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CHAMPION-1 STUDY

BPZE1, an intranasal live attenuated pertussis vaccine, evaluated in a *Bordetella pertussis* challenge study in healthy adults: a phase 2b, randomized, placebo-controlled study

Diane Gbesemete, Maheshi N. Ramasamy, Muktar Ibrahim, Alison R. Hill, Lucy Raud, Daniela M. Ferreira, Jonathan Guy, Adam Dale, Jay R. Laver, Tyween Coutinho, Lisa Weissfeld, Wei Lang, Camille Locht, Vivek Samal, Peter Goldstein, Ken Solovay, Keith Rubin, Stephanie Noviello, Robert C. Read

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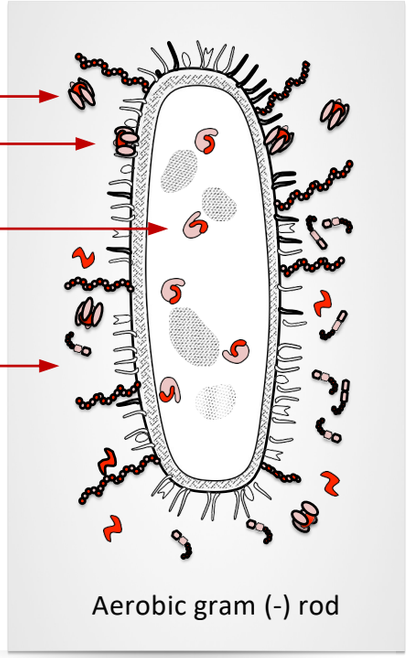
BPZE1: LIVE ATTENUATED VACCINE DESIGNED TO REDUCE TRANSMISSION AND PROVIDE SYSTEMIC PROTECTION

- BPZE1, a live attenuated intranasal vaccine, is designed to stop infection and reduce transmission
- BPZE1 is *B. pertussis* Tohama I strain with 3 genetic mutations to safely induce immunity (similar to wild-type exposure)

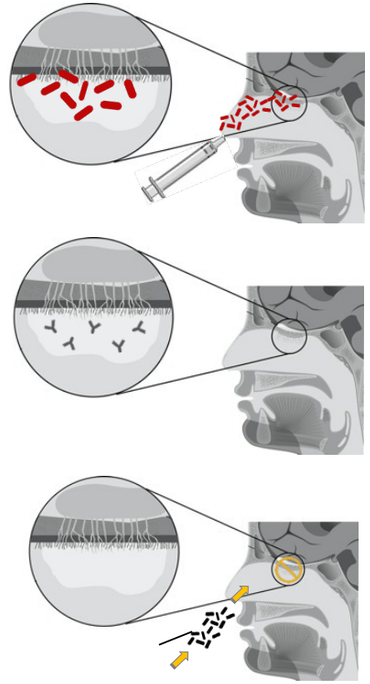
PT—Pertussis Toxin
Mutations create enzymatically inactive PT

DNT—Dermonecrotic Toxin
Removed via allelic exchange

TCT—Tracheal Cytotoxin
Gene replaced – reduces TCT release to <1%



Aerobic gram (-) rod



1. *Nasal vaccination with BPZE1 using VaxINator*
2. *BPZE1 stimulates mucosal and systemic immunity*
3. *B. pertussis* transmission interrupted at mucosal barrier[a]

[a]Keech et al. Lancet 2023

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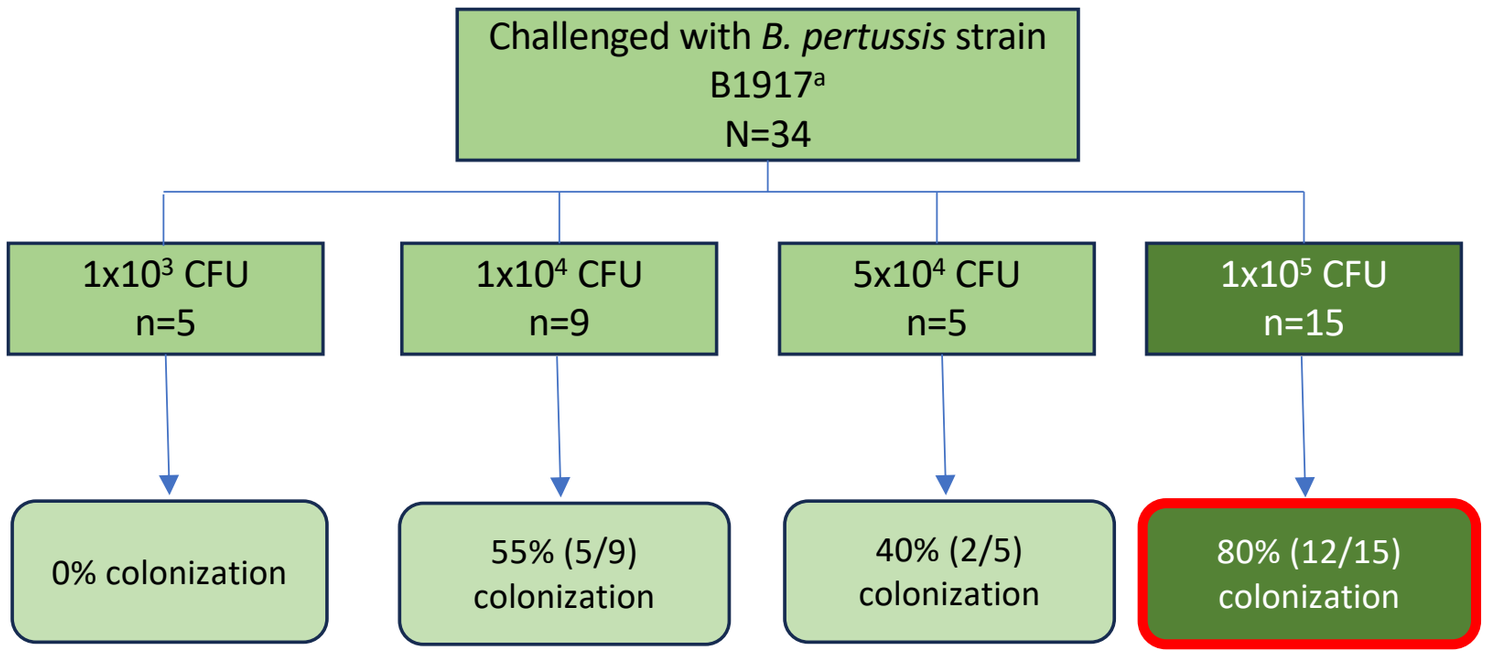
PERISCOPE HUMAN CHALLENGE MODEL

- PERISCOPE is a European consortium to accelerate development of new pertussis vaccines
- Primary objective: To determine inoculum dose to colonize at least 70% of challenged volunteers without *B. pertussis* disease
- Established challenge inoculum of 10^5 CFU of virulent *B. pertussis* strain B1917



[a]de Graaf et al. CID 2020

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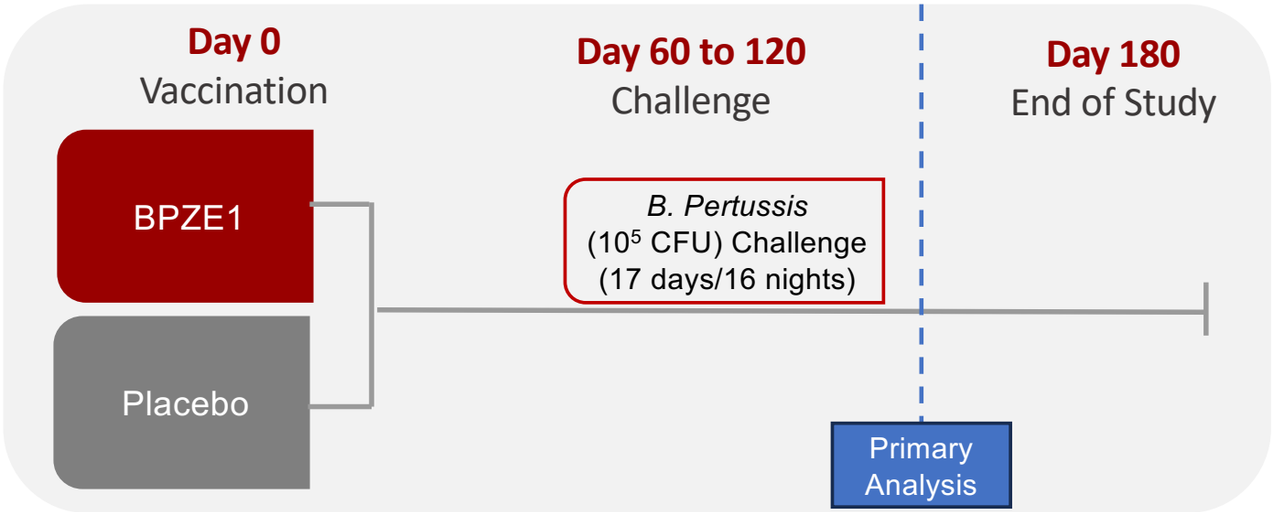
CHAMPION-1 (IB-202P) STUDY DESIGN & ANALYSIS SETS



Key Inclusion Criteria

18-50 years old

Non-smoker at time of enrollment

Stable health status

Key Exclusion Criteria

Anti-PT IgG >20 IU/mL

Anti-PRN IgG >30 IU/mL

- 141 participants screened
- 53 participants randomized and vaccinated (Intent-to-Treat)
- 45 participants challenged and evaluable (Modified Intent-to-Treat)
- 36 participants challenged and evaluable with an adequate challenge inoculum of ≥5 x 10^4 CFU *B. pertussis* (Per-Protocol Adequate Challenge Inoculum)
  - Prespecified sensitivity analysis for primary endpoint

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CLINICAL PROTOCOL ENDPOINTS

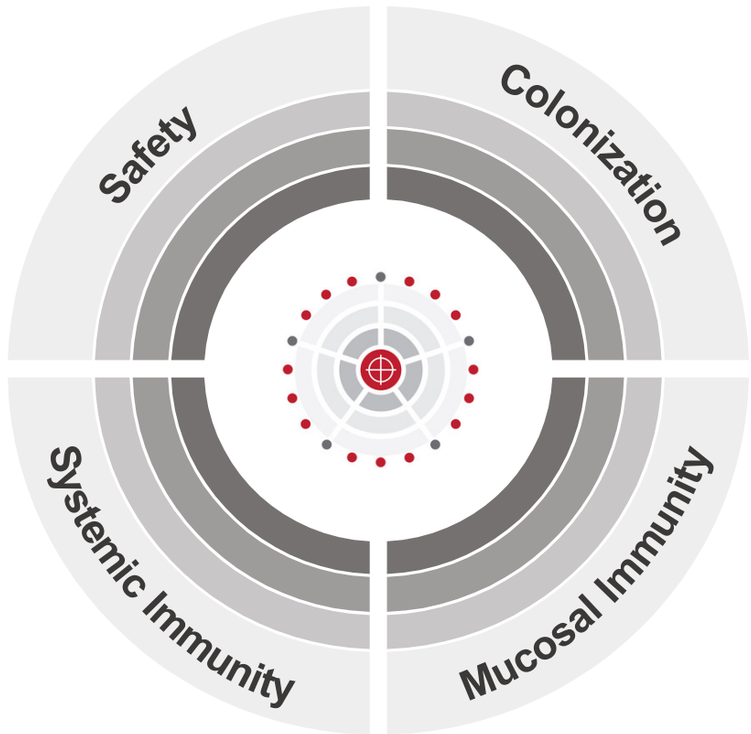
SAFETY

Reactogenicity

Unsolicited AEs

Safety Labs

Vitals/Physical Exam



COLONIZATION

1° - No colonization on Challenge Days C9, C11 and C14 following virulent challenge as determined by nasal wash culture

Colony counts from nasal wash culture

SYSTEMIC IMMUNITY

IgA and IgG WCE

Individual IgG antigens (PT, PRN, FHA)

Individual IgA antigens (PT, PRN, FHA)

NASAL IMMUNITY

S-IgA WCE

Individual S-IgA antigens (PT, PRN, FHA, FIM2/3)

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B. pertussis whole cell extract (WCE), pertussis toxin (PT), filamentous hemagglutinin antigen (FHA), and pertactin (PRN)

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DEMOGRAPHICS

- Demographics were similar between the BPZE1 and placebo groups

	BPZE1 n=26	Placebo n=27	Total N=53
Age, years, mean (±SD)	29.3 (7.8)	31.4 (9.2)	30.4 (8.5)
Male, n (%)	12 (46.2)	14 (51.9)	26 (49.1)
Race, n (%) White Black Asian	 22 (84.6) 3 (11.5) 1 (3.8)	 20 (74.1) 3 (11.1) 4 (14.8)	 42 (79.2) 6 (11.3) 5 (9.4)
Baseline Weight, kg, mean (±SD)	74.9 (17.3)	74.5 (12.2)	74.7 (14.8)
BMI, kg/m^2, mean (±SD)	25.3 (4.5)	25.5 (3.8)	25.4 (4.1)

BMI=body mass index; kg=kilogram; m=meter

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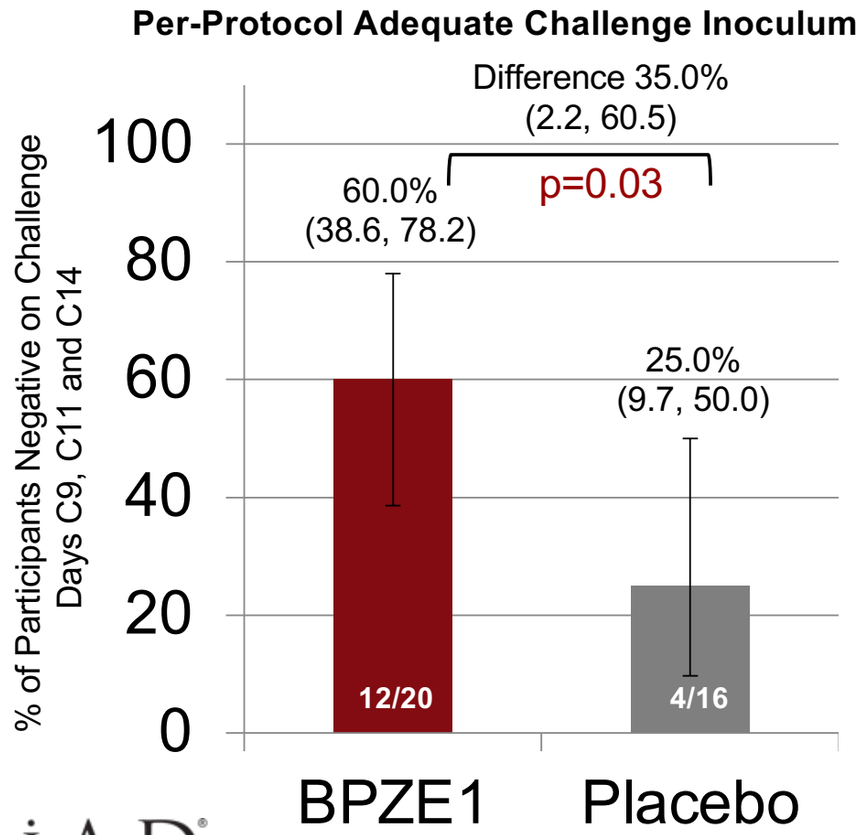
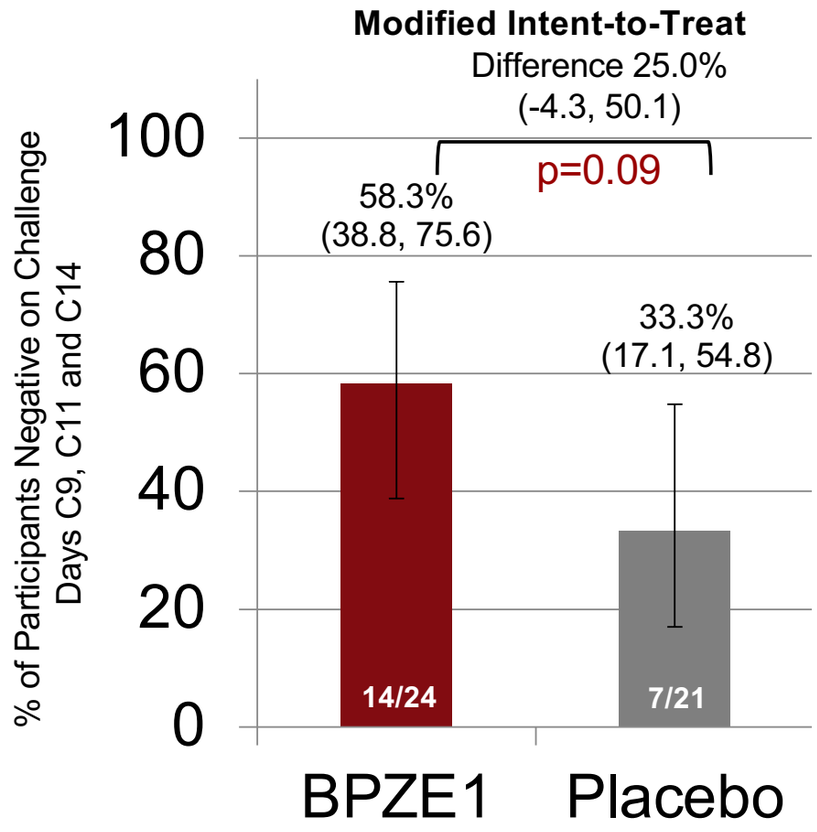
PRIMARY ENDPOINT- PROTECTION FROM COLONIZATION*

- Primary endpoint met in prespecified sensitivity analysis of BPZE1- compared with placebo-vaccinated participants who received an adequate virulent *B. pertussis* challenge dose (p=0.03)
- Primary endpoint showed comparable trends in the mITT participants (p=0.09)





*Defined as no colonization on Challenge Days C9, C11 and C14

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PROTECTION FROM COLONIZATION - CHALLENGE DAYS C9, C11, C14

- Challenge Days C9, C11 and C14 each showed BPZE1 protection from colonization (nominal p<0.05) in the mITT and Per-protocol Adequate Inoculum analysis sets

	Per Protocol Adequate Inoculum				Modified Intent-to-Treat			
Visit	BPZE1, n (%) (n=20)	Placebo, n (%) (n=16)	Difference (95% CI)[b]	p-value[c]	BPZE1, n (%) (n=24)	Placebo, n (%) (n=21)	Difference (95% CI)[b]	p-value[c]
Challenge Day C9	**13 (65.0%)**	**4 (25.0%)**	**40.0% (7.0, 64.7)**	**0.02**	**15 (62.5%)**	**7 (33.3%)**	**29.2% (-0.24, 53.8)**	**0.05**
Challenge Day C11	**13 (65.0%)**	**4 (25.0%)**	**40.0% (7.0, 64.7)**	**0.02**	**15 (65.2%)**	**7 (33.3%)**	**31.9% (2.2, 56.3)**	**0.03**
Challenge Day C14	**14 (70.0%)**	**4 (25.0%)**	**45.0% (12.0, 68.8)**	**0.006**	**16 (69.6%)**	**7 (33.3%)**	**36.2% (6.5, 59.9)**	**0.02**
Challenge Day C16[a]	19 (95.0%)	11 (68.8%)	26.3% (-0.6, 49.1)	0.07	21 (91.3%)	15 (71.4%)	19.9% (-4.3, 41.2)	0.13
Challenge Day C28	19 (100%)	14 (100%)	0	NA	22 (100%)	19 (100%)	0	NA

[a] Initiated azithromycin after culture on Challenge Day C14.
[b] 95% CI calculated by Agresti-Caffo method.
[c] p-value derived from likelihood ratio chi-square test (if expected cell counts ≥5) or Fisher's exact test (if expected cell count <5); Placebo reference.

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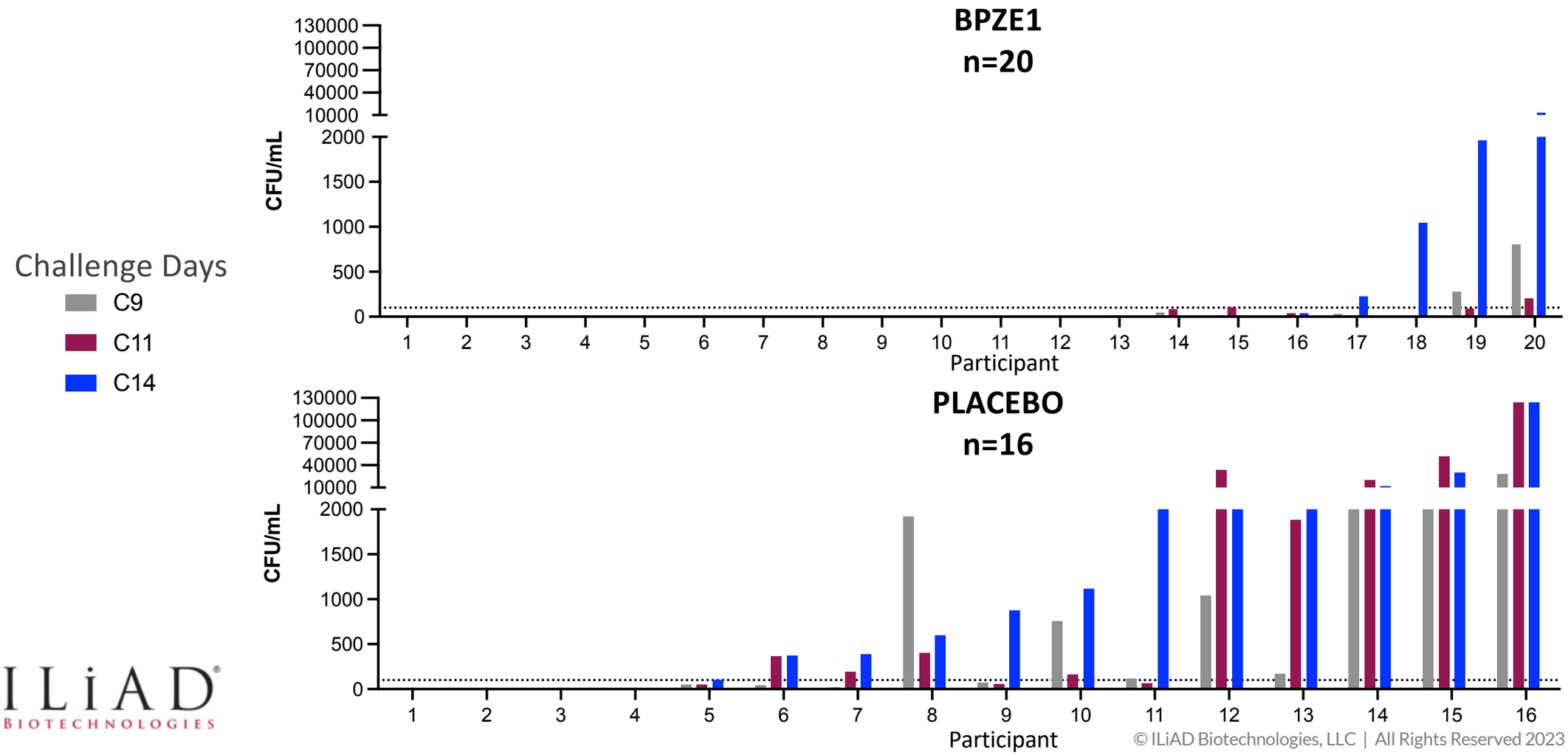
INDIVIDUAL PARTICIPANT *B. PERTUSSIS* CFU FROM NASAL WASH

PER-PROTOCOL ADEQUATE INOCULUM ANALYSIS SET

- 80% of BPZE1-vaccinated participants were protected from colonization >100 CFU/mL compared with 31% of placebo participants



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BPZE1 SUBSTANTIALLY REDUCED *B. PERTUSSIS* BURDEN

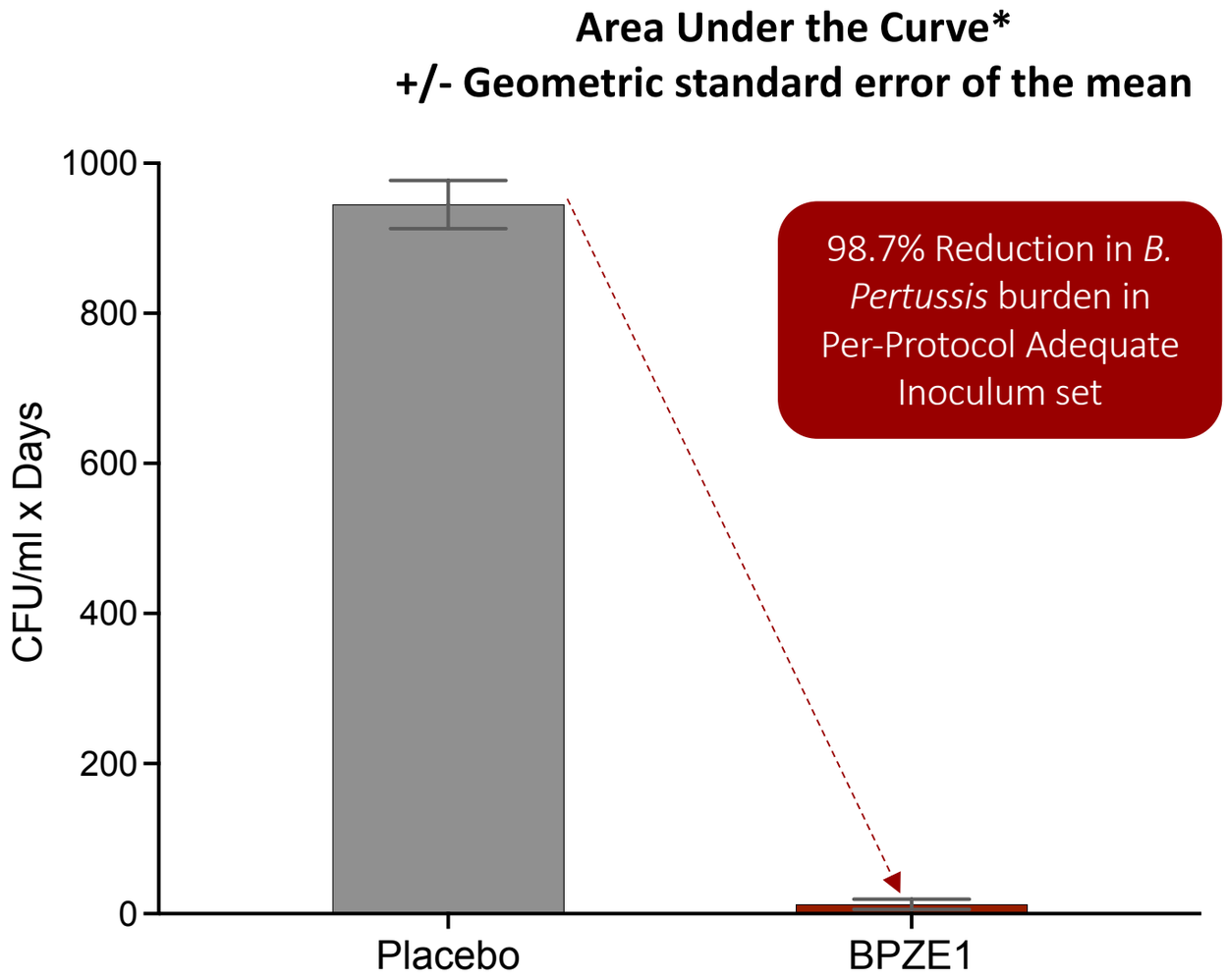
POST HOC ANALYSIS

<u>Per-protocol Adequate Inoculum</u>

- BPZE1-vaccinated participants had a 98.7% reduction vs placebo

<u>Modified Intent-to-Treat</u>

- BPZE1-vaccinated participants had a 97.1% reduction vs placebo



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*Geometric means of individual AUCs from C9 through C14 using the trapezoidal rule

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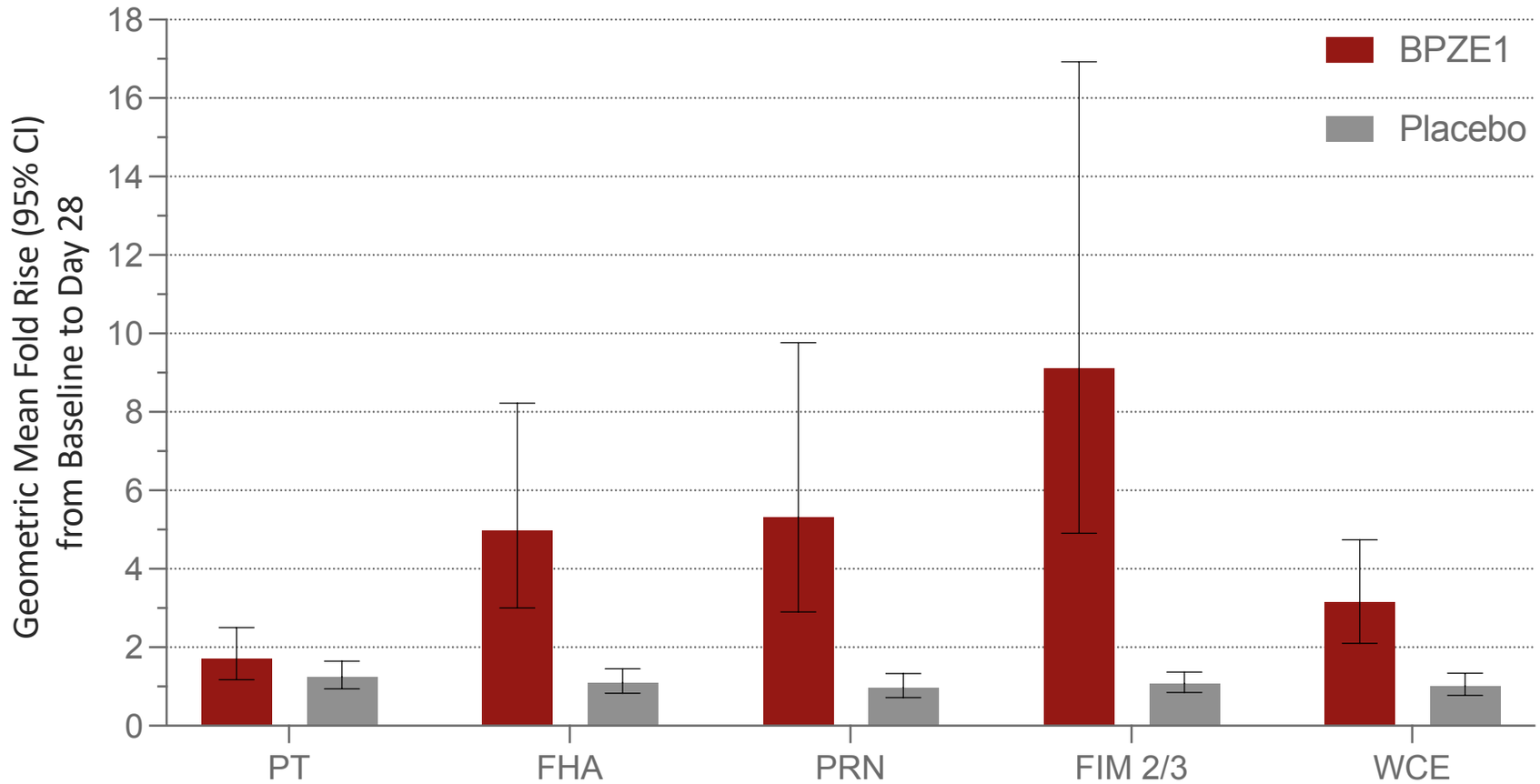
NASAL MUCOSAL S-IGA (NORMALIZED) IMMUNOGENICITY

ITT ANALYSIS SET

- Robust nasal mucosal immunological response



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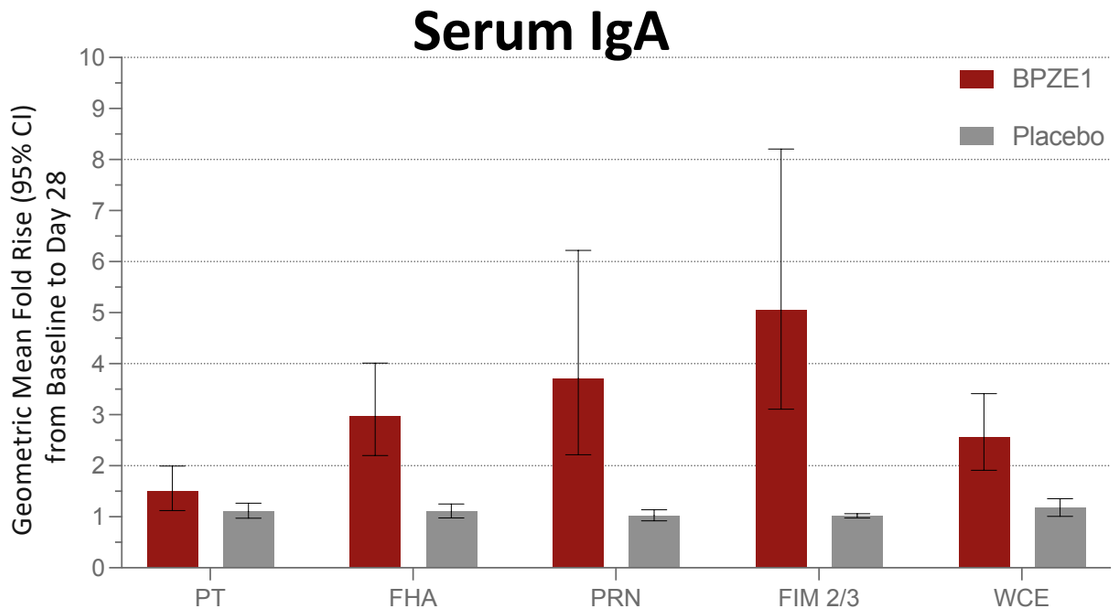
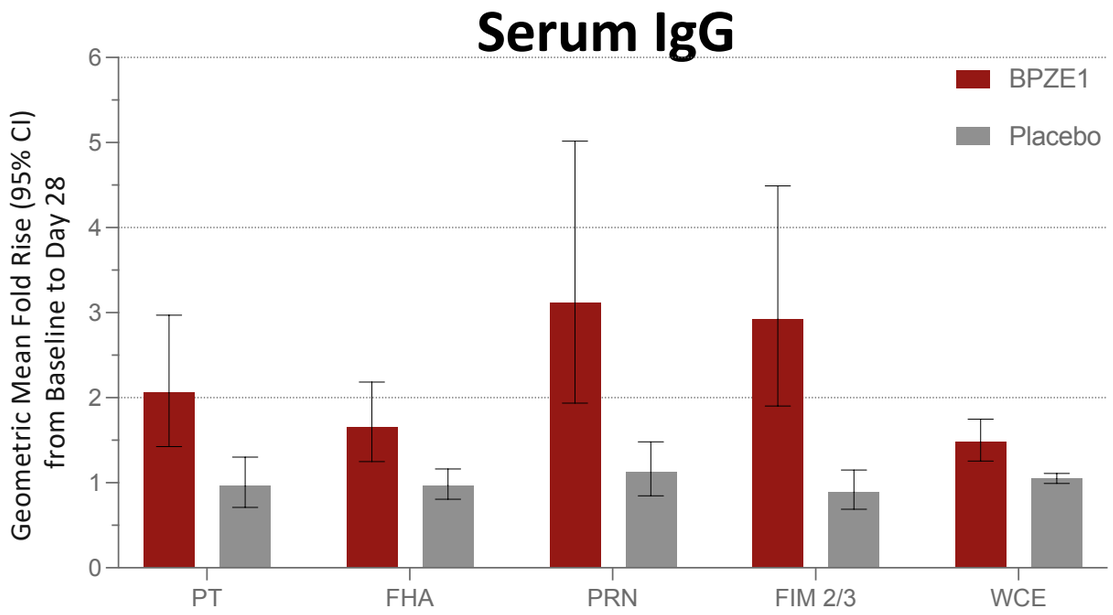
SERUM IGA AND IGG IMMUNOGENICITY

ITT ANALYSIS SET

- Robust immunological response in serum





- Seropositive response confirmed using the Ward criterion[a]
  - 85% of BPZE1-vaccinated participants had ≥2-fold increases in at least 2 antigen-specific (i.e., anti-PT, anti-FHA, anti-PRN and/or anti-FIM2/3) IgG and/or IgA titers from baseline to Day 28, as compared with 20% of placebo participants

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[a]Ward et al. NEJM 2005

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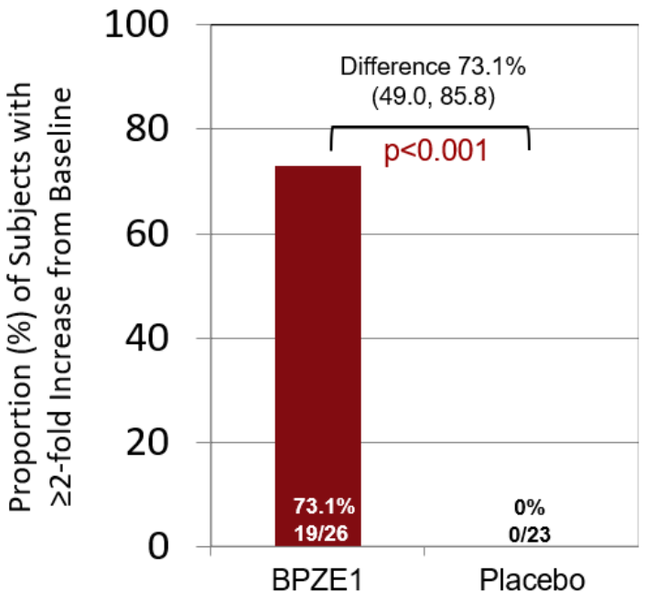
SERUM BACTERICIDAL ACTIVITY

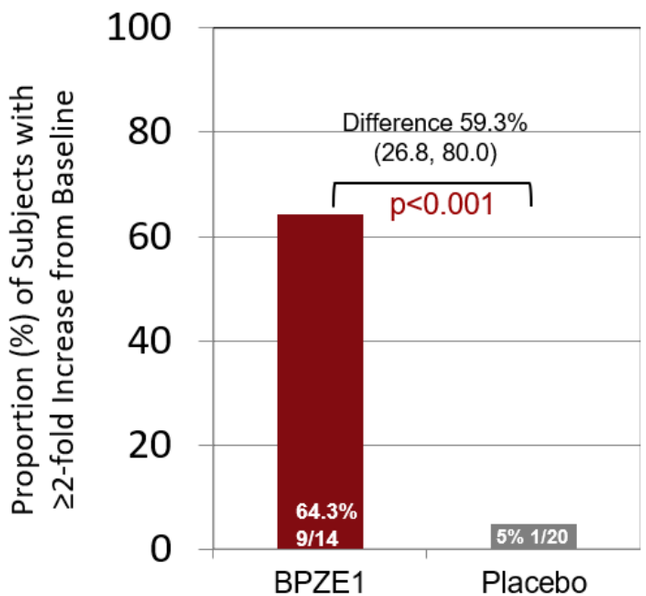
ITT ANALYSIS SET

- BPZE1 demonstrated serum bactericidal activity
  - Against PRN- strain: 73.1% of BPZE1 participants had ≥2-fold SBA response with 3.9x GMFR
  - Against PRN+ strain: 64.3% of BPZE1 participants had ≥2-fold SBA response with 3.6x GMFR
  - For participants that colonized, a ≥2-fold SBA response was observed indicative of systemic immunity

PRN- strain in SBA Assay



PRN+ strain in SBA Assay



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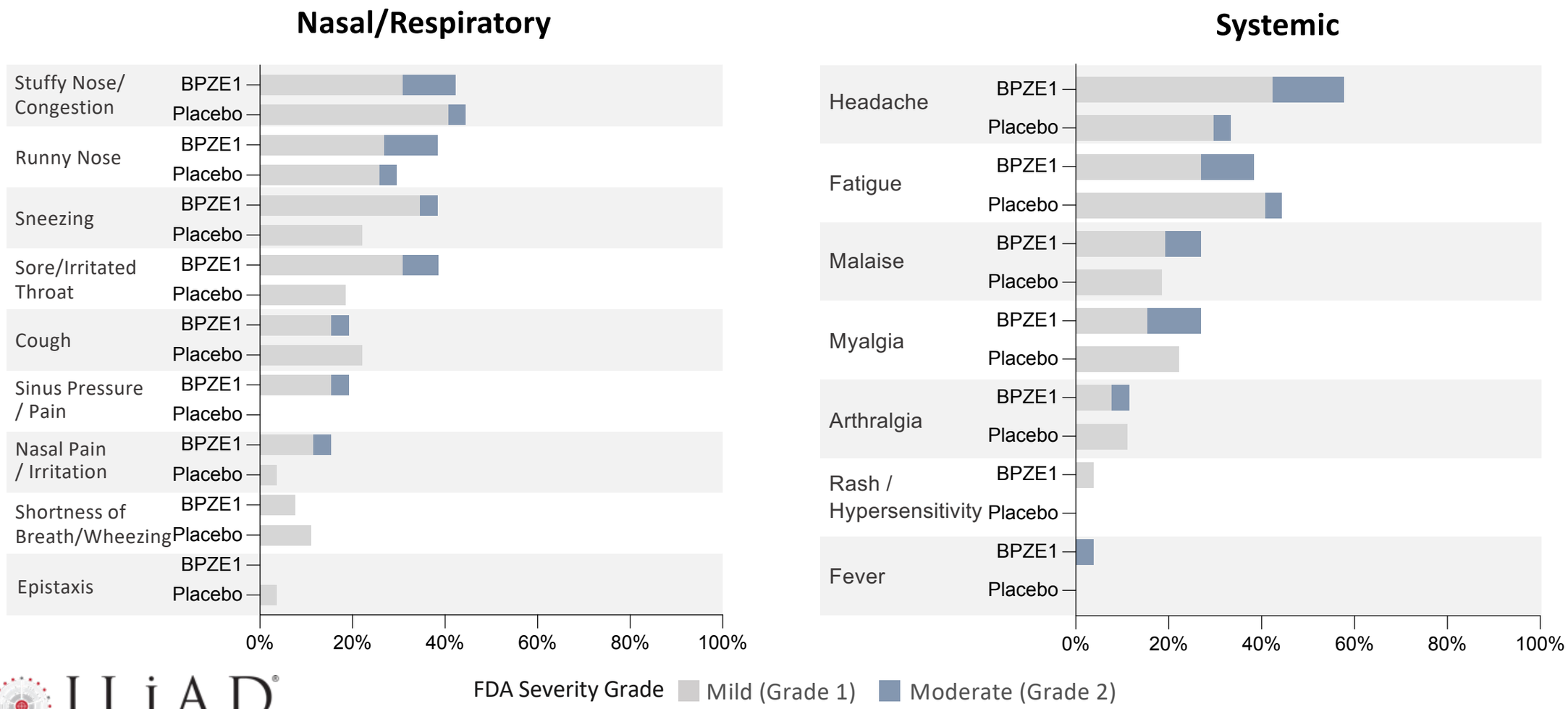
REACTOGENICITY OVER 7 DAYS POST VACCINATION

- No severe (Grade 3) reactogenicity events were reported



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UNSOLICITED ADVERSE EVENTS

- BPZE1 was well-tolerated and safe
- Similar safety profiles between BPZE1 and placebo groups

	BPZE1 n=26 n (%)	Placebo n=27 n (%)	Total N=53 n (%)
Death	0	0	0
SAEs	0	0	0
AEs leading to discontinuation	0	1 (3.7)	1 (1.9)
AE of special interest (COVID-19)	0	1 (3.7)	1 (1.9)
Any TEAEs	22 (84.6)	19 (70.4)	41 (77.4)
Through 28 days following vaccination	7 (26.9)	9 (33.3)	16 (30.2)
Through 28 days following challenge	20 (76.9)	16 (59.3)	36 (67.9)
Related	4 (15.4)	8 (29.6)	12 (22.6)
Vaccination	1 (3.8)	1 (3.7)	2 (3.8)
Mucosal atomization device	0	0	0
Challenge[a]	3 (11.5)	7 (25.9)	10 (18.9)

AE=adverse event; MAD=mucosal atomization device; SAE=serious adverse event; TEAE=treatment-emergent adverse event

[a] AEs were *B. pertussis* culture positive on Challenge Day 16.

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CONCLUSIONS

- Study IB-202P met the primary endpoint in pre-specified sensitivity analysis of participants who received adequate virulent *B. pertussis* challenge inoculum (p=0.03)
  - Primary endpoint showed comparable trends in mITT participants
- 98.7% reduction in bacterial burden was shown in BPZE1-vaccinated participants compared with placebo in Per-protocol Adequate Inoculum analysis set (post hoc)
- BPZE1 continues to induce consistent antibody responses across studies, including baboons, attenuated human challenge and virulent human challenge
- BPZE1 vaccinations were well tolerated and safe with no unexpected findings
- Results of this Phase 2 study reflect the favorable safety profile of BPZE1 and the potential of BPZE1 to offer protection against *B. pertussis* colonization
- Further investigation in a pivotal Phase 3 study is warranted

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ILiAD Biotechnologies thanks the investigators, study staff and participants in the CHAMPION-1 Study

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