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First-in-Human Clinical Trial Initiated for Novel Malaria Transmission Blocking Vaccine

Potential new tool in the control and eradication of malaria to be tested for safety, tolerability and reduction of transmission

Radboud University Medical Center (Radboudumc), Statens Serum Institut (SSI) and Novavax announce the initiation of clinical trials for a novel malaria transmission blocking vaccine candidate.

- The Phase 1, first-in-human clinical trial of a Pfs48/45 candidate, R0.6C, is being conducted at Radboud University Medical Center under the leadership of Dr. Matthew McCall in healthy volunteers to test the safety and efficacy of the novel vaccine
- Statens Serum Institut has produced a novel malaria protein derived from the *Plasmodium falciparum* protein Pfs48/45 to aid in malaria control and eradication through transmission reducing activity
- Preclinical data of SSI's Pfs48/45 candidate, termed R0.6C, together with Novavax' Matrix-M™ adjuvant has shown >80% reduction of transmission of the parasite that causes malaria in animal models

Nijmegen, Netherlands, Copenhagen, Denmark and Gaithersburg, MD, USA. – July 9, 2021 – Radboud University Medical Center, Statens Serum Institute, Novavax (NASDAQ: NVAX), with support from PATH, today announced the initiation of clinical trials of an investigational malaria transmission blocking vaccine, R0.6C, combined with Novavax's Matrix-M™ adjuvant. This new malaria vaccine candidate, manufactured by SSI, will be evaluated for safety and immunogenicity in healthy human adult volunteers in The Netherlands (Clinical Trial Identifier: NCT04862416) at Radboudumc, paving the way for further evaluation in West Africa later in 2021.

Malaria is one of the most common tropical infectious diseases. Despite the available medication, insecticides, and mosquito nets, more than 200 million people annually contract the disease, resulting in nearly half a million deaths. Malaria is caused by a parasite called *Plasmodium*, which is transmitted from one human to another via mosquitoes. When a mosquito bites a malaria patient, parasites can be transferred to the mosquito. The parasites continue to develop in the mosquito, ultimately making the mosquito's saliva contagious to other people the next time it bites.

R0.6C is a transmission blocking vaccine candidate (TBV) based on the *Plasmodium falciparum* protein Pfs48/45. Transmission blocking vaccines aim to induce antibodies that, together with the parasites in the bloodmeal, are taken up by the mosquito. The antibodies

inhibit parasite development inside the mosquito midgut, blocking onwards transmission. Several proof-of-concept studies in humans of this strategy have previously been conducted. However, the SSI candidate vaccine is the first to be based on the protective epitopes of the Pfs48/45 protein, a long-attractive vaccine target that others have been unable to produce due to the complex folding of the protein. The recent manufacture, under Good Manufacturing Practices (GMP) at SSI in 2020, was the direct result of several years of preclinical development and optimization supported and funded by PATH's Malaria Vaccine Initiative.

"PATH is very pleased to see the R0.6C project enter clinical testing," said Dr. Rick King, Director of R&D of PATH's Malaria Vaccine Initiative. "Transmission blocking vaccines provide the potential for a new mechanism to change the course of the effort to combat malaria."

Transmission blocking vaccines are designed to be used in combination with other malaria control measures, including other vaccines in development and testing that protect the individual from developing the malaria disease by neutralizing the parasite in infected individuals. A TBV, together with other vaccines that target different stages of the parasite's lifecycle, may provide a more effective control strategy and thereby help achieve the goal of malaria eradication.

The initiation of clinicals trials of R0.6C is a result of efforts by the Danish Statens Serum Institut team and investigators from the University of Copenhagen, including Dr. Michael Theisen, Dr. Susheel Singh and Jordan Plieskatt. Jordan Plieskatt, who led optimization of the manufacturing strategy with Dr. Susheel Singh, said "This week's activities are a direct result of the tireless efforts by a dedicated small team of scientists who for a decade have sought to bring safe, effective, and novel vaccines to clinical evaluation to help control the most burdensome diseases on the world's population. Despite the pandemic year of 2020, our scientific team together with Staten Serum Institut's Vaccine Development Unit was able to achieve our timeline to bring this and other vaccines forward for clinical evaluation."

"This is a momentous moment for me, having first identified this vaccine antigen more than a decade ago, and now to see it as a vaccine candidate in human volunteers," said Dr. Michael Theisen, lead Principal Investigator of the SSI malaria team.

The commencement of clinical trials in The Netherlands of R0.6C is the first of several planned clinical trials this year and in the near future to evaluate novel malaria vaccines. The R0.6C vaccine, with further funding by The European Developing Countries Clinical Trial Partnership (EDCTP, grant number RIA2018SV-2311) will later evaluate the R0.6C vaccine in the endemic setting of Western Africa including clinical trials in Burkina Faso and Mali together with a novel chimeric vaccine developed by Plieskatt, Singh and Theisen which combines the lead antigen on which the R0.6C vaccine is based, with a second antigen.

The clinical trial of the R0.6C malaria transmission blocking vaccine candidate will also be unique as it will be evaluating two adjuvants in a single trial -- the common aluminum hydroxide adjuvant, which is utilized in many vaccines, as well as Novavax's Matrix-M adjuvant, which is developing a record as a potent and well-tolerated adjuvant.

"This study represents potentially significant progress against a longstanding global health challenge that afflicts many of the world's most vulnerable populations," said Gregory M. Glenn, M.D., President, Research and Development, Novavax. "We are pleased to see that Novavax' Matrix-M™ adjuvant continues to be considered as a key component in the development of new vaccines, including R0.6C, that could have a worldwide impact in protecting underserved populations from debilitating diseases."

Jordan Plieskatt added, "One of the unique approaches to our vaccine development, is that after the identification of potent potential vaccine targets, we seek to evaluate these targets and adjuvants in multiple head-to-head clinical trials, reducing the often long clinical evaluation timelines, by providing direct results and parallel evaluation for down- or up-selection of the candidate to move forward versus the often-iterative approach applied by others."

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About R0.6C
R0.6C is a new vaccine that can block the spread of malaria. In this research (called STOP-TRANS study), the active substance R0.6C will be combined with the adjuvant Alhydrogel or with two adjuvants Alhydrogel and Matrix-M™ to enhance the immune response. The R0.6C vaccination with adjuvants has been tested in the laboratory and also on animals, but never before on humans. The vaccination does not cure or prevent malaria, but it blocks the transmission of parasites from humans to the mosquito and can thus prevent the spread of malaria in the population.

About Matrix-M™ Adjuvant
Novavax' patented saponin-based Matrix-M™ adjuvant has demonstrated a potent and well-tolerated effect by stimulating the entry of antigen presenting cells into the injection site and enhancing antigen presentation in local lymph nodes, boosting immune response.

About Statens Serum Institut (SSI)
SSI is a public enterprise operating as a market-oriented production and service enterprise. Statens Serum Institut is an enterprise under the Danish Ministry of the Interior and

Health, and the Institut's duties are partly integrated in the national Danish health services. The Statens Serum Institut aims to ensure advanced control of infectious diseases, including new infections and biological threats. The institute also strives to be a highly regarded and recognized national and international research, production, and service enterprise.

About Radboud Medical Center (Radboudumc)
Researchers of the Radboud university medical center (Radboudumc, in short) focus on today's scientific health challenges as well as keeping an eye on emerging diseases of the future.

About Novavax
Novavax, Inc. (Nasdaq: NVAX) is a biotechnology company that promotes improved health globally through the discovery, development and commercialization of innovative vaccines to prevent serious infectious diseases. The company's proprietary recombinant technology platform combines the power and speed of genetic engineering to efficiently produce highly immunogenic nanoparticles designed to address urgent global health needs. Novavax is conducting late-stage clinical trials for NVX-CoV2373, its vaccine candidate against SARS-CoV-2, the virus that causes COVID-19. NanoFlu™, its quadrivalent influenza nanoparticle vaccine, met all primary objectives in its pivotal Phase 3 clinical trial in older adults and will be advanced for regulatory submission. Both vaccine candidates incorporate Novavax' proprietary saponin-based Matrix-M™ adjuvant to enhance the immune response and stimulate high levels of neutralizing antibodies.

For more information, visit www.novavax.com and connect with us on Twitter and LinkedIn.

About PATH
PATH is a global nonprofit dedicated to achieving health equity. With more than 40 years of experience forging multisector partnerships, and with expertise in science, economics, technology, advocacy, and dozens of other specialties, PATH develops and scales up innovative solutions to the world's most pressing health challenges.