NEWSLETTER

Epic Crown 2 JANUARY 2024

As the EPIC CROWN 2 project nears completion, we invite you to take a look at the progress we've achieved. This newsletter provides an overview of our progress in the fight against COVID-19 with innovative antiviral therapies.

GENERAL OBJECTIVE OF THE PROJECT

The overarching goal of the EPIC-CROWN-2 project is to develop and optimize an effective COVID-19 therapeutic solution, assess its response against various SARS-CoV-2 variants, refine its application through comprehensive studies, and prepare for its integration into the healthcare market.

PROJECT CONSORTIUM

OBJECTIVES OF EPIC CROWN 2 PROJECT

OBJECTIVE 1

Pioneering a potent horse-derived anti-SARS-CoV-2 antibody treatment, rigorously validated through clinical trials, to revolutionize antiviral therapy.

OBJECTIVE 2

Unraveling the power of FBR-002 antibodies to neutralize COVID-19 variants, shedding light on our defense against the virus's evolving threats.

OBJECTIVE 3

Bridging bench to bedside by scaling production, preparing for varied outbreak scenarios, and fostering critical alliances in our battle against COVID-19.

> ***DEVELOP AND OPTIMIZE AN EFFECTIVE COVID-19 THERAPEUTIC SOLUTION***

FEW FIGURES

27 **deliverables submitted**
(including 8 public deliverables, available on the website)

6 **publications**

1 **team of 5 dedicated partners**
(from France, Spain, Greece, Germany)

3 **face-to-face meetings**

PARTNERS

FABENTECH Specific Polyclonal Antibodies

BNITM Bernhard Nocht Institute for Tropical Medicine

i+12 Instituto de Investigación Hospital 12 de Octubre

IRD Institut de Recherche pour le Développement FRANCE

Sepsis ΕΛΛΗΝΙΚΟ ΙΝΣΤΙΤΟΥΤΟ ΜΕΛΕΤΗΣ ΤΗΣ ΣΗΨΗΣ HELLENIC INSTITUTE FOR THE STUDY OF SEPSIS

FOCUS

ON EACH OBJECTIVE OF THE PROJECT

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OBJECTIVE 1

AMBITION

Our primary goal is to **evaluate the safety profile** and the efficacy of our COVID-19 treatment through Phase II a/b clinical studies across Europe.
The phase2a study will be performed on **two cohorts to assess the safety profile** and pharmacokinetic data of the two-dose treatment. the phase 2b will assess real-world efficacy and evaluate the prevention of severe respiratory failure (Phase IIb). We also aim to **confirm the effectiveness of our treatment,** FBR-002, against all SARS-CoV-2 variants.

RESULTS

Despite enrollment delays caused by the pandemic, **the Phase 2a clinical trial has achieved significant milestones.** The regulatory documentation for the trial has been successfully prepared and submitted, allowing the study to progress smoothly. **The completion of the first cohort and the initiation of the second cohort are a positive step,** demonstrating progress in patient enrollment.

Logistics and supply management have been effective, ensuring no shortages in the trial. Pharmacokinetics methods have been established and **the study is eagerly awaiting results**. Safety evaluations have shown no adverse events linked to the FBR-002 product, and the safety profile of the product has been validated by a DSMB (Data safety Monitoring Board). To date, patient inclusion in Europe is slowing down. As part of the European project, the consortium has assessed the best options for achieving its Phase IIb. For a few months now, **a clinical board has been evaluating** the product's repositioning phase towards an uncovered medical need. In parallel, **the consortium was funded by the European platform ISIDORe** for a thorough epidemiological study to confirm the repositioning and medical need in the immunocompromised population.

NEXT STEPS

- From the generated ideas :
- Select a few promising concepts and develop them further.
- Create sketches, rough prototypes, or digital representations to visualize and communicate the concepts.
- Evaluate each concept based on feasibility, desirability, and viability.

PROGRESS

72%

FOCUS

ON EACH OBJECTIVE OF THE PROJECT

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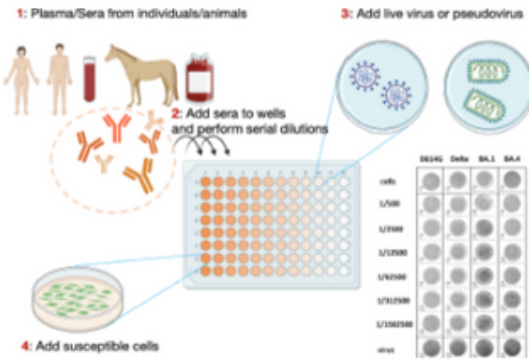
OBJECTIVE 2

AMBITION

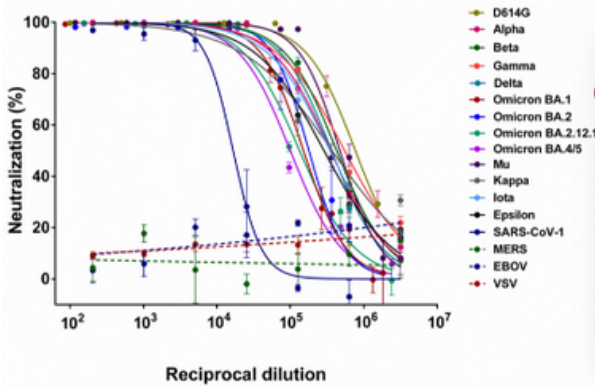
Our focus is to **study the interaction of SARS-CoV-2 variants of concern (VOCs) with our polyclonal FBR-002 antibodies.** We aim to understand the neutralizing potential of these antibodies against both existing and future VOCs through targeted in vitro and in vivo studies.



RESULTS

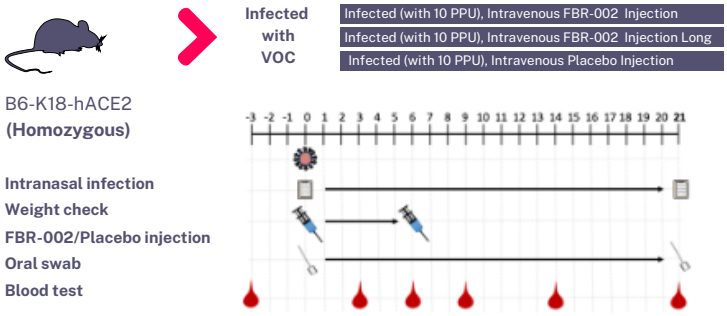
Objective 2 has made notable progress in studying the impact of SARS-CoV-2 Variants of Concern (VOCs) on clinical batches of FBR-002 antibodies. **The construction of a comprehensive collection of spike protein expression vectors and VOC isolates is a significant achievement**. The neutralizing potency of FBR-002 antibodies has exceeded expectations, surpassing levels typically seen post-infection or vaccination.

Despite the Omicron variant displaying lower neutralization, **the potency remains meaningful given the limited availability of effective antibodies for Omicron.**



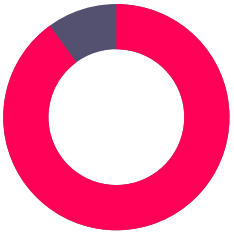
Also, **an in vivo proof of concept was performed,** demonstrating the neutralizing efficacy of purified F(ab')2 immunoglobulin against SARS-CoV-2 infection in different vivo models such as the reference model K18 – and an humanized model set hamster, mice, and non-human primates. **The development of a humanized mouse model has allowed for the investigation of SARS-CoV-2 infection and the identification of surfactant protein D (SP-D) as a disease severity biomarker.** Promising efficacy tests of FBR-002 in humanized mice are underway, with results forthcoming.

The studies realized in the K18 modele on two delivery routes and two variants demonstrated that **the product FBR002 prevents from death.**



PROGRESS

90%



GLOBAL REVIEW

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From the European Commission

THE EUROPEAN COMMISSION ASSESSMENT ON OUR PROJECT SO FAR :

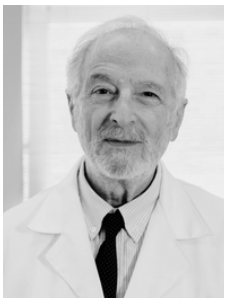
"The team has obtained very interesting preclinical research findings demonstrating the promise of polyclonal antibodies to address multiple VoCs."

"The product exhibits significant neutralizing activity against current described VoCs, including Omicron subvariants BA.4/5."

"An innovative ultrasensitive diagnostic procedure has also been developed that could have an immediate impact on the current epidemic if disseminated."

From the Scientific Advisory Board

Arribas Lopez, José Ramon
MD, PhD
Head of the Infectious Diseases and Clinical Microbiology Unit Sectop, 5 of Internal Medicine at Hospital Universitario La Paz.



Luis Enjuanes
MD, PhD
Professor of Virology at the University of Madrid and the Institute Pasteur of Paris, he has been working in the verology field for more than 40 years, including 36 years in coronaviruses.

Lucia Lopalco
PhD
Director of Research Unit at San Raffaele Scientific Institute, Universita degli Studi di Pavia.

Antonio Artigas Raventos
MD, PhD
Emeritus Director of the Critical Care Center at the Sabadell Hospital, is a member of the Scientific Council of the Lilly Foundation.

"The conclusions have been clear and convincing in relation with the evaluation of the protection of the mouse models against the challenge with virulent SARS-CoV strains, including prototypes of the most important variants of concern (VOCs)."

"Protection efficacy by the F(ab')2 using cell culture systems and humanized mouse models has already been demonstrated."

"The project made a reasonable progress, as different batches of the F(ab')2 have been generated and evaluated. These stocks of the antibody have shown protection in vitro (tissue culture) and in the mouse model."

FOCUS
ON EACH OBJECTIVE OF THE PROJECT

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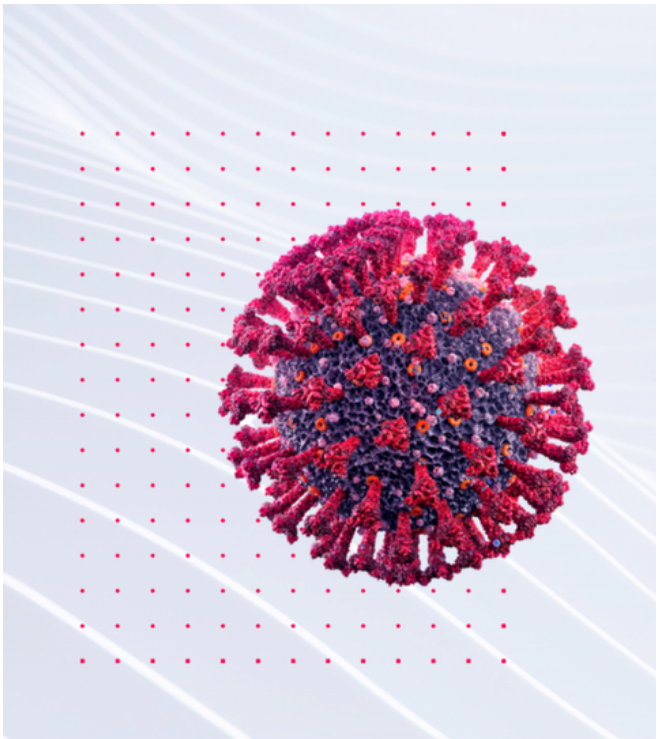
OBJECTIVE 3

INDUSTRIAL SCALE UP BATCH

We are preparing for market integration by **planning for upscaled production and trial readiness.** Our strategic approach accommodates varying outbreak scenarios and includes a flexible industrial production plan for FBR-002. Simultaneously, **we are working to increase awareness and engagement with key stakeholders in the scientific and medical community.**



RESULTS

The validation of the scaled-up process protocol, has been successfully accomplished, marking a significant achievement. The production of the first GMP-grade clinical batch, coupled with effective purification and adherence to control specifications and regulations, showcases our preparedness for human clinical trials. The yield has met expectations, providing an adequate supply to meet the treatment requirements for Phase 2a and a portion of Phase 2b. **Scale-up feasibility has been realized** through the production of a larger volume GMP batch, and is currently undergoing rigorous quality control assessment to ensure its release.

PROGRESS

100%

VISUAL RECAP

THROWBACK IN PICTURES

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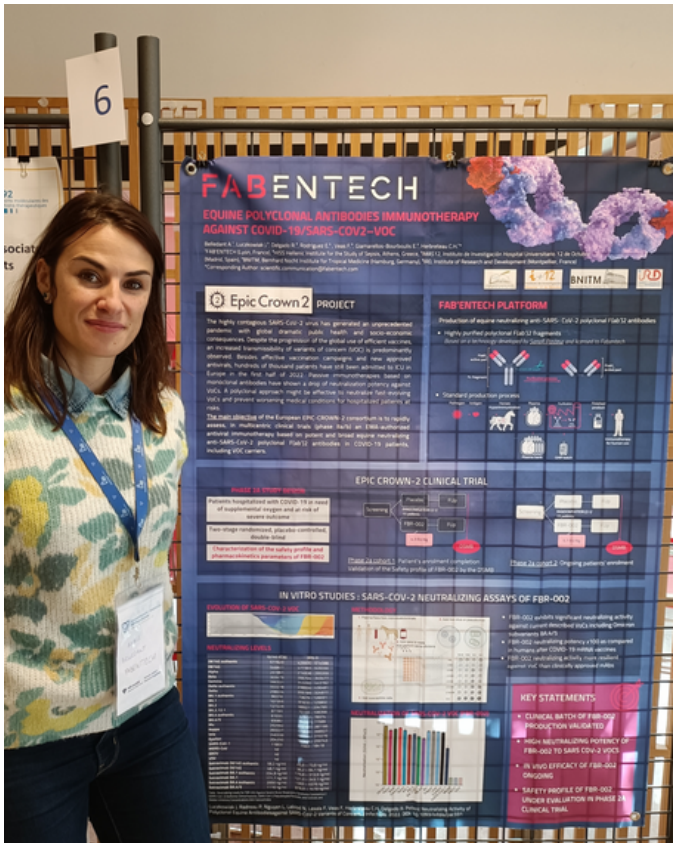
1st General Assembly in Athens

2nd General Assembly in Madrid



Best Poster Award – I4ID Conference 2023

Dinner with the consortium

CONTACT

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