



## ExeVir Bio and VIB Announce Data on a New Therapy for Prevention and Treatment for COVID-19

- **ExeVir Bio and VIB-UGent's bioRxiv pre-print reports on S2-binding camelid single-domain antibody-based drug, XVR013, that targets the Achilles' heel in the SARS-CoV-2 viral spike**
  - **Focus on protecting the millions of immuno-compromised patients, who are most vulnerable to COVID-19**

**Ghent, Belgium, 13 March 2023:** ExeVir Bio, a biotech company developing robust single domain antibody therapies for broad protection against infectious diseases, and its scientific founders at Belgium's VIB, Flanders' leading life sciences institute, today announced the publication of a pre-print paper by De Caestecker *et al.*, entitled "Ultrapotent SARS coronavirus-neutralizing single-domain antibodies that bind a conserved membrane proximal epitope of the spike". [The pre-print paper is available here.](#)

Nearly all SARS-CoV-2 neutralizing antibodies that have been used in the clinic show substantial loss of potency against currently circulating variants. The bioRxiv pre-print details a novel, highly potent, anti-S2 camelid single-domain antibody, discovered at the VIB-UGent Center for Medical Biotechnology, and developed as a candidate drug molecule by ExeVir as XVR013. It targets a conserved region in the spike S2 subunit that is essential for viral entry. It neutralizes all previous and current variants of concern and the currently most frequently circulating variants, including XBB, XBB.1.5, BQ.1.1 and BF.7.

These single-domain antibodies bypass the highly immunogenic spots on the S1 part of the COVID-19 virus, that were the targets of all first-generation anti-SARS-CoV-2 antibodies in the clinic. In addition, the anti-S2 single domain antibodies directly neutralize the virus without relying on the patient's own immune system, potentially providing protection for immunocompromised patients who typically do not, or only poorly, respond to COVID-19 vaccines.

The S2 subunit of the SARS-CoV-2 spike mediates membrane fusion, an essential step during virus entry. XVR013 prevents this membrane fusion and potently protects against SARS-CoV-2 infection *in vitro* and in an *in vivo* model.

ExeVir's COVID-19 pipeline includes XVR012, which is a combination product of the S2-targeting single-domain antibody-based XVR013 reported in the pre-print paper, and XVR014, a bispecific single-domain-based antibody construct which targets two conserved epitopes in the S1 subunit, using an innovative design that will be reported in the future. XVR012 has demonstrated very high neutralization activity against all previous and current variants of concern and the currently most frequently circulating variants and is advancing towards clinical trials for COVID-19.

**Dr. Torsten Mummenbrauer, CEO of ExeVir, said:** "The pandemic isn't over; it is an ongoing challenge for immunocompromised patients, who total around 3%<sup>1</sup> of the world population and remain at high risk of severe COVID-19 disease despite availability of current vaccines. We are therefore delighted to share our positive results in this pre-print paper with our VIB colleagues. It highlights XVR013's unique and powerful mode of action targeted to a highly conserved epitope of the coronavirus spike protein. This is but one asset in our arsenal of multiple epitope binders which offer the potential of multi-specific binders to the spike protein in one molecule or as a cocktail. XVR013 is a super potent molecule with a single digit nanomolar IC<sub>50</sub> against virtually all circulating known variants. It could add an additional layer of protection for the most vulnerable in our population who are unable to build an adequate immune response with current vaccines."



**Dr. Bert Schepens of VIB**, said: “As there is currently a strong need for antibodies that work against the newest omicron variants, we think it is useful to rapidly communicate to our scientific colleagues about the discovery that targeting this novel membrane-proximal S2 epitope can yield such strong neutralization of SARS-CoV-2. We will be submitting a comprehensive paper for peer review soon. As researchers, it is very motivating that ExeVir, who we have been working closely with, is finalizing the preclinical package to move into the clinic. Together we are enabling great strides towards bringing a long-lasting biologic to treat and protect immuno-compromised and elderly people. Our research, part of which is pre-printed today, has unveiled weak spots in the SARS-CoV-2 spike; a true Achilles’ heel that requires spears with a small tip to reach them well, in the form of our new single domain antibodies.”

The new S2-binding camelid single domain antibodies described in the bioRxiv pre-print paper by Sieglinde De Cae were identified and characterized in the lab of Xavier Saelens by the team of Bert Schepens (VIB-UGent Center for Medical Biotechnology). A hybrid molecule based on these camelid single domain antibodies and a human antibody was designed and built in the lab of Nico Callewaert (also VIB-UGent Center for Medical Biotechnology). The interaction between these single domain antibodies and the S2 protein was characterized by Inge Van Molle in the lab of Han Remaut (VIB-VUB Center for Structural Biology). Together these labs form VIB's pandemic drug development response team, which was assembled by the Center for Medical Biotechnology in January 2020. The pharmacodynamic and safety properties of candidate drug molecules based on these S2-binding single domain antibodies were extensively evaluated in vitro and in vivo by ExeVir Bio.

[1] Global, regional, and national estimates of the population at increased risk of severe COVID-19 due to underlying health conditions in 2020: a modelling study (thelancet.com)

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## About ExeVir Bio

ExeVir Bio is a clinical stage biotechnology company developing single-domain antibody based therapeutics focusing on infectious diseases. The company is harnessing its llama-derived antibody (VHH) technology platform to generate multi-specific antibodies for prophylaxis and treatment of infectious diseases. ExeVir's initial focus is on prevention of COVID-19 for the immunocompromised patient population, including active chemotherapy, immunosuppressive drugs, solid organ transplantation, hematological malignancies, and AIDS patients, where there remains a high unmet need due to the limitations of current vaccines and therapeutic approaches.

ExeVir's COVID-19 pipeline includes XVR012, a combination product of XVR013 and XVR014, a bi-specific single-domain-based antibody construct which targets two conserved epitopes in the S1 subunit. Together they target several S1 and S2 epitopes in one product.

ExeVir has demonstrated it can progress its candidates from research to the clinic in under one year, execute on Phase 1a and Phase 1b studies and conduct scale-up manufacturing. Leveraging this extensive experience, its XVR012 asset is being developed for regulatory submission in 2023.

ExeVir has also initiated research in dengue, a migrating disease becoming an increasing global health burden due to global warming and urbanization.

VHHs are smaller in size than whole antibodies, giving them access to hidden epitopes that traditional monoclonal antibodies are unable to reach with potential for deeper tissue penetration and simpler, more cost-effective manufacturing. VHHs can be linked together like building blocks into a single molecule to tackle different epitopes or act through different mechanisms of actions at once, to address the "arms race" in more complex and co-evolving infectious diseases.

ExeVir is a spin out of VIB, the leading Belgium-based life sciences research institute. It is backed by strong investors including Fund+, which led the series A of EUR 42 million, together with an international consortium including UCB Ventures, FPIM, V-Bio Ventures, VIB, SRIW, Noshag, Vives IUF and SambrInvest. ExeVir has received support from VLAIO, the SPW-Recherche and the European Union, leading to a total of €16.5M in non-dilutive funding. In 2023, ExeVir secured an option for EUR 25 million venture debt financing from the European Investment Bank.

Find out more on [ExeVir's LinkedIn](#) or on [ExeVir's website](#)

## About VIB

VIB's core mission is to generate disruptive insights in the molecular underpinning of life and to translate these actively into impactful innovations for patients and society. VIB is an independent research institute where some 1,800 top scientists from Belgium and abroad conduct pioneering basic research. As such, they are pushing the boundaries of what we know about molecular mechanisms and how they rule living organisms such as human beings, animals, plants, and microorganisms. Based on a close partnership with five Flemish universities – Ghent University, KU Leuven, University of Antwerp, Vrije Universiteit Brussel, and Hasselt University – and supported by a solid funding program, VIB unites the expertise of all its collaborators and research groups in a single institute. VIB's technology transfer activities translate research results into concrete benefits for society such as new diagnostics and therapies and agricultural innovations. These applications are often developed by young start-ups from VIB or through collaborations with other companies. This also leads to additional employment and bridges the gap between scientific research and entrepreneurship. VIB also engages



actively in the public debate on biotechnology by developing and disseminating a wide range of science-based information.

More info can be found on [www.vib.be](http://www.vib.be).