Title of Study:	**A 2-part Clinical Study Including a First-in-Human, Open-label, Single Ascending Dose Part (Phase 1) Followed by a Randomised, Double-blind, Placebo-controlled Part (Phase 2) to Evaluate the Efficacy and Safety of XVR011 in Patients Hospitalised for Mild to Moderate COVID-19**	
Studied Period:	**First subject screened:**	26 Aug 2021
	Last subject completed:	18 Mar 2022

Study Objectives:

The primary objectives of the study were:

Part 1: To evaluate the safety of a single intravenous XVR011 infusion in subjects hospitalised for COVID-19.

Part 2: To evaluate the efficacy of a single intravenous XVR011 infusion in subjects hospitalised for COVID-19, compared to placebo.

The secondary objectives of the study were:

Part 1:

To evaluate the efficacy of a single intravenous XVR011 infusion in subjects hospitalised for COVID-19.

To evaluate the antiviral activity of a single intravenous XVR011 infusion in subjects hospitalised for COVID-19.

Part 2:

To further evaluate the efficacy of a single intravenous XVR011 infusion in subjects hospitalised for COVID-19, compared to placebo.

To evaluate the antiviral activity of a single intravenous XVR011 infusion in subjects hospitalised for COVID-19, compared to placebo.

To evaluate the safety of a single intravenous XVR011 infusion in subjects hospitalised for COVID-19, compared to placebo.

Study Design:

This study was designed as a 2-part Phase 1/2 clinical study to evaluate the safety, efficacy and pharmacokinetics (PK) of XVR011 in subjects hospitalised for COVID-19. In March 2022, the Sponsor prematurely terminated the EXEVIR0101 study before Part 2 started due to changes in the COVID-19 landscape. This decision was not driven by safety concerns and a new Phase 2 trial was designed.

A total of 33 healthy male and female subjects were screened, and 27 subjects aged 26 to 73 years were enrolled and assigned to 1 of 3 dose levels, Cohort 1 (250 mg), Cohort 2 (500 mg), or Cohort 3 (1000 mg), 9 subjects per cohort to receive a single intravenous infusion of XVR011.

Two subjects in each cohort served as sentinel subjects and each were monitored for at least 24 hours (first sentinel subject were monitored for 24 hours before the second sentinel subject was treated and monitored for 24 hours) before the remaining subjects were dosed.

Hospitalised subjects who provided informed consent underwent Screening (Day -1) preferably within 24 hours of admission. In Treatment Period (Day 1), within 36 hours of admission to hospital, subjects received a single intravenous infusion of XVR011 in addition to standard of care treatment. In the Endpoint Assessment Period (Day 2 to Day 29)

subjects remained hospitalised until at least Day 4 (i.e., at least 72 hours after study treatment administration). Discharge prior to Day 4 was possible if clinically justified but needed to be discussed with the Sponsor upfront. After Day 4, subjects whose clinical condition had improved sufficiently in the opinion of the Investigator, could be discharged from the hospital. Subjects who were discharged from the hospital before the Day 29 visit were to attend an additional visit on the day of hospital discharge and to return to the study site for each study visit until Day 29 (end of study [EOS]). Study assessments were performed every day up to Day 4 and then weekly until Day 29.

Methodology:

When all subjects enrolled in Part 1 completed the Day 4 visit, an interim analysis was performed, and all available safety, tolerability, efficacy and PK data were reviewed by the independent data monitoring committee, which was to recommend whether Part 2 could be initiated (with or without modifications to the study design and protocol) and was to recommend the XVR011 dose for Part 2.

Conclusion:

Only the first of the 2 planned parts of this study was conducted. In March 2022 the Sponsor has made the decision to prematurely terminate the EXEVIR0101 trial before Part 2 starts and to design a new Phase 2 trial aligned with the changed COVID-19 landscape in terms of study design and population. This decision was not driven by safety concerns.

Safety data from Part 1 of the study show that a single IV administration of 250 mg, 500 mg, and 1000 mg of XVR011 was safe and well tolerated in hospitalised subjects with mild to moderate COVID-19 with no clear dose response pattern.

The absence of a placebo control in the design of Part 1 makes it impossible to assess the impact of XVR011 on clinical and virological outcomes of COVID-19. This would have been the main goal of Phase 2, which had a placebo-controlled design. Except for median time to hospital discharge and need for mechanical ventilation, there was no suggestion of a dose response pattern for clinical and virological outcomes.

A clear dose response relationship was documented for most PK parameters.

Overall, the 3 tested doses of XVR011 showed an acceptable safety and tolerability profile in adult patients hospitalised for mild to moderate COVID-19. There is no safety concern that would prevent further development of XVR011.