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HEALTH, EDUCATION, LABOR AND PENSIONS COMMITTEE'S
SUBCOMMITTEE ON HEALTH AND BIO-TERRORISM

REGARDING THE CURRENT STATE OF BIODEFENSE PREPAREDNESS IN THE UNITED STATES

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Chairman Burr, Senator Kennedy, and Members of the Committee, it is an honor for me to testify before you today regarding the current state of biodefense preparedness and the capacity of the biotechnology and pharmaceutical industries to respond to the biodefense needs of the United States.

I appear before you today as the Chief Executive Officer of Chimerix, Inc. Chimerix is an emerging biotechnology company based in Durham, North Carolina. The company was founded in 2002 to harness a technology developed by Dr. Karl Hostetler, professor of medicine at the University of California, San Diego, and is applying this technology to an existing, FDA licensed antiviral medication for AIDS patients in order to make it effective against orthopoxviruses, in particular, smallpox.

My testimony is based on over 25 years of experience in the biotechnology and pharmaceutical industry. During my career, I have worked for both large pharmaceutical companies such as Burroughs Wellcome Co. (now part of GlaxoSmithKline) and small biotechnology companies such as Triangle Pharmaceuticals, also based in North Carolina (now owned by Gilead Sciences). My primary focus and experience is in the development of effective treatments against viruses such as Hepatitis B and HIV, including being the inventor of lamivudine-HBV for the treatment of hepatitis B and being a member of the development team for AZT, perhaps the most widely used HIV treatment in the world.

Let me begin by thanking the Committee for its leadership in this critical public health and national security area. The work of this Committee's members, including the leadership of Senator Burr while in the House of Representatives and Senator Kennedy with former-Chairman Gregg in the Senate, in the passage of the Project Bioshield Act of 2004 was a credit to each of you. I applaud President Bush for his vision in announcing Project Bioshield in his 2003 State of the Union Address and look forward to working with Senator Gregg and this Committee to see passage of S.3 this year to further strengthen the Nation's bioprepardness.

From my perspective, there are two primary challenges facing the emerging biodefense industry. First, it is imperative that existing animal models of viral infection be further developed to a level that will allow drug developers to provide the Food and Drug Administration (FDA) with the data necessary to ensure the safety and efficacy of needed biodefense medicines. Second, the Department of Health and Human Services (HHS) must ensure that the Project Bioshield Act of 2004 is implemented in a way to convince investors in biotechnology companies such as Chimerix that a

successfully developed biodefense countermeasure can be purchased for the Strategic National Stockpile in a timely and predictable manner. Both of the goals are easily achievable.

With support and funding by the National Institute of Allergy and Infectious Disease (NIAID) and funding from private venture capital firms, Chimerix has initiated an aggressive program focused on the development of an oral antiviral drug for the prophylaxis and treatment of one of the most deadly diseases known to man, smallpox. While naturally occurring smallpox was eradicated almost 30 years ago by the World Health Organization's vaccination program, the events of 2001 have made it clear that terrorists can obtain and will use dangerous pathogens to attack our country. Originally, the primary goal of our efforts was to produce a therapeutic alternative to vaccination to provide protection for the up to 50 million Americans who cannot be vaccinated against smallpox as a result of compromised immune systems. This population includes people with cancer, people who have undergone organ transplant, pregnant women and infants, people and the families of people with common skin disorders such as eczema and atopic dermatitis and people living with HIV-AIDS. While this existing gap in our Nation's preparedness alone warrants investment in the development of safe and effective antiviral treatments against deadly smallpox, last year, straightforward genetic engineering techniques were used to create a model virus related to smallpox that can elude vaccines and produce 100% mortality in vaccinated mice. Were these methods successfully applied to the smallpox virus, variola major, the United States would be left completely vulnerable to attack despite the availability of smallpox vaccines.

Against this backdrop, Chimerix has worked diligently to pursue the development of a safe and effective smallpox drug and to expedite the drug development process as much as possible. Reaching this goal requires, in essence, that a new, accelerated paradigm for the discovery and development of antiviral drugs be defined. If successfully implemented, this new paradigm could help protect Americans not only against biological terrorist attacks, but also against emerging infectious diseases such as SARS.

The single most critical tool in this effort is relevant animal models that can provide data to ensure the efficacy and determine the appropriate human dose of these new drugs. It is both impractical and unethical to study the efficacy of a potential treatment for virulent diseases such as smallpox in humans. Therefore, critical efficacy data must be gathered in animal models. Under the FDA's animal efficacy rule, this data is used in place of the standard Phase II and Phase III clinical trials to support registration of the drug. Thus, animal models acceptable to both drug developers and the FDA are absolutely essential to the successful development of biodefense medicines. Simply put, without an appropriate animal model, neither

Chimerix nor any other maker of antiviral drugs will be able to develop medicines to treat smallpox infection. While a great deal of excellent research has been undertaken by both the Federal government and the private sector in response to this critical need, current animal models in mice, rabbits, and monkeys using test viruses such as mousepox, cowpox, vaccinia, monkeypox, and even human smallpox, are inadequate to fully support drug development under the FDA's animal efficacy rule. Thus, further development of treatments for smallpox is stalled.

Existing animal models cannot, for example, address two key issues that have arisen out of discussions between the FDA and Chimerix on the company's smallpox drug candidate. Firstly, the disease produced in animals needs to be as analogous as possible to the disease that would be seen in a human infected with smallpox. In current animal models, the rate and degree of appearance of the infection in the blood is dependent on the type and strain of the poxvirus used, the route of infection and how much virus is used to induce the infection. We currently do not know which test conditions produce the best model of human disease. Secondly, the treatment in animals needs to provide the basis for guiding physicians in the treatment or prophylaxis of human disease. In order to meet this condition not only must the disease model be correct but the uptake, distribution and elimination profile of the drug in the animal must be translatable to that in a human. Resolving these issues is absolutely critical in allowing us to determine what dose of the drug should be given, how soon before exposure the drug can be given to have a prophylactic effect, and how long after the disease has begun to manifest itself that we can treat someone and be assured of their recovery.

There is no doubt these issues can be resolved with more effort. However, from a practical standpoint this will require a significantly higher application of resource since animal experiments are both costly and time consuming. Additionally this process can be expedited by creating expanded working groups in which people with experience in drug development, animal modeling experts and representatives from the FDA CDER branch all participate. Finally, companies that are working to develop biodefense countermeasures and who are consequently gaining first hand experience in the use of the animal efficacy rule must be incentivized to participate in and contribute to these programs despite the fact that the models and their data will be made available to competitors.

On Friday, I returned from a trip to Russia with a delegation led by Congressman Curt Weldon (R-PA). On my own initiative, I was able to meet with and talk extensively to the leading former-Soviet virologists to obtain information and insight into their experience. Given the widely reported experience of the Soviet Union with smallpox long after the eradication of the disease, these scientists, many of whom are quite elderly, possess a great deal

of information about the course of the disease. While I have no doubt the United States has already learned a great deal of information from these individuals, their knowledge about the course of the disease could enormously supplement our understanding and help expedite development of animal models to allow drugs such as those being developed by Chimerix to enter the Strategic National Stockpile as quickly as possible. I would strongly encourage Congress to consider support of such interactions as part of Project Bioshield. I look forward to working with FDA and our partners at NIAID, to explore whether the information available from Russian scientists can help expedite development of proper animal models, and thus, the development of safe and effective treatments against smallpox.

The very practical concerns that require companies such as Chimerix to depend upon the animal rule creates enormous challenges in sustaining a private market solution for development and manufacture of medicines such as our smallpox antiviral. Chimerix, like most biotechnology companies, is funded by private equity investors that must be able to analyze and predict a reasonable return on their investment. Thus, the immediate development of animal models that produce data with the most predictive value is critical not only to ensure the safety and efficacy of these drugs to satisfy the FDA, but also to permit a sustainable business model to allow private entities to continue to participate in the emerging biodefense industry. Without addressing this problem, the United States and, indeed, the world will be left without a safe and effective drug for the treatment of smallpox.

In addition to addressing the animal rule, Project Bioshield must be implemented in way to allow the investment community the ability to assess and predict with some degree of accuracy the likelihood that a private entity such as Chimerix can generate an adequate return on investment through development of biodefense countermeasures. The recent award of a large contract for a single vaccine technology to a single company to address anthrax has caused some questions to be raised in the investment community about whether the market is viable for companies developing technologies such as Chimerix's that may be used as part of a drug cocktail. Moreover, it is unclear from the recent request for proposals issued by HHS for countermeasures whether there will be enough certainty regarding the number of doses that are to be procured to attract private investment.

Recognize that any uncertainty by investors in companies developing countermeasures caused by unpredictable markets and regulatory challenges such as the animal rule have the direct effect of increasing the cost of developing these countermeasures, which in turn, are passed on to the taxpayer when the drug is purchased for the stockpile. Of course, there is also the very clear danger that these challenges drive private investment away entirely, thereby threatening the capacity to produce countermeasures

at any price. Coupled with the already uncertain environment surrounding the creation of the emerging biodefense industry, the lack of a clear animal rule is potentially crippling to the development of the warm manufacturing base for needed countermeasures.

I very much appreciate the opportunity to offer testimony on this very important public health and anti-terrorism issue. Achieving the objectives of the Project Bioshield Act of 2004 and the Protecting America in the War on Terror Act of 2005 recently introduced in the Senate by Senator Gregg as S.3 are of the utmost importance to ensuring homeland and national security. Again, I applaud your efforts, and the efforts of President Bush and his Administration, and look forward to continuing our work with the Department of Defense, HHS and NIH in this critical area.

I am happy to respond to any questions you may have.