



Laura Holler, Rebecca Avila, Kaitlin Kestenber, Carley Armstrong, Adam Grossman  
ADMA Biologics, Boca Raton, FL, United States of America

## INTRODUCTION

Despite the widespread utilization of vaccines and antibiotics, *Streptococcus pneumoniae* remains prevalent globally. According to the 2021 Global Burden of Disease report, 2.1 million people died of pneumonia in 2021 and over half of those deaths were due to antimicrobial resistance<sup>1</sup>. In the United States an estimated >2 million cases of *S. pneumoniae* infections occur annually.<sup>2</sup> *S. pneumoniae* is responsible for half of all bacterial meningitis cases in the United States.<sup>3</sup> This is a major public health concern, given that an estimated 30% of pneumococcal bacteria are resistant to one or more antibiotics and that number is increasing. Vaccines for *S. pneumoniae* continue to increase serotype coverage; however, vaccines are limited due to the number of serotypes and there is a significant gap between vaccination and prevalent disease. Additionally, for immunocompromised patients, vaccine response conferring protection is likely to be diminished or absent.<sup>4</sup>

Currently, one of either PCV20 or PCV21 are recommended for adults 65+ years old, with no previous vaccination history. However, these two vaccines differ in their serotype coverage. Only 11 serotypes overlap in both vaccine options, and 19 serotypes are covered by one vaccine or the other, but not both.

Despite the fact that serotype 3 (Pn 3) is included within all currently recommended pneumococcal conjugate vaccines (PCVs) for *S. pneumoniae*, infection rates specific to Pn 3 have not declined since its 2012 inclusion in PCVs.<sup>5</sup> Pn 3 poses a high risk for invasive infections, even in vaccinated populations. Pn 3 is associated with more severe presentations of disease, including bacteremia induced septic shock, meningitis, and pneumonia.<sup>5</sup> From 2022-2023, Pn 3 had the highest rate of prevalence in the United States, composing 12.3% of the isolates identified<sup>6</sup> with a case mortality rate of 27.55%.<sup>7</sup> Additionally, a study demonstrated that Pn 3 requires a significantly higher number of protective antibodies to confer protection.<sup>8</sup>

The rates of penicillin resistance increased by approximately 400% within the United States after the introduction of PCV7.<sup>9</sup> In a general study of all *S. pneumoniae* serotype drug resistance, 56.8% of the isolates were resistant to at least 1 class of drug.<sup>10</sup> Pn 19A isolates often exhibit multi drug resistance. The addition of Pn 19A in PCV13 helped to reduce the rates of infections caused by the serotype by ~93%.<sup>9</sup> However, Pn 19A has a case mortality rate of 17.68%.<sup>7</sup>

The investigational product, SG-001, is a polyclonal high titer immune globulin designed to provide pre-exposure prophylaxis and treatment for *S. pneumoniae* based infections. SG-001 is a proprietary blended polyclonal composition exhibiting protective titers across serotypes unique to both PCV20 and PCV21.

## METHODS

### Multiplexed opsonophagocytic assay (MOPA) Titer Determination

High titer *S. pneumoniae* immune globulin, SG-001, was prepared by ADMA Biologics using a proprietary blend of plasma, from vaccinated donors. SG-001 pre-clinical lot titer levels were determined through multiplexed opsonophagocytic assay (MOPA) testing, at SunFire Biotechnologies. MOPA testing demonstrated a minimum of a 4-fold titer increase versus standard IVIG titer values (data shown for serotypes 3, 4, 8, 14, 19A, 24F, and 35B).

### Preclinical Animal Studies

Pre-exposure prophylaxis (PrEP) preclinical animal studies were performed for Pn 3 (ATCC 6303) and Pn 19A (ATCC 700904), in two groups (immunocompromised and immunocompetent). These studies were carried out using adult humanized gen-O-hFcγR mice of mixed gender, 6-7 weeks old. Bacterial isolates were animal passaged once prior to inoculation, in the study group. Studies were performed by Charles River Laboratories – Portishead, UK.

For the immunocompromised group, animals were rendered neutropenic via intraperitoneal (IP) injection of cyclophosphamide on days -4 and -1, at 150 mg/kg and 100 mg/kg, respectively. On Day -3, whole blood was collected from all animals to determine baseline colony-forming units (CFU). One day prior to infection, all animals were administered either saline or SG-001 at 400 mg/kg. On Day 0, all mice, excluding the naïve groups, were infected via intranasal administration of either  $1 \times 10^6$  CFU of Pn 3 (ATCC 6303) or  $1 \times 10^7$  CFU of Pn 19A (ATCC 700904). The immunocompromised groups were inoculated with either  $1 \times 10^5$  CFU of Pn 3 or  $1 \times 10^6$  CFU Pn 19A. Inoculation doses were based on initial dose response studies for Pn 3 and Pn 19A in humanized mice (data on file).

Animals were terminated 72 hours post infection, or earlier if endpoints were met.

Study readouts included bodyweight, clinical scores, survival, and CFU in lungs and blood pre-infection and at termination. Each animal was scored for each of the following criteria: (i) abnormal posture (hunched), (ii) abnormal coat condition (piloerection), (iii) abnormal activity levels (reduced activity), (iv) abnormal breathing and (v) presence of eye discharges and/or closed eyes. For each criterion, a score was given: (0) absence of signs, (0.5) intermittent signs and (1) persistent signs. A total score was calculated daily for each animal. Animals terminated early were given the maximum score (5) until end of experiment.

## RESULTS

### Functional Titers in SG-001

Investigational lots of SG-001 exhibit protective titers across serotypes within both PCV20 and PCV21. CDC uses a ≥4-fold increase in serotype-specific MOPA as a measure of vaccine effectiveness.<sup>11</sup> SG-001 functional titers are 4-fold higher compared to a standard IVIG reference material, providing protection across more serotypes than any vaccine alone.

Table 1. Selected *S. pneumoniae* functional titers contained in SG-001. Fold Increase SG-001 vs standard Ig

Serotype	SG-001 MOPA Titer Fold Increase vs. Standard IVIG
Pn 3	10
Pn 4	10
Pn 8	51
Pn 14	15
Pn 19A	160
Pn 24F	43
Pn 35B	6

## RESULTS (Continued)

### PrEP in Pn 3 challenged humanized mice

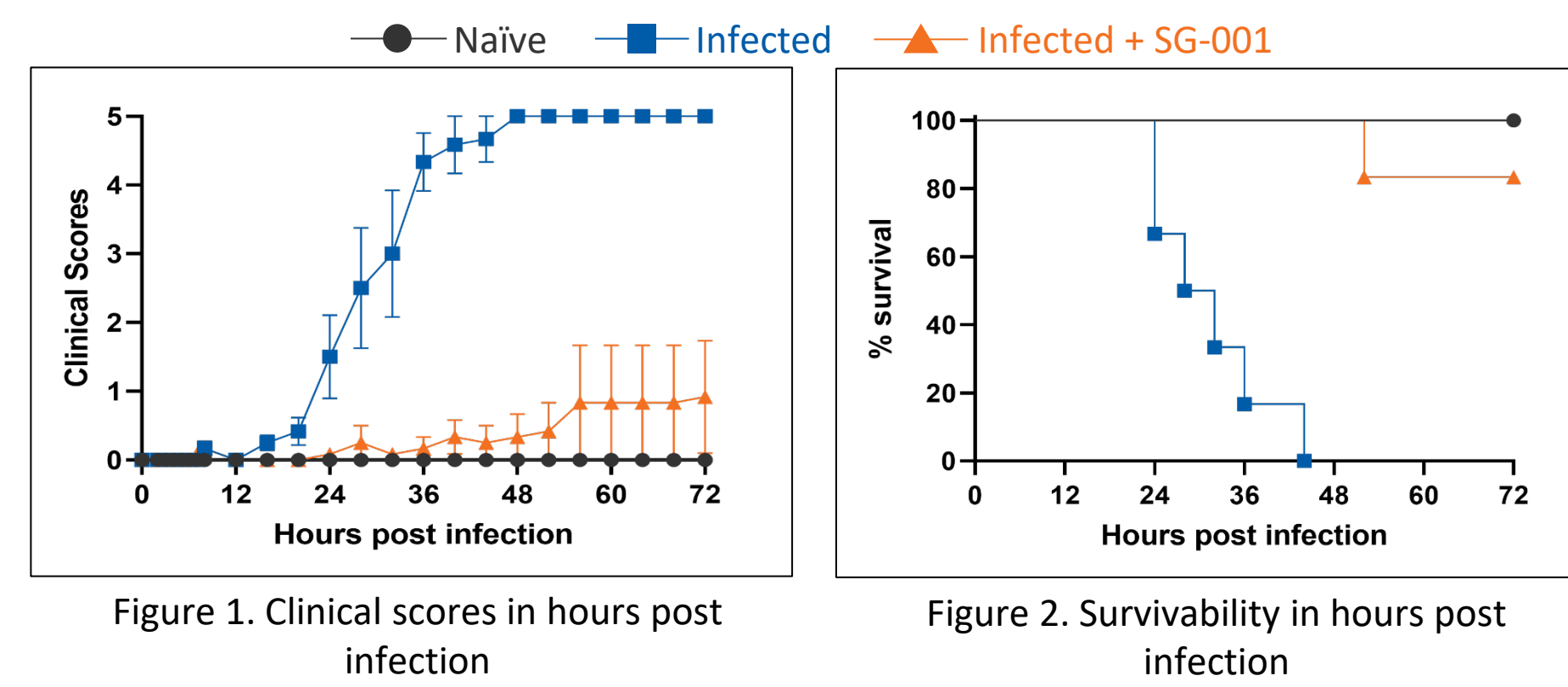


Figure 1. Clinical scores in hours post infection

Figure 2. Survivability in hours post infection

Animals that received SG-001 on Day -1 exhibited a statistically significant protection from infection, most noticeably showing greatly improved survival and reduced clinical scores. No untreated mice survived infection with Pn 3, while 83% of the SG-001 treated group survived to the end of the study.

### PrEP in Pn 3 challenged immunocompromised humanized mice

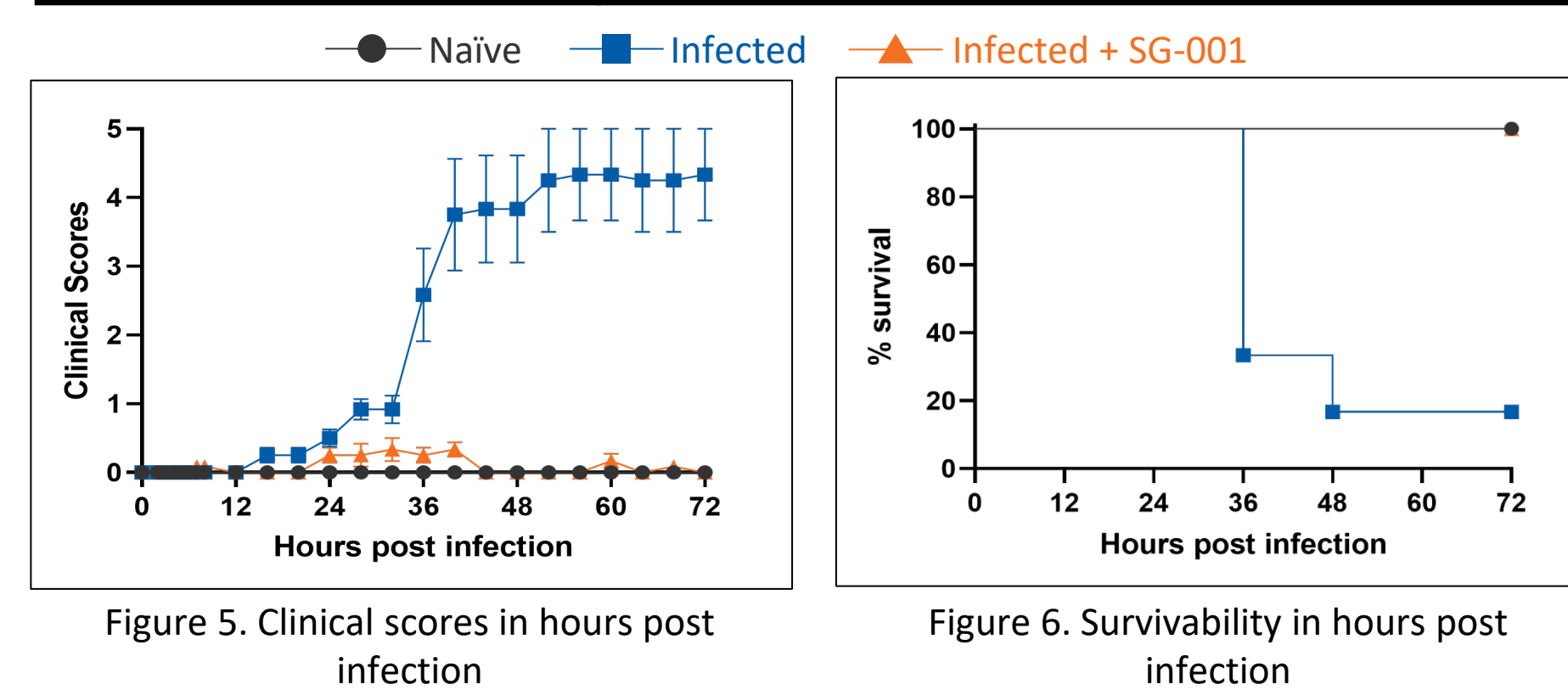


Figure 5. Clinical scores in hours post infection

Figure 6. Survivability in hours post infection

Animals that received SG-001 on Day -1 exhibited a statistically significant protection from infection. Survival was greatly improved compared to infected animals without SG-001, as well as reduced clinical scores. 100% SG-001 treated immunocompromised mice survived Pn 3 infection, with complete protection against blood or lung bacterial invasion.

### PrEP in Pn 19A challenged humanized mice

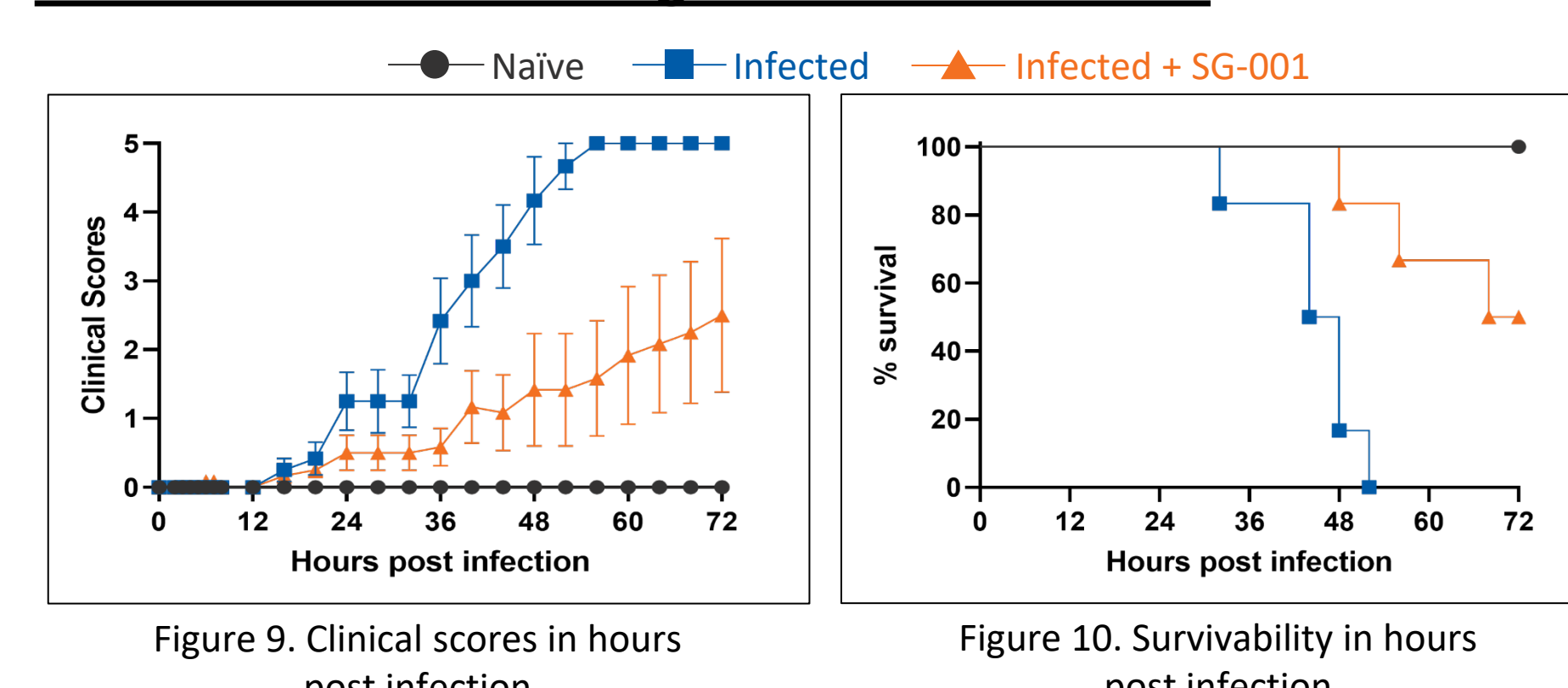


Figure 9. Clinical scores in hours post infection

Figure 10. Survivability in hours post infection

Animals that received SG-001 on Day -1 exhibited a statistically significant protection from infection. Survival was greatly improved compared to infected animals without SG-001 treatment.

### PrEP in Pn 19A challenged immunocompromised humanized mice

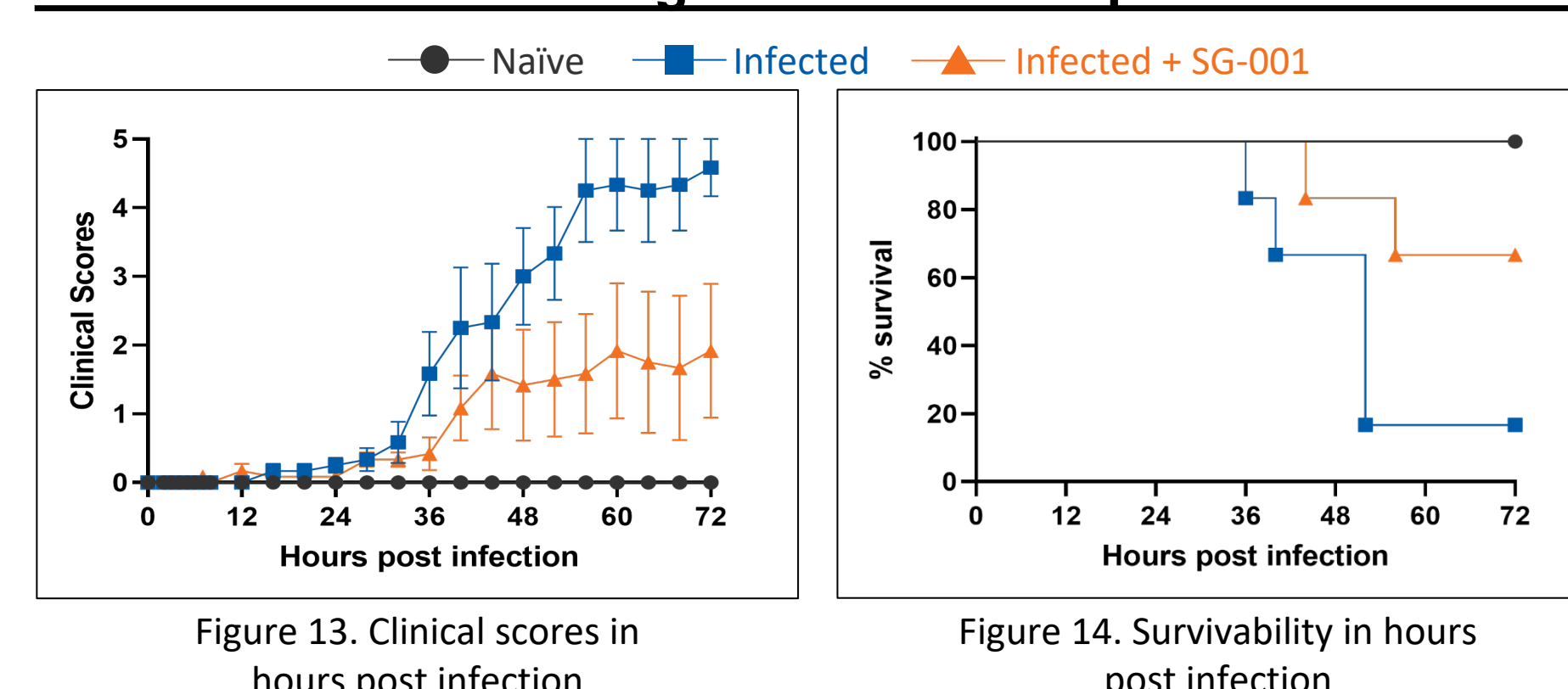


Figure 13. Clinical scores in hours post infection

Figure 14. Survivability in hours post infection

Animals that received SG-001 on Day -1 exhibited a statistically significant protection from infection. Survival was greatly improved compared to untreated, infected animals, with reduced clinical scores.

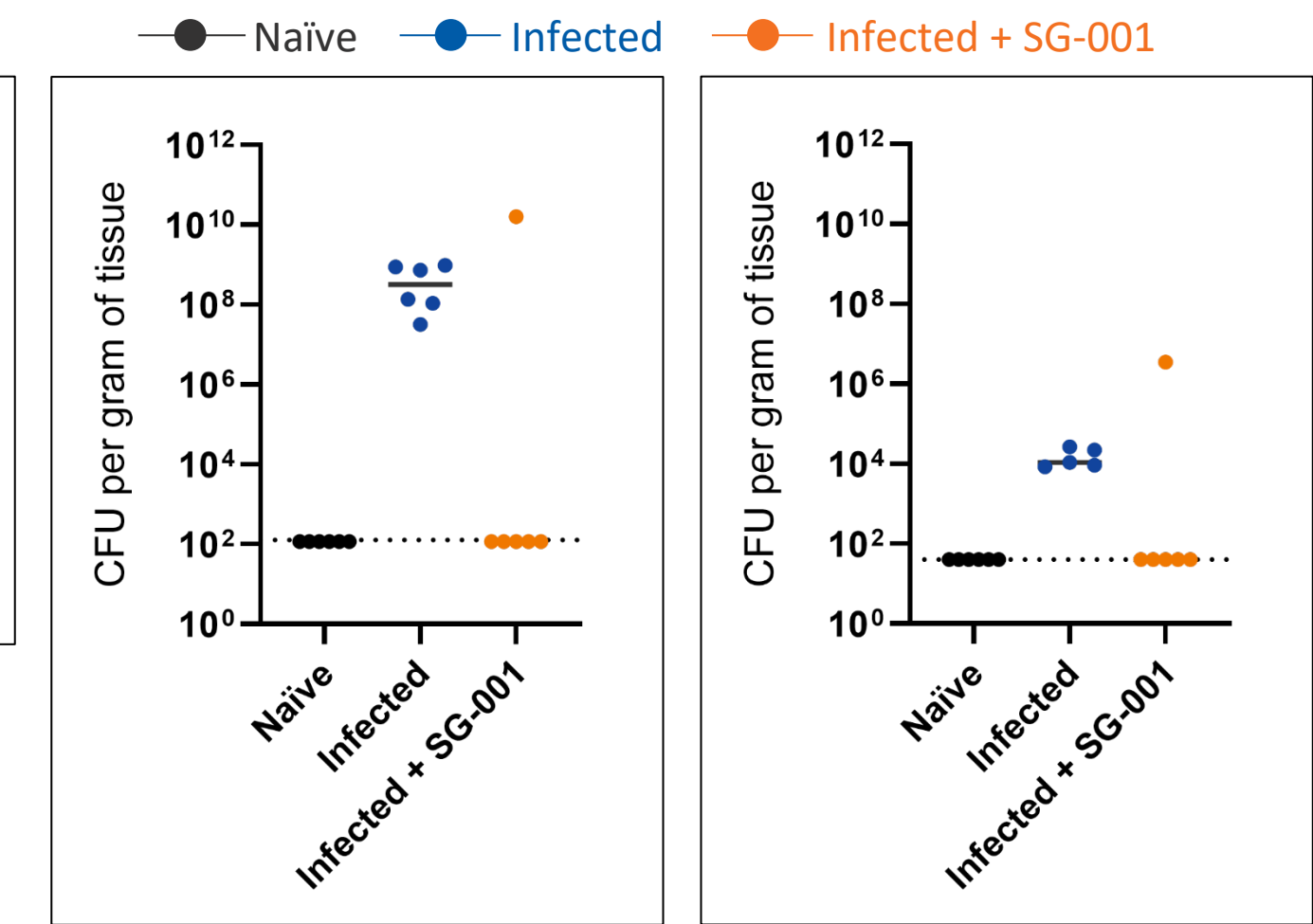


Figure 3. CFU in lung homogenates

Figure 4. CFU in whole blood following termination

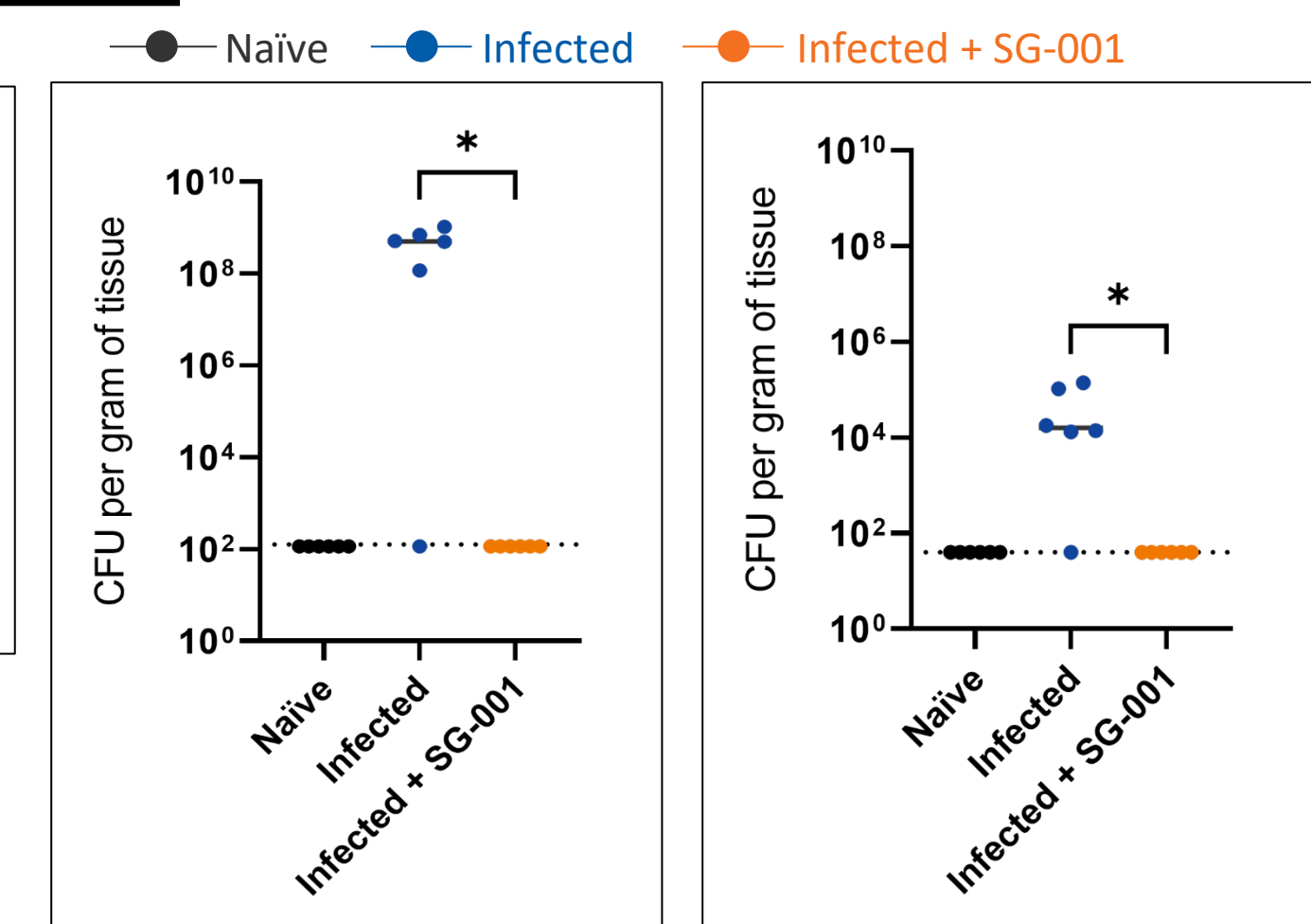


Figure 7. CFU in lung homogenates

Figure 8. CFU in whole blood following termination

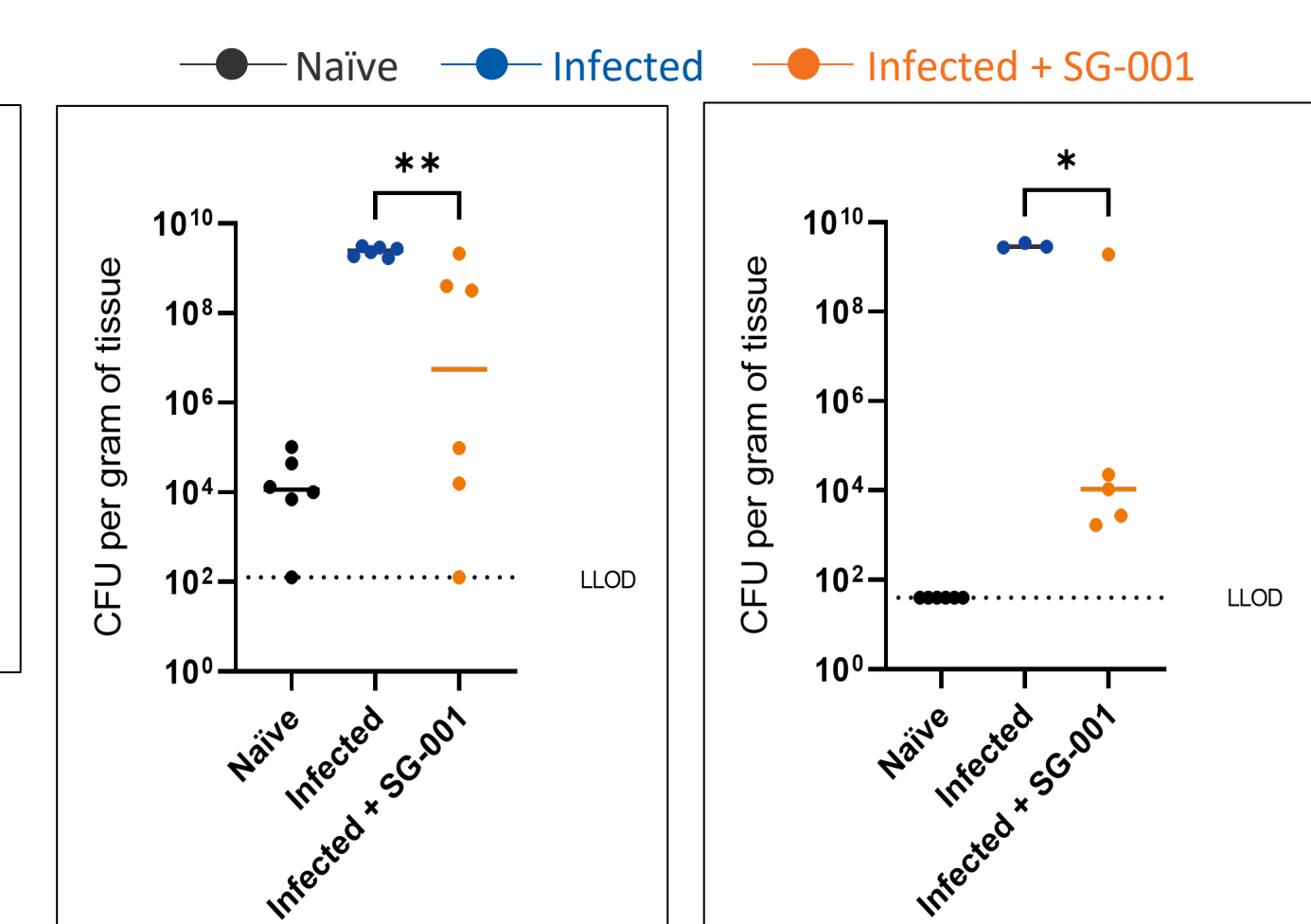


Figure 11. CFU in lung homogenates

Figure 12. CFU in whole blood following termination

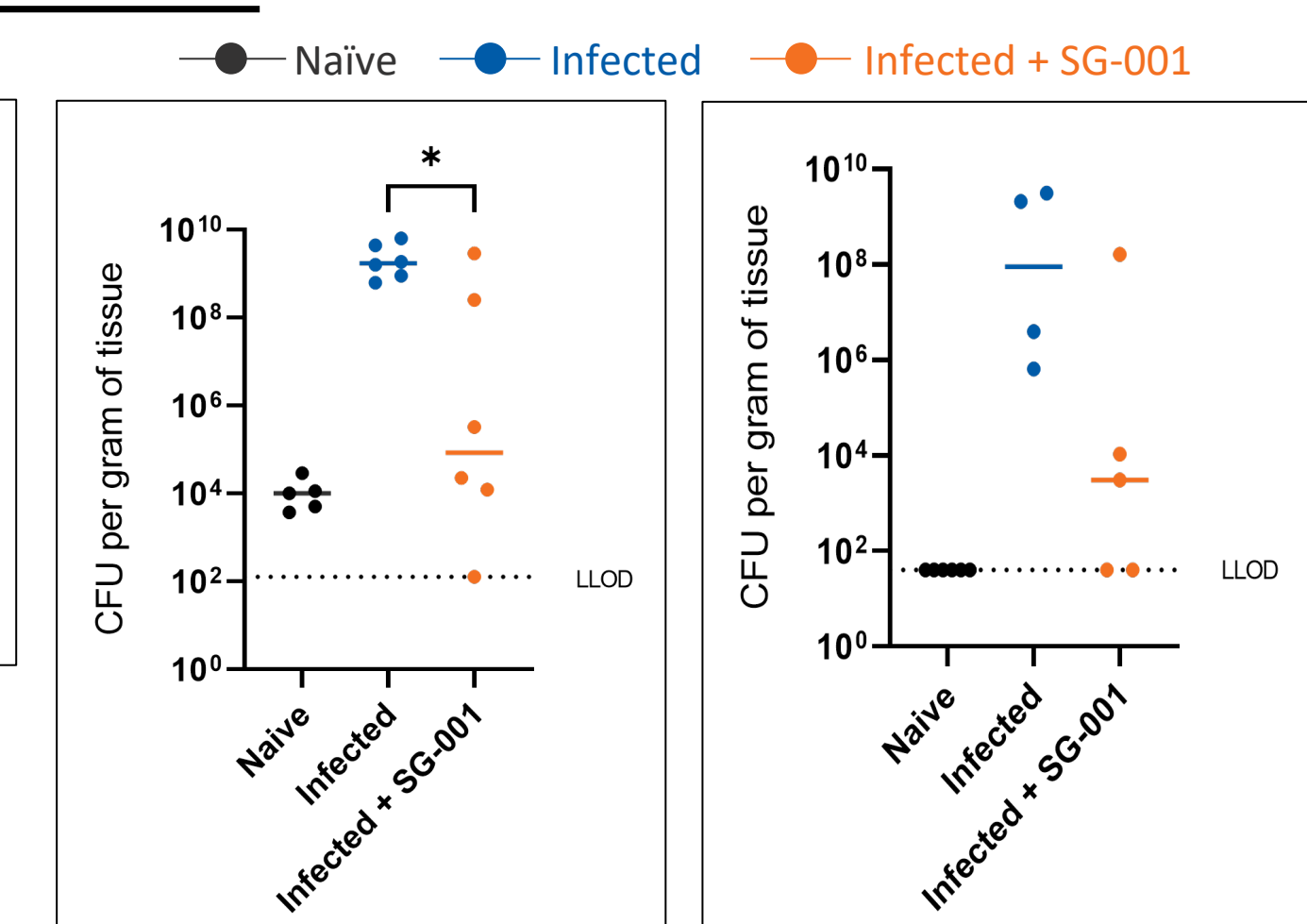


Figure 15. CFU in lung homogenates

Figure 16. CFU in whole blood following termination

## CONCLUSION

SG-001, a novel *S. pneumoniae* immune globulin, demonstrates a profound protective effect against Pn 19A and Pn 3, in a humanized mouse model, for healthy and immunocompromised cohorts. These data represent protective effect at the lower limit of standard Ig dosing range (400 mg/kg); at the upper limit of the dosing range it is expected that the protective effect would be markedly improved.

These data show that SG-001 is the first ever therapeutic that has demonstrated protection against *S. pneumoniae* in both healthy and immunocompromised models immediately following administration and does not rely on a delayed response from the individual immune system. As such, SG-001 would be invaluable for at-risk primary immunodeficient patients, ICU patients, and other vulnerable populations.

SG-001 is comprised of solely human immune globulins and will not negatively impact the microbiome or contribute to antibiotic resistance in bacterial populations. These are important features of SG-001 as the landscape of pneumococcal diseases continues to grow and increase in multi drug resistance. This is especially important for vaccine resistant serotypes such as Pn 3, for which SG-001 maintains high titers.

These data support further evaluation of SG-001 and we believe it would be highly successful as an effective treatment in at-risk populations, given the high titers observed in lots produced to date; studies are ongoing.

## REFERENCES

- Cilloniz C, Dela Cruz CS, Dy-Agra G, Pagcatipunan RS Jr; Pneumo-Strategy Group. World Pneumonia Day 2024: Fighting Pneumonia and Antimicrobial Resistance. Am J Respir Crit Care Med. 2024 Dec 1;210(11):1283-1285.
- Ryan Gierke, MPH; Sopia Chochua, PhD; Kristin Andrejko, PhD; Lesley McGee, PhD; Miwako Kobayashi, MD, MPH. Chapter 11: Pneumococcal. Manual for the Surveillance of Vaccine-Preventable Diseases. United States Centers for Disease Control and Prevention (CDC). January 17, 2025.
- Pennsylvania Department of Health. Pneumococcal Disease Fact Sheet. 10.22.2025.
- Bonilla, F. Update: Vaccines in primary immunodeficiency. J Allergy Clin Immunol. 2017. 141: 474-481.
- Luck JN, Tettelin H, Orihuela CJ. Sugar-Coated Killer: Serotype 3 Pneumococcal Disease. Front Cell Infect Microbiol. 2020 Dec 23;10:613287.
- Bensaci M, Bauer KAA, Klinker K, Cota J, Prusakov P, Mendes RE, Feemster K. P-1478. Trends in Streptococcus pneumoniae serotypes and antimicrobial resistance among US adults ≥18 years old with invasive and noninvasive pneumococcal disease (2022-2023). Open Forum Infect Dis. 2026 Jan 11;13(Suppl 1).
- Darkwah S, Somda NS, Mahazu S, Donkor ES. Pneumococcal serotypes and their association with death risk in invasive pneumococcal disease: a systematic review and meta-analysis. Front Med (Lausanne). 2025 May 14;12:1566502.
- Choi EH, Zhang F, Lu YJ, Malley R. Capsular Polysaccharide (CPS) Release by Serotype 3 Pneumococcal Strains Reduces the Protective Effect of Anti-Type 3 CPS Antibodies. Clin Vaccine Immunol. 2015 Dec 16;23(2):162-7.
- Isturiz R, Sings HL, Hilton B, Arguedas A, Reinert RR, Jodar L. Streptococcus pneumoniae serotype 19A: worldwide epidemiology. Expert Rev Vaccines. 2017 Oct;16(10):1007-1027.
- Mohanty S, Feemster K, Yu KC, Watts JA, Gupta V. Trends in Streptococcus pneumoniae Antimicrobial Resistance in US Children: A Multicenter Evaluation. Open Forum Infect Dis. 2023 Mar 7;10(3).
- CDC Advisory Committee on Immunization Practices (ACIP). Grading of Recommendations, Assessment, Development, and Evaluation (GRADE): 21-valent Pneumococcal Conjugate Vaccine (PCV21) Use among Adults Aged ≥19 Years Who Currently Have a Recommendation to Receive a Pneumococcal Conjugate Vaccine. United States Centers for Disease Control and Prevention (CDC). September 12, 2024.