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SPECIAL COMMUNICATION

Development and implementation of novel liquid biopsy NGS panels via the OncNGS precommercial procurement (PCP) initiative

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Background: Circulating tumor DNA (ctDNA) analysis is transforming oncology, but challenges such as insufficient analytical sensitivity, difficult variant interpretation, suboptimal turnaround time, limited deployment flexibility, and high costs hinder its broader adoption and raise concerns about reimbursement sustainability across European health care systems.

Materials and methods: To address these challenges, we created the OncNGS consortium, comprising academic, public, and private hospitals (buyers' group) and several supporting entities, to run a European precommercial procurement (PCP) initiative. The consortium defined ctDNA diagnostic testing requirements, conducted an open market consultation, and launched a call for tender. Suppliers were invited to develop an end-to-end, Conformité Européenne *In Vitro* Diagnostic (CE-IVD)-compliant solution integrating wet laboratory, dry laboratory, and reporting workflow in a single procedure, offering short turnaround time and reasonable cost.

Results: The OncNGS consortium defined criteria for a versatile, modular, cost-effective solution, deployable centrally or on-site, and adaptable to advancements in precision oncology. Launched in July 2022, the tender attracted seven companies, with four selected for phase I—OncNGS solution(s) design. From these, three advanced to phase II—prototyping. Ultimately, two contractors were awarded contracts for phase III to assess the clinical performance of their prototypes.

Conclusions: By leveraging the PCP approach, OncNGS aims to deliver innovative, affordable solutions to standardize ctDNA testing and reporting across European Union countries, improving diagnostic and therapeutic strategies for oncology patients.

Key words: liquid biopsy, ctDNA, OncNGS, comprehensive genomic profiling (CGP), precommercial procurement (PCP)

BACKGROUND

The use of liquid biopsy (LB) for the diagnostic profiling of circulating tumor DNA (ctDNA) is transforming oncology,[1,2] with proven benefit across major diagnostic, prognostic, and therapeutic applications. Although robust and reliable, ctDNA testing still suffers from a number of known pitfalls (summarized in Supplementary Table S1, available at https://doi.org/10.1016/j.esmoop.2025.105127) related to analytical sensitivity, specificity, variant interpretation, turnaround time, flexible deployment models, sustainable cost, and reimbursement schemes in European health care systems.[3] The impact of these pitfalls is roughly proportional to panel size/complexity. Nevertheless, the expansion

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of the actionable genomic space makes the comprehensive genomic profiling (CGP) of hundreds of genes highly desirable. CGP pitfalls were considered by a recent workshop organized by the European Liquid Biopsy Society (ELBS), resulting in expert consensus recommendations.[4]

To address at least some known challenges, a cross-border group of academic public and private health care providers responded to an innovation precommercial procurement (PCP) call launched by the European Commission in 2019 under the H2020 work program. This call [next-generation sequencing (NGS) for routine diagnosis] was an opportunity for our OncNGS consortium to address the equitable implementation of cost-effective ctDNA CGP into routine clinical practice across Europe. The OncNGS PCP project, launched in January 2020, aimed to deliver 'The best NGS tests, for all solid tumor/lymphoma patients, forever' (https://cordis.europa.eu/project/id/874467).

MATERIALS AND METHODS

The OncNGS PCP: specific features

The OncNGS PCP, a single framework contract for research and development (R&D) services, was launched by Sciensano as a lead procurer. Structured into three competitive phases, it ensured thorough development and evaluation. Phase I selected four suppliers to design the OncNGS solution over 4 months. Successful contractors submitted offers for phase II, and three awardees developed working prototypes over a 12-month period. Phase II applicants submitted offers for phase III, resulting in two suppliers being awarded a contract to demonstrate clinical performance in a real-world setting over a 15-month period (Figure 1). Figure 1 also shows the OncNGS PCP project timeline.

The OncNGS PCP is scheduled to end in March 2026. Based on its outcome, a value-based public procurement of innovative solutions (PPI) might be started.

Eligible OncNGS suppliers included universities, research centers, small and medium-sized enterprises, large companies, and consortia. More than 50% of the contracted work had to be carried out within the European Union (EU).

The OncNGS PCP: consortium and approach

The OncNGS consortium consists of a buyers' group and supporting entities. The buyers' group includes eight academic public and private hospitals: Institut Jules Bordet (IJB), Alleanza Contro il Cancro (ACC), Institut Curie (IC), Hospices Civils de Lyon (HCL), Institut Català d'Oncologia (ICO), Charité Universitätsmedizin Berlin (HC), and Ludwig

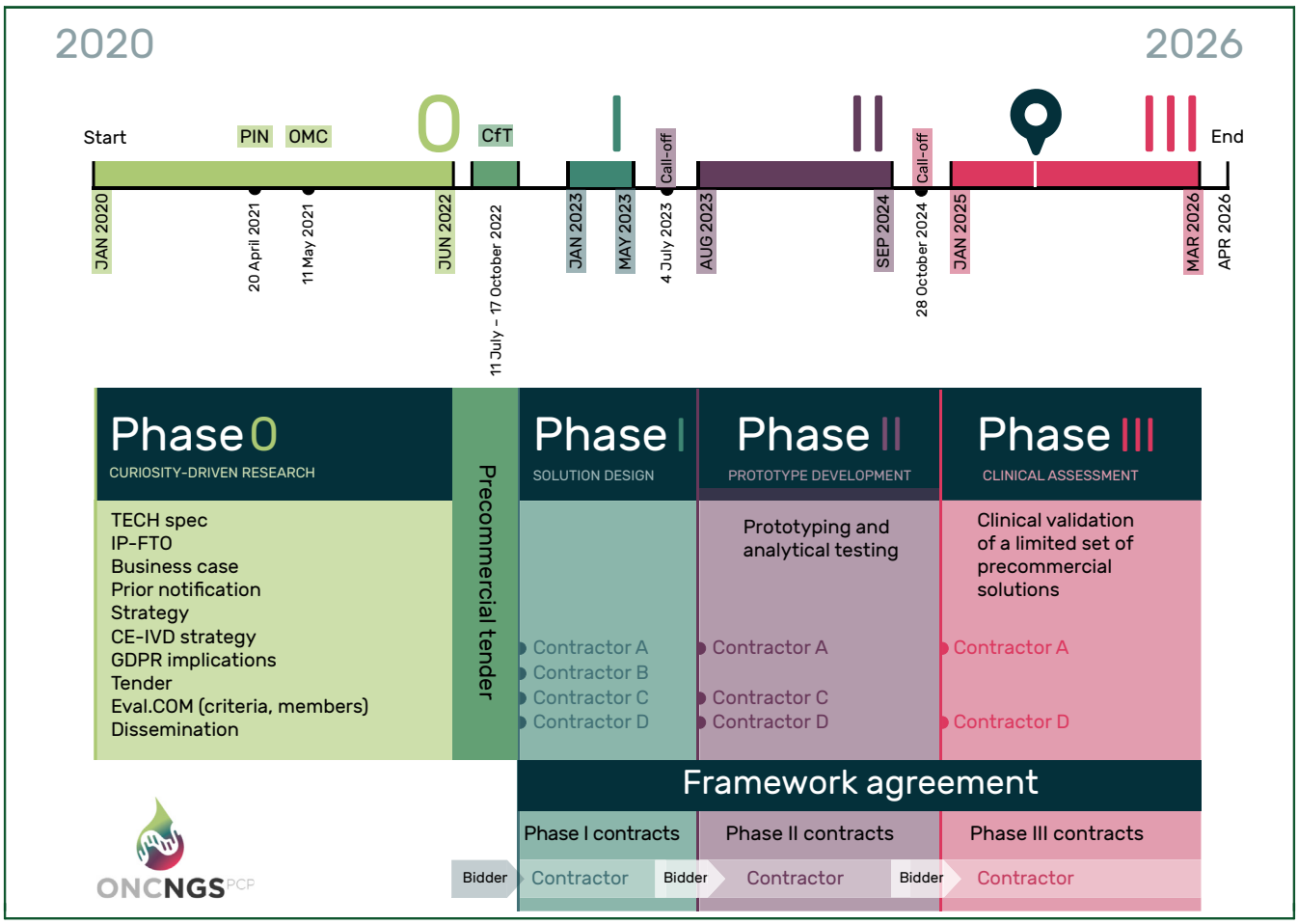

Figure 1. Overview of the OncNGS PCP procedure and project timeline.
CE-IVD, Conformité Européenne *In Vitro* Diagnostic; CfT, call for tender; GDPR, General Data Protection Regulation; IP-FTO, intellectual property freedom to operate; OMC, open market consultation; PCP, precommercial procurement; PIN, prior notice information.

Maximilians University (LMU). The six supporting entities are Agència de Qualitat i Avaluació Sanitàries de Catalunya (AQuAS), De Clercq & Partners, Institut National du Cancer (INCa), Belgian Cancer Registry (BCR), V*all d'Hebron Institute of Oncology* (*VHIO*), and Instituto De Investigación Biomédica De Salamanca (IBSAL).

Before launching the contract, buyers and supporting entities convened to identify and prioritize their unmet needs. Multiple workshops using the Miro visual platform (www.miro.com) helped experts (medical oncologists, pathologists, molecular biologists, and bioinformaticians) to assess technical and clinical needs and translate them into specific solution requirements. These sessions focused on describing the current environment and defining the desired future solution in terms of technology, data handling, patient needs, assets, resources, and input/output interfaces. Insights were categorized into five key areas: clinical workflow, wet laboratory, bioinformatics, molecular/clinical interpretation, and reporting. After reviewing state of the art and freedom to operate, an open market consultation assessed market readiness to address these unmet needs. The overall PCP tender ensured applicability of the results across the entire OncNGS value chain.[5,6]

Ethics approval and consent to participate were not applicable.

RESULTS

The OncNGS PCP: challenges identified

The OncNGS PCP aims for the broadest, most accurate, innovative, and affordable tumor ctDNA profiling.[7] It empowers international collaboration and foresees that data collected from various countries are merged and analyzed together.

The OncNGS PCP: state of the art

OncNGS solution(s) will operate in an LB market dominated by a few NGS panels originally designed and specifically approved for use in the United States, but used worldwide, e.g. FoundationOne®Liquid CDx and Guardant 360®.

The OncNGS PCP: goals defined

The OncNGS PCP set as major goals high performance, integration, security, affordability, and applicability (diagnostic, prognostic, and theranostic) to solid tumors and lymphomas. Lymphomas were prioritized over leukemias because of a more established role of ctDNA in diagnosis, prognosis, and treatment response monitoring, whereas, for example, myeloid cells may be easily sampled from blood. Similarly, ctDNA may have limited application to detect immunoglobulin rearrangements in myeloma. Six key improvement areas were defined: panel design, versatility, modularity, upgradability, cost, and data sharing/protection.

Panel design—hard-to-detect variants and joint solid tumor and lymphoma detection. The OncNGS PCP set stringent detection requirements for difficult-to-detect, clinically useful variants, such as gene fusions, copy number alterations, and multigene readouts (e.g. tumor mutational burden, microsatellite instability, and homologous recombination deficiency). To help rationalize resources, gene combinations were prioritized applicable to solid tumors, lymphomas, and cancer-predisposing inheritable variants.

Versatility. OncNGS was designed to be vendor-neutral (executable with no dedicated hardware), and compatible with available and future NGS platforms, new LB metrics, and federated learning from shared data.

Modularity. To meet both centralized and decentralized ctDNA CGP application models, the OncNGS consortium encouraged modular panel design. Modularity was promoted by grading target genomic alterations in two classes: 'must have' and 'nice to have'. The simpler/less inclusive NGS formats may be fit for routine diagnostics in small oncology centers, while the larger panels may be dedicated to complex cases typically seen by molecular tumor boards and for research and discovery in the clinical trial setting, particularly in large/comprehensive cancer centers.

Upgradability. Provisions were made for seamless incorporation of new alterations in future updates, extending the OncNGS solution lifecycle.

Cost. To ensure that a value-based contract would align with the PCP, the solution architecture was tailored to be affordable for European health care systems, which differ from the United States in reimbursement models and health policies.

Data sharing and protection. The OncNGS solution was meant to be cloud-based, ensuring General Data Protection Regulation (GDPR) compliance, and to support pooling and sharing of genomic data on a large scale (interoperability) using the Fast Healthcare Interoperability Resources (FHIR) standards.

Technical specification of the OncNGS solution

OncNGS solution specifications were grouped into five sections, described in detail in Supplementary Table S2-S6, available at https://doi.org/10.1016/j.esmoop.2025.105127. Any pre-analytical step (e.g. isolation of DNA/RNA from blood/plasma) was deemed out of scope. Target price was set below €1500, with suppliers required to project costs and benefits over different time horizons (1, 3, 5, and 10 years).

DISCUSSION: CURRENT AND NEXT STEPS

The OncNGS project aimed to develop a comprehensive LB solution for diagnostic, predictive, prognostic, and theranostic NGS profiling in solid tumors and lymphomas, enhancing access to advanced treatment options. Financial PCP support was foreseen to bridge the gap between new and established biotech companies. Desirable features designed by final users were introduced to help optimization and accelerate market acceptance, two crucial goals given the technological complexity of LB.

Several lessons emerged from the OncNGS PCP. Firstly, its format proved effective even in a complex regulatory setting like diagnostic ctDNA testing. Seven bidders responded with original, innovative solutions, demonstrating the viability of a pre-set PCP requirement scheme. Secondly, a buyer-for-buyers design followed by continuous monitoring led to progressive improvements, creating a scaffold for affordable and up-to-date real-world use. Thirdly, buyers gained insight into developing and producing new NGS solutions, highlighting an educational PCP value. By aggregating demand and driving innovation from the very beginning, this approach may increase the likelihood of successful future adoption. Fourthly, now that the project has entered phase III and prototypes are being tested, it has become clear that despite a common PCP architecture, each contractor implemented distinct wet-laboratory and dry-laboratory technologies. Small and large NGS panel blocks and gene sets for solid tumors and lymphomas were built to be combined by different, contractor-specified strategies. Both solutions offer optional add-ons, open-ended bioinformatic analysis, and intuitive visual reporting, expanding end-user choice and diagnostic pipeline flexibility. Both solutions implement optional add-ons, e.g. DNA methylomics and/or fragmentomics. Yet, customization does not compromise with turnaround times, which remained within 5-7 days for rapid therapeutic assignment.

Limitations of the OncNGS solutions that may be addressed in future PPI actions include extensive technical validation and demonstration of clinical utility. Cost—benefit analysis will have to take into account that target price was set in 2020, but cost per sequenced base pair has dropped since then, and will continue to decline over time.

Regardless, OncNGS will not be an improved 'carbon copy' of something existing, but a novel approach stimulating cohesion in the adopters. In the best possible scenario, cohesion includes a common design of precision oncology trials, real-world data re-use/interpretation, and, hopefully, common health care standards and strategies for all EU patients and citizens.

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DATA SHARING

All data and materials are included in the references.

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