Proposal Evaluation Form

EUROPEAN COMMISSION

Horizon Europe (HORIZON)

Evaluation Summary Report - Research and innovation actions

Call: HORIZON-HLTH-2025-01

Type of action: HORIZON-RIA

Proposal number: 101286237

Proposal acronym: APO2FOOT

Duration (months): 60

Proposal title: A randomized, open label, observer-blinded clinical trial to evaluate safety and efficacy of APO-2 in comparison to Standard of Care in the treatment of diabetic foot ulcers

Activity: HORIZON-HLTH-2025-01-TOOL-02

N.	Proposer name	Country	Total eligible costs	%	Grant Requested	%
1	[redacted]	[redacted]	1,250,000	9.54%	1,250,000	9.54%
2	[redacted]	[redacted]	1,056,250	8.06%	1,056,250	8.06%
3	Aposcience AG	AT	6,064,500	46.30%	6,064,500	46.30%
4	[redacted]	[redacted]	494,000	3.77%	494,000	3.77%
5	[redacted]	[redacted]	91,250	0.70%	91,250	0.70%
6	[redacted]	[redacted]	931,250	7.11%	931,250	7.11%
7	[redacted]	[redacted]	450,000	3.44%	450,000	3.44%
8	[redacted]	[redacted]	981,250	7.49%	981,250	7.49%
9	[redacted]	[redacted]	206,250	1.57%	206,250	1.57%
10	[redacted]	[redacted]	497,500	3.80%	497,500	3.80%
11	[redacted]	[redacted]	163,750	1.25%	163,750	1.25%
12	[redacted]	[redacted]	756,250	5.77%	756,250	5.77%
13	[redacted]	[redacted]	156,250	1.19%	156,250	1.19%
	Total:		13,098,500		13,098,500	

Abstract:

Diabetic foot ulcers (DFUs) are one of the most severe complications of diabetes, affecting nearly one million people in the EU every year. Chronic DFUs fail to heal within months, leading to infections, amputations, and a five-year mortality rate exceeding that of many cancers. Current standard care (blood sugar control, debridement, wound dressings, off-loading) is often insufficient, and available adjunctive therapies show limited efficacy, high costs, or lack regulatory approval. This situation creates an urgent medical, societal, and economic challenge for Europe's healthcare systems. APO2FOOT will demonstrate the safety and efficacy of APO-2, a novel off-the-shelf secretome therapy, in a clinical phase II study. It will be the first effective and reimbursable treatment to accelerate healing of chronic diabetic foot ulcers and reduce amputations
APO2FOOT clinically validates APO-2, a novel, cell-free secretome therapy. Unlike cell-based treatments, APO-2 is stable, virus-inactivated, easily stored, and can be applied topically as an "off-the-shelf" product. Early clinical trials have shown that APO-2 accelerates wound healing by promoting angiogenesis, re-epithelialisation, and anti-inflammatory effects, resulting in faster and more complete wound closure. The project will conduct a multicentre, multinational, observer-blinded phase II clinical trial with 120 patients across 5 EU countries, comparing APO-2 to SoC . Key innovations include central wound adjudication, digital imaging tools, and harmonised treatment protocols, ensuring robust and reliable clinical data. By delivering conclusive evidence of safety and efficacy, APO2FOOT aims to establish APO-2 as the first effective, accessible, and reimbursable active treatment for chronic DFU. The expected impact is fewer amputations, improved patient QoL, reduced mortality, and substantial savings for healthcare systems, while positioning Europe at the forefront of secretome-based regenerative medicine.

Evaluation Summary Report

Evaluation Result

Total score: 11.00 (Threshold: 12)

Criterion 1 - Excellence

Score: **3.50** (Threshold: 4 / 5.00 , Weight: -)

The following aspects will be taken into account, to the extent that the proposed work corresponds to the description in the work programme:
- Clarity and pertinence of the project's objectives, and the extent to which the proposed work is ambitious and goes beyond the state of the art.
- Soundness of the proposed methodology, including the underlying concepts, models, assumptions, inter-disciplinary approaches, appropriate consideration of the gender dimension in research and innovation content, and the quality of open science practices, including sharing and management of research outputs and engagement of citizens, civil society and end users where appropriate.

The objectives are well structured, specific, measurable, achievable, and realistic, demonstrating both clarity and relevance. They are fully aligned with the scope of the call, aiming to deliver a pivotal phase II clinical trial to support a marketing authorisation application for a secretome-based therapy derived from stressed peripheral blood mononuclear cells.

The proposal is ambitious and moderately goes beyond the state of the art by using the lyophilized secretome of allogeneic peripheral blood mononuclear cells (PBMC) to treat diabetic foot ulcers, an important unmet medical need. Although similar approaches exist, the concept still has merit and could potentially introduce a novel active substance that advances clinical care. However, the planned work relies on well-established methods. It does not clearly show how it will significantly advance the field and the extent to which the project truly goes beyond the current state of the art.

The proposed research and innovation work is at a mature stage and in-line with the topic description. It incorporates novel concepts at the medicinal and clinical level. However, the novelty of the biological development is not convincingly demonstrated.

The scientific methodology is generally clear, coherent, and technically sound, providing a solid basis for clinical translation. It integrates preclinical and early clinical work and follows a structured, stepwise approach. However, the approach relies primarily on a single mechanistic focus, angiogenesis, which may not fully capture the complexity of wound healing in chronic diabetic ulcers. Additionally, the rationale for key study design elements, including placebo selection and dosing, is insufficiently justified, all these aspects may limit the strength and interpretability of the clinical outcomes.

The research and innovation initiatives at both national and international levels are well integrated into the methodological framework. The consortium's prior experience in conducting clinical trials positions it to deliver fully in line with national requirements and international standards.

The methodology demonstrates a high level of interdisciplinarity, strengthening the conceptual basis of the work, supporting alignment with broader research and innovation priorities.

Gender aspects are overall addressed. However, important aspects such as the gender of the patient during their recruitment is not convincingly presented.

Open Science practices are well integrated throughout the project and its methodology, reflecting a strong commitment to open access and the sharing of results.

Criterion 2 - Impact

Score: **3.50** (Threshold: 4 / 5.00 , Weight: -)

The following aspects will be taken into account, to the extent that the proposed work corresponds to the description in the work programme:
- Credibility of the pathways to achieve the expected outcomes and impacts specified in the work programme, and the likely scale and significance of the contributions from the project.
- Suitability and quality of the measures to maximise expected outcomes and impacts, as set out in the dissemination and exploitation plan, including communication activities.

The pathways to achieve the expected outcomes and impacts are generally well described and credible. The project has potential for significant societal, clinical, and economic benefits, including improved patient care, safer therapies, and broader healthcare impact. It also strengthens technological capacity and expertise in the field, supporting Europe's leadership in translational therapies. Regarding wider impact, the project has strong potential, as it could deliver impact to other diseases. However, the absence of a clearly defined regulatory development pathway reduces confidence in achieving clinical and regulatory implementation.

The scale and significance of the project's contribution to outcomes and impacts are clearly described and quantified.

Potential barriers are overall credibly acknowledged and mitigated through standardized process. However, the proposal does not fully identify the barriers in regard to regulatory aspects.

The dissemination plan is comprehensive and credible, combining online and printed materials, stakeholder mapping, and targeted engagement with the scientific community, clinicians, industry, patients, and the public.

The communication measures are well developed, with tailored channels and a content management plan to ensure effective outreach, visibility, and uptake across all relevant audiences.

The exploitation strategy is robust, addressing clinical, commercial, and policy pathways and technology transfer through key partners, to scale up production and extend impact. The proposal includes a commitment to first deployment in the EU.

Responsibilities for IP protection, ownership, and access rights are well defined.

Criterion 3 - Quality and efficiency of the implementation

Score: **4.00** (Threshold: 4 / 5.00 , Weight: -)

The following aspects will be taken into account, to the extent that the proposed work corresponds to the description in the work programme:
- Quality and effectiveness of the work plan, assessment of risks, and appropriateness of the effort assigned to work packages, and the resources overall.
- Capacity and role of each participant, and the extent to which the consortium as a whole brings together the necessary expertise.

The work plan is overall well-structured, and logically sequenced, with work packages and tasks clearly aligned with the project's objectives. Deliverables are well defined and measurable, supporting progress monitoring. The plan covers all key areas, including manufacturing, clinical implementation, management, and dissemination. However, there are notable gaps: quality control measures for production and batch consistency are not fully defined, the effects of the IMP have not been adequately compared to standard-of-care. In addition, while the timeline is realistic, the milestones do not fully capture all critical decision points, and interdependencies and decision-gates between work packages are not fully described.

The allocation of resources, including personnel, time, equipment, and infrastructure, is overall appropriate and proportionate to the project objectives. However, the distribution of the budget among the beneficiaries is not duly justified.

In general, risks are identified. However, the likelihood of some non-technical risks may be underestimated, and mitigation and contingency plans are not always fully convincingly presented.

The consortium is strong and well-composed, bringing together complementary expertise and infrastructure across scientific, clinical, and industrial domains. It integrates all necessary competencies to advance the project toward its objectives, including preclinical validation, clinical evaluation, manufacturing, and regulatory expertise.

Partners' roles are generally well defined and balanced, and the consortium benefits from proven infrastructure, operational readiness, and an external advisory board to support project success.

The consortium demonstrates strong expertise in open science practices and in integrating gender aspects into research and innovation activities.

The consortium as a whole shows active industrial and commercial involvement, ensuring practical applicability and alignment with market and regulatory requirements.

Scope of the application

Status: **Yes**

Comments (in case the proposal is out of scope)

Not provided

Exceptional funding

A third country participant/international organisation not listed in the General Annex to the Main Work Programme may exceptionally receive funding if their participation is essential for carrying out the project (for instance due to outstanding expertise, access to unique know-how, access to research infrastructure, access to particular geographical environments, possibility to involve key partners in emerging markets, access to data, etc.). (For more information, see the HE programme guide)

Please list the concerned applicants and requested grant amount and explain the reasons why.

Based on the information provided, the following participants should receive exceptional funding:

Not provided

Based on the information provided, the following participants should NOT receive exceptional funding:

Not provided

Use of human embryonic stem cells (hESC)

Status: **No**

If YES, please state whether the use of hESC is, or is not, in your opinion, necessary to achieve the scientific objectives of the proposal and the reasons why. Alternatively, please state if it cannot be assessed whether the use of hESC is necessary or not, because of a lack of information.

Not provided

Use of human embryos

Status: **No**

If YES, please explain how the human embryos will be used in the project.

Not provided

Activities excluded from funding

Status: **No**

If YES, please explain.

Not provided

Exclusive focus on civil applications

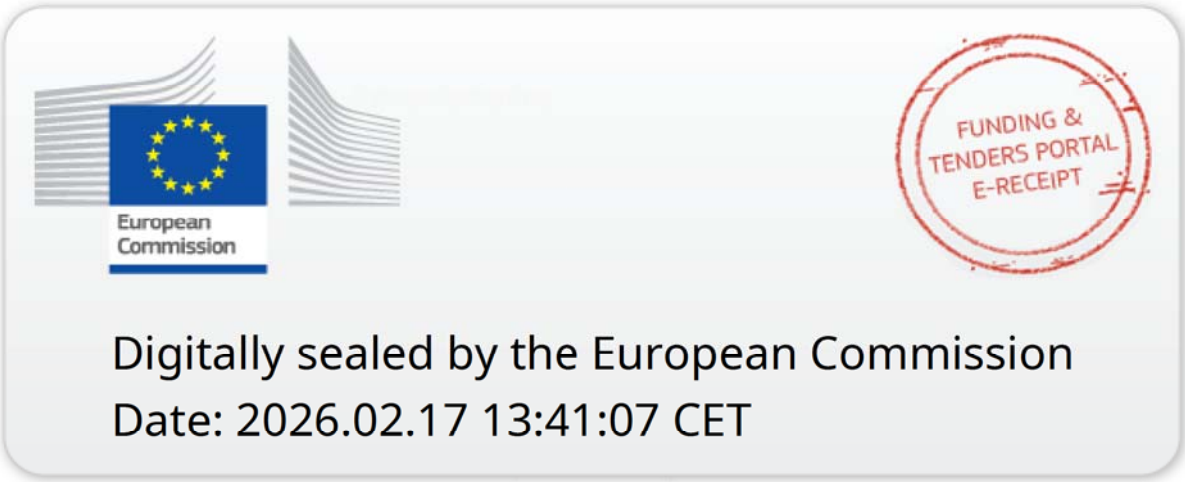
Status: **Yes**

If NO, please explain.

Not provided

Overall comments

Not provided



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