it will compile information from cancer gene testing, pharmacogenomics testing and e-medication in proper presentation to medical doctors for supporting therapy decision making at bedside widely applicable in health systems.

The EU co-funded PCP project provides funding for a public consortium to define unmet medical and technical needs based on an Open Market Consultation, which lays the foundation for a call for tenders addressing solution providers (companies) to develop their products to better meet user needs. At three cut-off periods, companies responding to this call will be evaluated regarding their ability to answer these users' needs from design perspective until the product phase. The total funding allocated to companies for product development (in total 8.55 M€) will finally lead to two integrated standardized NGS workflows, including decision support.

Major challenges to be addressed are:

- Improving the analytical performance by standardizing pre-analytical processes
- Integrating pre-analytical, analytical processes and data analytics into a standardized workflow
- Defining genetic variants with established medical implications for common and rare cancer of adult and pediatric cancers including pharmacogenomic variants relevant for drugs used in cancer care
- Developing reference material for quality control
- Meeting requirements of the European *in vitro*-diagnostics regulation
- Improving benefits for patients and health systems from NGS

Molecular diagnostics and subsequent medical decisions are often affected by the heterogeneity of pre-analytic conditions during sample preparation and DNA extraction, as well as by the compatibility of pre-analytical processes with analytical platforms and bioinformatic data analysis. Furthermore, there is a major gap between scientific progress and knowledge in NGS, pharmacogenomics and e-medication and the actual implementation of this complex information in routine healthcare.

Bringing NGS closer to bedside and increasing the benefit for patients is the objective of INSTAND-NGS4P. To achieve this goal, major emphasis is placed on actively involving patients through patient advocacy groups, as well as clinicians from the very beginning. By providing integrated information from NGS, pharmacogenomics and e-medication to medical doctors in an appropriate format, decision making on targeted therapies and additional medications will be supported at the bedside.

Instand-NGS4P is a 65-month PCP project – which started on January 1st 2020, with 18 partners federating:

- 7 European leading medical centres from 5 countries (two are coordinating European Reference Networks) as the buyers' group; they have major experience in using different NGS platforms in research and routine diagnostics: led by the **Medical University of Graz** (MUG - the lead procurer - AT), jointly with the **University of Florence** (UNIFI - IT), the **ERASMUS University Medical Centre** (EMC - NL), the **University of Milano-Bicocca** (UNIMIB - IT), the **University Clinics of Schleswig-Holstein** (UKSH - DE), and the two coordinating ERNs on cancer: **St. Anna Kinderkrebsforschung** (CCRI GmbH - AT) and the **Centre Leon Bérard** (CLB – FR), devoted to rare paediatrics cancers and adult rare cancers, respectively.
- 2 European patient advocacy groups, represented by the **Italian Patient Association** (FAVO – IT) and the **European Cancer Patient Coalition** (ECPC - BE),
- a standardization organization (**German Institute of Standardisation** (DIN)),
- partners participating in the European Research infrastructures: **BBMRI-ERIC** with the **Technical University of Munich** (TUM – DE) and **UNIMIB**, and **ELIXIR** through the Slovenian node, the **University of Ljubljana**,
- as well as several partners involved in NGS-related EU programs to cover all technical aspects and transversal needs & requirements: the **University of Manchester** (Uniman – UK) and the **University of Liverpool** (UoL – UK) connecting to the 100,000 Genomes Project and the **UK Biobank** with pharmacogenomics; the **Organisation of European Cancer Institutes** (OECI – BE) representing 92 entities, 13 Clinical Accredited Centres and 18 Accredited Comprehensive Cancer Centres, and the **University of Helsinki** (UH – FI) involved in the FIMM network,
- one SME, **BioXPedia**, who will act as future potential buyer, and
- **iPRI** (International Prevention Research Institute – FR), ensuring transparent dissemination of research worldwide.

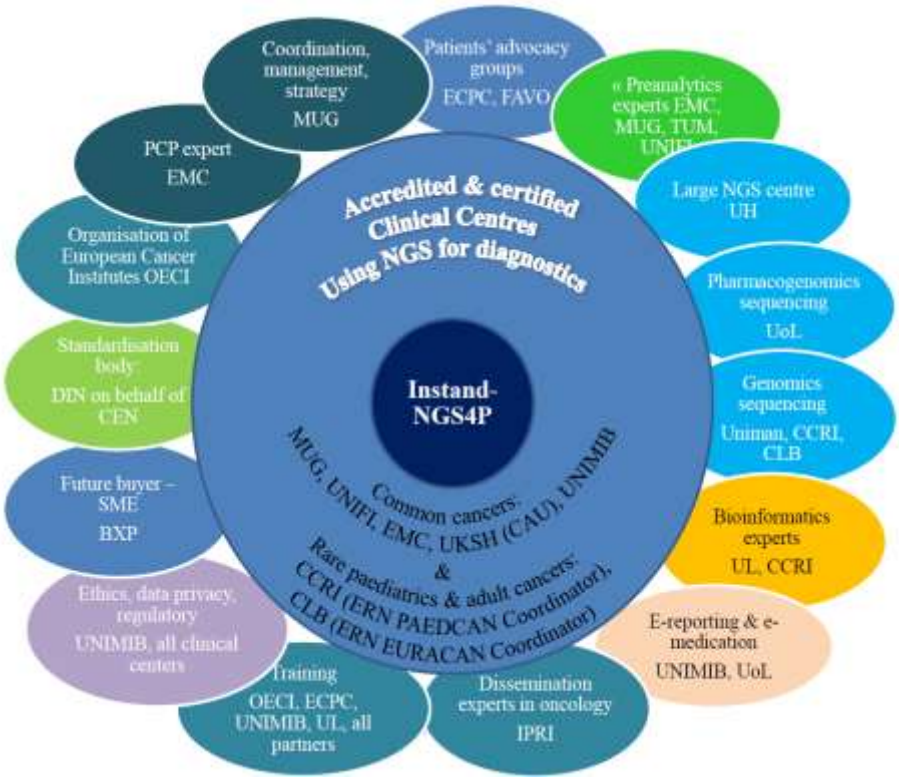
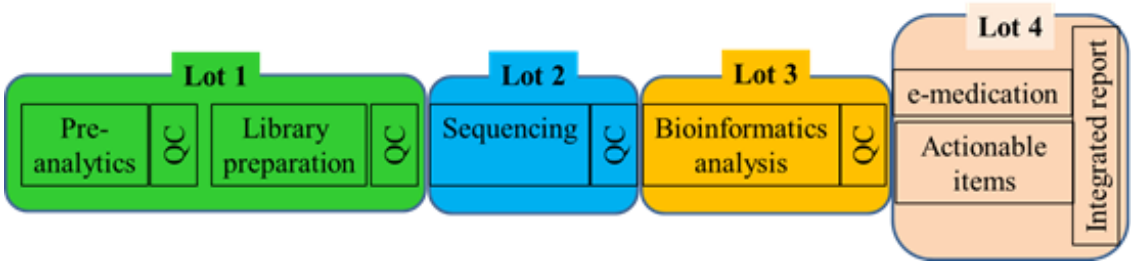


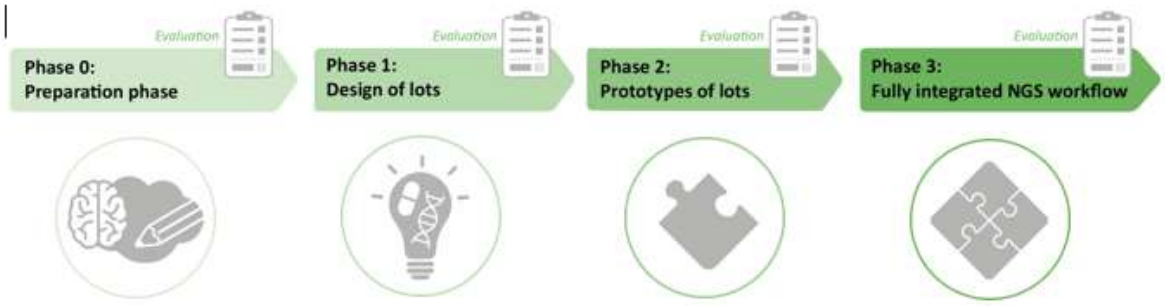
Fig 1 Participants in Instand-NGS4P

Driven by patient and clinical needs, two innovative NGS workflows (panel-based and whole genome sequencing) from sample pre-analytics to medical decision-making will be developed for routine diagnostics of common and rare adult and paediatric cancers complying with the IVDR. Criteria for inclusion of certain cancer types and subtypes are common patterns between adult and pediatric types, well-defined genetic markers for diagnosis, validated prognostic genetic markers and the availability of validated actionable genetic markers. The modular design of the workflow (4 lots) will enable SMEs in particular to contribute, and provides flexibility to adopt emerging user needs and technologies.



Specifications and upcoming development phases will also support the selected "PCP suppliers" in complying with regulatory requirements for IVDs. The last aspect concerns the joint contributions on international standards, requiring development of reference materials and implementation of external quality assessment schemes, covering the whole workflow.

Key figures: 12.22 M€ for Instand-NGS4P, with EC funding share of nearly 11 M€.
The 7 leading centres decide to procure jointly in a pre-commercial step, to achieve the ambitious objectives. 8.55 M€ is to be allocated to the R&D suppliers, who will be selected based on public tenders all along this PCP process comprising 3 phases according to the best value for money solution, after the closure of the preparation phase.



This preparation phase will involve an Open Market Consultation (OMC) (supporting the subsequent preparation of the call for tenders) to ensure proper alignment between the patient and clinical needs with the 7 leading clinical centres – representing a guarantee on developing the required critical mass to achieve this ambitious program, **and** the R&D service providers' community as well as the regulatory and payers' bodies. After gathering all feedbacks from the OMC, the 3 PCP phases will start with the publication of the call for PCP R&D suppliers. These 3 phases foresee the leverage of the 4 technical lots (i.e., on pre-analytics, sequencing, bioinformatics, e-reporting/e-medication) and their standardized interfaces, to be assembled in a full integrated NGS workflow.

- The first phase will address the design stage (Phase 1), for each lot.
- The second phase will concentrate on prototypes (Phase 2).
- The full integration will occur in Phase 3.

- At the end of Phase 3, Instand-NGS4P will provide 2 fully integrated, standardized NGS workflows for routine diagnostics of common and rare cancers from adults to children.

At the end of each phase, the PCP R&D suppliers are evaluated according to the defined published evaluation process - in a fair and transparent process - and the best R&D suppliers are retained for the next phase.
All the activities, including the evaluation process for all phases, are organised in partnership with the European Commission.

In order to enable broad implementation in healthcare systems throughout Europe and beyond, and to increase benefit to patients, a series of support activities are planned that include communication and dissemination activities targeting a broad stakeholder community, development of training and education material for healthcare professionals and patients, health economic assessment and engagement with healthcare payers and policy makers.

Stay tuned with our project website for the key events and dates:

- Publication of PIN/Open Market Consultation announced: End December 2020
- Open Market Consultation launched: End March 2021
- Publication for the PCP call for tenders – Phase 1: October 2021
- Closure of tenders' receipt – Phase 1: December 2021
- Start of Phase 1 with 15 Contractors: April 2022
- Start of Phase 2 with 11 Contractors: November 2022
- Start of Phase 3: March 2024
- End of Phase 3: May 2025

http://www.instandngs4p.eu/