

## **NON-TECHNICAL ABSTRACT**

We are conducting this clinical trial in individuals who are infected with Human Immunodeficiency Virus type 1 (HIV-1) to study the potential risks and benefits of a new type of treatment. The current medications used to attack HIV-1 are not able to eradicate the virus totally or relieve the symptoms fully for an extended period. They also produce many pronounced side effects including toxicity to the liver, kidney, pancreas, skin, and blood vessels. In addition, these anti-HIV drugs must be taken in combination and on an ongoing basis for life. This pill burden can be highly troublesome. The virus can also change its genetic sequence (mutate) so that the medications can no longer attack it. The trial that we are proposing is similar to the already approved Phase I trial at UCLA in that it uses an experimental approach called “gene therapy. The therapy involves removing some specialized white blood cells (known as CD34+ cells) from the blood of the individual with HIV-1 infection and inserting a gene into them. This gene produces molecules known as ribozymes or gene scissors, which cut up the genetic material of the HIV. The procedure of inserting the ribozyme gene into the CD34+ cells takes place in the laboratory. The CD34+ cells containing the new gene are put back into the same individual from whom they were collected and go back to the bone marrow where they produce white blood cells such as T cells, which also contain the new gene. It has been shown in laboratory experiments that T cells containing the ribozyme gene produce less HIV because its genetic material is cut up by the ribozyme. In the Phase I trial conducted in ten patients, there were no safety concerns related to the ribozyme gene. The CD34+ cells that were introduced to the patient survived and contributed to the various types of blood cells, including T cells which are important in fighting HIV-1 infection. In the Phase II trial presently proposed, we will further evaluate the safety of this approach. We will also determine whether the T cells and other cells containing the gene scissors reduce the load of HIV-1 in the body and improve the overall function of the immune system and its capacity to fight infection.