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Abionyx Looks To Next Steps As Renal Sepsis Candidate Succeeds At Phase IIa

Executive Summary

The French firm's lead asset has impressed in a Phase IIa trial in sepsis patients at risk of kidney injury, triggering discussions with regulators for a path forward in the challenging and life-threatening condition.

Abionyx Pharma's CER-001 has hit the mark in a Phase IIa sepsis-triggered acute kidney injury (AKI) trial, triggering regulatory discussions and a hunt for big pharma collaboration to support its further development.

The Phase IIa RACERS trial enrolled 20 people with Gram-negative sepsis at high risk for AKI. They received either standard of care treatment alone or in combination with one of three dosage regimens of CER-001 with the drug candidate meeting key primary and secondary endpoints, although Abionyx said it could not detail precise figures, which will be published at a later date.

Overall, CER-001 was associated with a rapid and sustained reduction in endotoxin levels, thus assuaging the inflammatory cascade more than standard-of-care alone. The drug candidate also normalized patient levels of apolipoprotein AI (apoA-I), a protein involved in lipid metabolism, low levels of which are predictive of long-term mortality following surgical sepsis.

CER-001 is a synthetic form of high-density lipoprotein, comprising a combination of human recombinant apoA-I and the phospholipids sphingomyelin and dipalmitoylphosphatidylglycerol.

Lead investigator Loreto Gesualdo of the University of Bari Aldo Moro, Italy, said, *"CER-001 was significantly able to scavenge endotoxins, modulate the cytokine storm, and provide endothelial protection." He added, "The trend observed in reducing renal damage, the need for organ support and ICU-day stay underscores the potential clinical significance of these results."* RACERS has established that a regimen of 10mg CER-001 twice a day is optimal, Gesualdo told *Scrip*.

Septic patients at a high risk of developing AKI currently have no treatment options meaning this is an area of high unmet need. *"Sepsis is a frequent disease with around 26 million people suffering from it worldwide each year and 50% mortality rate,"* Gesualdo explained. Antimicrobial agents are a mainstay of sepsis management but their use is hampered by increasing numbers of drug-resistant microbes.

Drug development for sepsis and related conditions is difficult because the complex syndrome is driven by host-environment interactions, meaning there is no 'typical' sepsis patients. Several clinical trials in the space to date have failed because they did not account for the heterogeneity of hosts, infectious agents and environments involved.

Even so, there are 18 drug candidates in active clinical development for the treatment of sepsis, according to Citeline database Pharmaprojects.

Besides sepsis, CER-001 has been studied in COVID-19, where it was shown to limit the effects of inflammation. Last year, the drug candidate received US Food and Drug Administration orphan drug designation for the treatment of the rare disorder LCAT deficiency when presenting as kidney dysfunction or ophthalmologic disease.

As for next steps, Abionyx said it would discuss the RACERS data with regulatory authorities later this year, starting with the EU and then moving on to the US. With the help of regulators, the firm hopes to design a clinical and regulatory development strategy to expedite the candidate through the pipeline, which could include a Phase IIb/Phase III trial.

Regarding the financing of a future trial, CEO Cyrille Tupin told *Scrip*, "*Right now, the cash position of the company is a little more than €4m,"* up slightly from the €3.8m Abionyx had reported on 30 September last year prior to its collection of the French Tax Credit for R&D expenses. At that time, the company revealed RACERS was fully financed without the need for dilutive financing.

"We'll for sure be looking for partners," Tupin said when asked about the prospect of teaming up with big pharma to develop CER-001. He added that *"all options are on the table,"* including fundraising.

Meanwhile, the firm's subsidiary IRIS Pharma, an ophthalmology-focused CRO, reported revenues of €4.2m in the first nine months of 2022.

Manufacturing Complexities Addressed

Back in 2021, following positive data in one patient with an ultra-rare kidney disease, Abionyx forged a strategic partnership with biological nanomedicine producers GTP Biologics and V-Nano to re-launch the manufacturing of CER-001. The asset is an engineered cell biology-based biomolecule, meaning the production process is complex.