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First vaccine against fatal visceral leishmaniasis enters clinical trial

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The first clinical trial of a new vaccine for visceral leishmaniasis (VL) has been launched by the Infectious Disease Research Institute (IDRI), a Seattle-based nonprofit that develops products to prevent, detect, and treat diseases of poverty. The Phase 1 trial is taking place in Washington State, with a companion Phase 1 trial planned in India, an epicenter of the disease.

Visceral leishmaniasis affects vital organs and bone marrow, destroying white and red blood cells. Because VL attacks the immune system, it has been called the parasitic version of HIV/AIDS.

"Visceral leishmaniasis is a persistent and deadly global health problem," said Steve Reed, IDRI founder and Chief Scientific Officer, who led the over twenty years of preclinical vaccine work. "Our partnership with India will speed the development of an effective vaccine and accelerate its control.

Leishmaniasis takes several forms, all of which are caused by the *Leishmania* parasite and transmitted by infected sand flies. VL is most common in India, Nepal, Bangladesh, Sudan, and Brazil and causes about 500,000 cases and 50,000 deaths each year. Cutaneous leishmaniasis, the most common form of the disease, causes serious skin lesions and often leaves its victims permanently disfigured. Leishmaniasis occurs in 88 countries, affecting 12 million people.

While the disease can be treated, current treatments are too expensive,

difficult to administer, or toxic for widespread use in poor countries. Drug resistance is also a growing problem, particularly in India. Left untreated, VL has a 90% case fatality, and death can come within two years—much more quickly than AIDS.

Furthermore, scientists warn that the geographical range for leishmaniasis is expanding. Spurred on by global warming, mass migration and rapid urbanization, cases are being reported in previously unaffected areas.

Given such challenges, a vaccine is considered essential to control and eliminate the disease.

"With this clinical trial, we hope to launch a new era in the fight against Visceral Leishmaniasis," said Franco Piazza, Medical Director at IDRI and leader of the vaccine's clinical development. "For the first time, an advanced vaccine to prevent this devastating disease is being tested in people."

The IDRI vaccine, known as LEISH–F3 + GLA-SE, is a highly purified, recombinant vaccine. It incorporates two fused *Leishmania* parasite proteins and a powerful adjuvant to stimulate an immune response against the parasite.

The Phase 1 clinical trial will enroll 36 adult volunteers in Washington State. They will be randomly assigned to receive one of three versions of the vaccine, which differ in the amount of adjuvant included. The trial will evaluate the safety and immunogenicity of each version.

A second Phase 1 trial will take place in India, where IDRI is transferring its vaccine technology to the Gennova Biopharmaceuticals. Last month, Gennova opened a vaccine formulation center that will be producing vaccines for neglected diseases in Pune, India, where the

company is based.

In India, VL is known as kala-azar, a Hindi word that means black fever, named after the fever that ravages affected individuals, whose skin becomes dark gray.

"Kala-azar is a significant health problem across northern India and neighboring countries," said Dr. Sanjay Singh, CEO of Gennova. "Bringing a vaccine to India will not only end deaths and disease, it will also help many of our poorest citizens to lead more productive lives and move out of poverty."

Beginning later in 2012, the Indian biotherapeutics and vaccine manufacturer will produce the LEISH-F3 + GLA-SE vaccine. It will be then tested in healthy Indian adults, in collaboration with the Banaras Hindu University in Varanasi, India.

"We are very pleased to be working with IDRI on this vaccine, which is critically important to the many people who suffer from this disease in India as well as to the millions of people who are infected around the world," said Dr. Shyam Sundar, Professor of Medicine at the University's Institute of Medical Sciences.

Subsequent clinical trials will involve larger numbers of people who are at high risk of developing VL during their daily lives, because they are frequently bitten by sand flies. Only such large trials, conducted in real-life situations of disease exposure, will determine the full effectiveness of the LEISH-F3 + GLA-SE vaccine.

"Vaccines can do what medicines can't – prevent the disease from even occurring," said Dr. N. K. Ganguly, a highly distinguished biotechnology professor and advisor in India, and former Director General of the Indian Council of Medical Research (ICMR), New Delhi. "Only with an

effective vaccine can we expect to control leishmaniasis in South Asia."

Provided by Infectious Disease Research Institute