MTBVAC, the first vaccine against Tuberculosis derived from a human source, begins clinical trials in adults in India.

- **Studying the safety, immunogenicity and efficacy of MTBVAC in the most populated country in the world and the one with the highest number of cases of this infectious disease is key to continue advancing in this vaccine.**

- **Bharat Biotech International Limited in collaboration with Biofabri have started a series of clinical trials to evaluate the safety, immunogenicity and efficacy of MTBVAC in India.**

- **MTBVAC is being developed for two purposes: as a more effective and potentially longer-lasting vaccine than BCG for newborns, and for the prevention of TB disease in adults and adolescents, for whom there is currently no effective vaccine.**

- **Next Sunday, 24 March, we commemorate World Tuberculosis Day, which causes more than 1.6 million deaths annually.**

Spain. 24 March 2024. MTBVAC, the Spanish tuberculosis vaccine, the first live attenuated vaccine of *Mycobacterium tuberculosis* isolated from a human, reaches a new milestone by starting clinical trials in India, the most populated country in the world and the one with the highest number of cases of this infectious disease.

The trials are carried out by Bharat Biotech in close collaboration with Biofabri. Trials to evaluate the safety and immunogenicity of MTBVAC have started with a pivotal safety, immunogenicity and efficacy trial planned to start in 2025.

After more than three decades of research, Esteban Rodriguez, CEO of Biofabri says: "It is a giant step to test in adults and adolescents in the country where 28% of the world's TB cases accumulate" and concludes that more effort and funding is needed to combat TB, which remains one of the world's leading infectious causes of death, especially in India.

It should be remembered that the only vaccine in use today, BCG (Bacillus Calmette and Guérin), is an attenuated variant of the bovine TB pathogen. It is more than a hundred years old and has a very limited effect on pulmonary

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tuberculosis, which is responsible for the transmission of the disease, hence the need to make progress on this new vaccine, which will be a milestone in global vaccinology and is an example of public-private, national and international collaboration.

Dr. Krishna Ella, Executive Chairman Bharat Biotech added, “Our quest for a more effective vaccine against Tuberculosis received a big boost today, with clinical trials in India. Our goal to develop TB vaccines to prevent disease in adults and adolescents has taken a big step today. We are honoured to partner with BioFabri, Dr. Esteban Rodriguez and Dr. Carlos Martin in this noble effort to reinvent TB vaccines.”

A long process, an example of public-private collaboration

The MTBVAC vaccine has passed several milestones before entering clinical trials in India.

The first is that after the recent completion of a Phase2 dose finding trial, a double-blind, controlled Phase3 clinical trial in newborns has started in 2023, comparing the vaccine with the current BCG vaccine. 7,000 newborns from South Africa, 60 from Madagascar and 60 from Senegal will be vaccinated. To date, more than 1,900 babies have been vaccinated.

The aim is to assess the immunogenicity and efficacy of MTBVAC which is administered intradermally to infants on the first day of life.

Vaccination began at a time of setback in the global fight against TB. Health restrictions imposed during the COVID-19 pandemic led to an increase in infections and a decrease in diagnosis and treatment. As a result, annual TB deaths have risen to over 1.6 million.

This Phase3 neonatal project, partially funded by the European Union through its EDCTP (*European & Development Countries Clinical Trial Partnership*) programme, is being coordinated by Biofabri, as part of a consortium that also includes the University of Zaragoza (Unizar), *TuBerculosis Vaccine Initiative* (TBVI), *The University of Cape Town* (UCT)/SATVI, Wits VIDA Health Consortium (WHC), Stellenbosch University (SUN-FAMCRU), Enhancing Care Foundation (ECF), *Center de Recherche Biomedicale Espoir Pour La Santé* (CRB-EPLS, Senegal) and *Institut Pasteur de Madagascar* (IPM).

Another important milestone is that after completing a dose escalation trial in HIV uninfected adults, a Phase2 study in HIV infected adults has started in 2024 to determine whether MTBVAC is safe in this population. This ongoing trial at 16 sites in South Africa - involving the vaccination of 276 adults – is evaluating safety

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and immunogenicity in HIV-negative and HIV-positive adults and adolescents vaccinated with MTBVAC.

A Phase2b efficacy study in adolescents and adults is planned to start in the second half of 2024 in Sub-Saharan Africa.

The studies in adolescents and adults in Sub-Saharan African are led by the American institution IAVI. The Phase2 HIV safety study is carried out by HIV Vaccine Trials Network (HVTN) and is funded by the Division of AIDS (DAIDS), National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH), Department of Health and Human Services (DHHS). The Phase2b efficacy study will be carried out by IAVI and will be funded by BMGF and Open Philanthropy.

About MTBVAC

MTBVAC is the only vaccine against tuberculosis in clinical trials based on a genetically modified form of the pathogen isolated from humans *Mycobacterium tuberculosis* which, unlike BCG, contains all the antigens present in strains that infect humans. This vaccine was developed in the laboratory of the University of Zaragoza, which has been part of CIBERES since its creation, in collaboration with Dr Brigitte Gicquel of the Pasteur Institute in Paris. The University of Zaragoza has the Spanish biotechnology company BIOFABRI as an industrial partner.

About BIOFABRI

BIOFABRI is a Spanish biopharmaceutical company founded in 2008 to research, develop and manufacture human vaccines. BIOFABRI has strong technical and scientific capabilities in vaccines and immunotherapy and is responsible for the clinical and industrial development of MTBVAC.

Biofabri is part of the Zendal Group, a Spanish pharmaceutical group of companies specialising in human and animal health.

About BHARAT BIOTECH

Bharat Biotech has established an excellent track record of innovation with more than 145 global patents, a wide product portfolio of more than 16 vaccines, 4 bio-therapeutics, registrations in more than 123 countries, and the World Health Organization (WHO) Pre-qualifications. Located in Genome Valley in Hyderabad, India, a hub for the global biotech industry, Bharat Biotech has built a world-class vaccine & bio-therapeutics, research & product development, Bio-Safety Level 3 manufacturing, and vaccine supply and distribution.

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Having delivered several billion doses of vaccines worldwide, Bharat Biotech continues to lead innovation and has developed vaccines for influenza H1N1, Rotavirus, Japanese Encephalitis (JENVAC®), Rabies, Chikungunya, Zika, Cholera, and the world's first tetanus-toxoid conjugated vaccine for Typhoid. Bharat's commitment to global social innovation programs and public-private partnerships resulted in introducing path-breaking WHO pre-qualified vaccines BIOPOLIO®, ROTAVAC®, ROTAVAC 5D®, and Typbar TCV® combatting polio, rotavirus, typhoid infections, respectively. The acquisition of Chiron Behring Vaccines has positioned Bharat Biotech as the world's largest rabies vaccine manufacturer with Chirorab® and Indirab®. To learn more about Bharat Biotech, visit www.bharatbiotech.com.

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About Tuberculosis

Tuberculosis, which is transmitted through the respiratory tract, kills more than 1.6 million people and infects more than 10 million worldwide each year. In 90% of TB infections, the immune system recognises and controls the bacillus without causing disease. However, in 5-10% of infected people, the bacillus develops tuberculosis, which is fatal in half of patients without treatment with several drugs over 6 months. If the TB is in the lungs, it can find a free path to progress, multiply and spread the disease.

Although there are antibiotics that can kill the bacilli at a higher rate than they reproduce, TB bacteria have a coat that protects them from the immune system and makes it difficult for many of these drugs to penetrate, and multidrug-resistant strains have emerged in recent decades. The World Health Organisation has therefore stressed the need and urgency to develop a new vaccine, following the example of the public-private partnership that led to the development of the covid-19 vaccine.

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