



# CLB-3000A: Pioneering the Path to Functional Cure in Hepatitis B Treatment

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## Why This Therapeutic Vaccine is Turning Heads in Hepatology

Imagine teaching your immune system to play chess against a virus that's been winning for decades. That's essentially what ClearB Therapeutics' CLB-3000A aims to do in chronic hepatitis B (CHB) patients. This investigational therapeutic vaccine has become the talk of EASL and AASLD conferences since 2021, showing 80% functional cure rates in murine models - numbers that make hepatologists sit up straighter in their conference chairs.

## The Science Behind the Hype

CLB-3000A isn't your grandma's vaccine. It combines two engineered hepatitis B surface antigens (CLB-405 and CLB-505) expressed in *Pichia pastoris* yeast, delivered with an Alhydrogel adjuvant. Think of it as a molecular "Wanted" poster that helps immune cells recognize HBV's most vulnerable spots.

- Targets critical loops in the "a" determinant region of HBsAg
- Induces antibody profiles matching those seen in spontaneous resolvers
- Utilizes hydrogel delivery for sustained immune exposure

## Clinical Previews: From Mice to Men

In CBA/CaJ mice models mimicking chronic infection, CLB-3000A achieved what many thought impossible:

Parameter  
Result

Functional Cure Rate  
80%

Anti-HBs Seroconversion  
100%

Safety Profile (NZW Rabbits)  
Clean through 15-week toxicity studies



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## The Tolerability Tightrope

Even the most promising candidates can stumble on safety. But in 9-15 week studies with recovery periods, New Zealand White rabbits showed no deal-breaking issues. As Dr. Rubio quipped at EASL 2022: "Our bunnies hopped through trials cleaner than a lab coat parade."

## Beyond Monotherapy: The Combination Horizon

Most experts agree functional cure will require tag-team approaches. CLB-3000A brings three unique advantages to potential combination regimens:

- Breaks immune tolerance through epitope-specific retraining
- Complements direct-acting antivirals' viral suppression
- Could reduce treatment duration through immune memory formation

## Manufacturing Muscle

Using *Pichia pastoris* expression gives ClearB big-league production advantages. This yeast workhorse:

- Produces properly folded HBsAg variants
- Enables cost-effective scaling
- Avoids mammalian cell culture complexities

## The Road Ahead: First-in-Human Trials

With Phase 1 studies on the horizon, the field watches for answers to critical questions:

- Will human immune responses mirror murine data?
- Can durability of response match natural resolvers?
- What's the optimal combination partner?

As the first therapeutic vaccine to demonstrate functional cure potential in animal models, CLB-3000A represents more than just another candidate - it's proof that immune reprogramming can work against HBV's sophisticated evasion tactics. The coming years will determine if this biological chess master can checkmate hepatitis B in humans.



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