

# The NL4Cure Dutch Research Agenda

## Accelerating a Cure for HIV

### Executive summary



NL4Cure (short for The Netherlands for Cure) is a Dutch initiative to advance an HIV cure through a collaboration of a variety of stakeholders, including people with HIV, researchers from Dutch universities, HIV nurses and physicians and the HIV Monitoring Foundation. It has been initiated and is being coordinated by Aidsfonds.

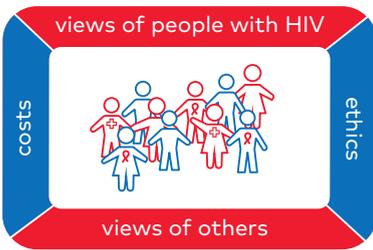
NL4Cure capitalizes on the opportunities and strengths of the Dutch HIV research and care infrastructure and in its research agenda sets out the research priorities for the next five years. The NL4Cure research agenda's overarching aim is to accelerate the development of an HIV cure with the goal to, among other benefits, end the dependence on lifelong antiretroviral therapy for people with HIV. This agenda is aligned with the global scientific cure strategy of the International AIDS Society.

NL4Cure has four main areas of focus that work in synergy towards the overall goal of curing HIV.



#### The four sections are:

1. Social engagement
2. Identifying and understanding the viral reservoir
3. Developing cure strategies
4. Clinical investigation and implementation



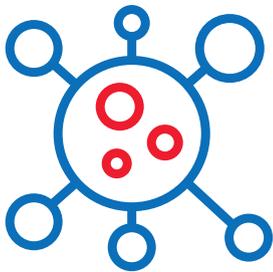
## 1. Social Engagement

The agenda is unique in its robust social engagement priorities that center around the views and preferences of people living with HIV, their partners and other key population groups. These priorities include: exploring the importance of a cure to these groups; the level of awareness of the global state of cure research; priorities around communicating decisions; potential impacts on stigma; and attitudes around HIV risk and prevention. The principles of MIPA (Meaningful Involvement of People with HIV) are upheld in the social engagement agenda from research to rollout with an emphasis on the ethical considerations of cure and what it means for affected groups. Additional considerations explore the inclusiveness of HIV cure trials, the support of policymakers and the financial and public health impacts of implementing specific HIV cure strategies.

## 2. Identifying and Understanding the Viral Reservoir

HIV establishes a lasting infection by integrating inside various immune cells in the body before going into a resting state, creating a reservoir of latently infected cells. This allows the virus to evade treatment while still maintaining the ability to reactivate and reproduce in the future. Quantifying and classifying the reservoir, the cells that can be reactivated, is central to testing an HIV cure and has remained a challenge for researchers.

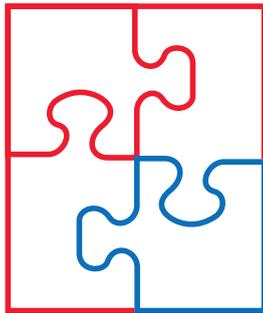
The NL4Cure agenda outlines priorities to define the size, cellular composition and location of the relevant reservoir inside the body. This work would facilitate our understanding of the molecular mechanisms and key players that trigger viral latency in host cells. Other research priorities include identifying the specific signals or markers produced by the body when HIV replication is under control in the absence of therapy. Elite controllers (individuals who are able to control HIV without therapy) and post-treatment controllers (Individuals, who after ceasing therapy, are able to control the levels of virus in their body) will be studied under the scope of the agenda to develop a greater understanding of the impact on the reservoir.



### 3. Developing Cure Strategies

The agenda focusses on controlling replication (functional cure) and viral elimination (traditional cure) as the two approaches to cure HIV. One strategy to control replication is 'lock and block'. This strategy targets mechanisms that allow infected cells to no longer produce copies of the virus forcing the cells to stay dormant or "locked" into place. It also involves strengthening the immune system to "block" new infections. Eliminating HIV is a two-part approach of reactivating the virus from its resting state ('kick'), followed by clearing ('kill') these newly-visible cells via targeted immune strategies.

Another strategy being pursued is cell or gene therapy to modify target cells in such a way that they are no longer susceptible to HIV infection. This can contribute to either a traditional or functional cure, depending on the chosen approach.



The agenda also highlights the need for models as close to the human setting as possible to investigate the safety and efficacy of various HIV cure strategies before they can progress to human clinical trials. The Dutch research enterprise has significant expertise in this area and is poised to lead an accelerated effort translating cure strategies from bench to the bedside.

### 4. Clinical Investigation and Implementation

The agenda envisions a multi-stakeholder platform to develop hypothesis-driven designs for preclinical studies, with the opportunity for promising strategies to advance to clinical trials. NL4Cure will utilize both existing and new Dutch cohorts of individuals with HIV to test candidate strategies and to engage people with HIV in all stages of the research continuum. There are three existing Dutch patient cohorts that will be utilized to facilitate clinical and translational research: the national HIV Monitoring Foundation registry of people with HIV in care (SHM), the Netherlands Cohort Study on Acute HIV Infection (NOVA) and the Biomarkers for the HIV Reservoir Cohort (CHRONO).



A patient-centered approach will be retained for clinical trials addressing the safety and efficacy concerns of cure strategies, whilst drawing from the social engagement agenda prioritized in the beginning of this document.

## Collaborating for Success

The combination of a well-organized infrastructure for care and research, highly-skilled professionals, the involvement of people with HIV and a collaborative culture makes the Netherlands a unique and high-impact environment to accelerate the HIV cure agenda globally.

With this research agenda NL4Cure seeks to accelerate the development of an HIV cure for all people with HIV utilizing the unique opportunities and strengths afforded by Dutch infrastructure. This agenda serves as a guiding document for those currently working in the field and as a tool to also engage disciplines not yet active in HIV research.

