RV144 was the first AIDS vaccine trial to show protection against HIV in humans. The prime-boost combination reduced HIV risk by an estimated 31.2 percent over three years of follow-up.

The field moved quickly and collaboratively to identify a set of tests to perform on available samples to identify correlates of risk. This effort yielded two correlates that are clues for future vaccine design.

The experience with RV144 is a powerful reminder of why human clinical trials of vaccines are essential to the search. The field has learned things it could not have predicted and pursued these results with new research and trials.

Modeling shows that a product like RV144 would make a significant impact in many settings—even in the context of scaled up combination prevention. Now is the time to invest energy, financial resources and time in the RV144 follow on agenda.

RV144, also known as the Thai Prime-Boost trial, evaluated a poxvirus vector plus protein vaccine combination, which found evidence of modest protection. At the end of the trial, efficacy was 31.2 percent overall; efficacy at 12 months after immunization was higher.

Within nine months of the result, an international initiative was underway to select the assays used to analyze RV144 samples for correlates of risk.

Correlates analysis identified one immune response (binding antibody to the V1/V2 region of HIV envelope) associated with vaccine-induced protection. High levels of the immune substance known as IgA, were associated with decreased protection.

Scientists are seeking to improve on the RV144 result in several ways:

- They are following up on the questions raised by the correlates analysis: Is the binding antibody to V1/V2 responsible for, or just a sign of protection? What’s the structure of the V1/V2 binding site?
- A clinical trial has begun to re-boost some of the volunteers in the RV144 trial to see if immune responses can be improved and sustained.
- Several partners from the Pox-Protein Public Private Partnership (P5) have developed a regimen that will be tested in follow-on trials to RV144 (planned for South Africa and Thailand). One goal is to seek to prolong the level of protection observed at 12 months in RV144.

Three follow-on trials are planned: (1) a South African efficacy trial of the P5 regimen to see if results can be repeated/improved in a high incidence setting; (2) a South African “discovery” trial with an adaptive design to gather information on multiple vaccine candidates; and (3) an efficacy trial using the P5, RV144-like regimen among MSM in Thailand.

**Adaptive design:** A trial in which the protocol predefines ways in which the trial can change on an ongoing basis (e.g., study questions, product, number of trial arms), with decisions guided by review of the available data by the trial team.

**Assay:** A laboratory procedure or test.

**Binding antibody:** An immune response that attaches to but does not completely inhibit (neutralize) the activity of a pathogen, like HIV.

**Correlates of risk:** An immune response that predicts whether those who receive the vaccine become HIV-1 infected. It may be causally related to protection or only a marker for the real immune factor(s) that caused protection.

**Re-boost:** Providing another dose of a previously-administered vaccine regimen.

**V1/V2 region:** A region on the envelope (outer coat) of HIV that is involved in viral entry into cells.

**RV144 (Thai Prime-Boost Trial):**
Building on a breakthrough

**KEY QUESTION**
Is an AIDS vaccine possible?

2009 - 2010

**KEY QUESTION**
What might explain the RV144 regimen’s protection against HIV?

2011 - 2012

**KEY QUESTION**
Can we do better?

2014...