



PHOENIX is a ground-breaking project revolutionising transplant medicine through next-generation nano-immunotherapy.

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1. Describe your project through key words/key phrases that identify it.

Organ transplantation has been a remarkable medical breakthrough since the first successful kidney transplant between twin brothers in Boston 70 years ago. Today, over 180,000 transplants are performed annually worldwide, saving lives through advancements in surgical techniques and immunosuppressants. However, these drugs, while preventing organ rejection, also weaken the immune system, making patients highly susceptible to infections, cancer, and metabolic disorders. The challenge remains: how can we ensure long-term graft survival while protecting the patient's overall health?

Enter PHOENIX—a ground-breaking project revolutionising transplant medicine through next-generation nano-immunotherapy. Rather than relying on lifelong immunosuppression, PHOENIX harnesses cutting-edge nanotechnology to reprogram the body's immune response. By using nanoparticle-based therapy to transform T cells into regulatory cells, this approach creates localised immune protection around the graft while preserving the body's overall immune defences.

Through kidney and liver transplant models in multiple species, PHOENIX aims to prove that this innovative therapy can eliminate the need for broad immunosuppression, significantly reducing complications and side effects. By bringing this concept to preclinical validation, the project is paving the way for a paradigm shift in transplant medicine—one that prioritizes both organ longevity and patient health.

Behind PHOENIX is a powerhouse of expertise. The Giuseppe Remuzzi group at the Istituto di Ricerche Farmacologiche Mario Negri leads in transplant immunology and tolerance-inducing therapies. At the Fundació de Recerca Clínic Barcelona-IDIBAPS, Pere Santamaria's team brings cutting-edge knowledge in nanotechnology, nanoimmunology, and immune-protein engineering. Their pioneering work on MHC-based nanotherapies spans from design and development to safety and clinical application. Meanwhile, experts at the Centre Hospitalier Universitaire de Rennes/INRAE specialise in liver transplantation, offering vital preclinical hepatology insights. Pintail Limited ensures seamless project coordination, communication, and administration.

By uniting nanoengineering, protein science, immunology, and transplant medicine, PHOENIX is bridging the gap between autoimmune disease treatments and organ transplantation. This revolutionary approach is poised to redefine the future of transplantation—offering patients a new era of safer, more effective treatments.

2. In terms of impact, what will be the most tangible your project will achieve?

The PHOENIX project is poised to revolutionise transplant medicine, delivering lasting benefits for patients, healthcare systems, and the broader scientific community. At the heart of this transformation is a game-changing breakthrough: the ability to achieve long-term graft survival without the need for lifelong immunosuppression. By reprogramming the immune system to accept transplanted organs naturally, PHOENIX will eliminate the dangerous side effects of current treatments—such as heightened susceptibility to

infections, cancer, and metabolic disorders. For transplant recipients, this means no longer living in constant medical fragility but instead embracing a healthier, longer, and more stable life.

Beyond improving individual outcomes, PHOENIX will help ease the burden on transplant waiting lists. By significantly extending the lifespan of transplanted organs, the project will reduce the need for repeat transplants, ensuring that more patients can access life-saving procedures sooner. This not only optimises the use of donor organs but also improves overall transplant success rates, making the system more efficient and equitable.

The economic impact of PHOENIX is just as profound. Today, managing transplant patients is a costly endeavour driven by the substantial price of immunosuppressive drugs, frequent hospitalisations, and treatment for complications. PHOENIX's innovative nano-immunotherapy—administered in just a few doses during the critical post-transplant period—aims to provide lasting immune tolerance with minimal ongoing intervention. This shift from lifelong medication to a short-term, highly effective treatment could dramatically cut healthcare costs while simultaneously improving patient quality of life.

But the results of PHOENIX do not stop at transplantation. One of its most ground-breaking outcomes will be the development of an "off-the-shelf" nanotherapy platform—an adaptable solution suitable for any patient and any solid organ transplant. This makes treatment more accessible, easier to prescribe, and simpler to monitor. Looking ahead, PHOENIX's pioneering approach lays the foundation for broader applications, from xenotransplantation to new immunotherapeutic strategies for inflammatory diseases.

By redefining how we approach immune tolerance, PHOENIX is not just changing transplant medicine—it's reshaping the future of healthcare.

3. Please describe your project's overall impact, if applicable, at the European level.

The PHOENIX project is set to make a profound impact across Europe, tackling urgent healthcare challenges while cementing the EU's leadership in next-generation immunotherapies. By pioneering a revolutionary nano-immunotherapy that removes the need for lifelong immunosuppression, PHOENIX is transforming the future of organ transplantation—directly reducing the disease burden and enhancing patient outcomes across the continent.

A key benefit of PHOENIX is its ability to ensure long-term graft survival, significantly reducing the need for repeat transplants. This breakthrough will help alleviate the strain on transplant waiting lists in EU

countries, ensuring that life-saving organs reach patients faster and more efficiently. By optimising organ allocation and increasing accessibility, PHOENIX is setting a new standard for fairness and effectiveness in European healthcare.

From an economic and healthcare sustainability standpoint, the project offers a game-changing solution. The costs associated with lifelong immunosuppressive drugs, repeated hospitalisations, and the treatment of severe side effects—such as infections and cancer—place immense pressure on national healthcare budgets. PHOENIX presents a cost-effective alternative: a short-term, highly targeted nanotherapy that integrates seamlessly into existing healthcare systems. This shift will not only save financial resources but also enable smarter, more sustainable long-term healthcare planning across Europe.

At its core, PHOENIX is a testament to European scientific excellence. By uniting leading experts and institutions across the continent, the project leverages cutting-edge research to deliver a breakthrough therapy that redefines transplant medicine. But its impact extends far beyond transplantation—by showcasing the power of precision immunotherapy, PHOENIX opens doors to new treatments for other high-burden diseases.

With the potential to improve patient outcomes, cut healthcare costs, and reinforce Europe's position at the forefront of medical innovation, PHOENIX is paving the way for a safer, more effective, and more sustainable future in healthcare—one where science and technology work hand in hand to improve millions of lives.

4. As an applicant, what advice would you have wanted in the Horizon project design process? What support did you receive from National Contact point (NCP) and your organisation, and what improvement of support would you benefit from?

The Italian NCP, APRE, provides efficient and easily accessible assistance that spans both administrative and scientific aspects of a project. They offer valuable suggestions on various elements of proposal development, including reviewing advanced drafts and providing constructive feedback for improvement.

Additionally, APRE offers grant preparation courses, although these are fee-based. The primary limitation we encountered was their exclusive reliance on email communication, which sometimes led to delays due to the lack of immediate responses via phone.

For the PHOENIX project, we did not contact APRE, as our partner, Pintail Limited (Ireland), had significant expertise in Horizon Europe applications. We collaborated with Pintail Limited to support proposal preparation and later partnered with them within PHOENIX for administration, dissemination, and future planning.

To enhance the impact and efficiency of the Horizon application process, a well-structured NCP support system could:

- Offer more interactive communication channels, including phone or virtual meetings, to reduce delays.
- Provide customised advisory services for organisations at different experience levels.
- Share practical resources, such as proposal templates, case studies, and best-practice insights.
- Organise targeted workshops and webinars to guide applicants in optimising their proposals.

5. Please highlight aspects of your Horizon project's strengths that you consider important and that may constitute good practice for other applicants.

The PHOENIX project exemplifies several key strengths that set it apart and serve as a model of good practice for future Horizon applicants. One of the most critical aspects of its success is its clear and well-defined research focus. From the outset, PHOENIX has aligned its objectives precisely with the priorities of the funding call, ensuring that its goals are both ambitious and achievable. This strategic alignment not only strengthens the proposal but also demonstrates a deep understanding of the call's scope, increasing the project's overall credibility and impact.

Another cornerstone of PHOENIX's success is the careful selection of consortium partners. By bringing together leading experts from diverse yet complementary fields—including nanotechnology, immunology, transplant medicine, and clinical research—the project has assembled a team with the highest level of expertise to drive ground-breaking innovation. A strong, multidisciplinary consortium ensures that each aspect of the research is approached with the right knowledge and technical capacity, maximising the project's potential for success.

Beyond expertise, PHOENIX embodies a mindset of innovation that goes beyond the status quo. While the project pushes the boundaries of what is possible in transplantation medicine, it remains grounded in a realistic assessment of what can be achieved within the constraints of the budget and timeframe. Striking this balance between ambitious innovation and practical feasibility is a crucial factor in making the project viable and ensuring a meaningful, lasting impact.

A final, yet equally vital, aspect of PHOENIX's approach is its commitment to collaboration, knowledge-sharing, and training. By fostering an environment of open communication within the consortium, the project promotes the exchange of ideas and best practices, enabling team members to learn from one another and drive collective progress. This culture of cooperation not only enhances the effectiveness of PHOENIX itself but also helps build capacity for future research, strengthening the broader scientific community.

Together, these elements—strategic focus, top-tier expertise, innovative yet realistic goals, and a strong collaborative spirit—make PHOENIX a model for excellence in Horizon projects. By adopting these principles, future applicants can position their proposals for success, increasing their chances of securing funding while making meaningful contributions to their respective fields.

