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# DNA Medicines FAQ

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INOVIO is focused on rapidly bringing to market precisely designed DNA medicines to potentially treat and protect people from a range of serious and life-threatening diseases and infections. INOVIO's first-of-their-kind DNA medicines are delivered directly into cells so that the body fights disease from within by producing a natural immune response robust enough to potentially treat and prevent diseases related to human papillomavirus (HPV), cancers, and infectious diseases.

With more than 2,000 patients receiving INOVIO DNA medicines in more than 6,000 applications across a range of clinical trials, INOVIO's DNA medicines have consistently activated safe, robust, and fully functional T cell and antibody responses against targeted pathogens and cancers.

## WHAT ARE DNA MEDICINES?

DNA medicines are composed of optimized DNA plasmids, which are small circles of double-stranded DNA that are synthesized or reorganized by a computer sequencing technology and designed to produce a specific response in the body. DNA medicines do not interfere with or change an individual's own DNA, which is the case with gene therapy and gene editing.

## HOW ARE DNA MEDICINES MADE?

INOVIO's investigational DNA medicines are made using a process called SynCon®. SynCon uses a computer algorithm that has been designed to identify and optimize the DNA sequence of the target antigen, whether it is a virus or a tumor. Once this sequence has been determined, the DNA is synthesized or reorganized, and manufacturing can begin.

## HOW ARE INOVIO'S DNA MEDICINES ADMINISTERED?

INOVIO's DNA medicines deliver optimized plasmids directly into cells intramuscularly or intradermally using one of INOVIO's proprietary hand-held CELLECTRA® smart devices. CELLECTRA uses a brief electrical pulse to reversibly open small pores in the cell to allow the plasmids to enter, overcoming a key limitation of other DNA and other nucleic acid approaches, such as mRNA. Once inside the cell, the DNA plasmids enable the cell to produce the targeted antigen. The antigen is processed naturally in the cell and triggers the desired T cell and antibody-mediated immune responses. Administration with the CELLECTRA device ensures that the DNA medicine is efficiently delivered directly into the body's cells, where it can go to work to drive an immune response.

## ARE DNA MEDICINES SAFE?

INOVIO's DNA medicines have been used in clinical programs treating more than 2,000 patients in more than 6,000 administrations. All results thus far have demonstrated favorable safety and robust immune responses.

## ARE THERE ANY DNA MEDICINES APPROVED FOR USE IN PATIENTS TODAY?

No. INOVIO is currently the only company with a DNA medicine in Phase 3 clinical trials: VGX-3100 for precancerous cervical dysplasia.

## **WHAT TYPES OF DNA MEDICINES ARE IN DEVELOPMENT?**

DNA medicines are being investigated for use as a vaccine or an immunotherapy to potentially treat and protect people from a range of serious and life-threatening infections.

## **HOW LONG DOES IT TAKE TO PRODUCE A DNA MEDICINE?**

INOVIO's technology enables the company to rapidly design and manufacture its DNA medicines. As an example, in contrast to typical vaccine development which requires harvesting viruses in eggs and takes several years, INOVIO advanced its DNA vaccine targeting the coronavirus (SARS-CoV-2) that causes COVID-19 from bench to human testing in less than three months.

## **ARE DNA MEDICINES IDEALLY SUITED FOR POTENTIAL INFECTIOUS DISEASES?**

DNA medicines may be the best modern approach to addressing potential infectious disease pandemics due to their rapid design and manufacture.

As an example, in the case of the coronavirus that causes COVID-19, INOVIO created an optimized plasmid in about three hours based on the virus's genetic sequence. The company began small-scale manufacturing of the DNA vaccine – INO-4800 – in the lab, followed by preclinical testing to assess its safety and immunogenicity. Less than three months after creating INO-4800, INOVIO announced the U.S. Food and Drug Administration authorized its Investigational New Drug (IND) application and the company began Phase 1 clinical trials in humans.

Further, INOVIO's DNA medicines are stable at room temperature and do not need to be frozen during transport or storage. This is an advantage since some vaccines need to be transported and stored in freezing temperatures. As an example, the Ebola vaccine needs to be transported and stored in temperatures four times colder than a home freezer, which can present significant challenges when mass vaccinations are required to address a pandemic.

## **ARE INOVIO'S DNA VACCINES BEING USED FOR OTHER INFECTIOUS DISEASES?**

INOVIO has seven programs in clinical studies to address infectious diseases, including COVID-19, HIV, Zika, Ebola, Lassa fever, and MERS (both COVID-19 and MERS are caused by coronaviruses). These programs are all externally funded by global public health organizations, including the Coalition for Epidemic Preparedness Innovations (CEPI), the National Institutes of Health, the Bill & Melinda Gates Foundation, and the International Vaccine Institute (IVI). For MERS, INOVIO's DNA vaccine INO-4700 is the first vaccine to progress to Phase 2 clinical trials. INOVIO also has the first-ever DNA-encoded monoclonal antibody (dMAb™), which is in clinical trials targeting the Zika virus.

## **WHAT IS THE FOCUS OF INOVIO'S DNA MEDICINES PIPELINE?**

INOVIO is leveraging its optimized plasmid design and delivery technology to develop DNA medicines to treat conditions and diseases associated with HPV, cancer, and infectious diseases. INOVIO's lead compound VGX-3100 is in Phase 3 development for precancerous cervical dysplasia caused by the high-risk HPV genotypes 16/18. VGX-3100 is the first medicine to show destruction/clearance of HPV 16/18 in a Phase 2b study. Other INOVIO DNA medicines are being studied to treat recurrent respiratory papillomatosis (RRP), a rare, life-long, and potentially life-threatening disease in which tumors obstruct the airway; glioblastoma multiforme (GBM), an aggressive brain malignancy; and several infectious diseases, including COVID-19, MERS, Zika, Ebola and Lassa fever.

*This document contains certain forward-looking statements relating to our business, including our plans to develop DNA medicines, our expectations regarding our research and development programs, including the planned initiation and conduct of clinical trials, and the availability and timing of data from those trials. Actual events or results may differ from the expectations set forth herein as a result of a number of factors, including uncertainties inherent in pre-clinical studies, clinical trials, product development programs and commercialization activities and outcomes, the availability of funding to support continuing research and studies in an effort to prove safety and efficacy of electroporation technology as a delivery mechanism or develop viable DNA medicines, our ability to support our pipeline of DNA medicine products, the ability of our collaborators to attain development and commercial milestones for products we license and product sales that will enable us to receive future payments and royalties, the adequacy of our capital resources, the availability or potential availability of alternative therapies or treatments for the conditions targeted by us or our collaborators, including alternatives that may be more efficacious or cost effective than any therapy or treatment that we and our collaborators hope to develop, issues*

*involving product liability, issues involving patents and whether they or licenses to them will provide us with meaningful protection from others using the covered technologies, whether such proprietary rights are enforceable or defensible or infringe or allegedly infringe on rights of others or can withstand claims of invalidity and whether we can finance or devote other significant resources that may be necessary to prosecute, protect or defend them, the level of corporate expenditures, assessments of our technology by potential corporate or other partners or collaborators, capital market conditions, the impact of government healthcare proposals and other factors set forth in our Annual Report on Form 10-K for the year ended December 31, 2019 and other filings we make from time to time with the Securities and Exchange Commission. There can be no assurance that any product candidate in our pipeline will be successfully developed, manufactured or commercialized, that final results of clinical trials will be supportive of regulatory approvals required to market products, or that any of the forward-looking information provided herein will be proven accurate. Forward-looking statements speak only as of the date of this document, and we undertake no obligation to update or revise these statements, except as may be required by law.*