DR. PETER HOTEZ STATEMENT FOR ALLIANCE FOR HEALTH REFORM AND KAISER FAMILY FOUNDATION BRIEIFING

Good afternoon, I would like to thank both the Kaiser Family Foundation and Alliance for Health Reform for inviting me to speak. My name is Peter Hotez I am an MD PhD physician scientist who heads a non-profit product development partnership – a so-called 'PDP' – which develops new vaccines for neglected tropical diseases.

Known as the Sabin Vaccine Institute and Texas Children's Hospital Center for Vaccine Development (based in Houston) our Sabin PDP has developed and is testing several NTD vaccines now in clinical trials. NTDs like Ebola virus infection, African sleeping sickness, kala-azar, hookworm, and schistosomiasis represent tropical infections that almost exclusively affect people living in extreme poverty. They are not rare diseases, but in fact are the most common afflictions of the poor, especially in Africa, the Middle East, Asia, and parts of Latin America.

Together with Seattle's Institute for Health Metrics and Evaluation at the University of Washington we have recently determined that practically every person living below the World Bank Poverty figure now suffers from at least one NTD, led by intestinal worm infections such as ascariasis and hookworm, as well as schistosomiasis. At the Sabin PDP we have advanced vaccines for these diseases now in clinical trials.

Let's talk about Ebola virus infection. It sure would be nice to have an Ebola virus vaccine now! As we speak brave men and women of the United States military are now in Liberia and elsewhere in West Africa creating a healthcare infrastructure for hospital beds, and for training healthcare personnel. Last month the WHO stated as many as 10,000 new Ebola cases per week could be reported by December. In order to slow the pace of this horrific epidemic and ultimately turn the curve downward, WHO has adopted a goal of "70-70-60" meaning that 70% of the people killed by Ebola need to be buried safely, and we need to get 70% of those with the disease treated in a hospital like setting within 60 days. From my perspective that is the roles of the US and now UK militaries as well as other international relief organizations.

The next few weeks will determine whether we can meet these targets, if not our only hope could rely on having a safe and effective Ebola virus vaccine ready to use. I'm hoping it's not the case, but if it is then we could find ourselves in a race against time. Even if turns out we won't need a vaccine, it may become a lifesaver for the next Ebola outbreak, especially when used in the context of a strengthened health system.

So I will state it again - it sure would be nice to have an Ebola virus vaccine! For me the terrible sadness is that we have had the technology for developing an Ebola virus vaccine for almost a decade, and possibly we could have had an Ebola virus vaccine stockpiled and ready roll out as soon as this epidemic began in Guinea earlier this year. But it wasn't developed, and we have

no vaccine simply because there was a market failure for Ebola virus vaccines, just as there are for other NTD vaccines such as the ones we are developing for hookworm and schistosomiasis.

The point is that our technical ability to develop Ebola and other NTD vaccines has outpaced our social, political, economic, and financial institutions that haven't yet figured out what to do for vaccines that target diseases of the extremely poor.

Let's take a moment to do a little deeper dive for the Ebola virus vaccine. One of the more promising ones is an Ebola vaccine comprised of an adenovirus encoding Ebola virus glycoprotein antigens. The vaccine was developed at the VRC – the vaccine research center – located on the main campus of the National Institute of Allergy and Infectious Diseases – NIAID – the US National Institutes of Health, just a few miles north of here in Bethesda, MD. At the time the VRC was headed by my good colleague Dr. Gary Nabel. Just retracing Gary's progress by looking at his papers in PubMed the database from the National Library of Medicine is instructive.

In 2000, almost 15 years ago they reported in Nature the Nabel group reported on a "highly effective vaccine strategy for Ebola virus infection in non-human primates…demonstrating that it is possible to develop a preventive vaccine against Ebola virus infection in primates". These findings were fine-tuned in 2006 when they reported in PLOS – the Public Library of Science – that a recombinant adenovirus vaccine, presumably similar to the one subsequently licensed to GlaxoSmithKline (Ad 3) and Crucell (Ad 26), was sufficient to confer protection against lethal challenge in a nonhuman primate model. Finally in 2010, almost 10 years after the initial publication they reported that a recombinant adenovirus-based Ebola vaccine is safe and immunogenic in healthy adults.

According to the NIH "the current candidate vaccine builds upon three earlier NIAID-developed investigational Ebola vaccines that began Phase 1 clinical trial testing in 2003." Proceeding to phase 2 and 3 trials – for further safety and efficacy - can be both lengthy and expensive, and require the backing of a major pharmaceutical company such as GSK or Cruzell.

My point is that we may have lost a few critical years, while things stalled waiting for GSK and Crucell, advance their vaccines through advanced clinical testing and scale-up production. But I believe we could have had a vaccine in hand ready to go a few years ago. Talking to industry colleagues we now realize how quickly we can move if all hands are on deck, including adequate investments from Pharma and the US and other governments, but also regulatory flexibility with the FDA and European EMEA. An additional gap is that Pharma is still waiting on projections of how many dosease will be required for this and future epidemics so they can plan accordingly.

I also think we need to consider mechanisms other than relying exclusively big pharma to see an opportunity in order to develop NTD vaccines. Mind you this is not a criticism of big pharma who have done great work donating repurposed essential medicines for NTDs and have in this case stepped up when a crisis arose to license and develop an Ebola vaccine. It's also not the fault of the NIH, which according to the group Policy Cures in their annual G-FINDER Report supports more neglected disease R&D than any other agency globally.

Perhaps we need additional institutions and organizations beyond big pharma to develop NTD vaccines like Ebola.

Our Sabin PDP in Houston is one of four or five PDPs making vaccines for neglected diseases such as AIDS, TB, malaria and NTDs. Ours is the smallest of the five and of course we struggle having sufficient funds to advance our vaccines through both product and clinical development. We were launched with support from the Gates Foundation, and over the years have been able to pull additional funding together from a variety of sources including the NIH, the EU, Texas Children's Hospital, and private foundations including the Slim Foundation. But it's a struggle to maintain meaningful funding to support advanced vaccine development.

In 2011 in the Public Library of Science Neglected Tropical Diseases – PLOSNTDs – I proposed a possible solution. In a paper entitled New Antipoverty Drugs, Vaccines, and Diagnostics: A Research Agenda for the U.S. President's Global Health Initiative (GHI). http://www.plosntds.org/article/info%3Adoi%2F10.1371%2Fjournal.pntd.0001133 I suggested Setting aside approximately 1%–2% of President Obama's billion dollar global health initiative (roughly US $100–200 million annually) for R&D on new antipoverty vaccines and drugs would dramatically increase the current support for new NTD antipoverty technologies, and simultaneously provide capacity building activities for key disease-endemic countries of strategic interest to the US. It could also provide a new and exciting role for PDPs committed to the NTDs, many of which are US based, to engage in vaccine diplomacy – international scientific cooperation to jointly produce new vaccines, and ultimately lead to the development of a new generation of poverty-reducing biotechnologies.

The mechanisms by which funds are distributed could require the establishment of peer-reviewed study sections, possibly not too dissimilar to those established by the NIH in order to ensure that only the best science is funded, and in addition there could be specific requirements and oversight to place the science in a diplomatic context. Such science and technology diplomacy to reach out to countries of America's strategic interests could create a new dimension in US foreign policy that also plays to our great strengths and intellectual prowess in biomedical R&D.

Thank you again to Kaiser and the Alliance for this opportunity.