Cristal Therapeutics and Intravacc Announce Strategic Collaboration to Advance Novel Vaccine Platforms

- First joint CriVac® vaccine candidate to target receptor-binding domain of SARS-CoV-2
- Evaluation of Cristal's CliCr® and Intravacc's OMV technology

Bilthoven and Maastricht, the Netherlands, 6 January 2021 – **Intravacc,** a world leader in translational research and development of vaccines, and Cristal Therapeutics, a technology leader in enabling safer and more effective therapeutics, today announced a strategic collaboration to develop novel vaccine programs against human diseases with the initial candidate targeting COVID-19.

Under the terms of the agreement, Cristal Therapeutics and Intravacc will collaborate with an initial focus on generating a CriVac® vaccine candidate based on the receptor-binding domain of the SARS-CoV-2 spike protein. In addition, Cristal Therapeutics will provide its powerful copper-free click chemistry reagent, CliCr®, for evaluation with Intravacc's proprietary outer membrane vesicles (OMV) technology. OMV vaccines allow for the native conformation of immunity-stimulating antigens. After completion of the evaluation period Intravacc and Cristal will jointly explore next steps to further advance the program.

Axel Mescheder, M.D., CEO and CMO of Cristal, commented:

> *"Over the past year, it has become evident that vaccines play a crucial role in protecting us, our families and those at high risk for infectious diseases. We have put great effort in optimizing our unique CriVac® platform based on our CriPec® nanoparticles and CliCr® conjugation technology. Our CriVac® technology platform mimics features of a live virus, inducing immunity in a safe and efficient way, providing a solid foundation for the development of novel vaccine approaches. We look forward to partnering with Intravacc to develop novel therapeutic candidates for vaccine-preventable diseases."*

As part of this agreement, Intravacc will also provide access to its proprietary, detoxified LPS technology to enhance immune activation. All technologies represent innovative approaches to vaccine development enabling an efficient presentation of antigens to the immune system. Combining the technologies will further allow swift development of vaccine candidates against a broad range of human diseases. This is particularly driven by a scalable GMP manufacturing process.

Dr. Jan Groen, Intravacc's CEO, said:

> *"Intravacc shares the belief that no one should be suffering from diseases that can be prevented by vaccines. We have a track record in translational vaccinology and an established infrastructure that enables the accelerated development of promising vaccine candidates such as Cristal's CriVac® approach. Combining Cristal's technologies with Intravacc's proprietary LPS and OMV technologies holds great promise. We look forward to working closely with the Cristal team to advance the program through preclinical evaluation."*

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About CriVac®

CriVac®, Cristal's proprietary vaccination platform, combines the tuneability and ease of manufacturing of biodegradable CriPec® nanoparticles with the CliCr® conjugation technology for fast and controlled conjugation of antigens on the nanoparticle surface. This generates coated nanoparticles that mimic the features of a live virus to induce a potent immune response, safely, and solely against the displayed

antigen. The tuneability allows Cristal to rapidly design candidates for any antigen, allowing swift development of vaccines against a broad range of different pathogens. CriVac® vaccines are easy to be (GMP) manufactured at large scale, and the final product can be freeze-dried, therefore not requiring cold chain storage, all contributing to key advantages over existing vaccines.

About CliCr®

CliCr® is a class of fast-reacting molecular entities for conjugating compounds to each other in a strain-promoted azide-alkyne cycloaddition click reaction. CliCr® is able to attach a broad range of small molecule active agents as well as large molecular entities including biologics, to CriPec® nanoparticles. The attractive functionalization possibilities, combined with its versatility, great reactivity and small size offer multiple opportunities for CliCr® reagents to become the new standard for non-copper catalyzed click reactions in a multitude of applications.

About Intravacc's OMV platform technology

For the development of vaccines, Intravacc has designed and developed a platform based on outer membrane vesicles (OMVs) - spherical particles with intrinsic adjuvant properties. The OMVs can be rigged with immunogenic peptides and/or proteins that stimulate effective adaptive immunity. The OMV carrier has been optimized to induce a more effective immune response against these newly introduced antigens. Intravacc has also developed genetic tools to increase the yield of OMVs, reduce the toxicity and achieve the desired antigenic composition. Intravacc's OMV platform is fully scalable and allows rapid and efficient modification of the antigen composition, either through genetic modification of the bacterial host or by associating antigens with stored OMVs.

About LPS

Intravacc's proprietary LPS technology is based upon the detoxification of the Lipid A moiety of the LPS derived from *Neisseria Meningitides.* LPS is an effective TLR-4 agonist. Intravacc has developed a panel of detoxified LPS mutants with tailored safety/immune stimulatory profiles. A cGMP production and purification process is in place to bring the LPS molecules as standalone adjuvants into clinical testing.

About Intravacc

Dutch Intravacc, located at Utrecht Science Park Bilthoven, is a leading global contract developer of innovative vaccines against infectious diseases. As an established independent CDMO organization with over 100 years of experience in the development and optimization of vaccines and vaccine technologies, Intravacc has transferred its technology related to polio vaccines, measles vaccines, DPT vaccines, Hib vaccines and influenza vaccines around the world. Around 40% of childhood disease vaccines are based on Intravacc's technology. Intravacc offers a wide range of expertise for independent vaccine development, from concept to Phase I/II clinical studies for partners around the world, including universities, public health organizations (WHO, Bill & Melinda Gates Foundation), biotech and pharmaceutical companies. For more information, visit www.intravacc.nl

About Cristal Therapeutics

Cristal Therapeutics applies three distinct and interconnected technologies together with biologic insight to improve the therapeutic profile of our partners' programs in development. Based on over 10 years of real-world experience, Cristal's CliCr®, CriPec® and CriVac® technologies provide superior conjugation, enhance target specificity and engender highly selective immune responses, thereby increasing efficacy and reducing toxicity. The company aims to be the partner of choice for overcoming challenges and enabling the full potential of ADCs, immuno-oncology treatments, vaccines, among a broad range of therapeutics, tuned to modality and indication.

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