Live attenuated *Bordetella pertussis* intranasal vaccine (BPZE1)

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Disclosures

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Novartis					X		X (former)	
Bristol-Myers Squibb					X		X (former)	

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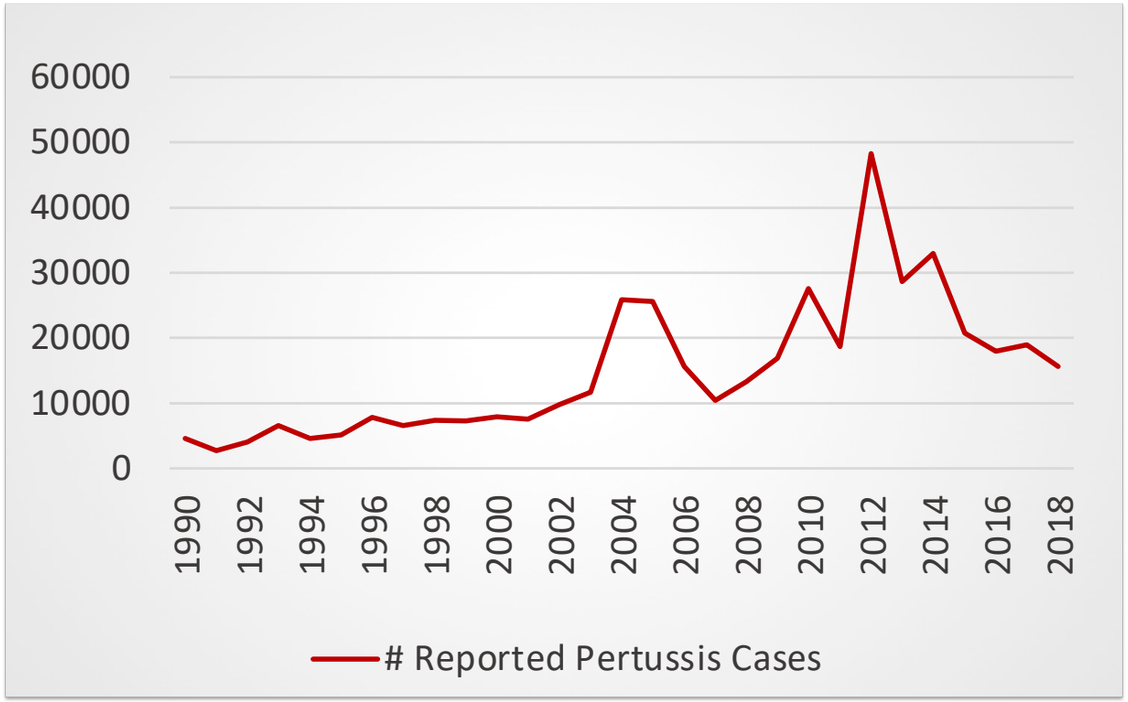
Acellular Pertussis Vaccination and Resurgence of Pertussis in the United States

- Relative to other vaccines, acellular pertussis (aP) vaccine immunity wanes rapidly; requiring multiple boosters
- aP vaccine introduction is associated with *B. pertussis* resurgence (by surveillance and modeling estimates)
- WHO recommends to continue wP vaccines if switching to aP has not yet occurred

B. pertussis Cases Reported U.S. 1990-2018



WHO Position Paper, 2015; CDC surveillance, https://www.cdc.gov/pertussis/surv-reporting/cases-by-year.html

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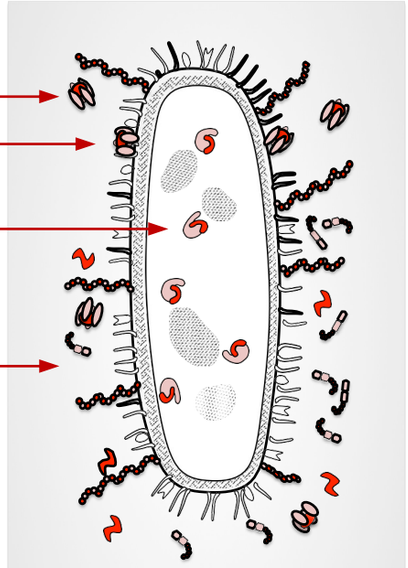
BPZE1: Live Attenuated Vaccine Designed to Reduce Transmission and Provide Systemic Protection

- 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 induce immunity (similar to wild-type exposure)

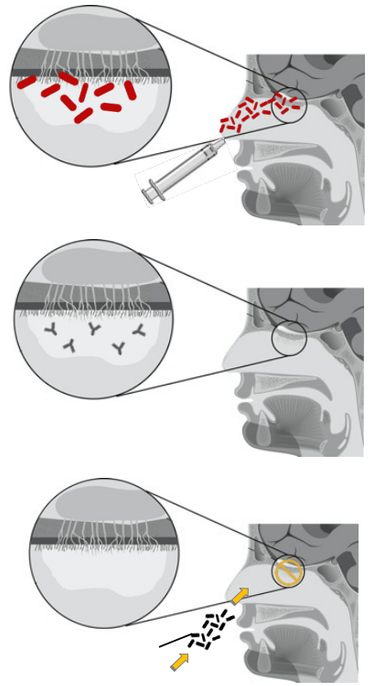
PT—Pertussis Toxin
Mutations create enzymatically inactive PT

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 is interrupted at mucosal barrier

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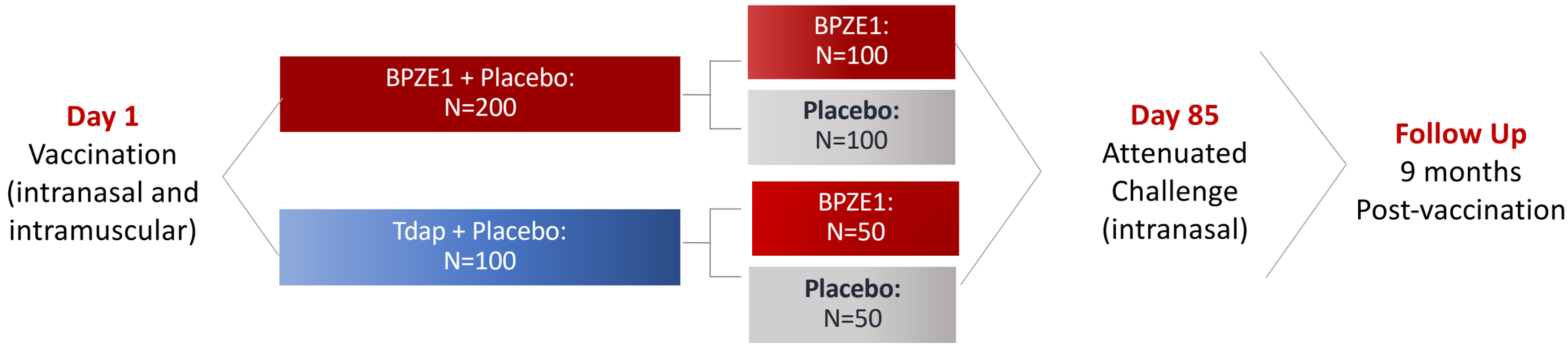
BPZE1 Adult Ph2b Study Design

- Phase 2b study was a multicenter, double-blind randomized study enrolled 300 healthy adult volunteers (18-50 years)
- First 48 subjects were randomized to BPZE1 10^7 CFU or 10^9 CFU doses in safety lead-in cohort
  - No safety issues noted by safety monitoring committee in safety lead-in
- 10^9 CFU analysis set used for analysis of primary and secondary endpoints



Tdap = Boostrix™

Clinical Protocol Endpoints*

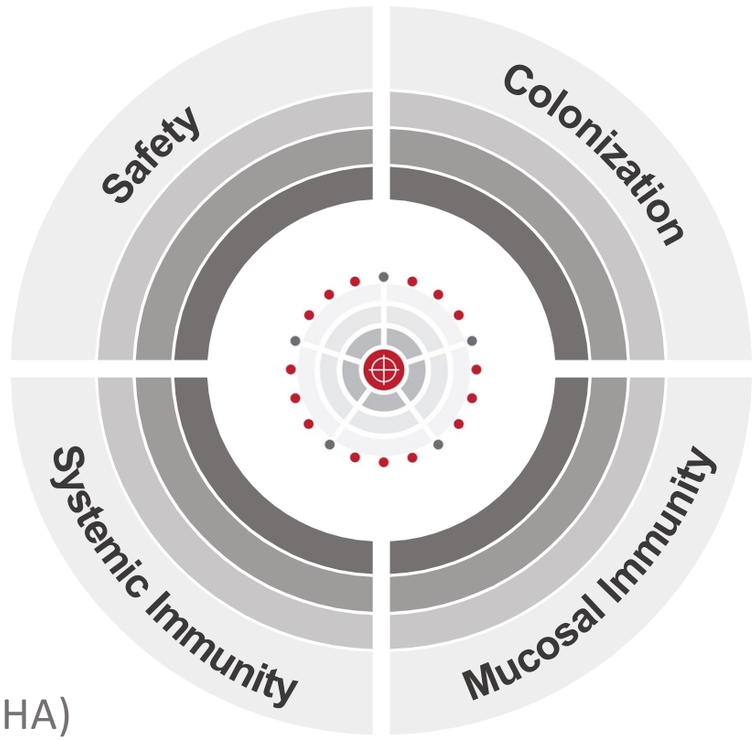
SAFETY

Reactogenicity (1°)

Safety Labs (cohort)

Vitals

Unsolicited AEs



COLONIZATION

Effect of BPZE1 Revaccination/Challenge

B. pertussis culture and colony counts

SYSTEMIC IMMUNITY

IgG Whole cell extract (WCE)

Individual IgG antigens (PT, PRN, FHA)

Individual IgA antigens (PT, PRN, FHA)

MUCOSAL IMMUNITY

IgA Whole cell extract (WCE) (1°)

Individual IgA antigens (PT, PRN, FHA)

*Descriptive only, no adjustments for multiplicity

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

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Safety

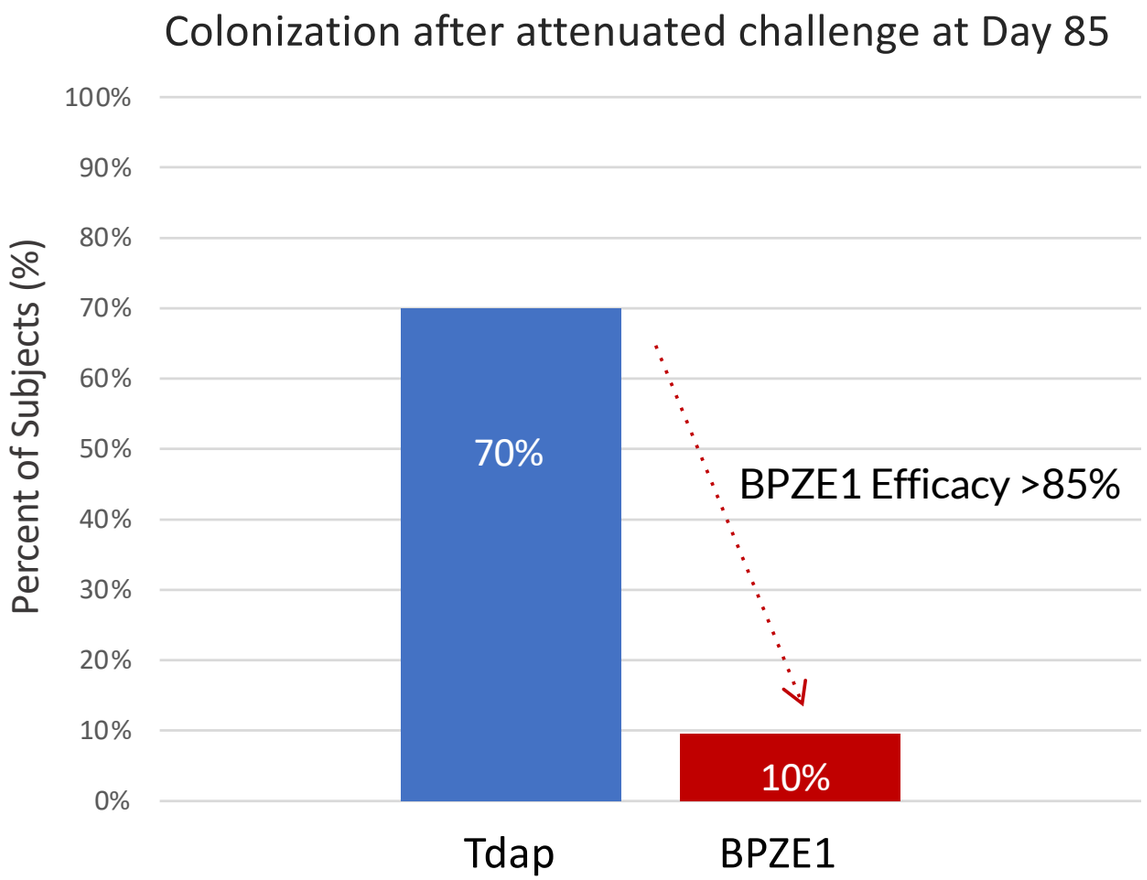
- BPZE1 vaccination was well tolerated
- Reactogenicity (nasal/respiratory and systemic) during 7 days after vaccination graded mainly as none to mild using the FDA toxicity scoring, with similar incidence and intensity to Tdap and placebo groups
- Majority of vaccination-related events were respiratory with similar incidence between treatment groups (7.7% vs 6.3%, BPZE1 and Tdap, respectively, Days 1-84)
- No serious adverse events related to vaccination

Adverse Events (AEs), n (%)	Vaccination 1 (Days 1-84)		Vaccination 2 (Days 85-113)	
	BPZE1 (n=183)	Tdap (n=96)	BPZE1 (n=133)	Placebo (n=146)
Any treatment-emergent adverse events (TEAEs)	54 (29.5)	30 (31.3)	22 (16.5)	37 (25.3)
Vaccination-related TEAEs	21 (11.5)	11 (11.5)	5 (3.8)	12 (8.2)
Serious adverse events	3 (1.6)	0 (0)	0 (0)	1 (0.7)
Vaccination-related SAEs	0 (0)	0 (0)	0 (0)	0 (0)
AEs leading to study discontinuation	0 (0)	0 (0)	0 (0)	0 (0)
Death	0 (0)	0 (0)	0 (0)	0 (0)

*SAEs were bacterial sepsis and cellulitis of leg; post-procedural hemorrhage post-tonsillectomy; diabetic metabolic decompensation; all considered not related to study vaccine.

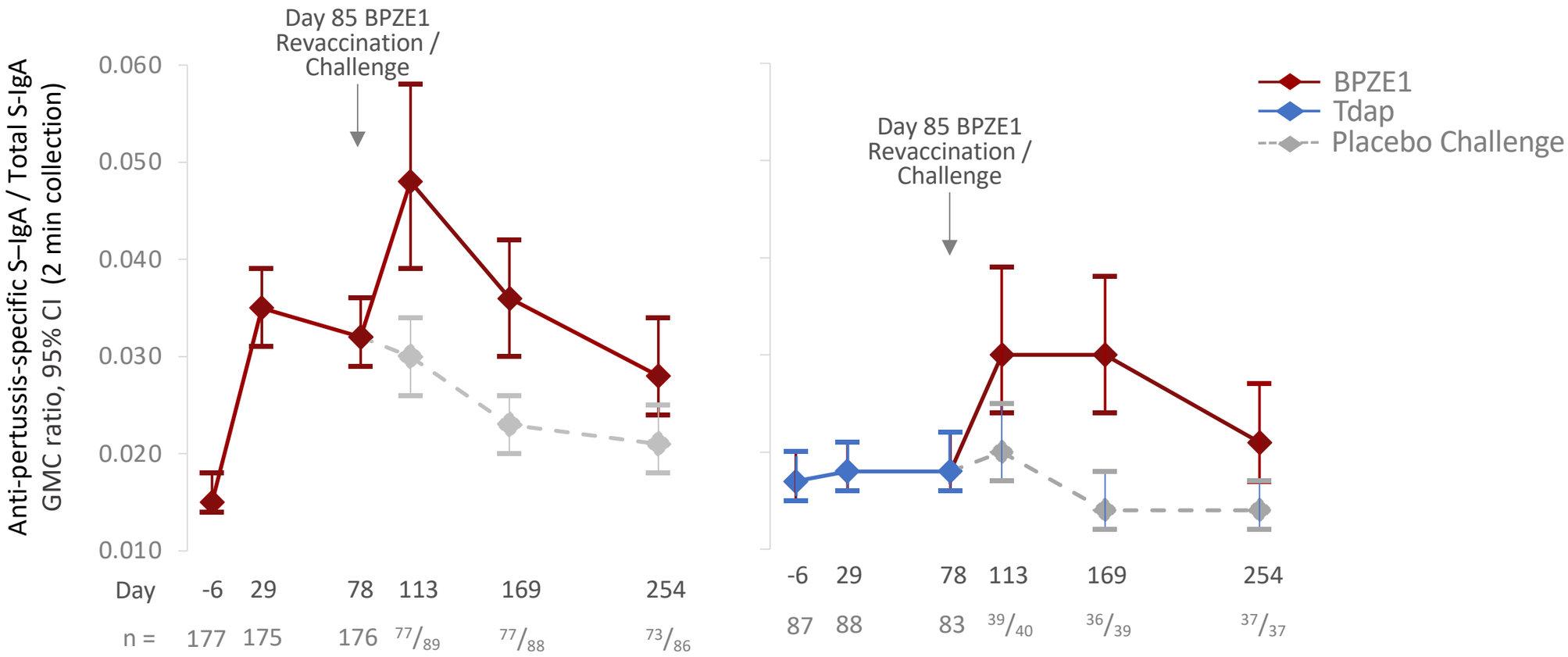
Colonization Rates

- BPZE1- and Tdap-primed subjects were challenged with attenuated *B. pertussis* (BPZE1) at Day 85
- BPZE1 vaccination demonstrated ability to prevent colonization in 90% of subjects
- Tdap provided minimal protection against attenuated *B. pertussis* challenge



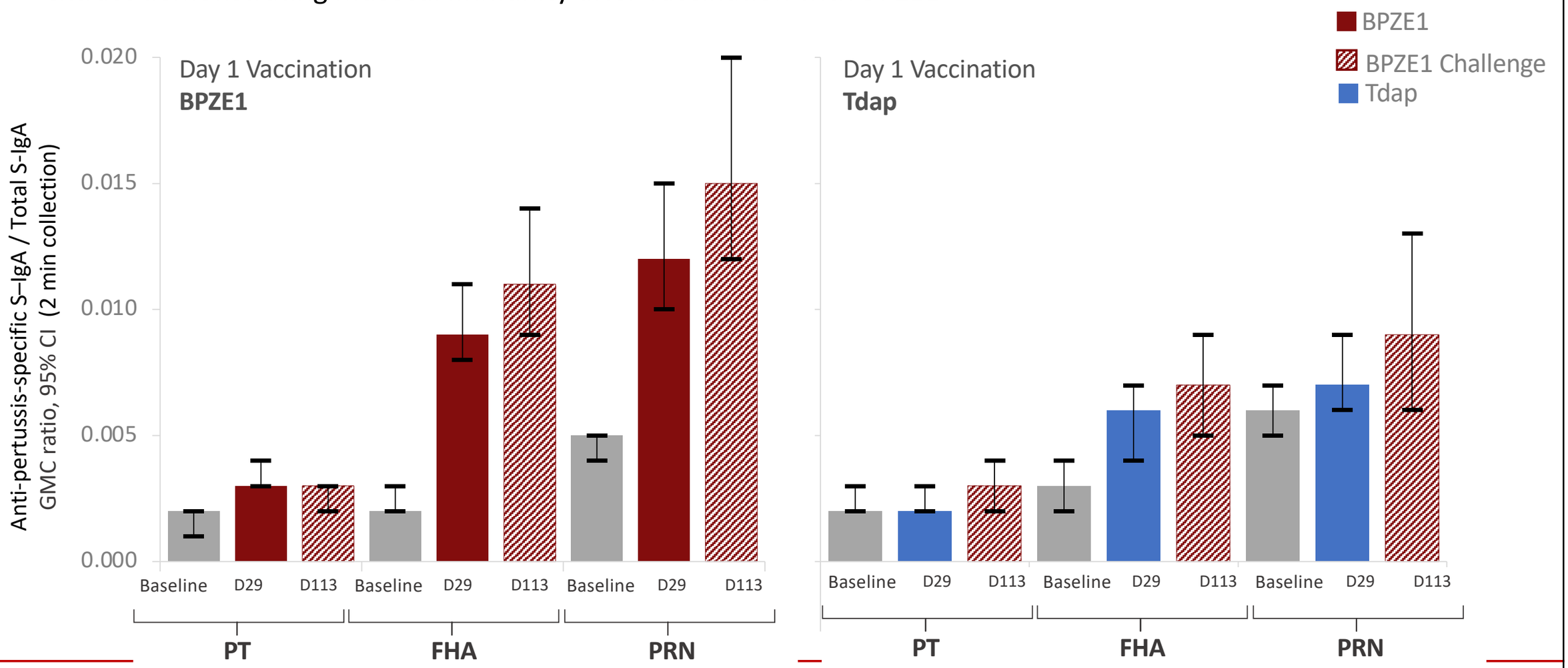
Mucosal S-IgA Pertussis Whole Cell Antibody Responses Over Time

- Mucosal immunity after vaccination with BPZE1 demonstrated, unlike in the Tdap group



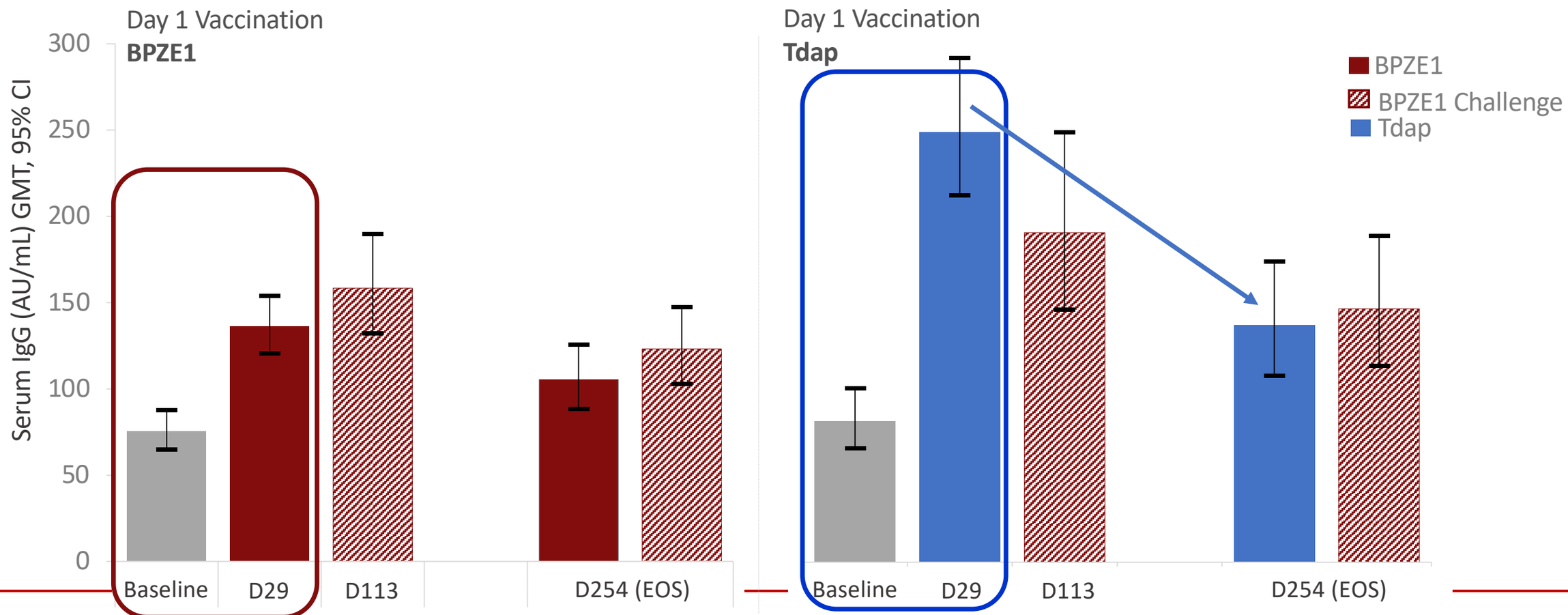
Mucosal S-IgA Pertussis Protein Antibody Responses

- Specific antigen responses against PT, FHA and PRN were consistent with the response seen using whole cell extract demonstrating mucosal immunity after vaccination with BPZE1



Serum IgG Pertussis Whole Cell Antibody Responses

- BPZE1 induced sustained systemic IgG immunity at 28 days following vaccination to end of study
- Tdap induced significantly greater serum antibody responses, although IgG levels rapidly decayed over 9 months



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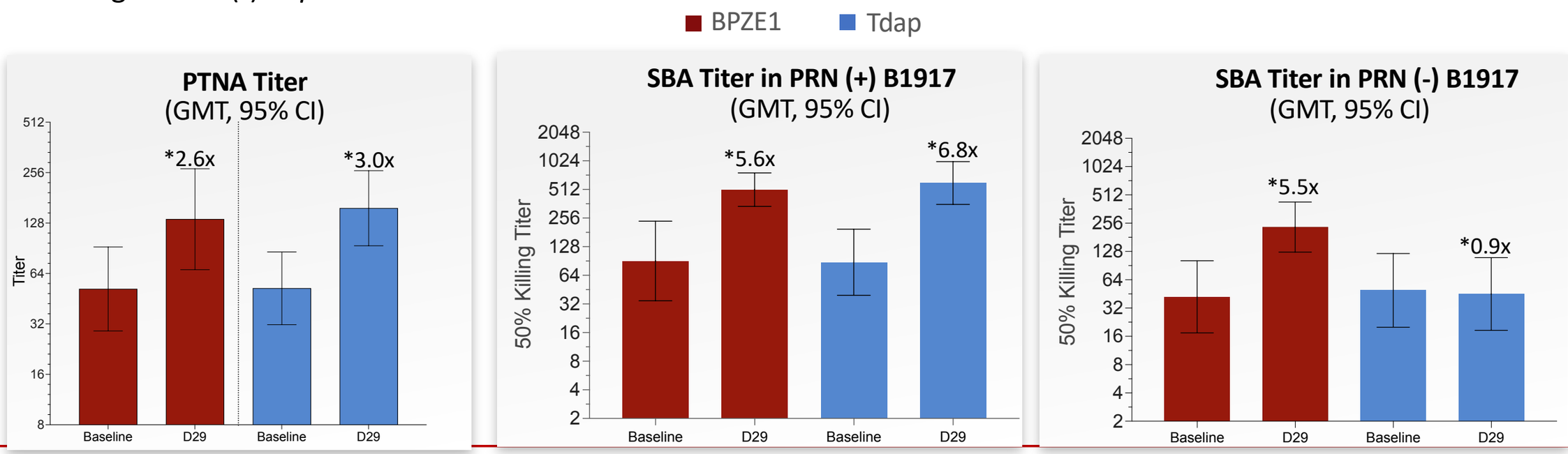
Functional Antibody Responses (post-hoc analysis)

- Methods for pertussis toxin neutralizing antibody (PTNA) and serum bactericidal activity (SBA) assays
  - Randomized convenience set from 2 of 4 treatment arms: BPZE1/BPZE1 (n=13) and Tdap/Placebo (n=17)
  - Laboratory personnel blinded to treatment assignment
- Results
  - BPZE1 and Tdap induces similar functional PTNA responses
  - BPZE1 and Tdap induces comparable SBA killing in PRN (+) *B. pertussis,* but only BPZE1, not Tdap, induces SBA killing in PRN (-) *B. pertussis*



*GMFR

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*GMFR over baseline

BPZE1 Adult Phase 2b Study Conclusions

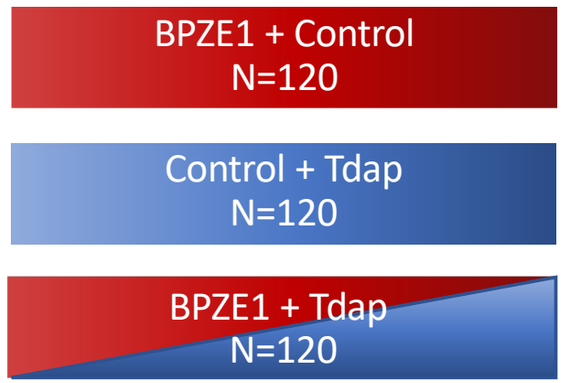
- BPZE1 vaccination was well tolerated, and no safety concerns were noted
- BPZE1 prevented colonization following attenuated challenge and induced sustained mucosal and serum immunity
  - In contrast, Tdap did not prevent colonization nor induce mucosal immunity; Tdap did induce systemic immunity as expected
- PTNA CHO assay showed comparable functional protection with BPZE1 and Tdap and SBA assay demonstrated similar 50% killing titers against PRN (+) *B. pertussis, although o*nly BPZE1 antibodies were bactericidal against PRN (-) *B. pertussis*
- BPZE1 may provide broader sustained protection against pertussis than currently achieved with acellular pertussis vaccines

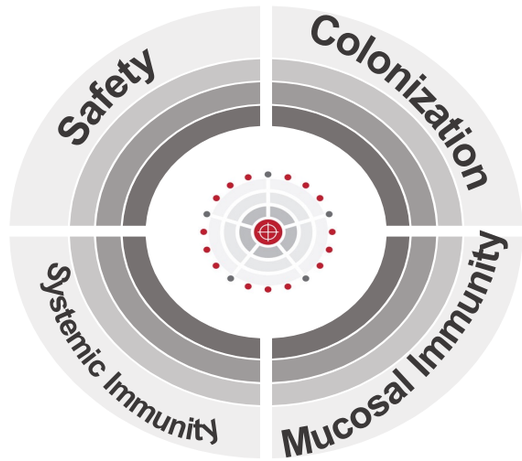
ONGOING

Phase 2b School Age Study Design (IB-201P)

- Study population is acellular-pertussis-vaccine-primed only (highest risk of breakthrough pertussis)
- Study population is 6-17 years of age, inclusive
  - Safety subgroup (n=45 of 11 to 17 years) reviewed by Safety Monitoring Committee
- Substudy includes up to 120 subjects receive open-label BPZE1 at Day 85 as attenuated challenge
- Safety follow-up for 6 months after Day 1 vaccination
- Study sites in UK, Australia and Costa Rica

Day 1
Vaccination
(intranasal and
intramuscular)





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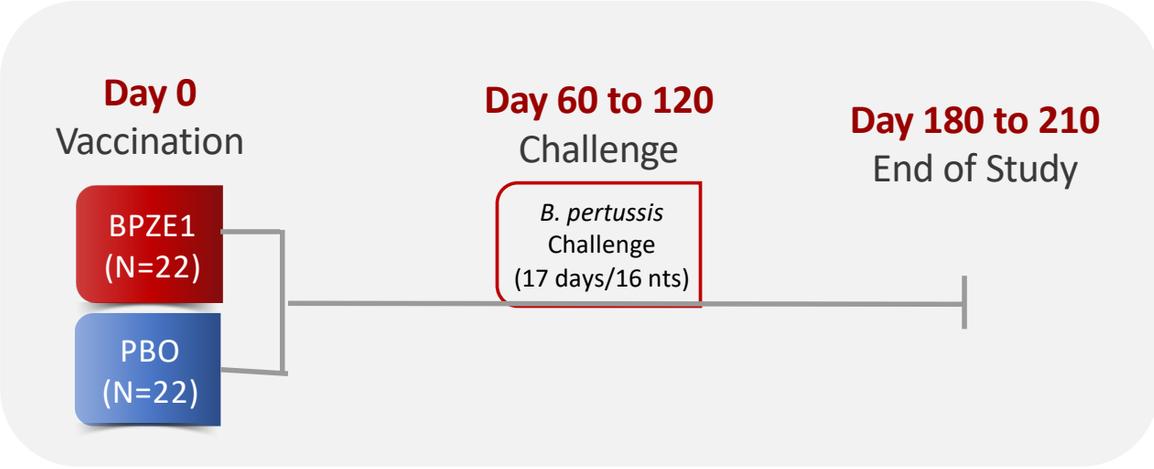
Phase 2b Virulent Challenge Study Design (IB-202P)

ONGOING

- Study population is 18-50 years of age
- Study vaccine administered on Day 0
- After 60 to 120 days, 17 days/16 nights in-unit stay after virulent challenge of wild-type *Bordetella pertussis* (strain B1917) administered
- Safety follow-up for 6 months after Day 1 vaccination or 3 months after challenge, whichever is longer
- Study sites in UK including University of Southampton where original model was developed



Primary endpoint: Proportion of subjects by treatment group (BPZE1 and placebo) colonized on any day (Challenge Day 9, 11 or 14) following virulent challenge as determined by culture
Secondary endpoints: GMFR mucosal S-IgA, serum IgA and IgG levels; safety of vaccine

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Thank you for your attention!

ILiAD Biotechnologies would like to thank the participants, investigators, study coordinators, and site staff for their participation in the BPZE1 clinical development program.