



PRESS FILE

# AN INNOVATIVE VACCINE PLATFORM

FOR A LARGE NUMBER  
OF PATHOGENS

Longer lasting and more effective vaccines  
to address health challenges

**LinKinVax** 

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**Linkinvax, a vri spin-off**

# A NOVEL APPROACH TO VACCINATION

*“We developed this dendritic cell-based vaccine technology at the Vaccine Research Institute (VRI/INSERM).”*

Prof. Yves Lévy  
Co-founder of LinKinVax



## The LinKinVax Technology

- Exclusive worldwide license
- **13 patent families**
  - Numerous scientific publications from the VRI



*“LinKinVax develops next generation protein-based vaccines using a platform designed by French researchers. These vaccines will be adaptable to viral changes and mutations, with lasting efficacy.”*

André-Jacques Auberton-Hervé  
CEO and Co-founder of LinKinVax

Accelerating the production of more effective prophylactic or therapeutic vaccines and adapting them to emerging or rapidly mutating pathogens is a major public health challenge.

The Covid-19 pandemic highlighted the need for new strategies to address epidemic risks in the coming decades. Such strategies will require innovative vaccines.

To respond rapidly and effectively to these global health challenges, LinKinVax is developing next generation protein-based vaccines providing truly disruptive alternatives to conventional vaccine technologies and those currently under development.

## MAIN CHARACTERISTICS OF LINKINVAX VACCINES:

- Stimulate broad-spectrum cellular and humoral responses
- Expand the range of anti-infection and anti-cancer responses
- Induce long-term immunological memory
- Use proven production processes for protein-based vaccine

The LinKinVax scalable vaccine platform is based on the excellent academic research conducted for over 10 years by VRI and led by Prof. Yves Lévy, Co-founder of the company, and on the entrepreneurial and industrial expertise of its Co-founding Chairman André-Jacques Auberton-Hervé.



VACCINE  
RESEARCH  
INSTITUTE

### Vaccine Research Institute (VRI)

Vaccine Research Institute (VRI), Laboratory of excellence, was established by the French National Agency for Research on AIDS and viral hepatitis (ANRS) and the University of Paris-Est Créteil (UPEC), to foster the development of effective vaccines against HIV/AIDS and (re)-emerging infectious diseases. VRI is designed to strengthen the links between basic and translational research, patients' associations, and social and economic parties. Its research teams with multidisciplinary expertise draw on a network of nationally and internationally recognized scientists, bioinformaticians and data scientists specializing in genomic analysis, as well as a network of clinicians, state-of-the-art equipment, and innovative platforms.

### Since its inception in 2011, the VRI vaccine program has been focusing on the development of next-generation vaccines targeting the dendritic cells.

The scientific objective of VRI is to develop innovative vaccine strategies based on existing knowledge of infectious diseases and cancers, in collaboration with immunologists, virologists, cell biologists, molecular biologists, specialists in primate models and clinicians, thereby creating new partnership with the industry.

The program is developed nationally by the VRI teams in France, and internationally through the multidisciplinary partnership European HIV Vaccine Alliance (EHVA) for the development of combined HIV vaccine strategies.

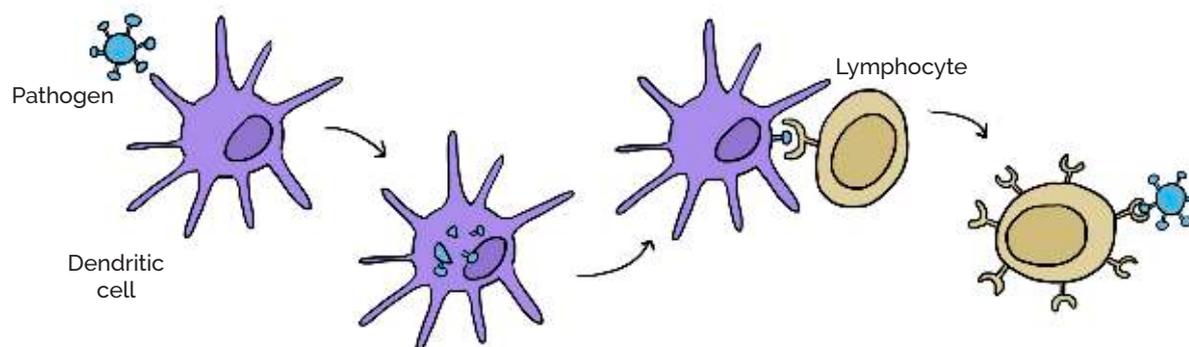
# DENDRITIC CELL-TARGETED VACCINE PLATFORM

## NEXT GENERATION PROTEIN-BASED VACCINES ADAPTABLE TO VIRUS CHANGES

LinKinVax vaccines are unique in that they target directly dendritic cells, the first point of entry into the immune system and the body's main line of defense.

In the 1970s, researchers found that dendritic cells present throughout the body (skin, mucous membranes, blood, lymph nodes, brain, etc.) are responsible for the immune system's initial activation when it meets a pathogen or a vaccine.

When a pathogen or antigen enters the body, it is first recognized as foreign, captured and dissected by dendritic cells. Dendritic cells then present the intruder to the immune system's B cells, responsible for humoral immunity (production of antibodies), and to the T cells responsible for cellular immunity (activation of killer cells).



### Dendritic cells, the keystone of the LinKinVax vaccine platform

Dendritic cells are white blood cells that specialize in presenting antigens to T cells. These cells, the keystone of the LinKinVax vaccine platform, were discovered in 1973 by Ralph Steinman and Zanvil Cohn while working on the mechanisms of immune response in mice. They knew that an immune response required the presence of lymphocytes but also of an accessory cell to present the antigen. Until then, immunologists had thought that this accessory cell was a macrophage, but R. Steinman, Nobel Prize in Physiology or Medicine 2011, and Z. Cohn identified a population of rare cells, so far unknown and surrounded by long extensions which they named dendritic cells.

Since then, these dendritic cells have been the subject of much fundamental research. They are distributed in all tissues of the body in immature form, and in greater quantities in lymphoid organs. The capture of an antigen or detection of potential danger signals (infection, inflammation, necrosis) by a dendritic cell triggers its maturation to fulfil its mission. The existence of specialized subsets of dendritic cells combined with their extreme intrinsic plasticity helps them decode potentially dangerous microenvironmental signals and induce appropriate T cell responses.

#### Sources:

Médecine/Sciences Med Sci (Paris) 2015; 31: 725-727

EM Consulte: Les cellules dendritiques - 26/11/08, Cécile Voisine, Benjamin Trinité, Régis Josien, Institut de transplantation et de recherche en transplantation (ITERT) Inserm U437 30, bd Jean-Monnet 44093 Nantes cedex 1, France

Each vaccine candidate is based on a unique and fixed dendritic cell-binding antibody. However, the protein antigen varies depending on the targeted pathogen (HIV, SARS-CoV-2, HPV, etc.).

## Delivering the vaccine antigen directly to the dendritic cells

The LinKinVax approach is based on the use of an antibody targeting directly CD40 receptors expressed on the surface of dendritic cells. This antibody is attached to the vaccine antigen to drive optimum immune responses. The vaccine antigen is a protein extracted from the targeted pathogen. **Protein vaccines have been used for over 30 years with excellent efficacy and safety results.**

## Optimizing the immune response

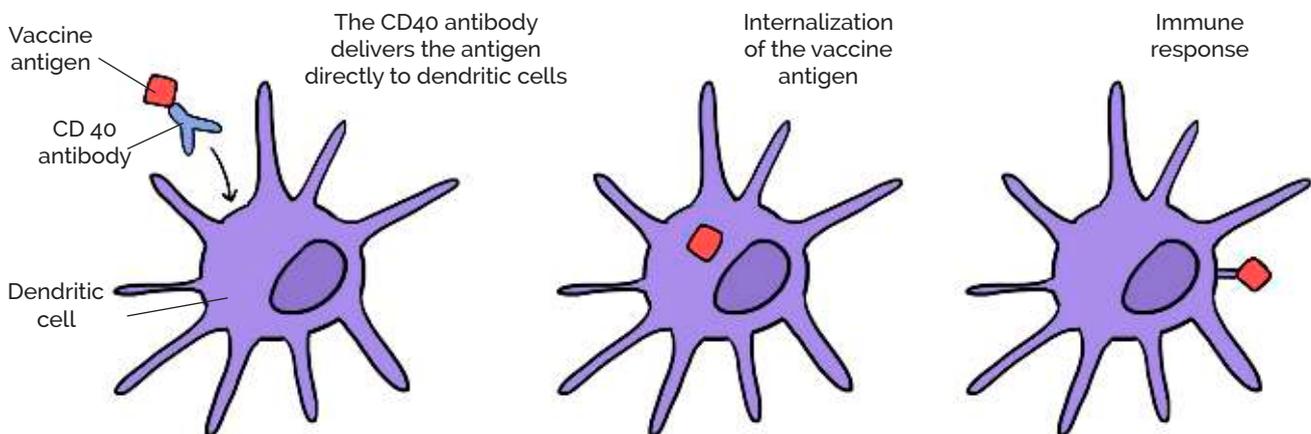
The CD40 antibody was developed using biotechnology techniques to target dendritic cell receptors. The LinKinVax strategy consists of attaching to this antibody a protein from the pathogen to be fought. This protein antigen will then be delivered directly to the dendritic cells, which will trigger an immune response against the targeted pathogen.

## Induction of a specific and lasting immune response demonstrated in numerous preclinical studies

Studies using different animal models have shown that several viral antigens (influenza, HIV, SARS-CoV-2, papillomavirus) attached to the vaccine antibody targeting the CD40 receptors induced persistent antibody and cell-mediated responses capable of controlling the targeted pathogen. Toxicology studies of the vaccine candidates in clinical development have shown their good tolerance. This vaccine platform is therefore **flexible and adaptable to different viruses and their variants.**

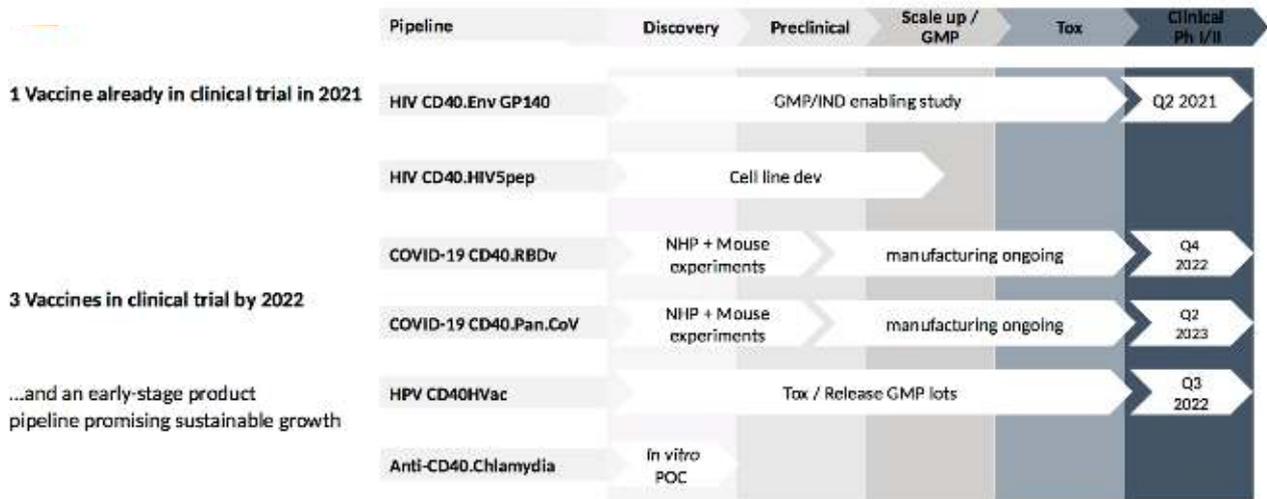
*“With conventional vaccines, the pathogen’s antigen reaches dendritic cells in a random way, whereas our strategy optimizes the stimulation of the immune system by delivering it directly to the DCs. This approach also reduces the quantities of vaccine to be injected and to be produced.”*

André-Jacques Auberton-Hervé



Activation of humoral and cell-mediated immunity by the viral protein attached to the CD40 antibody

# VACCINE PIPELINE: SIX PRODUCTS ON THE MARKET WITHIN 5 YEARS



6 products within 5 years. (HIV Prophylactic & Therapeutic, COVID-19, HPV cancer induced immunotherapy (oncology), Chlamydia)

## Each vaccine candidate tested reinforces the proof of concept

The LinKinVax clinical development program is based on a first phase I/II trial of the prophylactic HIV vaccine, aiming to demonstrate the safety and immunogenicity of the vaccine in volunteers currently enrolled in the trial. This proof of concept study strengthens the clinical development of other vaccine candidates planned for late 2022 and early 2023 (therapeutic vaccine for HPV-associated malignancies, second generation SARS-CoV-2 vaccine).



# 1 - CLINICAL DEVELOPMENT OF TWO HIV VACCINES, THE 'EVEREST OF VACCINE STRATEGIES'

## A prophylactic vaccine

A phase 1 clinical trial targeting the AIDS virus was launched in volunteers in May 2021 in France and in Switzerland<sup>1 2</sup>.

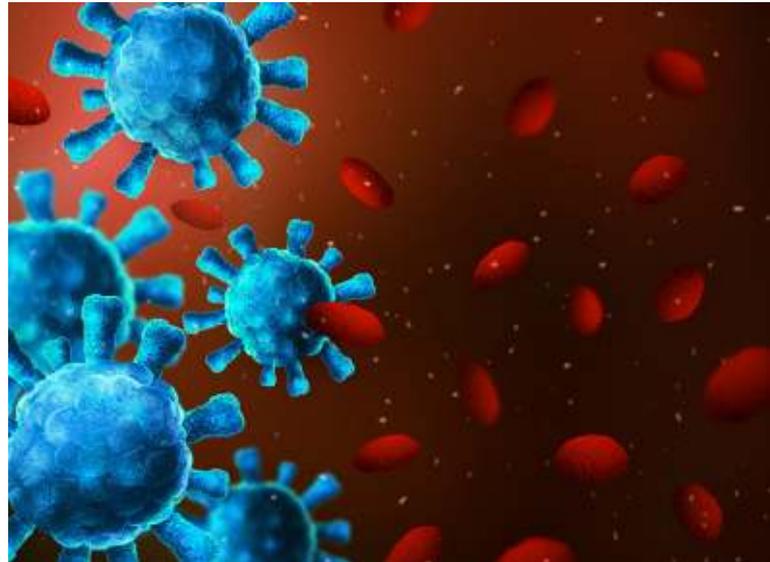
## A therapeutic vaccine

This second vaccine targets HIV sanctuary sites, which persist under antiviral treatment and are difficult to reach with current treatments. This is why, for the time being, antiviral treatments must be taken for life. When tested in humanized HIV-infected mice, the LinKinVax vaccine candidate eliminated the virus reservoirs<sup>3</sup>.

First-in-human studies will be launched following the very promising results obtained in numerous preclinical trials.

*"VRI was created in 2011, with the primary objective of developing an HIV vaccine. This 'Everest of vaccine research' has been ongoing for 35 years."*

André-Jacques Auberton-Hervé



1 Godot V, Tcherakian C, Gil L, Cervera-Marzal I, Li G, Cheng L, et al. (2020) TLR-9 agonist and CD40-targeting vaccination induces HIV-1 envelope-specific B cells with a diversified immunoglobulin repertoire in humanized mice. PLoS Pathog 16(11) <https://doi.org/10.1371/journal.ppat.1009025>

2 Flamar A-L, Bonnabau H, Zurawski S, Lacabaratz C, Montes M, Richert L, et al. (2018) HIV-1 T cell epitopes targeted to Rhesus macaque CD40 and DCIR: A comparative study of prototype dendritic cell targeting therapeutic vaccine candidates. PLoS ONE 13(11): e0207794. <https://doi.org/10.1371/journal.pone.0207794>

3 Liang Cheng, Yves Levy, Lishan Su et al. TLR3 agonist and CD40-targeting vaccination induces immune responses and reduces HIV-1 reservoirs J Clin Invest. 2018;128(10):4387-4396. <https://doi.org/10.1172/JCI99005>.

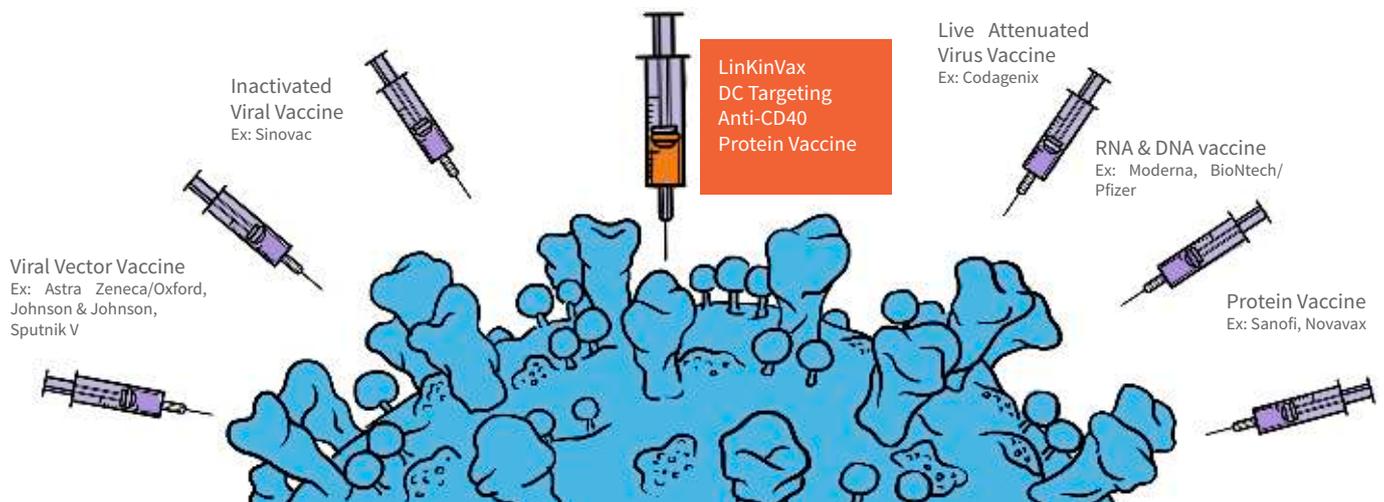
## 2 - TWO CORONAVIRUS VACCINES

According to the WHO, there is an urgent need to develop a vaccine protecting against coronaviruses and their new variants to provide an effective and lasting protection against the disease.

The LinKinVax Covid-19 vaccine candidates are based on analyses of the spike protein and virus mutations. Bioinformatics tools were used to identify the most relevant antigens to attach to the CD40 antibody.

These vaccine candidates contain a fragment of the spike protein that includes the different virus mutations, combined with protein fragments from other regions of the virus that never mutate and are common to all coronaviruses.

**The LinKinVax objective is to develop a pan-sarbecovirus vaccine for SARS-CoV-2 and its variants, as well as other viruses of the same family.**



Different Covid-19 vaccine strategies

Studies have shown that convalescent monkeys vaccinated with a single dose of LinKinVax vaccine six months after a first infection, and later re-exposed to the virus, were protected from infection and cleared the virus within two days. In the control group, convalescent, unvaccinated and infected monkeys cleared the virus in an average of six days<sup>1</sup>. Furthermore, in vitro studies showed that this vaccine produced cross-reactive antibodies against all variants of SARS-CoV-2.

*“Our objective is to develop a pan-coronavirus vaccine,” said André-Jacques Auberton-Hervé. “We are eager to initiate Phase 1 clinical trials and demonstrate its potential in humans against SARS-CoV-2 and several of its variants.”*

1 Marlin, R., Godot, V., Cardinaud, S., et al. Targeting SARS-CoV-2 receptor-binding domain to cells expressing CD40 improves protection to infection in convalescent macaques. Nat Commun 12, 5215 (2021). <https://doi.org/10.1038/s41467-021-25382-0>

### 3 - A THERAPEUTIC VACCINE FOR HPV-ASSOCIATED MALIGNANCIES

**Human papillomaviruses (HPV) cause cancer of the cervix in women and of other areas, such as the throat and anus, in both men and women.**

Despite the availability of an underused prophylactic vaccine, these malignancies are not disappearing. *“LinKinVax is evaluating a DC-targeted therapeutic vaccine with an HPV protein. It is intended for patients with HPV-associated oropharyngeal cancer previously treated by surgery and/or radiation therapy,”* explained Prof. Yves Lévy. *“The aim of the vaccine is to eliminate the virus, which may persist in certain residual tumor cells, and thus prevent recurrence. In mice grafted with HPV-infected tumor cells, this vaccine was shown to foster the elimination of cancer cells.”*

A study evaluating the vaccine’s therapeutic potential is due to start in 2022 at Gustave Roussy in patients with head and neck cancer, using several injections of the vaccine administered 4 to 6 weeks apart.

**The LinKinVax papillomavirus vaccine will be developed for the treatment of cervical lesions.**

HPV is responsible for 99% of cervical cancers. It induces initially pre-cancerous dysplastic lesions that may lead to cervical cancer. Depending on their severity, these lesions need to be monitored or treated with laser or surgery. The LinKinVax therapeutic vaccine may eliminate these lesions.

The LinKinVax approach targets viral infectious diseases, as well as virus-associated cancers. The vaccine candidate identifies and eliminates virus-infected cells.

*“The HPV therapeutic vaccine developed by LinKinVax could be used to prevent the development of cancer lesions. The antibodies and specific T cells generated by our vaccine neutralizing the viruses in the dysplastic cells and eliminates infected cells,”* explained Prof. Yves Lévy. *“This technique which does not compete with prophylactic vaccines.”*



## 4 - A CHLAMYDIA VACCINE CANDIDATE

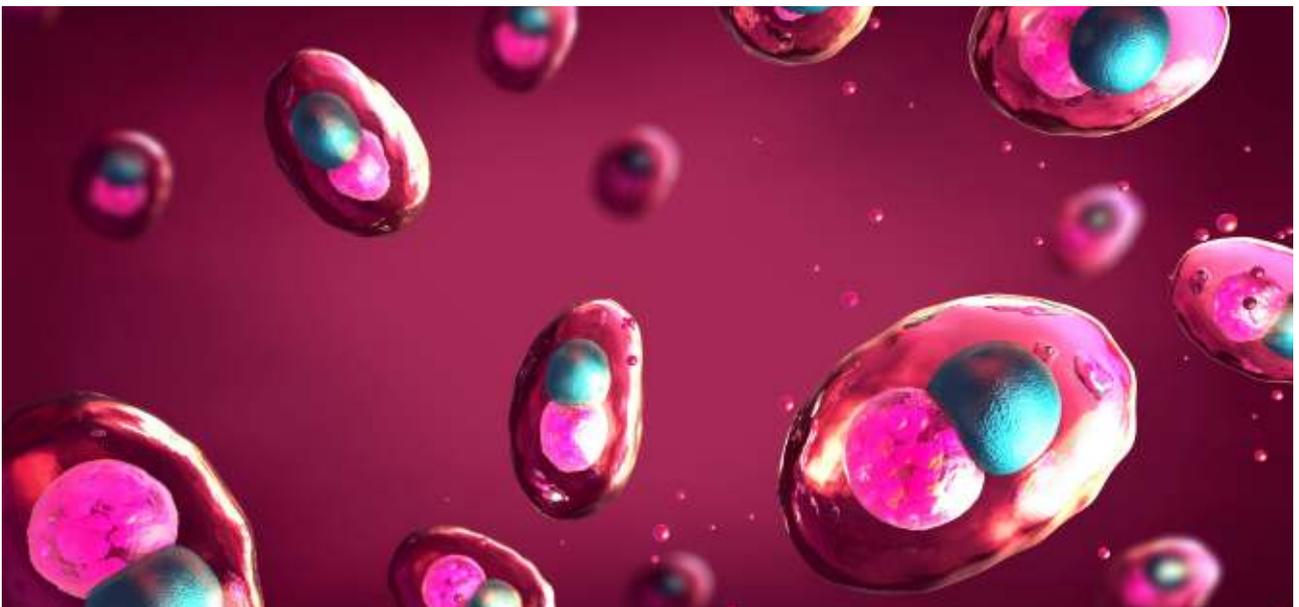
Chlamydiae are pathogens responsible for common sexually transmitted infections that cause few symptoms and sometimes go unnoticed. If left untreated, these infections can lead to tubal factor infertility in women and urethritis or prostatitis in men. In developing countries, infants born vaginally to infected mothers with genital disease may contract trachoma, a disease that causes blindness. Antibiotics are effective, provided the infection is diagnosed and treatment is available, which is far from always being the case.

*“Our vaccines could also potentially be used for other infectious diseases with unmet medical needs.”*

André-Jacques Auberton-Hervé

*“We are looking for the Achilles heel of chlamydia, i.e. the antigen which could be targeted by the vaccine to block its development, prevent it from entering the cell and eliminate it. This vaccine would be used particularly in adolescents to protect them from this STD. It could also help prevent trachoma in developing countries.”*

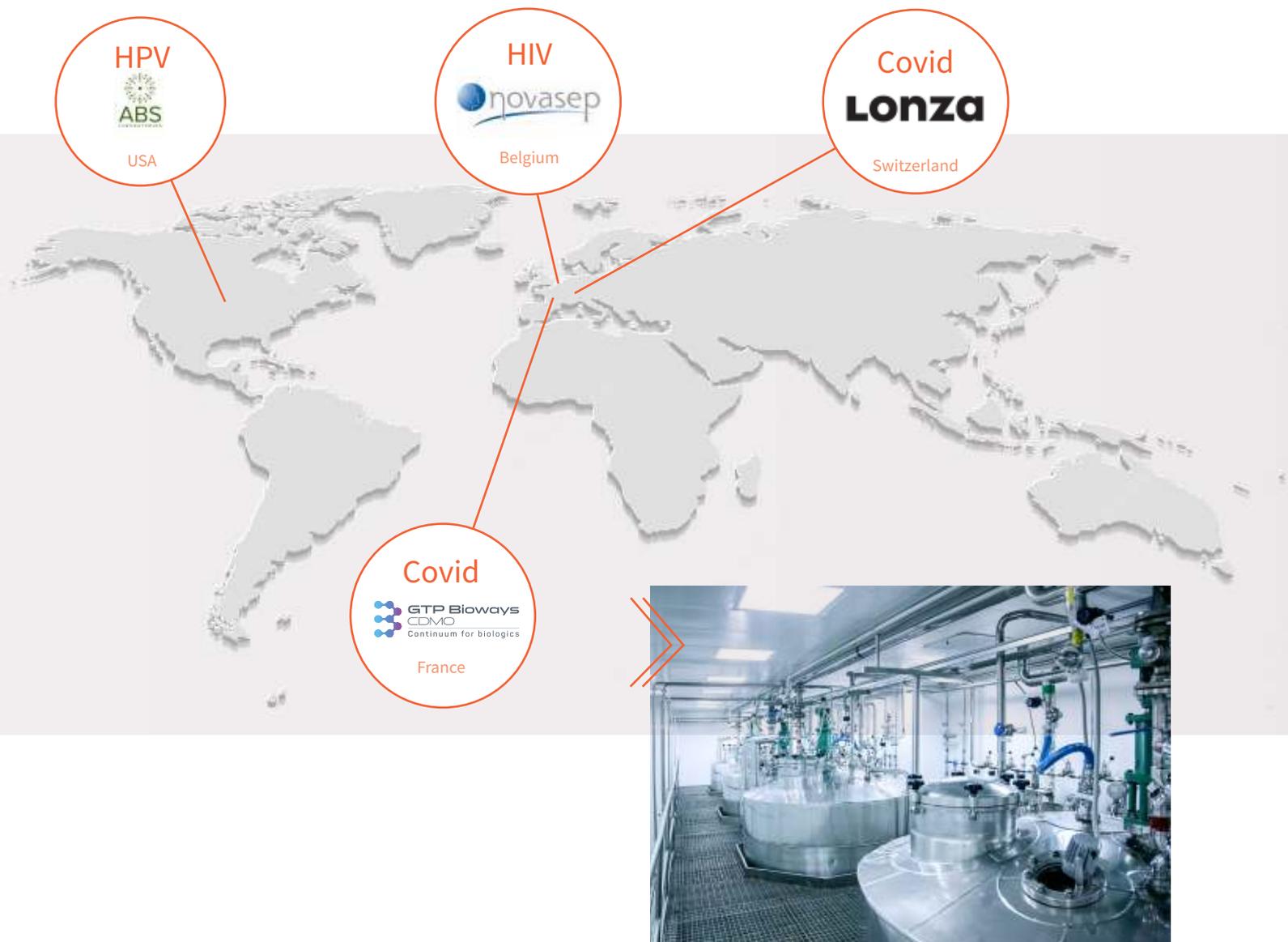
Prof. Yves Lévy



# LINKINVAX INDUSTRIAL STRATEGY

LinKinVax collaborates with several biomanufacturing companies to develop and produce its protein vaccines.

- HPV vaccine candidates are produced in the USA by ABS.
- AIDS vaccine batches are produced in Belgium by Novasep.
- One of the Covid-19 vaccines is manufactured by LONZA in Switzerland, the other by GTP Bioways in France.





**André-Jacques Auberton-Hervé**  
**CEO and Co-founder of LinKinVax**

André-Jacques Auberton-Hervé holds a doctorate in physics from Ecole Centrale Lyon. In 1992, he co-founded Soitec with Jean-Michel Lamure, where he acted as Chairman and CEO for 23 years.

He was responsible for the company's strategic, operational and financial activities and turned Soitec into a world leader in the semiconductor industry. He built an international high-tech group present in 10 countries, with 5 manufacturing sites in Europe, Asia, and the USA. In 1999, he listed Soitec on the Euronext market. It is currently valued at over USD 5 billion and is a leading Industry 4.0 company.

Since 2010, André-Jacques Auberton-Hervé has been a member of the European Commission's Group on Key Enabling Technologies (KETs), which brings together European industrial and academic experts to develop a common long-term strategy for technologies such as nanoelectronics, nanotechnologies, photonics, advanced materials and biotechnology.

André-Jacques Auberton-Hervé is very involved in the emergence of innovative sectors. He sits on the board of several companies and contributes to the financing and governance of fast-growing companies in sectors such as digital imaging (Enlaps) and robotics (Hoomano).

André-Jacques Auberton-Hervé was appointed Chevalier de l'Ordre du Mérite in 2007 and Chevalier de la Légion d'Honneur in 2014.



**Prof. Yves Lévy**  
**Co-founder of LinKinVax**

Prof. Yves Lévy, MD, PhD, Professor of clinical immunology, specializes in immunotherapies, HIV vaccines, immune deficiency diseases and infectious diseases.

Since 1985, Prof. Yves Lévy has worked successively in various Inserm research units, the French National Institute for Health and Medical Research which he chaired from 2014 to 2018. He was Head of the Department of Clinical Immunology and Infectious Diseases at Henri Mondor University Hospitals. In 2006, Prof. Yves Lévy was appointed Scientific Director of the vaccine program of the ANRS Agency for Infectious and Emerging Diseases (formerly the French Agency for Research on AIDS and Viral Hepatitis). In 2011, he created the Vaccine Research Institute (VRI), Laboratory of Excellence, under the French Investments for the Future (PIA) program and was appointed Executive Director.

Prof. Yves Lévy is recognized by international institutions for his major research work which led to changes in the management and treatment of infectious diseases worldwide. He also held several positions and carried out missions at national and international levels. From 2010 to 2012, he was Vice-Dean of the University of Paris-Est Créteil Val de Marne (UPEC), special advisor to the Ministry of Research, and the French government's special envoy for the Ebola epidemic in the DRC in 2018. He also served as a special State Counsellor. Prof. Yves Lévy published over 250 scientific articles.



### **Corinne Margot**

#### **Chief Corporate Development Officer**

Corinne Margot specializes in the growth and structuring of highly innovative industrial companies, particularly in the high-tech sector. Prior to joining LinKinVax, she was HR Director of the Beneteau Group where she was responsible for the Group's transformation program as well as its corporate communications. Before that, Corinne had worked for 18 years as Vice President Human Resources and Communications at Soitec, the world leader in innovative semiconductor materials. She started her career as HR Director for several high-tech companies and start-ups. Corinne Margot holds a postgraduate degree in European law and a postgraduate degree in business administration.



### **Alessandra Powell-Smith Ph.D**

#### **Regulatory Affairs Director**

Alessandra has 20 years of experience in regulatory affairs in the pharmaceutical industry. She has developed and registered drugs worldwide and has acquired an in-depth knowledge of sterile injectable drugs. She has successfully devised development strategies for therapeutic products at all stages of their life cycle (toxicology studies, clinical studies, and especially analytical development, manufacturing, regulatory and sales), to bring them to market.

Alessandra holds a PhD in Pharmacy from the University Paris V and an Executive MBA in Health Management from IAE Sorbonne Business School.



### **Thierry Menguy Ph.D**

#### **CMC Director**

Thierry has worked for over 20 years in preclinical and phase 3 clinical studies, and in Chemistry, Manufacturing and Controls (CMC) for therapeutic proteins, including monoclonal antibodies (MABs) and protein and viral vaccines (poxvirus, adenovirus). He has gained extensive and in-depth knowledge of the pharmaceutical and biotech sectors, notably at Transgène, Elsalys Biotech (which he co-founded in 2013), Biométhodes and Genodyssee, where he successfully led the different development stages, from R&D strategy design to implementation and management of outsourced activities of various CDMOs.

Thierry holds a PhD in Structure, Function and Engineering of Proteins from the University Paris Sud.



### **Pascal Pincemin**

#### **Financial Director**

Pascal has 35 years of experience as financial advisor for disruptive technology companies in various sectors, as well as large organizations and CAC 40 groups on structural transactions, risk management and governance. He joined LinKinVax early 2021 to boost the company's development, particularly its industrial partnership agreements and fundraising. Pascal has already led two major financings for the company. He has extensive international experience and a multicultural understanding gained through senior positions at Deloitte.



### **Dr. Mireille Centlivre Ph.D**

**R&D Director**

**Co-founder of LinKinVax**

Mireille is responsible for the scientific coordination and follow-up of national and international projects, acting as liaison with the VRI Director and the 17 international VRI teams. She holds a PhD from Institut Pasteur (Paris, France) and a post-doctorate degree from the Amsterdam Medical Centre (Amsterdam, The Netherlands) and CIMI-Paris (Paris, France).

Her research activities focus on the pathophysiology of HIV infection, HIV vaccination and the preclinical HIS mouse model.



### **Hasnae NIANG**

**Director of Quality Operations**

Hasnae is a quality operations specialist with 18 years of experience in various sectors of the healthcare industry: pharmaceutical industry, forensic laboratories, CROs, CMOs, biotech companies (biomarkers, companion diagnostics and IVD), such as Tc-land and Eurofins. Before joining LinKinVax, Hasnae oversaw Global Quality at Voisin Consulting Life Sciences. Hasnae holds a postgraduate degree (DESS) in Quality Control and Assurance in gene and cell therapy from the University Paris XI, and an MBA from Audencia in responsible management, innovation and CSR.



### **Valérie Bouchara Pomar Ph.D**

**Clinical Operations Director**

In close to 30 years, Valérie acquired a solid expertise in clinical research and its operational models in France and internationally, particularly at GSK and Amgen, where she held various positions, including director of clinical operations in France.

Valérie holds a PhD in Pharmacy and an Advanced General Management degree from ESSEC. Her leadership skills have led her to work regularly for university management programs and in senior management positions at Deloitte.

# LINKINVAX, A VRI SPIN-OFF



VACCINE  
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VRI historical partners



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