

**The 2nd IAS Conference on HIV Pathogenesis and Treatment
Extraordinary Plenary Session
“20 Years of HIV Science”
“From Science to Action: Challenges in Managing AIDS”
7/14/03**

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MALE VOICE: We'd like to start this extraordinary session on "20 Years of HIV Science" and I guess you've all been looking at the program. You've all been impressed by the people that will be here. Nelson Mandela will come. Do not worry. He will arrive a little bit late, but he will come and it's now my extreme pleasure to introduce our special guest that will chair this meeting, Professor Robert Gallo and Professor Luc Montagnier. As you know, they are the co-discoverers of HIV, which is a tremendous accomplishment, but I also think that they have a lot of other accomplishments and this is upon me (misspelled?) to introduce the first speaker, but before doing that, I'll get you a little, I'll get the exact order of speakers from Alhambra (misspelled?), but we've got to do a brief introduction first, then Dr. Anthony Fauci, whose is also a first one of the most preeminent paramedical scientists in the world who will give the keynote lecture on HIV and AIDS 20 Years of Science. He will be followed by a few introductory remarks by Professor Luc Montagnier and then we will have Mr. Mandela, President Mandela here. And I'd like to introduce Dr. Gallo to do his introductory remarks. As I said, he has had an extraordinary scientific career in virology. He not only discovered HIV; he discovered a number of betavars (misspelled?) as well, including Helv (misspelled?). He's made other great contributions; data growth factor (misspelled?) being one of them and I don't think we would be where we are in

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virology if he hadn't been there and if you look at this accomplishment, it could actually fill 10 cc (misspelled?). I just found out how he does it because his watch is about five minutes fast, but I'd like to introduce you to him (unintelligible). I thank you for coming.

ROBERT C. GALLO: Thank you very much. We have to be on time and if there're a few minutes for general remarks before the introduction of our first special lecturer, Dr. Fauci. I first want to thank President Lange and also Dr. Kazatchkine and Mr. Peter Hale for their kind invitation and for making life so easy while I've been here in Paris. The few general remarks I want to make go back in time to beginning with the late 1970s and I'd like to see if we can take lessons from this period. At that time, a dramatic shift in thinking occurred in the scientific community, when it fostered three viruses. The first virus was that viruses, which were once suspected as possible causes of some human cancers, in fact, never caused human cancer was (unintelligible). Evidence of this was the closure of the Virus Cancer Program of the National Institutes of Health in conclusions at various scientific meetings, particularly in the United States. The second virus was that retroviruses, which caused many interesting diseases in animals and were long sought for in humans, in fact, did not exist in humans. Worse it stated that human retroviruses could not exist. The third and most

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troubling virus was that microbes causing serious epidemic diseases were no longer a problem for us; namely those people in the industrial world. This is evidenced at the time, by the closure of the Departments of Microbiology in several U.S. medical schools and the threat of the reduction of closure for the Center of Disease Control in the United States and by groups from Europe, including France that were in agreement with this thinking. Amazingly and ironically, within a few years that is by the early 1980s these viruses were shattered. Viruses were identified as involved in the cause of about 20% of all human cancer. Human retroviruses, HTLVs were discovered, shown to cause some forms of leukemia and neurologic disease. And finally, the greatest pandemic in history emerged, AIDS, ultimately shown to be caused by another human retrovirus, HIV. It's important to note that background is important, technological and so on, referred to a little bit by Dr. Lange. A discovery of the new virus, and its evidence that it causes disease, can almost never occur in a vacuum. In the case of HIV, at least for our group, it was preceded by about 13 years of basic science aimed to find human retroviruses, particularly in the 1970s. This was two-fold really; it was the development of sensitive and specific (unintelligible) for a human fetus human (misspelled?) reverse-transcriptase, which could be used as a footprint for a surrogate mother for a human retrovirus and the development of techniques could grow primary human T-

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cells in rats cell culture for the first time, notably by the finding of what we called T-cell growth factor, later renamed InterLeukin-2 or IL-2. For us, and I think for others, these techniques were very important for finding human retroviruses. Unlike, as was, in my opinion, naively reported in the current issue of the journal, "Nature Medicine". The eight viruses were not found or discovered by a simple electron micrograph. Critically, first came the culture retrovirus and showing it was unique by Luc Montagnier and his co-workers. Second, the demonstration that the new retrovirus found in '83 was the cause of AIDS, that is for the (unintelligible) virus or the Human Immunodeficiency Virus, took another full year of intense solid basic research, and recorded in early 1984, nineteen years ago. Finally, in my mind, it is notable that no individual or group were really responsible for finding the cause or developing a blood test, and so on. Certainly in my group, and I think Luc Montagnier's group certainly got involved from interest, maybe even by chance. Briefly, what are the lessons from this history? The first is that scientists should never believe they have concurred nature, to realize that microbes will always be with us and second; that the microbe could come from any class. We shouldn't be limited in our thinking of particular classes not infecting humans. The third lesson is that detecting a new virus must follow by demonstrating it is the cause of a disease, and not just

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technology, preparation and ideas. I believe this can be best fulfilled in the future by the creation of centers of excellence in human biology throughout the world, covering every known class of virus. Each center responsible for new epidemic diseases, especially a center with experience that best fits the new epidemic problem or challenge. Each center in turn should be intent intimately related through a few centers in a few developing nations, as we are trying to do with a few now. Finally, you know it would be great to have massive funding for anti-HIV drugs for the developing nations; this must come with massive infrastructure improvement or we make create new epidemics of HIV drug-resistant mutants. New drugs will also likely be continuously needed and they are coming, particularly entry inhibitors. A preventive vaccine, in my view, is possible. Medical science can and will solve this problem. I believe there is now much more, not less, reasons for hope in this regard than only a few years ago. It is now time, my duty, and more so my great pleasure and privilege to introduce colleague, friend, much admired scientist, and science administrative leader, Dr. Anthony Fauci. Tony Fauci trained in New York at Cornell University. He studied Infectious Disease and Immunology in particular. He took his first and his last career job at NIH, the National Institutes of Health in Bethesda Maryland in the U.S. Specifically, the National Institute of Allergy and Infectious Disease, where in

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1984, he became its Director and continues to this day in that job. You will of course note, that that institute also includes the largest AIDS effort (misspelled?) in the world. Tony Fauci is known by all his scientific colleagues as a leader in the field of HIV pathogenesis from the beginning to this day. He has been widely recognized with a variety of awards for his science contribution, including membership in the U.S. National Academy of Sciences, but it does not end there. The super and superb organizational skills, brilliance and a tremendous work ethic. He has combined science and scientific administrative leadership. More than anyone, he is responsible for bringing into the field diverse scientists to work on AIDS. He was also the first to include the activist community in decision-making. He has been a house advisor for several American Presidents and most recently, he played an important role in the development of President Bush's \$15 billion plan for AIDS relief. In conclusion, Tony Fauci has been a marathon man of AIDS. It is interesting that he also runs the marathon and it is now time to let him do a bit of that marathon.

DR. ANTHONY FAUCI: Thank you very much Bob for that very nice introduction. I would like to thank the organizers of the meeting for giving me the opportunity and the honor to discuss with you the extraordinary journey of 20 Years of

HIV-AIDS Science. When Michelle Sebastian (misspelled?) asked me several months ago to undertake this task, to outline

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in 25-minutes my impression of what the salient features of advances were in HIV-AIDS, I really would see the daunting task, but I did not realize until I started to dig into it, the extraordinary magnitude and scope of science that has been put into HIV-AIDS. Now I cannot promise you that I wrote every one of these 135,000 papers, but it seems that way. If one looks at the science, it really has various components to it. The first component was plain, simple observational epidemiology. The realization back in the summer of 1981 that we were dealing with a new disease, as shown by these original morbidity, mortality weekly reports from the CDC. Over the ensuing months, it became very clear that we were dealing with something much more than just handfuls of gay men in New York and in San Francisco, as the epidemiology began to unfold involving hemophiliacs, infants, sexual partners of infected individuals. And, in fact, what we see now in the year 2003, is most extraordinary and in many cases and in many sense, tragic. The scope globally of this epidemic with more than 16 million people having been infected and currently 40 plus million living with HIV-AIDS, now back in the early '80s, it was unclear what we were dealing with. There were some far-fetched theories as to what the etiology of this strange and frightening disease was and it was only after patient ports (misspelled?) from different risk groups began to accumulate that it was very clear to summarize in this editorial that we

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were dealing with a transmissible agent, but what transmissible agent. At that time, as Bob mentioned, there were a number of laboratories involved in looking at retroviruses, and since this was a disease that was clearly compatible with an atrophic and immunosuppressant disease, a number of laboratories began, with intensity, examining the possibility of an etiologic agent, and this is got now very well known issue of science and with multiple laboratories, including Luc Montagnier, and Bob Gallo's and others, he grabbed a circle around and really get their arms around the idea of this being a retrovirus. Now it was the paper of Luc Montagnier, as shown here, from the EM (misspelled?), from Francoise Barre-Sinoussi, which shows them clearly came from lymph nodes from an individual that was then grown in for blood lymphocytes, that we were dealing with a new agent that was not HTLV-1 and over the ensuing months, the information that began to be gathered as shown by this cluster of papers from 1984, putting the causal link of HIV and AIDS definitively where we know it to be today, hence HIV, the immunological agent of AIDS. A few months later, this was confirmed in San Francisco by J. Meaty (misspelled?) and his colleagues. We are talking about 20-years of science, but we really must remember that science is a continuum and as alluded to by Bob just a few moments ago, we drew very heavily on previous discoveries, such as the Nobel Prize winning discovery of reverse transcriptase by Renato Dulbecco, David Baltimore

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and Howard Temin. The ability to could grow T-cells long-term in culture, was essential for our ability to isolate atrophic viruses such as HIV and also the realization that retroviruses can, in fact, cause human disease as shown here by the link and etiological cordiality (misspelled?) between HTLV-1 and certain types of lymphomas and leukemias. Now what followed the development and the realization of HIV as a cause of AIDS came a succession of extraordinarily important observations that had major impact. Second to none, was the development of an antibody test for HIV, which had a number of important implications. First and foremost is the protection of the blood supply, but also the ability to diagnose HIV infection in asymptomatic individuals to allow for appropriate screening and appreciation of the epidemiological scope and magnitude of the epidemic that we were dealing with. The science of molecular biology, the molecular cloning of the virus, the determination of the nucleotide sequence opened up new disciplines for us, such as the disciplines of molecular biology and molecular epidemiology, whereby we were able to determine the actual origins of HIV. With HIV-2 directly linked to SIV in the pseudo macaques and over the most recent years, just the past few years, the appreciation of the link between a virus in chimpanzees and HIV-1. In addition, this adversity of heterogeneity, as shown by this bio-genetic tree, breaking down the viruses of multiple sub-groups that has important relevance

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when one looks at the geographic distribution of HIV, early on thinking that we had a homogeneous virus, what we now call the blue (misspelled?) sub-type has been a part of the United States and Western Europe, but now we see from molecular examination that the C-subtype is actually globally the most predominant one. Molecular biology also allowed us to hone in on the nine genes, the three structural and the six regulatory genes, which are so important in what followed in pathogenesis and even today at this meeting, we are learning more about the function of these important genes. What about pathogenesis? This is probably the best-studied virus, literally, in history. We've learned an awful lot, but there are many, many challenges. The first pathogenic observations were really rather simple. It was the link to the epidemiology, an appreciation that those early patients had an acquired cellular immunodeficiency that seemed to be focusing on the CD4 positive T-cells. If you look at the right-hand side of this slide, it was where we were in 1981, functional and quantitative depletion of CD4 positive T-cells that we now know after years of experience that the first viremia is responsible directly and indirectly for the insidious and inevitable evolution of CD4 positive T-cells leading to the disease that we call HIV-AIDS. There are a number of proposed mechanisms for the loss of CD4 positive T-cells. Several of them are listed on this slide. They are not mutually incompatible with each other, and it is

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likely an example of many approaches, all of which are possibly correct, but the one overwhelming clear observation is that lymphocyte turnover is increased in a state of heightened immune activation, but why T-cells? The answer came early on from these two classic papers that identify the CD4 molecule as a primary receptor for HIV. But with power over the next few years because we knew, the field knew, that it couldn't just be CD4 alone because when you transect the gene CD4, for example, into a mouse head, you did not get sufficient height infection and replication. This led to a search of other receptors and in this regard, I considered this and many of my colleagues do, one of the most beautiful examples of the convergence of two separate fields. Investigating interesting and receptor biology and those who are interested in cytercon (misspelled?) biology, particularly for soluble suppressors of HIV, which led to the HIV co-receptor discovery. In fact J. Meaty and his colleagues early on in the epidemic were the first to recognize that a soluble factor could actually suppress HIV replication. There is still work going on in sorting out the precise nature of these factors, but the big breakthrough came with the discovery of (unintelligible) in Bob Gallo's lab that (unintelligible) data could directly block R5 viruses. We didn't call them R5; we called them macrophage-tropic viruses at that time. But simultaneously with this work for a number of phenomenally interested and talented investigators who were working on

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receptor biology (unintelligible) showing by functional CDA cloning could even identify what we now today know to be CXCR4. A number of other investigators looking at a receptor that might bind the macrophage-tropic strain led to an appreciation of the dual co-receptors and it was an experiment of nature, namely individuals who appeared to be relatively protected and whose lymphocytes could not be infected in vitro for the now five hours that led to depreciation of the 32 (unintelligible) which narrowed down the importance and the necessity to that co-factor. That in and of itself, opened up yet again another field, closing the loop on the true replication cycle of HIV as shown in this slide with the need for the dual-receptors that as in all science, it was much more complicated than that. First what this did was open up the door to understanding things like cryptic epitopes, because it was the binding of the virus of the CD4 which allowed for the confirmation of change to allow then envelope that binds snugly the CCR5 (unintelligible). In and of itself that was important, but it also exposed cryptic epitopes that we are now perusing in vaccinology, which I'll get to in a moment, as well as vulnerable targets like the Hampton Loop (misspelled?), which is now the target for therapeutic information with certain peptides. So all of these things were connected with each other, also the role of lymphoid tissue in the pathogenesis of HIV. The appreciation that the virus continuously replicates in

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lymphoid tissue, even during the quasi latent period of HIV and an appreciation of the clustering for the reservoir of HIV in lymphoid tissue in patients who otherwise appear well. It was not until the technical advance of being able to measure very small amounts and very large amounts of virus that led to the appreciation of the magnitude of viral turnover. The sensitive PCR assays, together with the ability to study people before and during therapy, led to the breakthrough work of David Ho (misspelled?) and George Shaw on delineating the rapid turnover of (unintelligible) and CD4 lymphocytes leading to this mathematical mirroring from (unintelligible) as shown on this slide, which would have predicted that one could, in fact, eradicate the virus if there was no further replication and if there was not a reservoir that could continually be present to blunt and frustrate eradication. As a matter of fact, Bob Cillacono (misspelled?) and his colleagues were the first to recognize the importance of the resting, (unintelligible) infected CD4 positive pool, which I'll get back to in just a moment when we talk about eradication. The new response to HIV and (unintelligible) of immunity have very important components of the scientific advances over 20-years. They're probably one of the most frustrating and problematic. One fact looms prominent, and that is the somewhat frustrating observation that no infected, HIV-infected individual has ever been reliably reported to have cleared HIV following the

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establishment of well-documented infection. So we're going to show on this very familiar slide, we know we have HIV-specific responses. CD8 responses, CD4 responses, neutralizing antibody, the time to appear later on following the drop in viremia that we see seemingly associated with CD8-positive responses, but there appears to be an escape for each of these. There is some encouraging news. Some clinical observations that suggest actually that there is potential for immune protection for long-term non-progressors, the highly exposed uninfected individuals, such as the Cambrian, Kenyan commercial sex workers. In addition, the temporary control of HIV after treatment of primary infection associated with CD8 responses, as Bruce Walker and others have reported. There are a number of animal studies, vaccine studies in non-human primates. The relationship between CD8 response and the level of viremia, such as when you deplete CD8 from chimps, you have a temporary burst of viremia, also the passive transfer study using neutralizing antibodies. Now the treatment of an HIV infected individual. Perhaps the most important advance following the discovery of HIV has been the road to affective therapy. It started off rather simply, screening already existing drugs, such as AZT, which was made for an entirely different purpose, the treatment of cancer and failed. This is the classic first taker showing the positive impact on morbidity and mortality of AZT as a single mono-therapy. This is great news, but it was

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soon sobering news because the effect did not last, and it was only in evolution of the realization and over time, throughout years, that we needed combinations of therapies that would leave a more profound drop in plasma viremia as well as an enduring affect, as shown on the right-hand side when the introduction of combination therapy occurred. This could only have been occurred by applying what we now call targeted drug developing aimed at the targets on this slide. A classic example of that was the basic science, the exquisite science that went into the identification, isolation and ultimate crystallization of the protease enzyme leading to the ability to tailor make a protease inhibitor that rapidly went into clinical trials and led to new therapies. We see now, most recently, refusion (misspelled?) the same philosophy, the identification of a vulnerable target in the fusion process, which led to the synthesis of a peptide, which is now going to become an important drug. This is a risk of the 22 formulations and the 19 drugs that have been approved for HIV. This is an extraordinary accomplishment, but many challenges remain. The results have been remarkable. This is the drop in mortality of the United States and just last week, the European results so strikingly similar are of positive results. Getting back to the question that I introduced a few minutes ago of eradication versus control. Can we cure this disease? Well in harking (misspelled?) back to the realization that we have probably

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many latent reservoirs and some not so latent. The studies from Cilacono and others, a number of groups indicating that the natural attrition of that reservoir will make eradication extremely problematic, unfortunately, this has shown scientifically in 1997 with three separate groups examined patients who had been treated to the point of being aviremic for three years, and unfortunately, in every one of those patients, you could isolate replication competent virus and to make matters worse, when we empirically stopped therapy, almost invariably, you had rebound of viremia to the level of the original set-point, again making eradication very problematic, which forced us to focus now on some of the limitations and challenges of the current anti-HIV drugs, such as those listed on this slide and I need not read them to you because you are very familiar with them. So the challenges of new and better drugs is an important part of our scientific agenda for the coming years. What about prevention? Prevention is indeed a science. And there have been scientific advances in prevention from simple education and behavior modification, to the use of treatment, such as the treatment of an infected mother and a baby at birth to block transmission, so in drug abuse programs, the use of condoms and clean needles and needle exchange, topical microbicides. The treatment of other sexually transmitted disease, but foremost among challenges is the question of an HIV vaccine. This is the cost of risk, of some

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of the vaccine strategies that are being employed and that have been employed, but the stumbling blocks have been substantial, this is an historical pathway of which we're still on that road. Initially taking an antibody-focused approach and then getting discouraged and gradually moving to a cell-mediated approach and then now, in the future also, looking at both, and let me explain what I mean. This has been a bumpy road. The antibody focus had some problems. We could neutralize, but not primary isolates. When you vaccinate an animal, they made antibody against the homogenous challenge, but not the heterologous challenge. Neutralizing antibodies rapidly, a symmetric for escape mutants, and although we had monotonal antibodies about five, derived from individuals that clearly were broadly neutralizing, we didn't know how, and still don't know how to reduce the immune system to make those sensitivities, and also there are numerous structural problems with the envelope themselves that is causing us great difficulty in being able to prime for a adequate response. And so early attempts at antibody focused vaccines were in some respects, unfortunately and retrospectively doomed to failure because of either a lack of appreciation for a failure to adequately address the points on this slide. Things were a little bit more optimistic with cell-mediated responses, even though CD8 could select for escape mutants and even though you need good helper cells, which are not necessarily around

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(unintelligible) disease, animal studies were able to protect against progression of disease, but not primary infection and you are all familiar with those studies. So the currently employed CD8 focused direction gives us some considerable promise, but it is not as itself adequate, which gets me back to this historical slide and where we need to go in the future and the challenges are extraordinary. For CD8, we must have novel designs for immunogens. We've got to look at how we present antigen to CD8 cells, much more difficult than that of CD4 cells. We need a broader range of epitopes and for both cell-mediated and antibody; we need better antigens, but the potential for marrying basic science. The classic vaccinology lies in the joining of modern day structural biology with classic immunology and we are starting to see that now. For example, with the crystallization of the structures of what happens when an antibody binds to envelope in the presence of CD4. What about the exposing of cryptic epitopes? Do we use that to inform vaccine development and most recently utilizing our knowledge that there exists broadly reacting neutralizing antibody in some patients to be able to use structural biology to point us in the direction of an appropriate immunizing antigen? Now again to reiterate, a safe and effective vaccine is absolutely critical and it is probably the most important and difficult scientific challenge in AIDS research. Now I would not be able to close without, for one minute, reflecting on, we

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are talking about science now, but the importance of the role of activism in HIV-AIDS science. Which my experience personally and we experienced in the United States very early on, and it was activism that demanded that those who were infected with HIV, or who were at risk of infection, play a role in determining the nature of clinical trials and the access to drugs which could only be accessed through clinical trials, and it was more than a decade and a half ago that we decided to address that problem. We brought the activist to the table and I can tell you from personal experience how clinical trials process and the process of access is much the better for it; for history has a way of repeating itself, because this is what we saw in South Africa a few years ago. The risk factor was demand on the part of the people to whom it mattered for treatment access. Something that is now the topic of intensive and appropriate discussion here today at this meeting and certainly throughout the world most recently and so I'd like to close with this line: We've spoken for the last 20 some-odd minutes on the basic and clinical research associated with HIV over the past 20-years, but we must keep in mind, it's mandatory that everything that we have done, that we are doing, and that we will do in the future should and must be directed towards the common goal of all of us and that is the treatment, prevention and care of HIV infection. Thank you.

MALE VOICE: Thank you Dr. Fauci for that wonderful

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review. I don't think that anybody doubts that, that there is any other person who could have done this. There is no other person that could have done this better. I may get it wrong here, but you know what I want to say. It's now my pleasure to invite Professor Luc Montagnier to give his introductory remarks. He subsequently will introduce President Mandela to the podium. Professor Luc Montagnier, like Professor Gallo, (unintelligible) has the basis of 20-years of HIV science, this was the first (unintelligible) in 1983 was a thing LAV, as some of you may recall, and he (unintelligible) as the cause of AIDS. It's hard to believe now, but this was initially met with considerable skepticism and I think that both Professor Montagnier and Professor Gallo are a testimony to the fact that persistence pays. Professor Montagnier.

PROFESSOR LUC MONTAGNIER: Thank you Dr.

(unintelligible). In 1986, a few of us created the International AIDS Society in this very same place on the occasion of the 2nd International AIDS Conference in Paris. I wish I get to see during my life the (unintelligible). It is no longer necessary for an organized meeting on AIDS (unintelligible) would be over. It is clearly it is not going to happen soon. Despite there are many advances in HIV-AIDS, as just reported by my colleague, Anthony Fauci. We are still facing a very (unintelligible). It means we (unintelligible) have not been able to find ways to eradicate this disease

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(unintelligible) to make a preventive vaccine. Of course, we are not only responsible. We need also to mobilize the forces of the war on this disease, the political world, the (unintelligible) world and also the generalized public opinion. And I think we have (unintelligible) and we should be aware of this. We, of course, have to design a rational approach for preventing AIDS, this has been done by (unintelligible) I'm not pretending to be alone in this (unintelligible) but I'd like to mention that there are several steps we should go through in order really eradicate this epidemic. Of course, the first, (unintelligible) is to make accessible to (unintelligible) to all people, which really need it in the world, especially in the developing world. This, of course, involves a decrease in the prices and this, of course, has been already started, but it is more difficult to achieve with the most recent (unintelligible) and I don't see (unintelligible) being used in Africa right now or for the coming years, but we need also to set up structure, because we know that HIV is a long-lasting disease. We can monitor it by some foreign nations political parties and of course, we need structure to use (unintelligible). This is unfortunately lacking in most parts of the developing world. So this has (unintelligible). We need also to tell people HIV is now a medical specialty and needs, of course, (unintelligible) from the developed countries to developing countries. But we need also to do more research

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because of course, we can see patients, especially those we shall (unintelligible) for some time, but it is written by Dr. Fauci, (unintelligible) because we cannot dictate why they actually use drugs for this infection, and this needs some more research to find a treatment which will be progressively added to this treatment like in a new drug, we have vaccine therapy and there are some other treatments as well. But we have also to consider that it not sufficient to restrict (unintelligible). We have to, I would say that most patients are in an asymptomatic phase and those patients are not that visible (misspelled?) for the drug treatment, the (unintelligible) treatment and most of them do not know and they just want to know whether they are (unintelligible) chasing in may African Countries and also in Asia. Most people do not what to be tested because they have no hopes to be treated after the (unintelligible) will actually make them stigmatized in their family (unintelligible) so we have to propose to everybody who is going to be tested, a treatment. I know it is difficult, (unintelligible) which needs to be broken if he really wants to restrict the spreading of the epidemic in many European countries, this also needs research and unless (unintelligible) I'd like to tell you that early (unintelligible), it is probably caused by HIV proteins; it could be caused also by some other factors as well. So we have to deal with that by the use of (unintelligible) Finally, a

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word for the vaccine (unintelligible) toward the AIDS vaccine.

I could add something, which also makes this more difficult. It

is (unintelligible) are associated with those (unintelligible)

Finally, I'd like having the unique pleasure and honor to

introduce President Nelson Mandela. Nelson Mandela is one of

the great modern political leaders of our time.

(unintelligible) or the lifelong education to the fight against

racial oppression and (unintelligible) throughout the world.

Today he's (unintelligible) fight against (unintelligible).

Thank you.

NELSON MANDELA: I wish to thank the organizers for inviting me to this prestigious conference on the advances in HIV science and treatment over the 20 years. The scientific advances in understanding HIV, the virus that causes AIDS have been truly remarkable. It demonstrates what we can do when faced with a global health crisis.

We now know more about the virus. We understand more about the natural history of the disease from infection to death. We named the virus and (unintelligible) that have already been undertaken to better understand the virus and its implications to our lives. Science has set the ground for improved prevention and care.

We know that there is still a long way to go, but science has already given us the powerful tools to stop the disease. The problems is that the world is not using them where

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they are needed most.

Consider the facts: 1The United Nations estimates that about 75 million people are living with HIV. Second: 10,000 people die everyday from AIDS and third: Over 26 million people have already died. 95% of them in the developing world.

These numbers are staggering, in fact, incomprehensible. By all accounts, we are dealing with the greatest health crisis in human history. By all measures we have failed in our quest to contain and treat this scourge. And the disparity between its impact in the developed world and the developing world is a shocking reality that we cannot hide from. In poor countries, the disease is weakening ravished, shaky economies, worsening famines, and orphaning millions of children.

Why have we failed? What are we going to do in the end? It boils down to one inappropriate fact. We have failed to translate our scientific focus into action where it is most needed in the communities of the developing worlds, in the poorest regions of the world. This is a gross injustice, which cannot be tolerated. It is a travesty of human rights from a global scale.

The world must do more, much more on every front in the fight against AIDS. Of course, it means dramatically expanding our prevention efforts, but the most striking inequity is our failure to provide the lifesaving treatment to the millions of people who needs it most. It is our belief, and we are sure it

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is shared by most of you in this conference hall, that the single most important step we must now take is to provide access to children throughout the developing world. There is no excuse for today. We must start now.

We are happy to say that the usual excuse of lack of funds is rapidly coming to an end. The Global Fund to fight AIDS, TB, and Malaria is up and running. It has approved grants totaling \$1.5 billion over three years in 93 countries and have already signed grant agreements totaling \$600 million to 49 of the poorest countries in the world. This is a remarkable and exceptional achievement supported by all the governed nations of the world, by private foundations, and increasingly by private sector businesses.

On this subject, we need to recognize the leadership of the of the people of the United States, and if President George W. Bush, who has given in U.S. emergency plan for AIDS relief. The amount of \$15 billion has been authorized over five years. It is a crucial contribution to the fight against AIDS. This quantum leap in global funding has moved the debate from hundreds of millions of dollars to tens of billions of dollars. At least \$1 billion of this money is earmarked for the Global Fund. We would like it to be more, but we believe that this is a floor from which to start. If the Global Fund delivers results, and if other nations of the world and the private sector contribute their fare share, there is nothing preventing

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the U.S. from being persuaded to increase the proportion of the \$15 billion that goes to the Fund. We and the people of Africa will follow the delivery of this critical commitment with great interest.

President Chirac has joined the leadership of President Bush by committing France to a tripling of its investment in the Global Fund.

Europe as a whole has historically been a leader in development assistance and it is now time for other European nations to substantially increase their commitments to the Global Fund. Given the size of its collective population and economy, Europe should at least match it, if not exceed it, the United States contribution. Likewise donor countries in the Pacific Rim also need to review whether their contributions, match up to expectations.

It is common knowledge that the Global Fund needs more money. We have spoken with the executive director Dr. Richard Feachem, and we are convinced that this is the ideal multilateral partnership to finance a dramatically scaled up global response to AIDS. It is incumbent on all of us whether public or private, individuals or organizations, big and small to support the Fund in whatever way we can.

Through my foundation, we will be running a fund-raising campaign centered around the Worlds AIDS Day on December 1 this year. We are pleased to announce that the Global Fund is a

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partner in this effort. We will ask people from around the world to give one minute of their life to AIDS, to hope to mobilize this effort, we have already invited some of the largest corporations in the world who support this effort and we look forward to (unintelligible). This is my way of working with the Global Fund. What will yours be?

With regard to the delivering effective HIV-AIDS responses on the ground, we must sadly point out that many of the countries that most highly affected by HIV/AIDS have not done nearly enough to fight the epidemic, especially in Sub-Saharan Africa. This is completely unacceptable. It too is a travesty of human rights. Yes these countries are poor, but we know they have the capacity to do more, much more. This is the least that can be expected. More importantly, it is the least they can do for the millions of our citizens struggling with HIV-AIDS. There are notable exceptions to this rule of course, I speak of Uganda, Senegal and more recently Botswana. These are countries that have demonstrated leadership from the very top and have made remarkable progress in both prevention and care. Botswana now has over 6,000 people receiving antiretroviral therapy.

I cannot end this address without mentioning our very great concern about India, China, and Russia, which have rapidly evolving epidemics. If they follow the trends of Africa, the results will be calamitous; not only for the countries concerned, but for the whole world.

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These countries must learn from our many mistakes and also from those few countries that have succeeded in containing the epidemic. One of the crucial lessons that we have learned is to fight denial, stigma, and discrimination with everything we have got. We have also recognized the importance of voluntary counseling and testing for HIV—it is essential that every sexually active person should know his or her HIV status.

Is it possible for political will to catch up with scientific progress? Time will tell, but we put it to you that there can be no other option. If we discard the people who are dying from AIDS, then we can no longer call ourselves decent people. We must act now for the sake of the world.

Thank you.

[SINGING IN AUDIENCE]

[END OF RECORDING]