



CYNBIOSE AND VIRNEXT CONGRATULATE THE PHARMACEUTICAL COMPANY HIPRA UPON COVID-19 VACCINE'S, BIMERVAX[®], APPROVAL BY THE EUROPEAN MEDICINES AGENCY (EMA).

Lyon, France, April 25th, 2023 - CYNBIOSE, a service company specializing in the development of innovative preclinical models, in partnership with VIRNEXT, a technological platform specializing in respiratory infectious diseases and evaluation of prophylactic and therapeutic treatments, have contributed actively to the preclinical assessment and accelerated transfer to clinical trial of HIPRA's Covid-19 vaccine.

At the time the SARS-CoV-2 pandemic was at its peak, HIPRA, a biotechnological pharmaceutical company, initiated a preclinical evaluation of its vaccine candidate to confirm its safety and efficacy in a translational model.

The active component of the HIPRA Covid-19 vaccine is an heterologous recombinant heterodimer protein that emulates the receptor binding domain (RBD) of the Spike (S) protein of the Alpha and Beta variants of the SARS-Cov-2 virus. The antigen, which is the active component of the vaccine, requires an adjuvant to amplify and enhance the immune response. The preclinical trials were completed in 2021. The European Commission announced in August 2022 it had signed a pre-purchase agreement with HIPRA to supply its Covid-19 vaccine, subject to approval by the European Medicines Agency (EMA). The agreement involves 13 countries and should allow the purchase of up to 250 million doses, said the European executive in a statement¹.

CYNBIOSE and VIRNEXT were selected to perform the preclinical studies in a SARS-CoV-2 large animal efficacy model. Indeed, thanks to their synergistically complementarity, they had developed a non-human primate efficacy model from the first half of 2020 thanks to the COVIBIOSE project labeled by the French Health cluster Lyonbiopôle and supported by an exceptional grant provided by the Région Auvergne-Rhône-Alpes.

The efficacy, safety, and immunogenicity of HIPRA's vaccine (PHH-1V) in cynomolgus macaques showed that PHH-1V prime-boost vaccination induces high levels of RBD-specific

¹ Health Union: Commission signs Joint Procurement contract with HIPRA for COVID-19 vaccines. Press release, August 2, 2022. https://ec.europa.eu/commission/presscorner/detail/en/ip_22_4782

IgG and IgA binding and neutralizing antibodies against several SARS-CoV-2 variants of concern, as well as a balanced Th1/Th2 cellular immune response. Remarkably, PHH-1V vaccination prevents SARS-CoV-2 replication in the lower respiratory tract and significantly reduces infectious viral load in the upper respiratory tract after an experimental infection challenge. This highlighted the potential use of the PHH-1V vaccine in humans. These results were presented in three scientific congresses² in 2022 and a scientific publication has been submitted.

HIPRA believes that “having the structures and capabilities ranging from the research and development to the production of vaccines in Europe is a key factor in being able to guarantee a rapid response in the event of future health emergencies and reinforces the strategic autonomy of Europe in the field of health. If the vaccine is a reality, it is thanks to the knowledge, effort and perseverance of the HIPRA team and the teams of all the research sites, private companies specialising in research, institutions, public and private hospitals that have collaborated”.

A STRONG AND EFFECTIVE PUBLIC-PRIVATE PARTNERSHIP SERVING THE BIOPHARMACEUTICAL INDUSTRY AND HUMAN HEALTH

Thanks to a strong public-private partnership initiated in 2017, CYNBIOSE and VIRNEXT teams have completed several R&D programs in the field of respiratory infectious diseases. Both organizations, settled in the Auvergne-Rhone-Alpes region, have developed and deeply characterized *in vitro* and *in vivo* models of infections by respiratory viruses such as influenza, pneumovirus (human Respiratory Syncytial Virus/hRSV, human metapneumovirus/HMPV) and coronavirus (SARS-CoV-2).

As of 2020, CYNBIOSE and VIRNEXT have joined forces to **offer a comprehensive preclinical package of services** for drugs, vaccines and antibodies candidates in the field of respiratory infectious diseases:

- A unique and large-scale library of respiratory viruses,
- A complete range of services from *in vitro* and *ex-vivo* screening to a continuum of relevant preclinical *in vivo* models (rodents, non-rodent and large animals) for respiratory infectious diseases,
- The evaluation of aerosol therapies with a screening offer using an *ex-vivo* model based on reconstructed human airway epithelium cultivated at air/liquid interface.

Beyond VIRNEXT and CYNBIOSE's capacity of innovation and research, this partnership combines their strengths in terms of expertise, unique know-how including logistics (BSL-2/BSL3 and A2/A3 facilities), flexibility, agility and outstanding customer relationship and scientific support.

² Preclinical efficacy, safety and immunogenicity assessment of a vaccine candidate in a cynomolgus monkey model of SARS-CoV-2 infection. Confais J. et al. Festival of Biologics, Nov 2-4, 2022 & Immunotherapies & Innovations for Infectious Diseases congress, November 23-24, 2022.

Preclinical efficacy, safety, and immunogenicity in cynomolgus macaques of the PHH-1V COVID-19 vaccine candidate based on a recombinant RBD fusion heterodimer of SARS-CoV-2. Moros A. et al. Spanish Society for Virology national congress, Sept 6-9, 2022.

Thanks to CYNBIOSE's new state-of-the-art facility that will start operating mid-2023, France and Europe gain a unique facility and highly focused scientific and technological expertise to deal with future pandemics and the evaluation of therapeutic and prophylactic candidates in the field of infectious respiratory diseases.

" CYNBIOSE is one of the only private CRO in Europe able to implement studies in primates involving infectious challenges warranting a biosafety level 3, as required by SARS-CoV-2. CYNBIOSE has more than 15 years of experience conducting studies on major infections such as the Dengue or Zika virus for the biopharmaceutical industry. In addition, our company has developed specific expertise in NHP model of infections by hRSV and HMPV, notably in collaboration with the technology research platform VIRNEXT (METABIOSE project accredited by Lyonbiopôle and financed by the Région Auvergne-Rhône-Alpes) and the Laboratory of Immunobiology of Viral Infections (IBIV) of CIRI. We sincerely thank HIPRA for trusting our private-public partnership for the non-clinical evaluation of their vaccine as well as for our collaborative relationship with their pre-clinical and development teams." said Hugues Contamin, CEO of CYNBIOSE.

"VIRNEXT has been committed for several years in the development of in vitro and in vivo preclinical models of infections dedicated to the screening and evaluation of antiviral, antibody and vaccine candidates against emergent and re-emergent respiratory viral pathogens. The synergy of our public-private partnership with CYNBIOSE and the very strong support of the Région Auvergne-Rhône-Alpes have enabled us to offer an NHP model of SARS-CoV-2 infection very quickly in 2020. We are very proud to have been able to contribute to accelerating the clinical transfer of HIPRA's Covid-19 vaccine. This gives meaning to our commitment and our research and development work for human health.", says Manuel Rosa-Calatrava, INSERM Research Director, Director of the VirPath Laboratory and VIRNEXT technology Research platform.

"The Région Auvergne-Rhône-Alpes has mobilized extensively since the beginning of the crisis in order to best support its territory in the fight against the Covid-19 and its consequences. Among its many areas of intervention, research and innovation is particularly important, especially when initiatives are able to quickly provide solutions at the scientific and medical levels. In 2020, the COVIBIOSE project convinced us of its strategic interest in the fight against Covid-19 and demonstrated the capacity of our territory's actors to urgently set up an effective consortium to innovate. We are very honored to have contributed to the evaluation of this new vaccine for the Europeans. It enhances the Auvergne-Rhône-Alpes region's position of excellence in the field of infectious diseases." said Catherine Staron, Vice-President of the Région Auvergne-Rhône-Alpes in charge of higher education, research and innovation.

About CYNBIOSE

CYNBIOSE is the only Contract Research Organization (CRO) of its kind in Europe and is AAALAC accredited. The company specializes in the development and commercialization of innovative non-human primate models to accelerate the preclinical development phases of drug candidates. It works on exploratory pharmacokinetics and toxicology studies, as well as proof of concept studies in different human pathologies, such as infectious diseases and respiratory conditions, the central nervous system and inflammatory, musculoskeletal disorders and cardiovascular/neurovascular diseases. The company provides its services in line with quality guidelines that meet industry requirements.

CYNBIOSE has expertise in every stage and technique required to manipulate these preclinical models. It boasts an extensive network of experts and partners in the academic and private domains, allowing complex studies to be conducted with dedicated project teams. CYNBIOSE is committed, responsible and proud to contribute to advancing healthcare research by participating in numerous preclinical development programs for new therapies.

The SME CYNBIOSE was founded in 2008 by CEO Dr Hugues Contamin (DVM, PhD) and is based in Marcy l'Etoile near Lyon, France. It currently has 25 staff. CYNBIOSE is a founding member of the French Association of Service and Innovation Companies for the Life Sciences (AFSSI).

www.cynbiose.com

About VIRNEXT

The Technology Research Platform VIRNEXT is a spin-off of the Université Claude Bernard Lyon 1 (UCBL1), and its subsidiaries EZUS Lyon and Lyon Ingénierie Projet, which was created in 2012 by Manuel Rosa-Calatrava, PhD, within the VirPath laboratory to foster industrial partnerships and enhance translational research. VIRNEXT provides expertise in the field of respiratory viruses and is committed for several years in the development of *in vitro* and *in vivo* preclinical models of infections dedicated to the screening and evaluation of antiviral, antibody and vaccine candidates against emergent and re-emergent respiratory viral pathogens within its BSL-2 and BSL-3 facilities. Very mobilized since January 2020, VIRNEXT has isolated and constituted working banks of several variant strains of the SARS-CoV-2 virus and evaluated numerous prophylactic and therapeutic treatments against SARS-CoV-2 and contributed to the implementation of several clinical trials. VIRNEXT currently has 10 staff and is based in Gerland Biodistrict, Lyon, France.

www.virnext.fr

About HIPRA

HIPRA is a pharmaceutical company focused on prevention for animal and human health, with a wide range of highly innovative vaccines and an advanced diagnostic service. The biotech company has a strong international presence in more than 40 countries with its own subsidiaries, 3 R&D centres and 6 production plants strategically located in Europe (Spain) and America (Brazil). In addition, its extensive international distribution network keeps marketing channels open in more than 100 countries, covering all 5 continents.

HIPRA is the company that has launched the most biotechnological vaccines in the last 10 years, with a total of 22 vaccines. HIPRA occupies the fifth place in the world's leading ranking of animal health vaccine manufacturers.

www.hipra.com

About the Région Auvergne-Rhône-Alpes

As a leader in innovation, research and higher education, the Région Auvergne-Rhône-Alpes has made the training, research and innovation continuum one of the priorities of its action, with the aim of creating more sustainable and skilled jobs and developing strong and competitive companies in strategic fields. It is producing, under the leadership of the Vice-president Catherine Staron, an unprecedented effort to support higher education in all territories, foster the training of engineers and technicians for regional companies and invest in public-private partnerships. Since 2016, the Région Auvergne-Rhône-Alpes

has invested more than 500 million euros in the field of higher education, research and innovation through structuring devices, which also benefit from the leverage of the FEDER funds up to 153 million euros.

About LyonBiopôle

As a French biocluster, Lyonbiopole Auvergne-Rhône-Alpes is the gateway to healthcare innovation in Auvergne-Rhône-Alpes, France. It aims to federate the actors of innovation, to connect and promote them internationally and to support the emergence and development of innovative technologies, products and services to address global healthcare challenges. In 2022, Lyonbiopole Auvergne-Rhône-Alpes gathers a community of 270 members among which world-class leaders, innovative small and medium size companies, research centers and university hospitals. At the center of this ecosystem, Lyonbiopole brings its members altogether to imagine the future of medicine and to develop breakthrough HealthTech innovation available for tomorrow's patients.

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