Combioxin

PRESS RELEASE

The Lancet Infectious Diseases publishes the first clinical results with CAL02

Geneva (Switzerland), 3 May 2019

Combioxin SA announcement: *The Lancet Infectious Diseases* published today the first clinical results with CAL02, a first-in-class drug, in severe pneumonia patients, showing safety and consistent superiority over placebo in all efficacy parameters (*Online First*).

REVOLUTION in the treatment of severe infections?

CAL02 provides a totally new and eagerly awaited solution for patients and doctors around the world. This simple, affordable and highly efficient drug has the potential to transform standard of care for millions of individuals with severe infections. By neutralizing bacterial toxins over which antibiotics are powerless, CAL02 creates a new paradigm in the field of infectious diseases.

BEYOND ANTIBIOTICS' limitations

CAL02 does not induce resistance, and can be administered before pathogen identification and on top of antibiotics, whether old or new. CAL02 consists of liposomes engineered to catch and neutralize a large panel of bacterial toxins known to cause severe and deadly complications.

Clinical results published today in THE LANCET INFECTIOUS DISEASES

The clinical trial – reported today in *The Lancet Infectious Diseases* – aimed at assessing the safety and efficacy of CAL02 administered in addition to standard of care. The trial was carried out in intensive-care-unit (ICU) patients with severe community-acquired pneumococcal pneumonia.

Despite best antibiotic treatments, pneumonia is still the first cause of infectious mortality in the world. The World Health Organization estimates that pneumonia affects 450 million people every year worldwide, 20% of whom require hospitalization. Pneumonia is also the single largest cause of death in children worldwide, killing approximately 2,400 children aged <5 every day. Besides the suffering and high mortality rates, severe community-acquired pneumonia also represents a high economic burden due to prolonged hospitalization and to the fact that more than 20% of hospitalized patients require ICU management.

This first-in-human trial was a randomized, double-blind, placebo-controlled study conducted in hospitals in Belgium and France. This study was carried out in a severe population where 58% of the 19 recruited patients were in septic shock and 42% under invasive mechanical ventilation at the time of treatment. Patients received two intravenous administrations of CAL02 or placebo, with a 24-hour interval, and were followed during 29 days. A sentinel group of patients received CAL02 at a dose of 4 mg/kg, and then the trial focused on a dose of 16 mg/kg.

The primary objective of the study was met: CAL02 was shown to be as safe as placebo. Furthermore, *The Lancet Infectious Diseases* reports that, as compared to patients under placebo, patients who were treated with CAL02 presented a faster clinical improvement, including a significantly faster resolution of organ dysfunctions (as per SOFA score). Efficacy was in line with the mode of action of the drug, which aims at protecting organs, including the respiratory and cardiovascular systems. Within one week the cardiovascular and hemodynamic status of treated patients were fully normalized and stable, while no improvement was observed in the placebo arm during the same period. Moreover, CAL02-treated patients remained under invasive mechanical ventilation for an average of 4.5 days, as compared to 12 days for patients receiving standard of care without CAL02. Cure of pneumonia was more rapid with CAL02. Inflammatory biomarkers, such as C-reactive protein (CRP) and procalcitonin (PCT) showed immediate decrease and full normalization within the first 48 hours after the start of treatment with CAL02, as opposed to immediate increases in the placebo arm. *The Lancet Infectious Diseases* also reports that CAL02-treated patients were kept in the ICU for an average of 5 days, as opposed to 12 days in the placebo arm.

Along with this publication, *The Lancet Infectious Diseases* issued a 2-page Comment, by Prof. Mathias Pletz, Prof. Michael Bauer, and Prof. Axel Brakhage, entitled "One step closer to precision medicine for infectious diseases" ranking "***this study a medical breakthrough***". The authors assert that "***CAL02 represents a milestone***" and that CAL02 is "***potentially suitable for adjunctive empirical treatment***". They conclude: "*We keep our fingers crossed that CAL02 will not get lost on its way to the patients who need it*".

"*CAL02 provides a totally new and eagerly awaited solution for patients and doctors around the world. This unique approach addresses important medical issues posed by severe pneumonia. We look forward to the next trial which will assess CAL02 in a much larger patient population*" said **Dr. Toni Perez**, Combioxin's Chief Medical Officer.

"*CAL02 addresses the fundamental damages of severe community-acquired pneumonia. Results published today in The Lancet Infectious Diseases provide a first set of evidence that targeting virulent effectors protects patients from organ dysfunction and has the potential to dramatically improve the outcome of patients in critical situations*" said **Prof. Pierre-François Laterre**, Head of the medical-surgical intensive care unit of Saint Luc University Hospital at the Université Catholique de Louvain (Brussels, Belgium).

"*This innovative and simple solution may well transform standard of care. For several decades, no treatment has improved the outcome of severe pneumonia that is still the deadliest communicable disease. We look forward to carrying out the next trial in severe CAP patients regardless of the causing pathogen*" said **Dr. Bruno François**, head of the medical-surgical intensive care unit at the University Hospital of Limoges, France.

"*Critical care costs represent a considerable percentage of overall health expenditures and hospital costs today. By significantly reducing the length of stay in intensive care and by limiting the duration of mechanical ventilation, this treatment has the potential to lead to a tremendous economy on cost of care*", said **Dr. Samareh Azeredo da Silveira Lajaunias**, Director at Combioxin.

About CAL02:
CAL02 is a disruptive, non-antibiotic drug addressing the severity and complications of infections. It consists of liposomes engineered to catch and neutralize virulent effectors, including bacterial toxins produced by pathogens most commonly responsible for severe infections. CAL02 does not give rise to resistance, can be administered before pathogen identification and regardless of antibiotics patients receive. CAL02 stems from a technology discovered at the University of Bern, Switzerland.

About Combioxin:
Combioxin SA is a Swiss-based clinical-stage biotechnology company founded in 2015. The company is committed to the development of disruptive treatments for severe infections.

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Link to the Article: *http://www.thelancet.com/journals/laninf/article/PIIS1473-3099(18)30805-3/fulltext*
Link to the Comment*: http://dx.doi.org/10.1016/ S1473-3099(19)30070-2*
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