activities and may consider covering the costs of any other potential joint activities without the prerequisite to detail concrete joint activities at this stage. The details of these joint activities will be defined during the grant agreement preparation phase.

Applicants should provide details of their clinical studies[286] in the dedicated annex using the template provided in the submission system. As proposals under this topic are expected to include clinical studies, the use of the template is strongly encouraged.

HORIZON-HLTH-2027-02-DISEASE-14-two-stage: Clinical trials for advancing innovative interventions for neurodegenerative diseases

Call: Cluster 1 - Health (Two stage - 2027)	
Specific conditions	
Expected EU contribution per project	The Commission estimates that an EU contribution of around EUR 10.00 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 39.30 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).
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.

[286] Please note that the definition of clinical studies (see introduction to this Work Programme part) is broad and it is recommended that you review it thoroughly before submitting your application.

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 "Tackling diseases and reducing disease burden". 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:

- The scientific and clinical communities make effective use of state-of-the-art knowledge, data, technologies, tools, methods, best practices, and trainings to underpin and complement the development of innovative interventions aimed at more effective treatments for neurodegenerative diseases.

- The scientific and clinical communities benefit from the exchange of data, knowledge and best practices, thereby strengthening their collaboration in the EU, the Associated Countries and beyond.

- The scientific and clinical communities make wide use of relevant databases and/or integrate them with existing infrastructures for storage and sharing of collected data according to FAIR[287] principles, thereby encouraging further use of the data.

- Policymakers, funders, scientific and clinical communities, patient organisations, regulators, and other relevant bodies are informed of the research advances made and the

[287] See definition of FAIR data in the introduction to this Work Programme part.

requirements for a widespread implementation of the innovative therapeutic interventions and complementary approaches.

- Patients and caregivers are constructively engaged with the research, ensuring that their needs are catered for, with the aim of tangibly benefitting from the interventions.

Scope: Neurodegenerative diseases are a high burden for patients, caregivers, health systems and society. Given the limitations with current therapeutic solutions, including that they primarily address symptoms rather than underlying causes and can have serious side effects, together with the increasing prevalence of neurodegenerative diseases in an aging population, there is a huge need to develop more innovative, safer and more effective therapeutic solutions for these diseases. To further enhance their safety and effectiveness, the therapeutic solution based on an active substance should be combined/complemented with another multidisciplinary approach (e.g. lifestyle changes, cognitive training, rehabilitation therapies). Together this innovative intervention should lead to an improved quality of life and reduce the societal impact of these diseases.

Rare neurodegenerative diseases are excluded[288].

Proposals should address most of the following aspects:

- Perform rigorous early-stage[289] clinical trials into the safety and efficacy of the innovative interventions and their mode of administration, ensuring adequate cohorts/sample sizes with adequate representation of the patient population, including in terms of age, sex and ethnicity.

- Through the clinical trials and to the extent possible of additional studies, gain further insight into the potentially novel mechanism(s) of action of the innovative therapies and complementary approaches. This could entail analyses of imaging (e.g. MRI, ultrasound, nuclear imaging), as well as physiological, molecular, biochemical or omics signatures revealing potential perturbations prior to the intervention and recovery/improvement thereafter, and it could lead to the development of surrogate endpoints. This insight should open the path to more personalised interventions and approaches.

- Use and/or develop technologies, including digital ones (e.g. (generative) Artificial Intelligence - AI[290], wearable technologies) to help implement and monitor the long-term efficacy of the intervention(s), as well as manage the disorder and/or monitor their progression (e.g. with unobtrusive technologies suitable for patient monitoring at home

288 Rare diseases, as defined by the European Union Regulation on Orphan Medicinal Products (1999), being a disease that affects not more than 1 person per 2000 in the European population (https://www.orpha.net/).

289 For pharmacological-based interventions: phase 1 and/or phase 2 clinical trials.

290 Generative AI is a type of AI technology that can generate various forms of new content such as text, images, sounds, and even code, such as for programming or gene sequencing (https://ec.europa.eu/newsroom/dae/redirection/document/101621).

and in real-world conditions), whilst also ensuring they are bias-free, inclusive, and ethically sound.

- Utilise existing data, biobanks, registries and/or cohorts, together with the generation of new data that should be managed in line with the FAIR principles.

- Engage all relevant stakeholders (especially patients and patients' representatives for the disease, caregivers, clinicians, counsellors, regulators, etc.) to design end-user optimised interventions, applying gender-sensitive and intersectional approaches.

- Advance research by leveraging already existing and emerging state-of-the-art research infrastructures (e.g. EuroBioImaging [291], European Genomic Data Infrastructure [292], ECRIN[293], EATRIS[294], EBRAINS[295], BBMRI[296], etc.), as well as results stemming from EU-supported research projects, where applicable[297].

- Engage with national public health authorities and regulators to ensure a robust development pathway and further uptake of the intervention.

The participation of start-ups, micro, small and medium-sized enterprises (SMEs) [298] is encouraged with the aim of strengthening their scientific and technological foundations, enhancing their innovation potential, and exploring possibilities for commercial exploitation.

Funded projects should liaise with the co-funded European Partnership for Brain Health[299], covered by topic HORIZON-HLTH-2025-02-DISEASE-01: "European Partnership for Brain Health".

The topic requires the effective contribution of social sciences and humanities (SSH) disciplines and the involvement of SSH experts, institutions as well as the inclusion of relevant SSH expertise, in order to produce meaningful and significant effects enhancing the societal impact of the related research activities.

All projects funded under this topic are strongly encouraged to participate in networking and joint activities, as appropriate. Therefore, proposals should include a budget for the attendance to regular joint meetings and may consider covering the costs of any other potential joint activities without the prerequisite to detail concrete joint activities at this stage. The details of these joint activities will be defined during the grant agreement preparation phase.

291 https://www.eurobioimaging.eu
292 https://gdi.onemilliongenomes.eu
293 https://ecrin.org
294 https://eatris.eu
295 https://www.ebrains.eu
296 https://www.bbmri-eric.eu
297 Consult databases e.g. CORDIS (https://cordis.europa.eu) & the JPND Research Database (https://neurodegenerationresearch.eu/search-our-database).
298 https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32003H0361
299 https://cordis.europa.eu/project/id/101259512, https://www.brainhealth-partnership.eu

Applicants should provide details of their clinical studies[300] in the dedicated annex using the template provided in the submission system. As proposals under this topic are expected to include clinical studies, the use of the template is strongly encouraged.

[300] Please note that the definition of clinical studies (see introduction to this Work Programme part) is broad and it is recommended that you review it thoroughly before submitting your application.

Destination - Ensuring equal access to innovative, sustainable, and high-quality healthcare

Topics under this destination are directed towards the Key Strategic Orientation 2 “The Digital transition” and Key Strategic Orientation 3 “A more resilient, competitive, inclusive, and democratic Europe” of Horizon Europe’s strategic plan 2025-2027[301].

Research and Innovation supported under this destination should contribute to the following expected impact, set out in the strategic plan impact summary for the Health Cluster: “healthcare systems provide equal access to innovative, sustainable and high-quality healthcare thanks to the development and uptake of safe, cost-effective and people-centred solutions. This is to be accompanied by management models focusing on population health, health systems resilience, and health equity and patient safety, and also improved evidence-informed health policies”.

Health systems are affected by limitations in sustainability and resilience, and face inequalities in access to high-quality and acceptable healthcare services. Health systems need to become more effective, efficient, accessible, fiscally and environmentally sustainable, and resilient in order to cope with public health emergencies, support healthcare workforce, adapt to environmental challenges like climate change, and contribute to social justice and cohesion. The transformation and modernisation of health systems will remain an important challenge for many years to come, but it also holds a significant opportunity to generate evidence, leverage existing and emerging solutions, implement digital and data-driven innovation and develop more accessible, cost-effective, flexible and equitable health systems.

Research and Innovation under this destination should aim to support the transformation of healthcare systems ensuring fair and inclusive access to high-quality, acceptable, sustainable healthcare for all. Funded activities will focus on developing innovative, practical, scalable and financially sound solutions, that improve governance, provide decision-makers with new evidence, tools, and technologies, and ensure long-term fiscal, environmental and climate sustainability. A patient-centred approach should be adopted, improving patients’ health outcomes, empowering patients, fostering active dialogue among stakeholders (e.g. citizens, patients, caregivers, healthcare providers), and encouraging social innovation. Research and Innovation actions should prioritise supporting healthcare professionals and providers, ensuring they have the resources and tools needed to meet the diverse needs and preferences of citizens. Research and Innovation should facilitate scalable and transferable solutions that can be applied across different healthcare systems and national, regional, and local contexts. This should include generating knowledge that supports the transfer of solutions between countries, including measures to address health inequalities. Research and Innovation activities under this destination will contribute to, among other things, the European Care Strategy[302], the digital

301 https://research-and-innovation.ec.europa.eu/funding/funding-opportunities/funding-programmes-and-open-calls/horizon-europe/strategic-plan_en

302 Communication from the European Commission on the European care strategy, COM(2022) 440, 7.9.2022

transformation of health and care in the EU[303], the European Pillar of Social Rights[304, 305], the EU strategy on adaptation to climate[306], the Pharmaceutical Strategy for Europe[307], the European Health Data Space (EHDS)[308], the Strategy for European Life Sciences[309] and the European Green Deal[310]. They align with the Commission's Political Guidelines for 2024-2029[311], which include efforts to complete the European Health Union by promoting access for all to high-quality and affordable healthcare, fostering a resilient and innovative health ecosystem, and strengthening the competitiveness of the European Union[312].

In this Work Programme part, the focus of this destination will be on public procurement of innovative solutions for integrated or personalised care, aiming to develop and test solutions that improve access to and provision of healthcare. It will also support personalised medicine approaches to reduce adverse drug reactions due to the administration of multiple medication, and research to identify and address low-value care in health and care systems, improving healthcare outcomes, efficiency, and fiscal sustainability.

To increase the impact of EU investments under Horizon Europe, the Commission encourages and supports cooperation among EU-funded projects to foster cross-fertilisation and synergies. This includes networking, joint activities such as workshops, knowledge exchange, best practices development, and joint communication activities. Synergies can be explored not only between projects funded under the same topic, but also between projects funded under other topics, Clusters or Pillars of Horizon Europe. For instance, collaborations may arise between projects related to European health research infrastructures (under Pillar I), the EIC[313] strategic challenges on health (under Pillar III), or across the Clusters of Pillar II such as Cluster “Culture, Creativity and Inclusive Society” focusing e.g. on the long-term sustainability of public health systems (e.g. economic and organisational models and measures for cost effectiveness and fiscal sustainability), or Cluster “Digital, Industry and Space” focusing on the digitalisation of the health sector, including the use of Artificial Intelligence (AI).

The Commission aims to foster synergies between Horizon Europe and other EU programmes. To this end, applicants are encouraged to explore the funding opportunities available through

303 Communication from the European Commission on enabling the digital transformation of health and care in the Digital Single Market; empowering citizens and building a healthier society, COM(2018) 233, 25.4.2018

304 https://employment-social-affairs.ec.europa.eu/policies-and-activities/european-pillar-social-rights-building-fairer-and-more-inclusive-european-union_en

305 Commission Communication on Artificial Intelligence for Europe; COM(2018) 237 final: https://digital-strategy.ec.europa.eu/en/policies/european-approach-artificial-intelligence; https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=COM:2018:237:FIN

306 https://climate.ec.europa.eu/eu-action/adaptation-climate-change/eu-adaptation-strategy_e

307 https://health.ec.europa.eu/medicinal-products/pharmaceutical-strategy-europe_en

308 https://health.ec.europa.eu/ehealth-digital-health-and-care/european-health-data-space-regulation-ehds_en

309 https://research-and-innovation.ec.europa.eu/strategy/strategy-research-and-innovation/jobs-and-economy/towards-strategy-european-life-sciences_en; https://ec.europa.eu/commission/presscorner/detail/en/ip_25_1686

310 https://commission.europa.eu/strategy-and-policy/priorities-2019-2024/european-green-deal_en

311 https://commission.europa.eu/about/commission-2024-2029_en

312 https://commission.europa.eu/topics/eu-competitiveness_en

313 https://eic.ec.europa.eu

the EU4Health Programme (2021-2027)[314], the EU's public health programme, as a means of capitalising on potential collaborations and maximising impact.

Expected impacts:

Proposals for topics under this destination should set out a credible pathway to contributing to ensuring access to innovative, sustainable, inclusive and high-quality healthcare, and more specifically to one or several of the following impacts:

- Health and social care services and systems have improved governance mechanisms, making them more effective, efficient, accessible, resilient, trusted and sustainable, from fiscal, organisational and environmental perspectives. This includes shifting from hospital-centred to community-based, people-centred and integrated healthcare structures, embedding technological innovations and prioritising health promotion and disease prevention and management.

- Healthcare providers are trained and equipped with the skills and competences needed for future healthcare systems that are modernised, digitally transformed and equipped with safe innovative tools, technologies and digital solutions for healthcare. This will involve better patient management, improved patient engagement and health outcomes, reorganised workflows, and improved resource management.

- Citizens play a key role in managing their own healthcare, informal carers (including unpaid carers) are fully supported (e.g. by preventing overburdening and economic stress) and the specific needs of groups in a vulnerable situation are recognised and addressed. This includes improved access to healthcare services, financial risk protection, timely access to quality healthcare services including essential medicines and vaccines.

- Health policy and systems adopt a holistic approach -considering individuals, communities, organisations, society- in evaluating health outcomes, public health interventions, healthcare organisation, and decision-making. They benefit from evidence based, scalable and transferable healthcare solutions (e.g. between countries and healthcare settings) including for addressing health inequalities and ensuring environmental and climate sustainability in the health sector.

The actions resulting from the topics under this destination will also create strong opportunities for synergies with actions stemming from the EU4Health programme, in particular contributing to the goals under the general objective “protecting people in the Union from serious cross-border threats to health” and specific objective 4 “to strengthen health systems, their resilience and resource efficiency”.

Legal entities established in China are not eligible to participate in both Research and Innovation Actions (RIAs) and Innovation Actions (IAs) falling under this destination. For

314 https://commission.europa.eu/funding-tenders/find-funding/eu-funding-programmes/eu4health_en