strategy. Appropriate measures should be considered to expand or widen the network during the roadmap's implementation.

- Create an advisory board with diverse stakeholders, as a forum to provide guidance and advice for ensuring maximum utility of the generated outputs.
- Develop common education and training programmes for the next generation of scientists including outreach activities to better inform i) the public and patients on the benefits of ATMPs and ii) the stakeholders about access to the CoEs facilities and support.

Proposals should build on the experiences and outcomes of previous or ongoing actions such as RESTORE[383], Join4ATMP[384], PRECISEEU[385] and T2EVOLVE[386], and liaise with the relevant partnerships such as the co-funded European Partnership on Rare Diseases[387], the co-funded European Partnership for Personalised Medicine[388] and the Innovative Health Initiative Joint Undertaking (IHI-JU)[389] as appropriate.

HORIZON-HLTH-2027-02-TOOL-01-two-stage: Development of predictive biomarkers of disease progression and treatment response by using AI methodologies for chronic non-communicable diseases

Call: Cluster 1 - Health (Two stage - 2027)	
Specific conditions	
Expected EU contribution per project	The Commission estimates that an EU contribution of between EUR 6.00 and 8.00 million would allow these outcomes to be addressed appropriately. Nonetheless, this does not preclude submission and selection of a proposal requesting different amounts.
Indicative budget	The total indicative budget for the topic is EUR 44.20 million.
Type of Action	Research and Innovation Actions
Admissibility conditions	The conditions are described in General Annex A. The following exceptions apply: Applicants submitting a proposal for a blind evaluation (see General Annex F) must not disclose their organisation names, acronyms, logos nor names of personnel in the proposal abstract and Part B of their first-stage application (see General Annex E).

383 https://cordis.europa.eu/project/id/820292
384 https://ec.europa.eu/info/funding-tenders/opportunities/portal/screen/how-to-participate/org-details/999999999/project/101137206/program/43108390/details, https://cordis.europa.eu/project/id/101137206
385 https://cordis.europa.eu/project/id/101161301
386 https://cordis.europa.eu/project/id/945393
387 https://cordis.europa.eu/project/id/101156595, https://erdera.org
388 https://cordis.europa.eu/project/id/101137129, https://www.eppermed.eu
389 http://www.ihi.europa.eu

Eligibility conditions	The conditions are described in General Annex B. The following exceptions apply: In recognition of the opening of the US National Institutes of Health's programmes to European researchers, any legal entity established in the United States of America is eligible to receive Union funding. If projects use satellite-based earth observation, positioning, navigation and/or related timing data and services, beneficiaries must make use of Copernicus and/or Galileo/EGNOS (other data and services may additionally be used). Subject to restrictions for the protection of European communication networks.
Award criteria	The criteria are described in General Annex D. The following exceptions apply: For the first stage, the thresholds for each criterion will be 4 (Excellence) and 4 (Impact). The overall threshold applying to the sum of the two individual scores will be set at a level that ensures the total requested budget of proposals admitted to stage 2 is as close as possible to four times the available budget, and not less than three and a half times the available budget. For the second stage, the thresholds for each criterion will be 4 (Excellence), 4 (Impact) and 4 (Implementation). The cumulative threshold will be 12.
Procedure	The procedure is described in General Annex F. The following exceptions apply: The first-stage proposals of this topic will be evaluated blindly.
Legal and financial set-up of the Grant Agreements	The rules are described in General Annex G. The following exceptions apply: The granting authority may, up to 4 years after the end of the action, object to a transfer of ownership or to the exclusive licensing of results, as set out in the specific provision of Annex 5.

Expected Outcome: This topic aims at supporting activities that are enabling or contributing to one or several expected impacts of destination "Developing and using new tools, technologies and digital solutions for a healthy society". To that end, proposals under this topic should aim to deliver results that are directed at, tailored towards and contributing to all the following expected outcomes:

- Clinical researchers and developers have access to novel predictive biomarkers to guide a more accurate assessment of disease progression and treatment response and tackle the unmet clinical needs of non-communicable chronic diseases.

- Clinicians and healthcare professionals use clinically validated predictive biomarkers for implementing more effective clinical research and personalised medicine with better health outcomes in chronic non-communicable diseases.

- Key stakeholders have access to trustworthy Artificial Intelligence (AI) tools to guide the development of multimodal predictive biomarkers of higher accuracy and clinical value when compared to the established practice.

- The citizens benefit of better health outcomes thanks to improved clinical guidelines and the implementation of effective biomarker-guided clinical research and personalised healthcare.

Scope: Biomarkers[390] are invaluable tools for improving patient outcomes, guiding treatment decisions, accelerating personalised medicine, more effective clinical research and the development of better medicines.

However, despite the scientific discoveries of many clinically relevant biomarkers, estimated on the scale of tens of thousands, only a few biomarkers have been implemented in clinical practice. The traditional 'one biomarker' paradigm is insufficient for addressing the unmet clinical needs of chronic, progressive and multifactorial diseases, due to the complexity of the clinical phenotypes characterised by broad inter-and intra-patient heterogeneity. The established biomarkers have limitations in their use as prognostic and predictive indicators, for the assessment of the disease progression and the choices of the optimal therapeutic interventions tailored to the patients' characteristics.

Therefore, the topic focuses on the clinical development of predictive biomarkers of disease progression and treatment response for chronic non-communicable diseases (excluding cancer) by using established AI methodologies able to combine data of clinically used and candidate biomarkers, with available data from relevant clinical studies, longitudinal and Real-World Data (RWD)[391]. This topic is expected to support collaborative projects paving the way for future innovations in personalised medicine and enabling more timely and effective therapeutic interventions.

The proposals should address all the following research and innovation activities:

- Set-up a multidisciplinary collaboration to map and evaluate the available information and data on biomarkers currently used in the clinical setting, candidate biomarkers from past and ongoing clinical studies, which are scientifically proven as clinically relevant to the disease progression and treatment response for the chronic non-communicable diseases under study. This should include stratification by biological sex, and where feasible,

390 See definition as in the Strategic Research and Innovation Agenda of the Innovative Health Initiative Joint Undertaking: http://www.ihi.europa.eu/sites/default/files/uploads/Documents/About/IHI_SRIA_ApprovedJan22.pdf

391 EMA definition: "Real-World Data are routinely collected data relating to patient health status or the delivery of healthcare from a variety of sources other than traditional clinical trials (e.g. claims databases, hospital data, electronic health records, registries, mhealth data, etc.)".

integration of gender-related variables and sociodemographic determinants that may modulate disease trajectories or treatment efficacy.

- Adapt and apply of established AI methods rather than developing novel ones from scratch, to deliver novel predictive biomarkers of disease progression and treatment response, by integrating data of currently used and candidate biomarkers, with suitable data from available longitudinal and other relevant clinical studies, including RWD, as necessary. To guarantee a solid and fast optimisation and training of the AI tools, the applicants should provide information in their proposal that the appropriate high-quality clinical data are readily available, and when necessary generate small-scale new data for the AI optimisation needs. The biomarkers under study should be multimodal, covering for instance molecular, cellular, physiological, imaging, behavioural and digital markers, and/or their combinations. The applicants should justify why the development of the biomarkers proposed is imperative to tackle the unmet clinical needs of the chronic non-communicable diseases under study.

- Use AI and, where needed, other relevant data and knowledge integration methods, to describe the relationships among different biomarkers and support the robust prioritisation of predictive biomarkers tailored to the characteristics of the patients' and their disease stage and treatment response. Proposals should have strong emphasis on the AI trustworthiness[392] and develop the adequate performance metrics to assess their accuracy, reliability, reproducibility, including the assessment of possible inherent bias. Use of AI and dataset should comply with existing privacy-preserving legislation. Moreover, proposals should consider the development of user-friendly and fit-for-purpose visualisation and decision-support tools to guide clinicians in evaluating the clinical plausibility of the biomarkers under study across diverse patient groups.

- Establish a biomarker validation platform to assess the clinical utility of the predictive biomarkers identified. To this end, the applicants should implement clinical validation studies in independent disease cohorts, RWD and exploratory clinical studies, as appropriate, to demonstrate their clinical value as prognostic and predictive indicators for more effective clinical research and better patient health outcomes as compared to the established clinical practice of chronic non-communicable diseases. Prospective clinical studies are expected to be led by entities in the EU/EFTA and/or Associated Countries.

- Develop a comprehensive exploitation plan for the valorisation of the research outputs and a regulatory strategy to support the alignment to the regulatory requirements for the qualification of the biomarkers and/or AI tools and engage with the regulators in a timely manner. The applicants should prioritise the exploitation of their research results in the

[392] See introduction to this Work Programme part as well as the Ethics Guidelines for Trustworthy AI, published by the European Commission's High Level Expert Group on Artificial Intelligence https://digital-strategy.ec.europa.eu/en/library/ethics-guidelines-trustworthy-ai and the Ethics by Design and Ethics of Use Approaches for Artificial Intelligence https://ec.europa.eu/info/funding-tenders/opportunities/docs/2021-2027/horizon/guidance/ethics-by-design-and-ethics-of-use-approaches-for-artificial-intelligence_he_en.pdf