and aid the selection of novel vaccine candidates. New tools to help identify the correlates of immunity, optimize vaccine regimens, and improve immunization strategies, combined with reservoir mobilizer and immunomodulators must be explored in the development of functional cure strategy.

To achieve its goal, EHVA has brought together experts in the fields of molecular biology, structure biology, virology, adjuvants delivery, immunology, clinical science, biostatistics, virology manufacturing, and industrial development. The partners of EHVA are leading scientists in their correspondent field with proven publication track records and international recognition of their leadership within the scientific community, working in close collaboration with representatives of the HIV community.

EHVA brings together the complementary skills and expertise of 39 groups with an integrated approach to tackle the scientific challenges.
Despite enormous progress in the prevention and treatment of HIV and AIDS, the global response cannot keep pace: almost 37 million people are living with HIV worldwide with around 6,000 new HIV infections each day. Whilst the vast majority of new infections occur in Sub-Saharan Africa, the past year has also seen over 142,000 new infections in the European region. HIV vaccine is essential to cut new HIV infections, ensure a sustainable response to HIV/AIDS, save the lives of millions of people and ultimately help achieve an end to the epidemic.

**PREVENTIVE VACCINES**

In the more than 30 years of HIV vaccine research, a variety of vaccine approaches including those generating antibodies and activating T-cells have been developed and evaluated. One of these candidates showed an ability to partially reduce the risk of HIV infection – but insufficient to justify plans for roll-out. In a new efficacy trial, recently initiated in South Africa, researchers will test an adapted vaccine regimen in order to improve on these results. In addition, more than 20 HIV vaccine candidates are in early clinical development, and innovative approaches are being evaluated in preclinical settings. Whilst these could generate new promising vaccine candidates, in the absence of correlates of protection and a proven selection platform, researchers are facing difficult choices on how to select the best candidates and immunization strategies, including but not limited to the different stages, i.e. pre-clinical and clinical, of vaccine development.

**Objectives & strategy**

**Fostering a multidisciplinary approach to HIV vaccine development**

The European HIV Vaccine Alliance (EHVA) programme aims to develop a Multi-disciplinary Vaccine Platform (MVP) for prophylactic and therapeutic HIV vaccines through four major approaches.

1. **Discovery Platform**, to generate novel prophylactic and therapeutic vaccine candidates that can induce potent neutralising and non-neutralising antibody responses and T-cell responses. Specifically, improving HIV envelope protein-based vaccine immunogenicity and vaccine regimens and achieving the transient break of immunological tolerance.

2. **Immune Profiling Platform**, to rank novel and existing (benchmark) vaccine candidates in pre-clinical and human clinical trials; the ranking will be performed through the use of a large set of validated, qualified and standardised immunological assays and access to the most advanced technologies in the profiling of the immune responses.

3. **Data Management and Down-Selection Platform**, to provide powerful statistical tools for the analysis and interpretation of complex data and algorithms for the efficient selection of vaccine candidates at the different stages, i.e. pre-clinical and clinical, of vaccine development.

4. **Clinical Trials Platform**, to accelerate the clinical development of novel vaccine candidates and the early prediction of failure of vaccine candidates. This will be achieved through innovative trial designs such as Experimental Medicine (EM) Trials and Adaptive Design, aimed at identifying improved vaccine regimens in the prophylactic setting and of immune correlates of protection in the therapeutic setting.

**Expected Outcomes**

EHVA will contribute to achieving safe and effective prophylactic and therapeutic vaccines to combat HIV/AIDS, notably by enhancing the identification and accelerating the development of promising vaccine candidates. The programme will develop novel vaccine concepts and a robust screening platform for vaccine candidate selection, supported by appropriate clinical trial design and infrastructure, capabilities for broad immunological profiling, standardized assays and data management and integration. The expertise, knowledge and resources that EHVA aims to develop will provide an indispensable resource for the HIV vaccine research community, and can help to achieve:

- Reduced R&D cost through improved methods for selecting best-in-class vaccine candidates by increasing the number of candidates that can be evaluated with limited resources, thus increasing the chance of achieving effective vaccines
- Increased capacity and resources for the further clinical development of promising vaccine candidates at early stages of clinical development and integration of new knowledge, notably through close collaboration with the industrial partners for product development
- Improved innovation capacity and the integration of new knowledge, notably through the relationship with the European and Developing Countries Clinical Trial Partnership (EDCTP)

**Context**

**Objectives**

On the basis of the Objectives outlined above, the following hypotheses will be tested:

1. **The increase in the immunogenicity of novel Env protein-based vaccine candidates together with the selection of optimal prime/boost combinations and transient break of immunological tolerance will result in the induction of improved quantitatively and qualitatively antibody responses as compared to benchmark vaccine regimens**.

2. **The immune profiling using an algorithm of EHVA immunological assays will provide the delineation of the diversity of the immune response induced by different vaccine candidates and the identification of immune correlates of protection**.

3. **The down-selection criteria for the novel vaccine candidates will allow efficient progression of the best-in-class vaccine candidates from the pre-clinical to the clinical development and early prediction of vaccine failure**.

4. **The innovation in clinical design will allow the elimination of poorly immunogenic vaccine candidates at early stages of clinical development and accelerate the progression of the best-in-class vaccine candidates into large clinical trials.**