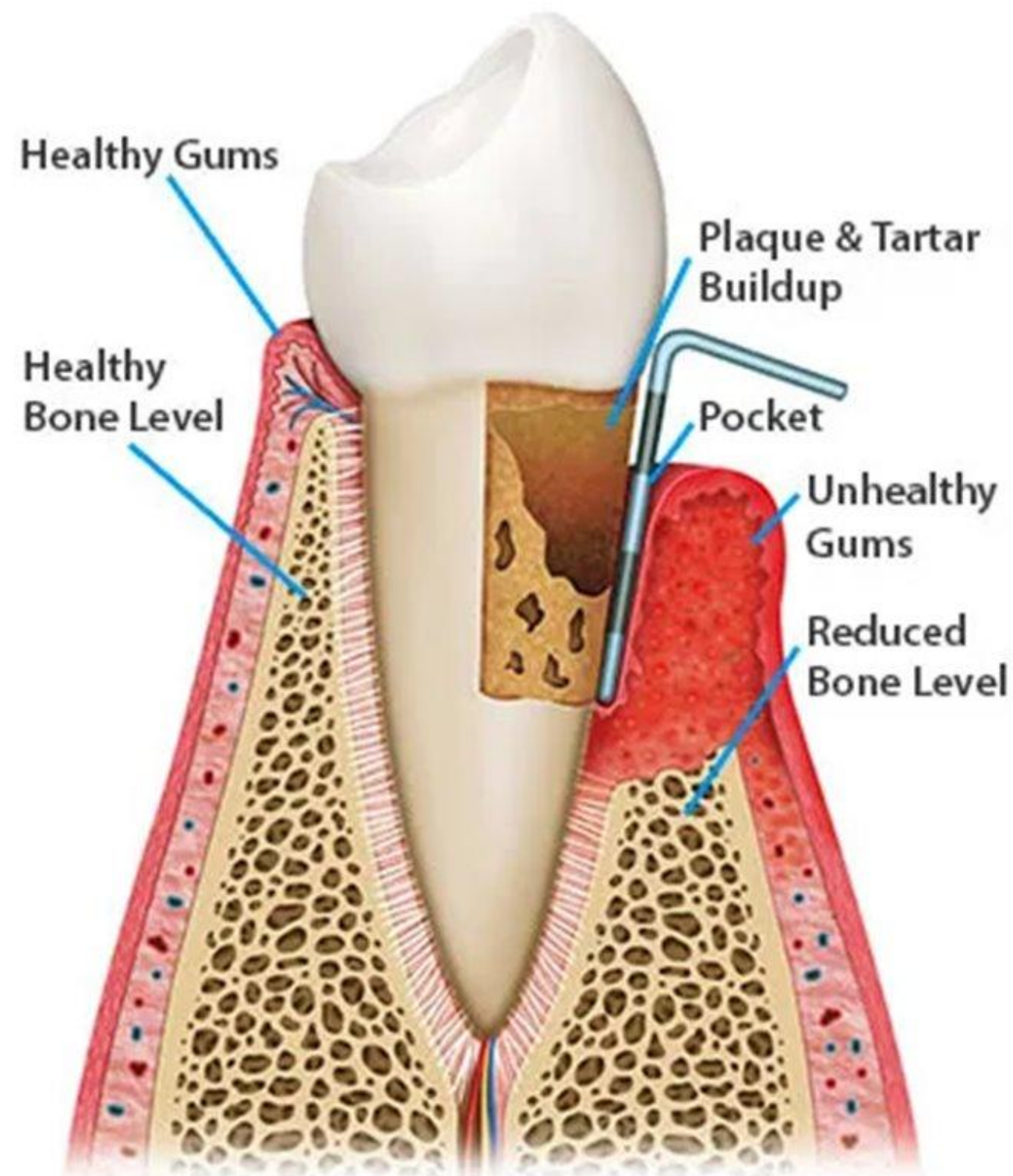


GPV381: A first-in-class therapeutic vaccine neutralizing gingipain toxins that drive chronic inflammation



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Pg drives severe disease through gingipain toxins



- *Porphyromonas gingivalis* (Pg) is an anaerobic bacteria and its levels increase with pocket depth
- Higher Pg levels correlate with **increasing disease severity** and bone loss
- While many bacteria are present in periodontitis, only Pg produces **gingipain toxins**, the central drivers of **immune dysfunction** and **chronic inflammation**.
- Current SoC is Scaling and Root Planing (SRP), a mechanic process that removes plaque, which only provide **short term benefits**

Scientific rationale behind GPV381

Gingipain toxins drive immune dysfunction

- Gingipain toxins are upstream drivers of chronic inflammation, keeping inflammatory pathways activated in immune cells while impairing effective bacterial clearance

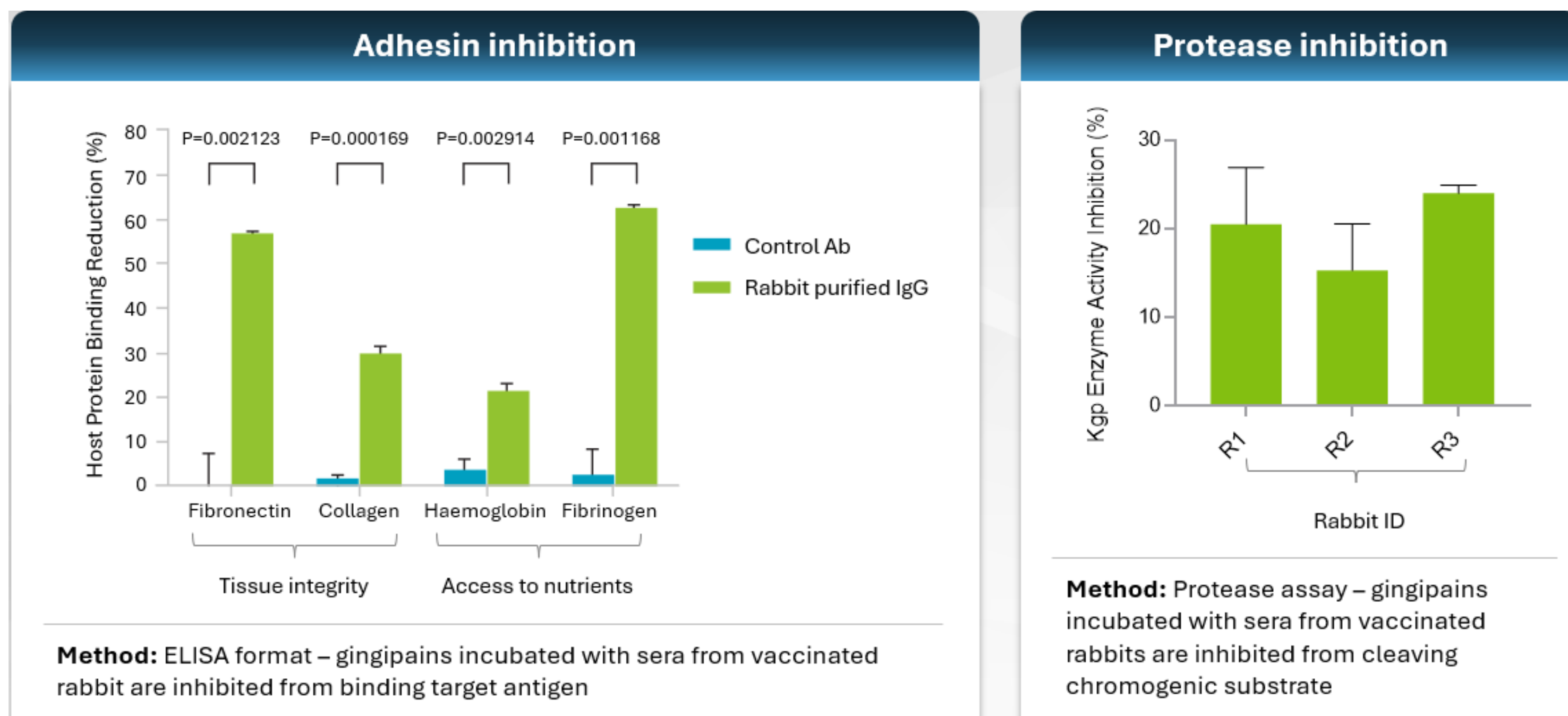
Neutralizing gingipains restores immune control

- Neutralizing gingipain toxins restores immune control, allowing inflammation to resolve and bacterial clearance to resume

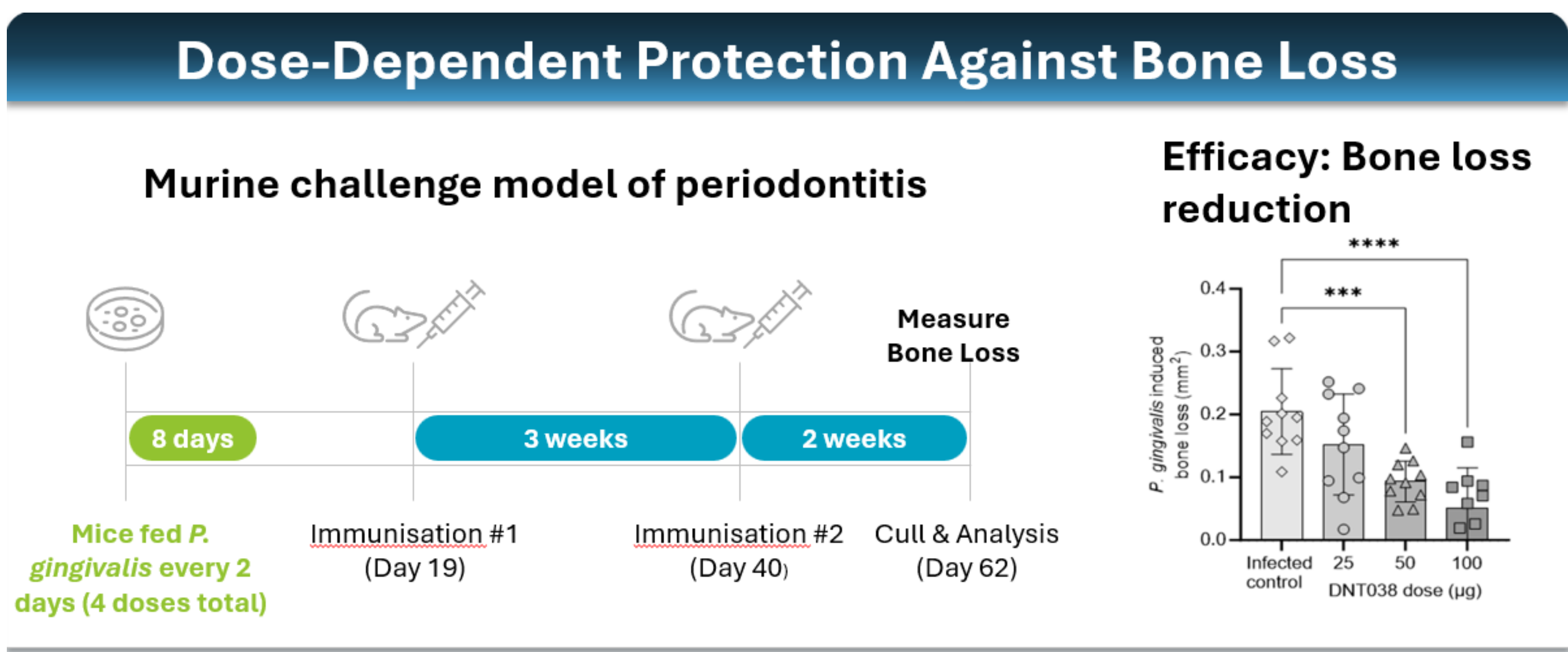
GPV381 induces gingipain neutralizing antibodies

- GPV381 generates durable neutralizing antibodies against gingipain toxins
- Phase 2 is designed to demonstrate clinically meaningful disease modification, including reduction in inflammation and healing in periodontal pockets
- Delivering this would shift treatment guidelines and redefine how periodontitis is managed

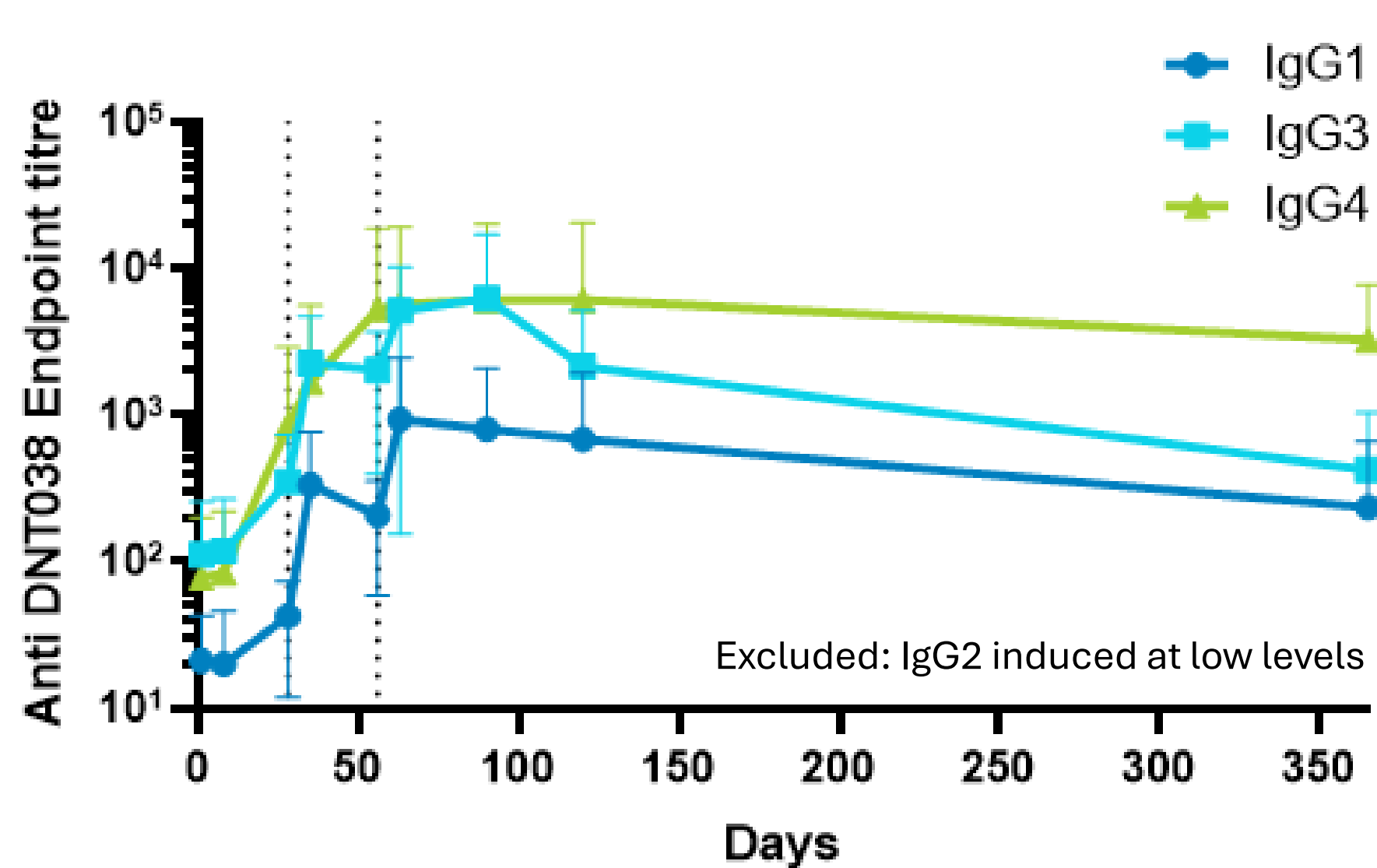
GPV381-induced antibodies neutralize the two critical domains of gingipain toxins



By neutralizing gingipain toxins, therapeutic dosing of GPV381 can limit bone loss in a challenge model

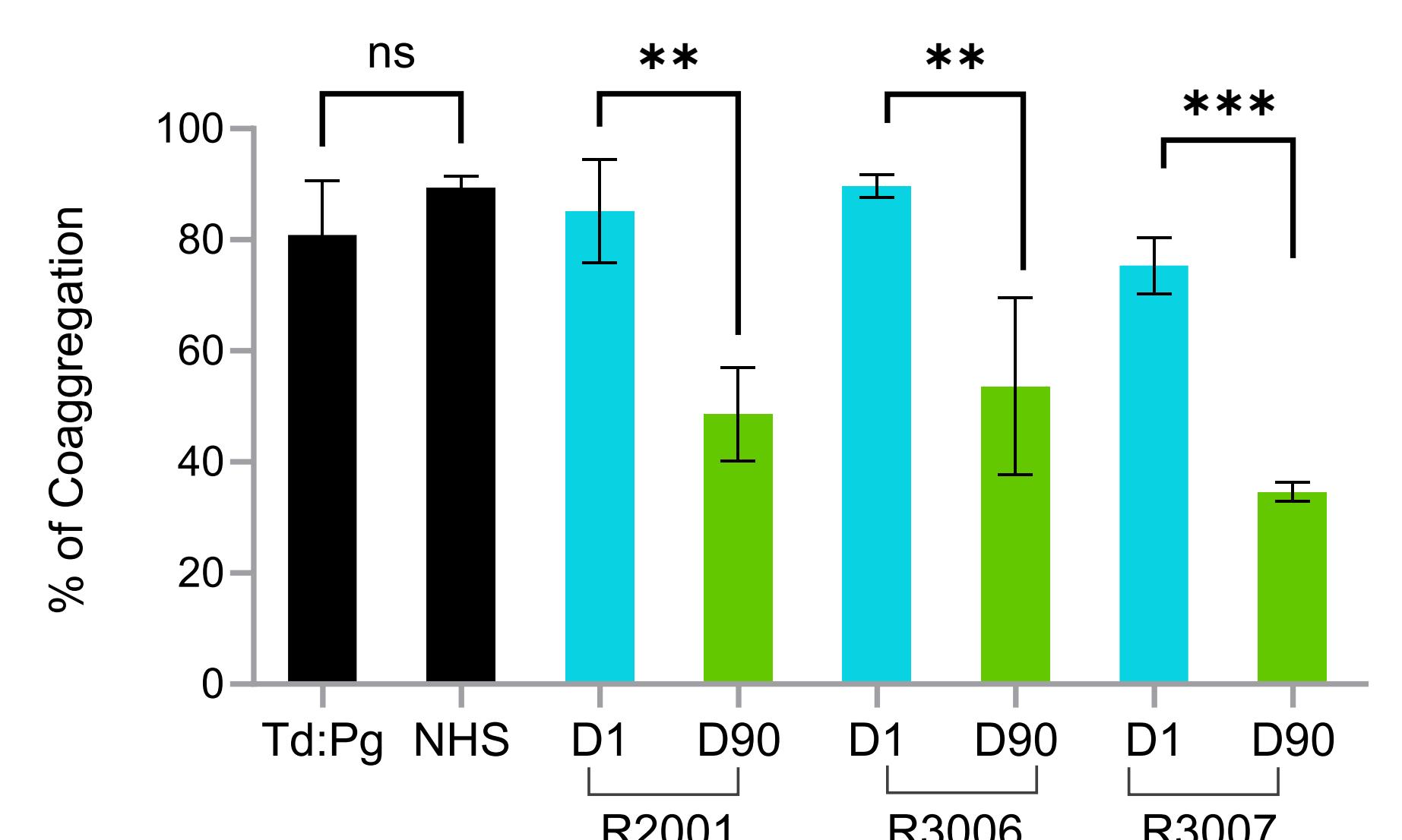
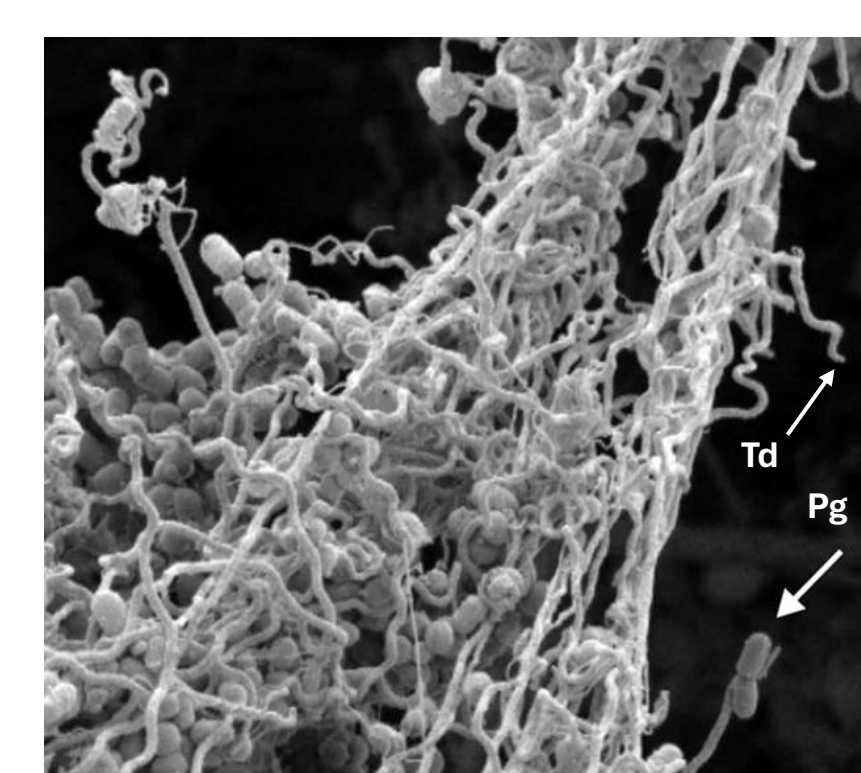


Phase 1: Safe and well tolerated with durable, functional anti-gingipain antibodies for 12 months



- High titers persist for 12-months, especially IgG4
- These subclasses provide a range of functionality including the inhibition of inflammatory signaling

Neutralizing gingipains disrupts the pathogenic periodontal ecosystem



- Surface gingipains enable coaggregation that enhances pathogenicity
- Ph1 Abs significantly inhibit coaggregation, collapsing the pathogenic ecosystem

REGAIN Phase II is designed to demonstrate disease modification in advanced periodontitis

REGAIN:

Restoration of symbiosis through Eradication of Gingipain-Associated Inflammation

A randomized, double blind, placebo-controlled study (n=174)	
Population	Patients with advanced periodontitis (pockets ≥6 mm)
Arms	SRP + GPV381(Lo) vs. SRP + GPV381(Hi) vs. SRP + Placebo
Primary Objectives	Safety, dose finding, pocket depth reduction (primary efficacy endpoint)
Secondary Objective	Efficacy: Pocket closure and Bleeding on Probing (BoP); local and systemic inflammatory biomarkers
Doses	3 x intramuscular doses, administered 3 months apart
Trial Length	19 months: (3Q26 – 1Q28)

- GPV381 administered adjunct to SRP, with design similar to Arestin® clinical trial
- Primary endpoint: PPD reduction – FDA accepted primary endpoint
- Secondary endpoint: includes % Pocket closure (<4 or 5mm PPD and no BoP) demonstrating **healing and disease modification**

GPV381 has the potential to treat Periodontitis – a \$154B gingipain-driven chronic inflammatory disease

- ✓ **Large Unmet Need:** Periodontitis is a \$154B chronic inflammatory disease affecting ~90M Americans, with ~14M patients suffering severe disease
- ✓ **First-in-class:** GPV381 is a disease-modifying therapeutic vaccine designed to neutralize gingipain toxins, upstream drivers of immune dysfunction and chronic inflammation
- ✓ **Clinically De-risked:** Phase 1 data demonstrate safety and durable neutralizing antibodies against gingipain toxins lasting 12 months.
- ✓ **Next Inflection Points:** IND Accepted, Phase IIb study planned for mid-2026, supported by a \$40–50 M raise to demonstrate clinical efficacy
- ✓ **Pipeline in a Product Potential:** Gingipain-driven inflammation is implicated in multiple systemic conditions including cardiovascular disease, diabetes, and Alzheimer's disease.