# A Phase 2 Randomized, Double-Blind, Placebo-Controlled Multicenter Study to Evaluate the Efficacy and Safety of CAL02 in Patients with Severe Community-Acquired Bacterial Pneumonia: Trial in Progress

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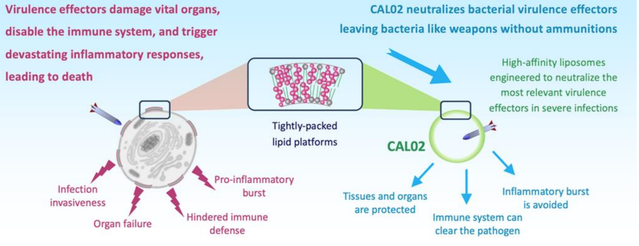
## Introduction

***There is a current unmet need for new treatment modalities that are safe and effective in improving outcomes in severe community-acquired bacterial pneumonia (SCABP)***

- Worldwide, Community-acquired pneumonia is a major cause of death due to infection[1]
- For patients with SCABP, mortality rates approach 50% in the ICU, and high rates of treatment failure persist, even with advanced antibiotic therapies[2,3,4,5,6]
- Unknown bacterial speciation and antibiotic resistance can complicate clinical management[7]

**CAL02 is a first-in-class liposomal, non-antibiotic, virulence factor neutralizing agent[8]**




- CAL02 is a proprietary mixture of empty liposomes engineered to mimic the cholesterol and sphingomyelin-enriched lipid platforms targeted by many bacterial toxins
- It is a high-affinity, irreversible trap that binds, sequesters and neutralizes virulence factors, preventing pathogenic consequences of toxin activity
- It is administered by IV infusion within 12 hours of severe infection diagnosis (2 doses, 24 hours apart)
- It is proposed for use in conjunction with and agnostic of antibiotic therapy

## Preclinical Rationale[9]

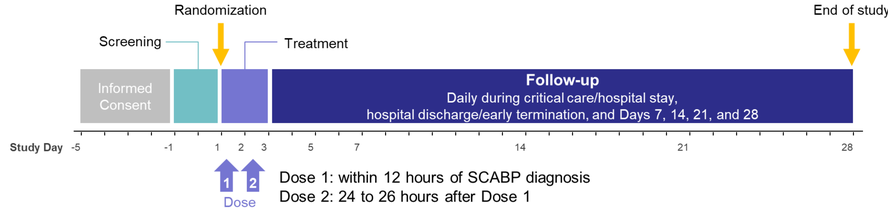
- In vitro studies showed that CAL02 binds virulence factors from both Gram-positive and Gram-negative bacteria with greater affinity than cells, protecting against cell lysis and cytotoxicity and preventing biofilm formation.
- In animal models of lethal pneumonia and bacteremia, CAL02 improved survival, enhanced organ protection, accelerated the rate of bacterial clearance from the blood, and reduced proinflammatory cytokines independently of infection etiology or antimicrobial resistance.

## First-in-Human Study[10]

***CAL02 has been investigated in a randomized, double-blind, multicentered, placebo-controlled study of patients with Streptococcus pneumoniae SCABP who required ICU admission (N=19)*** **(Study:CAL02-001;Clinicaltrials.gov NCT02583373)**

- CAL02 showed promising safety and tolerability, consistent with the profile of the study population
- CAL02 demonstrated faster resolution for clinical cure at both 8 and 15-22 days; increased the rate of organ function recovery (SOFA score); reduced duration of mechanical ventilation support and ICU stay; and faster decrease in inflammatory biomarkers, versus placebo treatment

## Study Design




- EGL-6535-C-2202 (NCT05776004) is an adaptive, Phase 2 randomized (1:1), double-blind, placebo-controlled study to evaluate the efficacy and safety of IV-administered CAL02 in addition to standard of care (SOC) in subjects with SCBAP (N=276)
- Subjects diagnosed with SCABP and requiring critical care measures will receive either two IV infusions of either CAL02 (13.7 to 24 mg/kg bracketed dose by weight), or placebo administered 24 to 26 hours apart.
- All subjects will receive standard of care therapy for SCABP, according to the local clinical guidelines

## Study Objectives

### Primary Endpoints

- Time to clinical recovery, defined as the number of days until resolution of all protocol-defined severity criteria, which qualified the subject at randomization, with no re-occurrence or additional severity criteria emerging within 24h after recovery
- Incidence and severity of TEAEs including infusion-related reactions

### Secondary Endpoints

- Days to critical care management discharge
- Days to hospital discharge
- Proportion of subjects achieving clinical recovery by Day 5
- Relative change from baseline in whole SOFA score at Day 7

### Safety Monitoring

- Independent unblinded DSMB will monitor safety and efficacy
- Blinded Clinical Event Committee to confirm adequacy of standard of care therapy

## Eligibility

### Key Inclusion Criteria

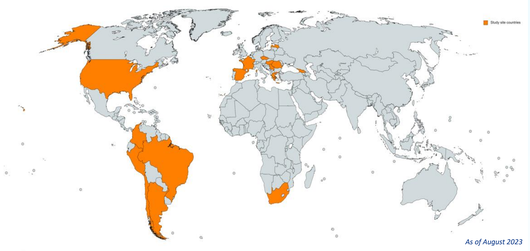
- Age ≥18 years with clinical diagnosis of SCABP or radiographic evidence supporting pneumonia with likely bacterial origin requiring ICU management
- Severity criteria (≥1) requiring critical care management, including respiratory failure requiring high-flow oxygen, invasive mechanical or noninvasive positive pressure ventilation support

### Key Exclusion Criteria

- Pneumonia of any other origin (viral co-infection is permitted if primary cause is suspected to be bacterial)
- >12 hours from SCABP diagnosis

## Enrollment Progress

**120+ sites planned in 20+ countries**




**First site activated:** May 2023
**First patient enrolled:** July 2023

## Summary

- CAL02 is a novel, first-in-class, liposomal agent, engineered to neutralize virulence factors, initially being evaluated for the treatment of SCABP in combination with standard of care[1]

### Study Rationale

- Extensive nonclinical studies have shown that CAL02 sequesters virulence factors and protects cells from a broad range of clinically relevant bacterial pathogens in vitro and in animal models of lethal infections[2]
- A first-in-human multicenter, double-blind, placebo-controlled study in patients with SCABP showed that CAL02 is safe, well-tolerated and efficacious as an adjunct treatment to current standard of care treatments for SCABP[3]
- Based on the extensive and promising preclinical and first-in-human studies, the FDA has designated CAL02 for fast track and as a Qualified Infectious Disease Product (QIDP)
- QIDP and fast-track designations underscore the significant unmet medical need for treatment of SCABP

### Trial in Progress

- A Phase 2 study investigating the efficacy and safety of CAL02 in addition to standard of care for patients with SCABP requiring critical care is in progress.

### Abbreviations

FDA, Food and Drug Administration; ICU, intensive care unit; IV, intravenous; SCABP, Severe Community Acquired Bacterial Pneumonia; SOFA, sequential organ failure assessment; TEAE, treatment-emergent adverse event, SOC, Standard of Care..

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