UNIVERSITY of MARYLAND
SCHOOL OF MEDICINE
CENTER FOR VACCINE DEVELOPMENT
AND GLOBAL HEALTH

Clinical Development of a Trivalent *Salmonella* Conjugate Vaccine (TSCV)

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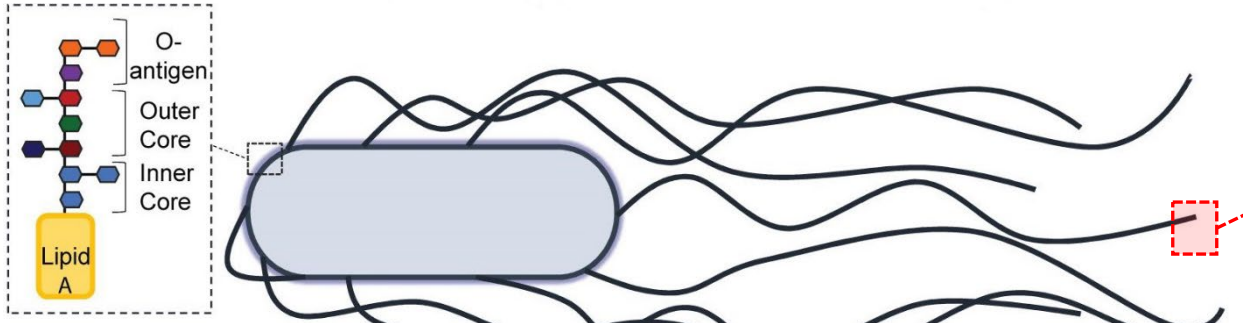
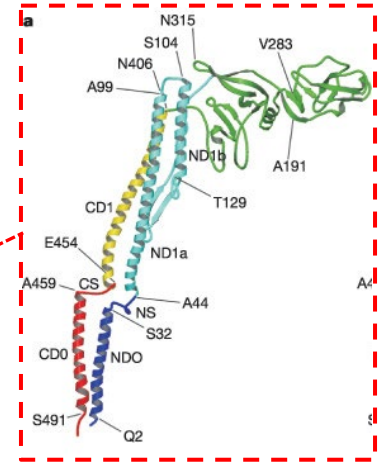
BHARAT BIOTECH
Lead Innovation

Trivalent *Salmonella* Conjugate Vaccine (TSCV) Components

- *S.* Typhimurium COPS-FliC conjugate
- *S.* Enteritidis COPS-FliC conjugate
- *S.* Typhi Vi-TT conjugate (Typbar-TCV)



Core and O-polysaccharides of LPS (COPS)



Flagellin monomer (FliC)

Phase 1 First-in-Human trial (Salmonella CVD 1000)

- Phase 1, adaptive, 3 dose-escalating cohorts & confirmatory cohort

Cohort	Vaccine	Dose of each COPS and of Vi (µg)	No. Subjects	Dose #1	Dose #2	Vaccination Days
A (Step 1)	Trivalent Placebo	6.25 0	8 2	Vaccine Placebo	- -	1
B (Step 2)	Trivalent Placebo	12.5 0	10 2	Vaccine Placebo	- -	1
C (Step 3)	Trivalent Placebo	25 0	12 2	Vaccine Placebo	- -	1
D (*Expanded, confirmatory cohort*)	Trivalent Trivalent Placebo	(*highest, well-tolerated dose among cohorts A-C*)	25 25 10	Vaccine Vaccine Placebo	Vaccine Placebo Placebo	1 & 29* 1 & (29)* 1 & (29)*
		Total	N = 96			

N=22 enrolled

Interrupted by COVID-19 Pandemic

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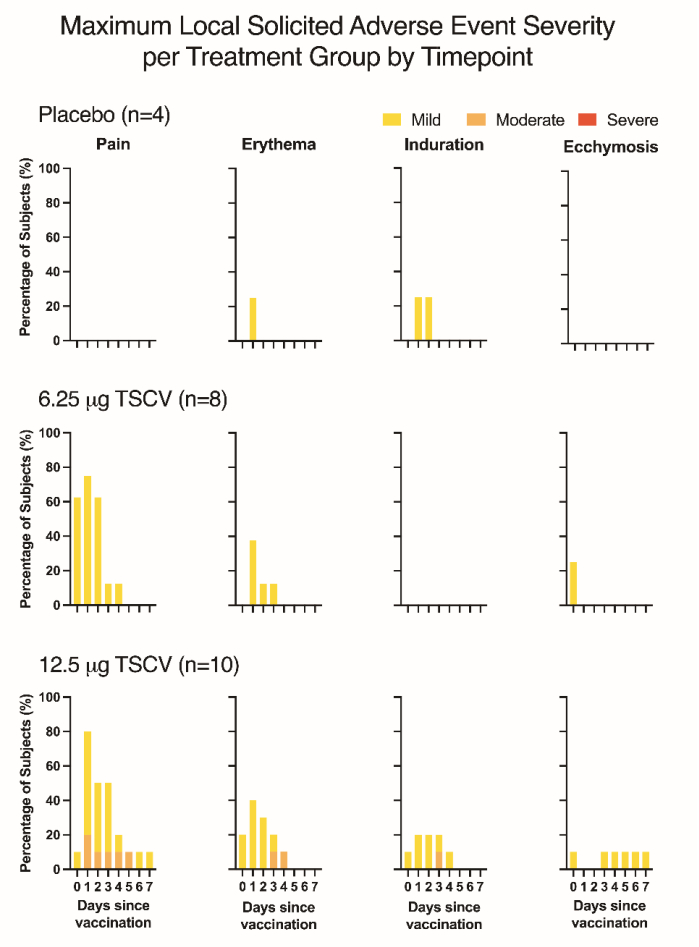
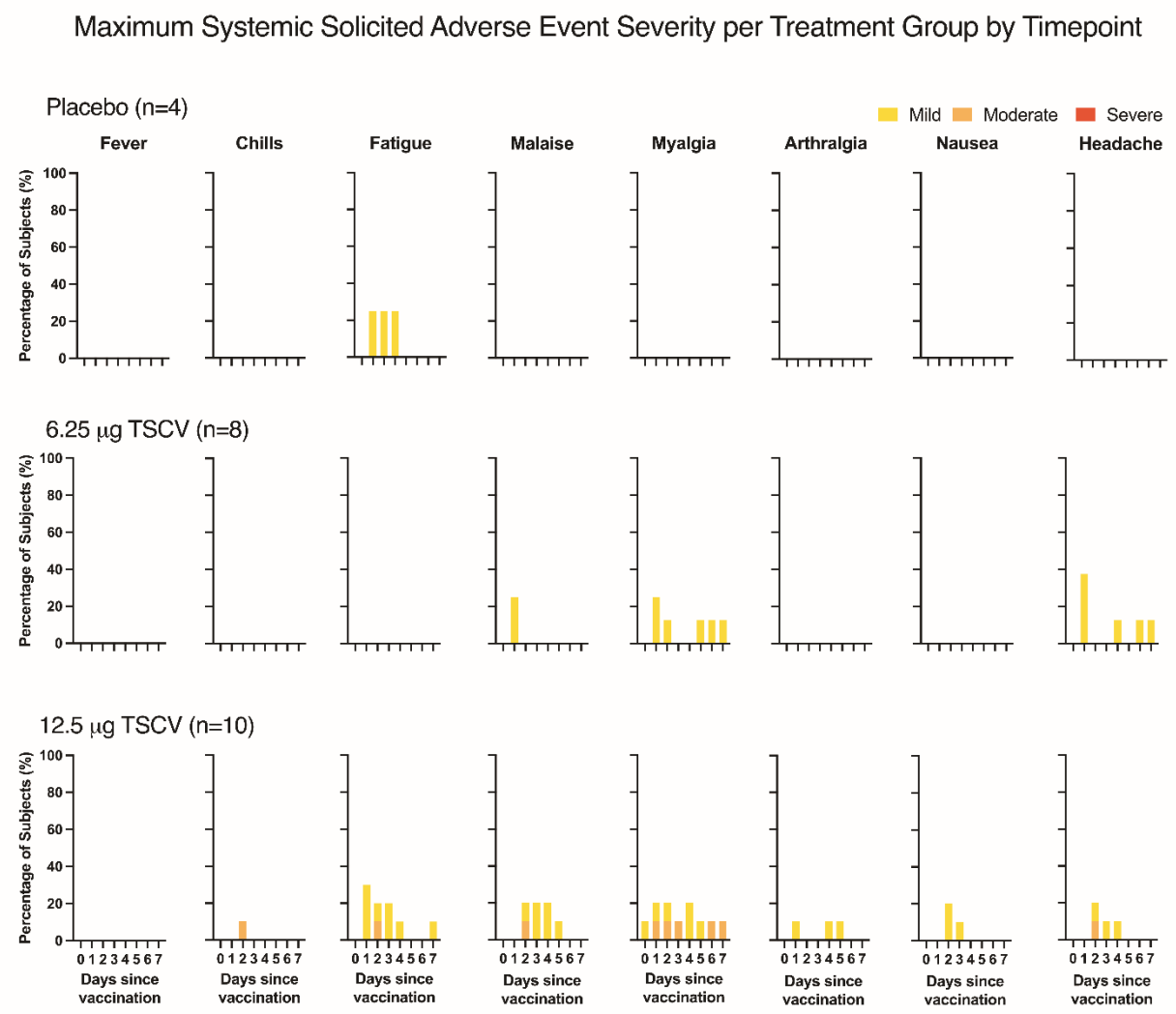
Phase 1 FIH: No Safety Concerns



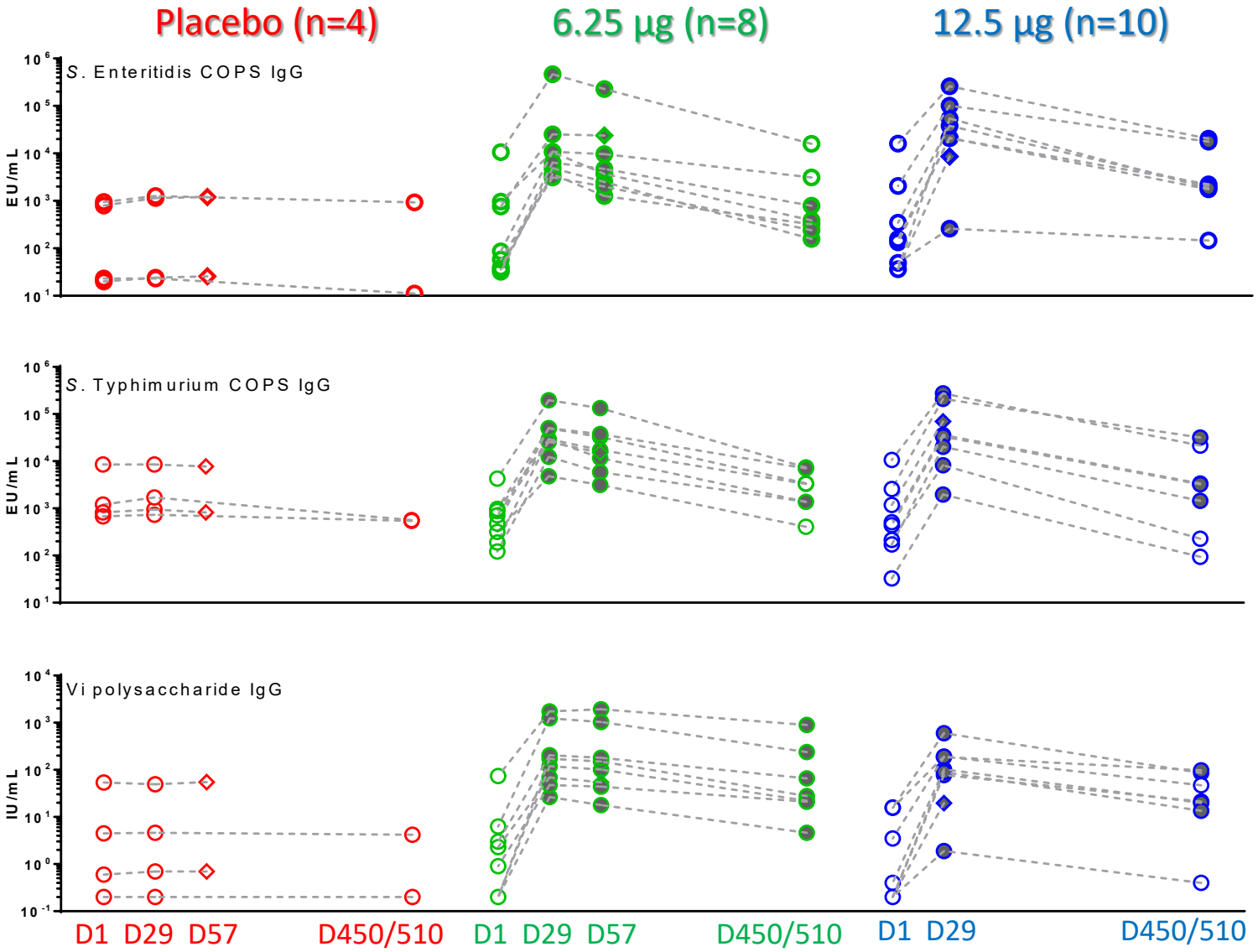


Phase 1 FIH: serum ELISA IgG

<u>100% seroconversions</u>† for all 3 primary aim antigens:

- SE COPS
- ST COPS
- Vi PS

† 4-fold or greater increase in titer, compared to baseline



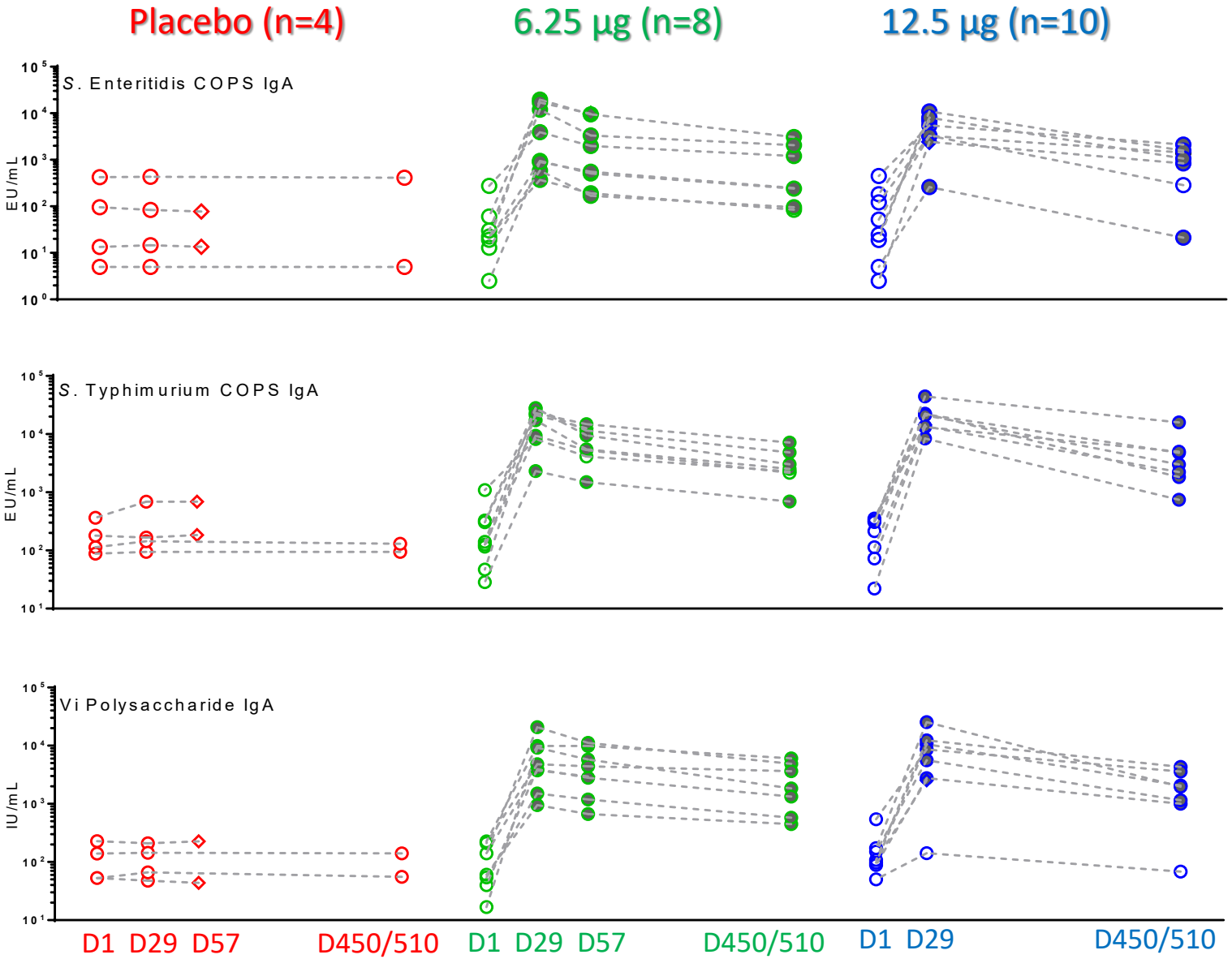
Due to the pandemic, the duration of antibody response was documented as elevated ≥4-fold-rise from baseline at **Day 450/510**!

Phase 1 FIH: serum ELISA IgA

<u>100% seroconversions†</u> for all 3 primary aim antigens:

- SE COPS
- ST COPS
- Vi PS

† 4-fold or greater increase in titer, compared to baseline



Phase 1/2a Bridging (Salmonella CVD 2000)

- Phase 1 Randomized, Blinded, Placebo-controlled trial
- “new” cGMP lots of TSCV

Group	No. Subjects	Study Product	*S.* Enteritidis (µg)	*S.* Typhimurium (µg)	*S.* Typhi Vi (µg)
A	25	**Full**-strength formulation TSCV	25	25	25
B	25	**Half**-strength formulation TSCV	12.5	12.5	25
C	15	Dilutional **half**-strength TSCV*	12.5	12.5	12.5
D	15	Placebo	0	0	0

*formulation which bridges to First-in-Human Phase 1

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康龙化成 PHARMARON

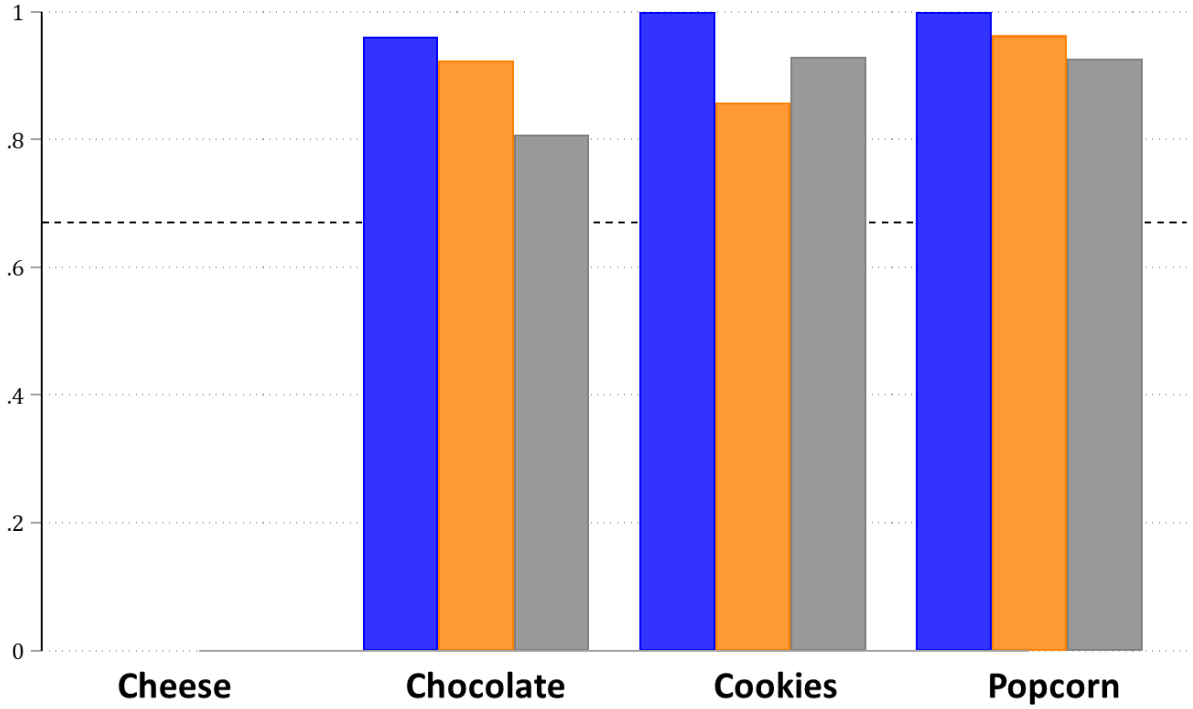
Phase 1/2a Bridging: Safety

(remains blinded)

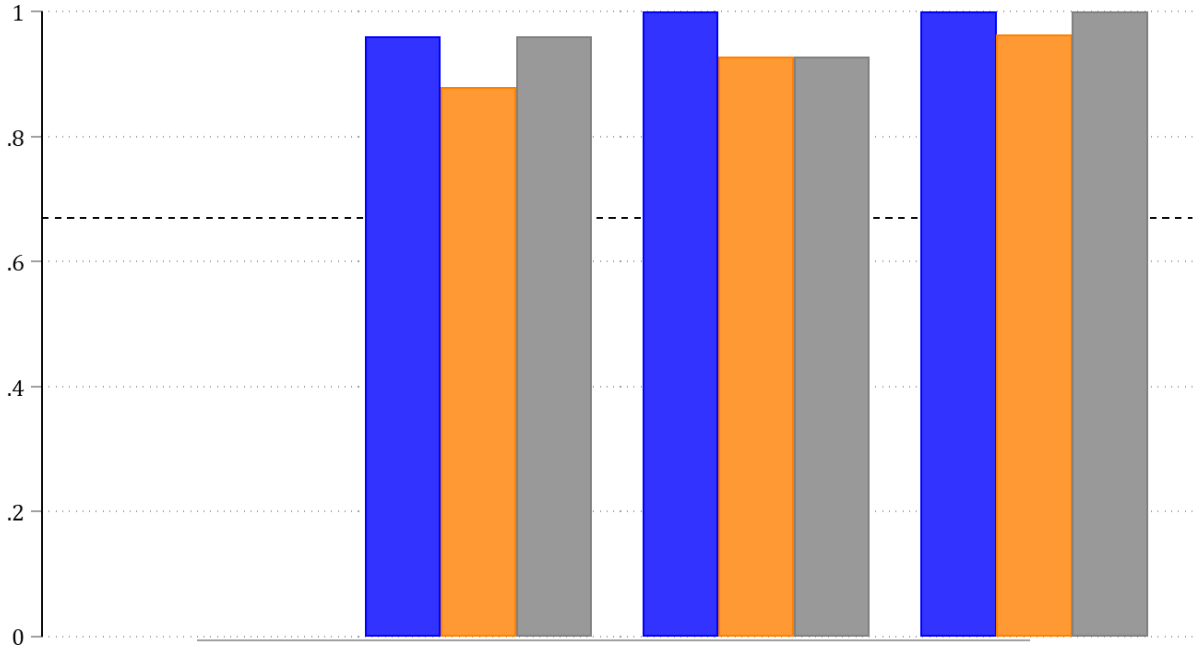
- Fully enrolled (n=80 evaluable) and all study visits completed
- No SAEs
- No halting rules
- No safety concerns

Phase 1/2a Bridging: Immunogenicity

7-days post-vaccination



28-days post-vaccination



	Cheese	Chocolate	Cookies	Popcorn
GMT	351	25,293	15,714	41,516
GMT	334	17,847	12,787	25,657
GMT	1.55	130	127	165

Proportion of subjects per group who manifested ≥ 4-fold rises in antibody titer *S.* Enteritidis COPS, *S.* Typhimurium COPS, and *S.* Typhi Vi antigens

Phase 2 Age de-escalation (Salmonella CVD 3000)

PI: Mili Tapia

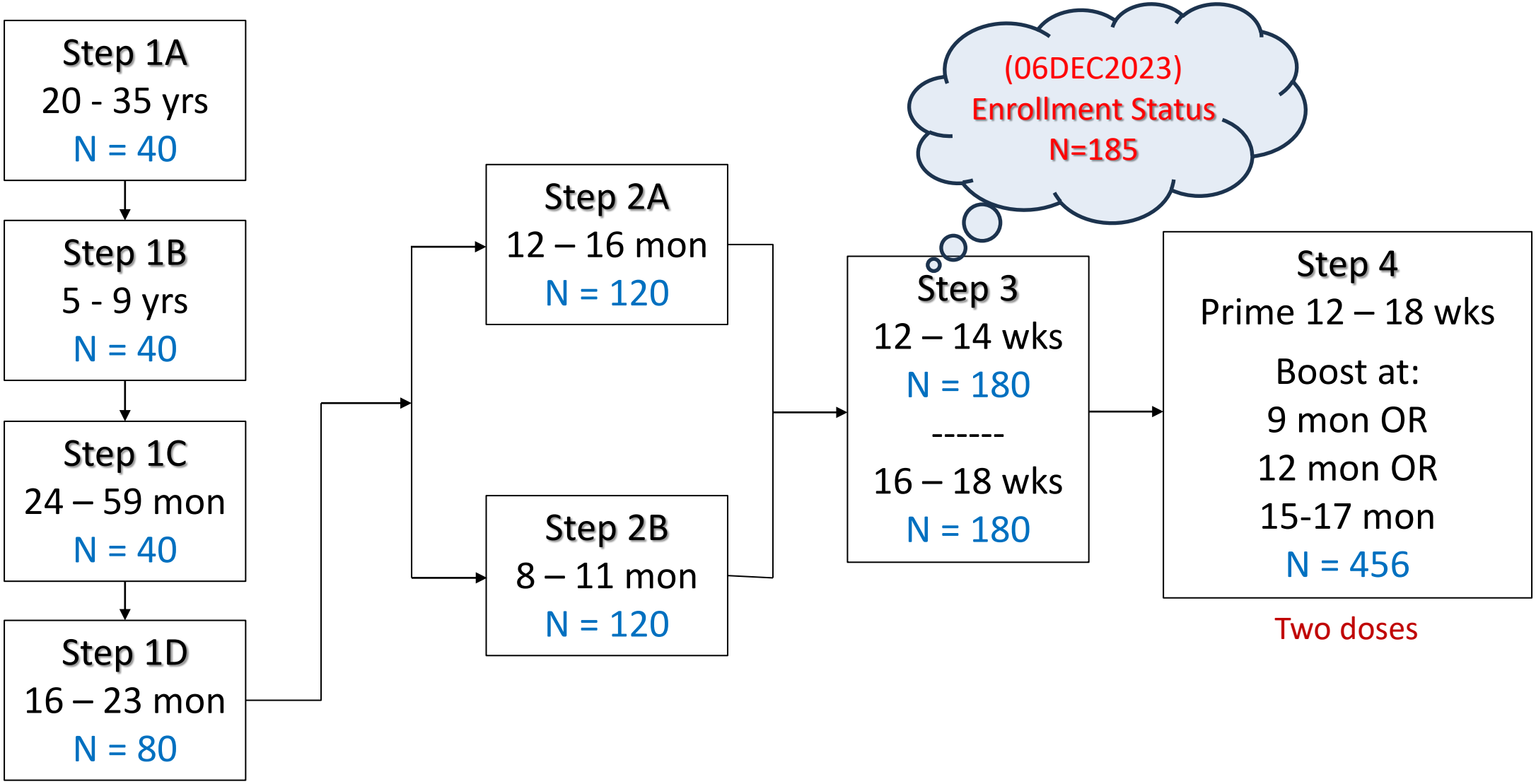
Sites:

- Centre pour le Développement des Vaccins du Mali (CVD-Mali), Bamako, Mali
- Centro de Investigaçao em Saude (CISM), Manhiça, Mozambique
- Kenya Medical Research Institute Center for Global Health (KEMRI-CGH), Kisumu, Kenya

Participation Duration:

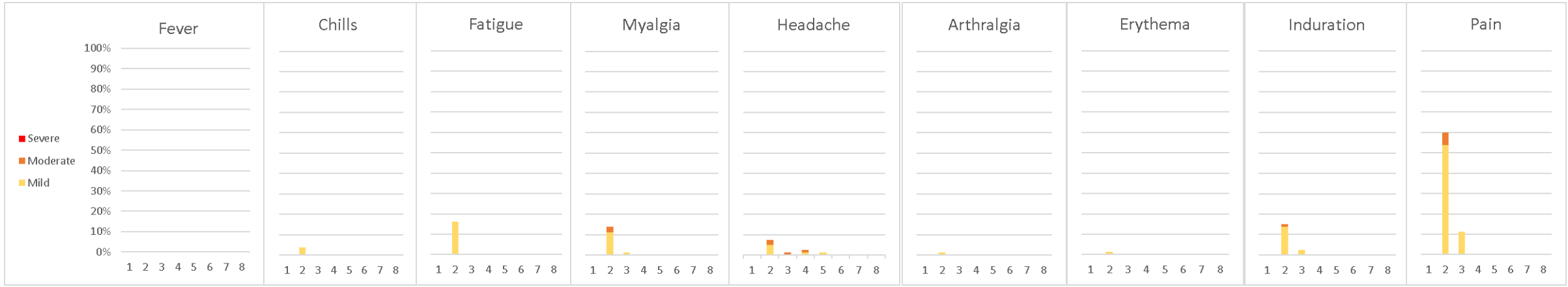
For Steps 1-3, ~6 months
For Step 4, ~12 months to 18 months

Phase 2 Age-de-escalation (Salmonella CVD 3000)

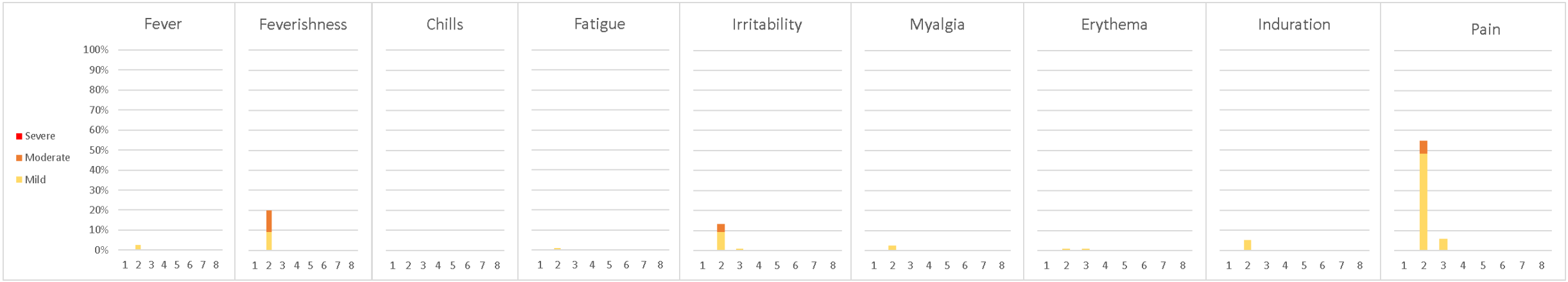


Phase 2: Blinded Safety Results

Step 1A (20-25 yrs) and Step 1B (5-9 yrs)



Step 1C (24-59 mons) and Step 1D (16-23 mons)



Acknowledgments

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  - Pharmaron (Drs. Al-Ibrahim and Beckett)
  - Mili Tapia
  - CVD-Mali
  - CISM
  - KEMRI-CGH
  - Likak Research
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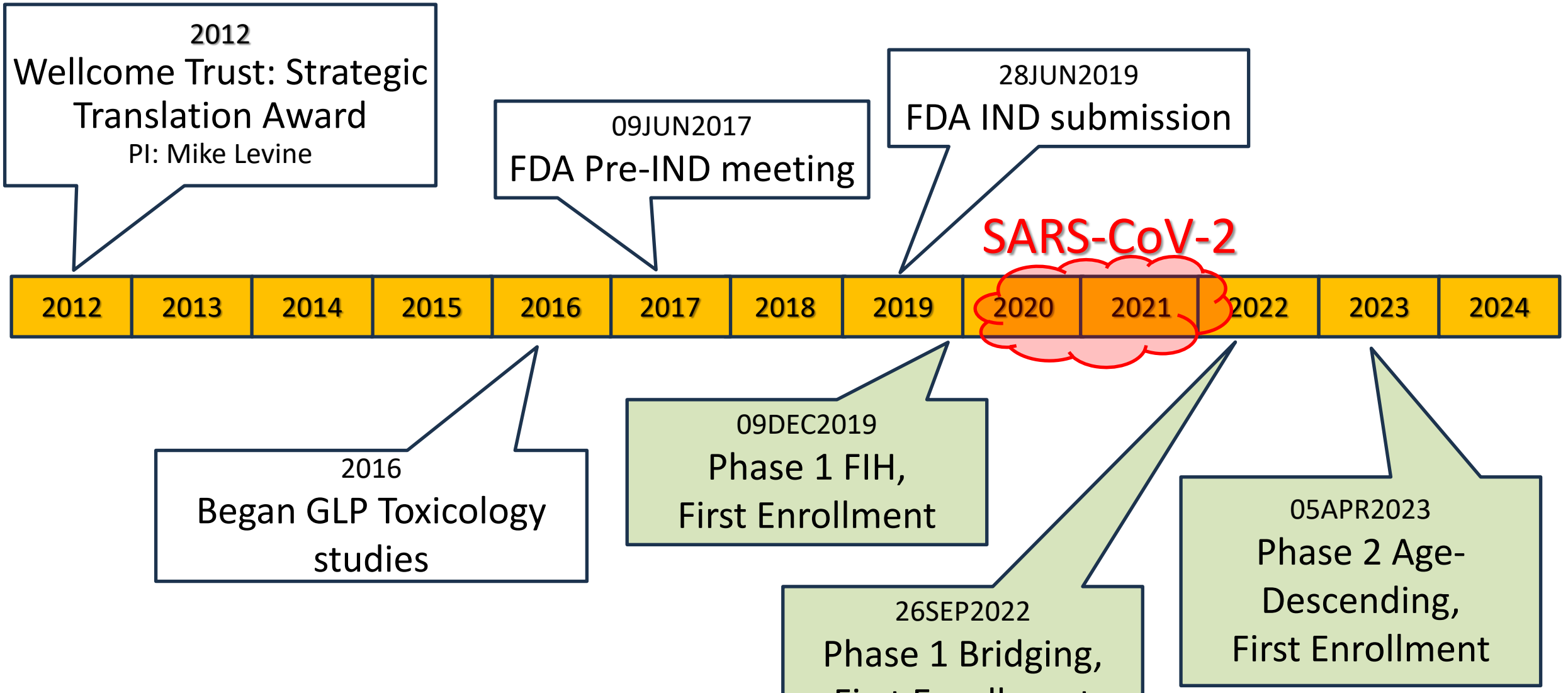
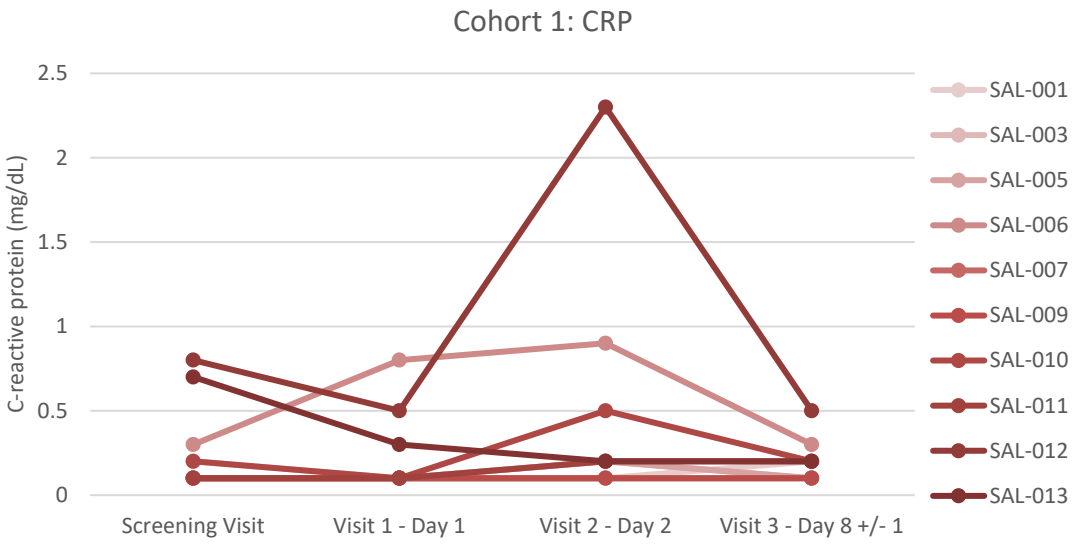
  - Marcelo Sztein Lab
  - Aly Kwon, Fleesie Hubbard
  - Khristine Bozylinski-Bulos, Lynnee Roane
- ❖ Supported by NIAID and Wellcome Trust

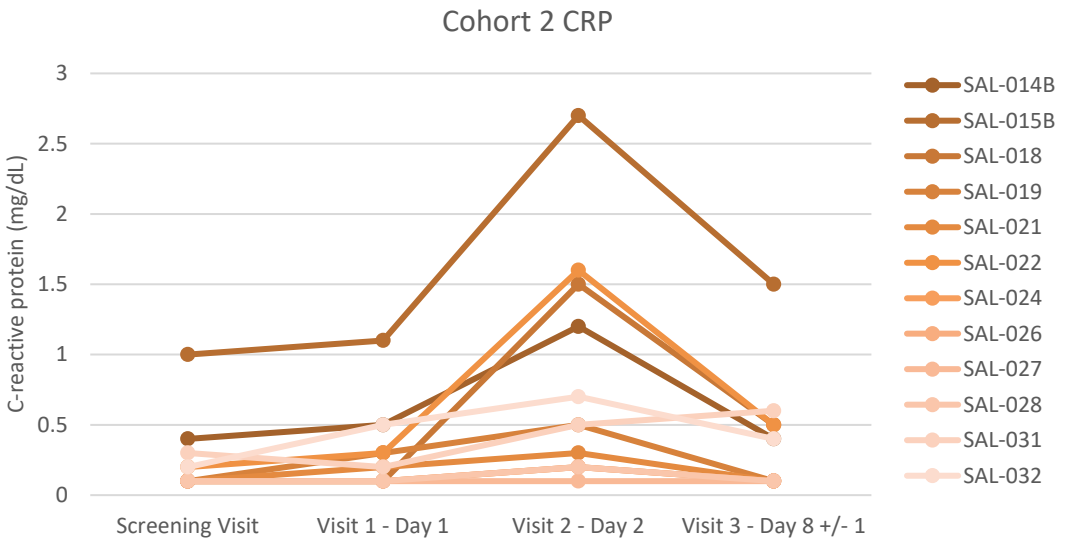
Back-up Slides

Timeline of TSCV



Phase 1 FIH: C-Reactive Protein



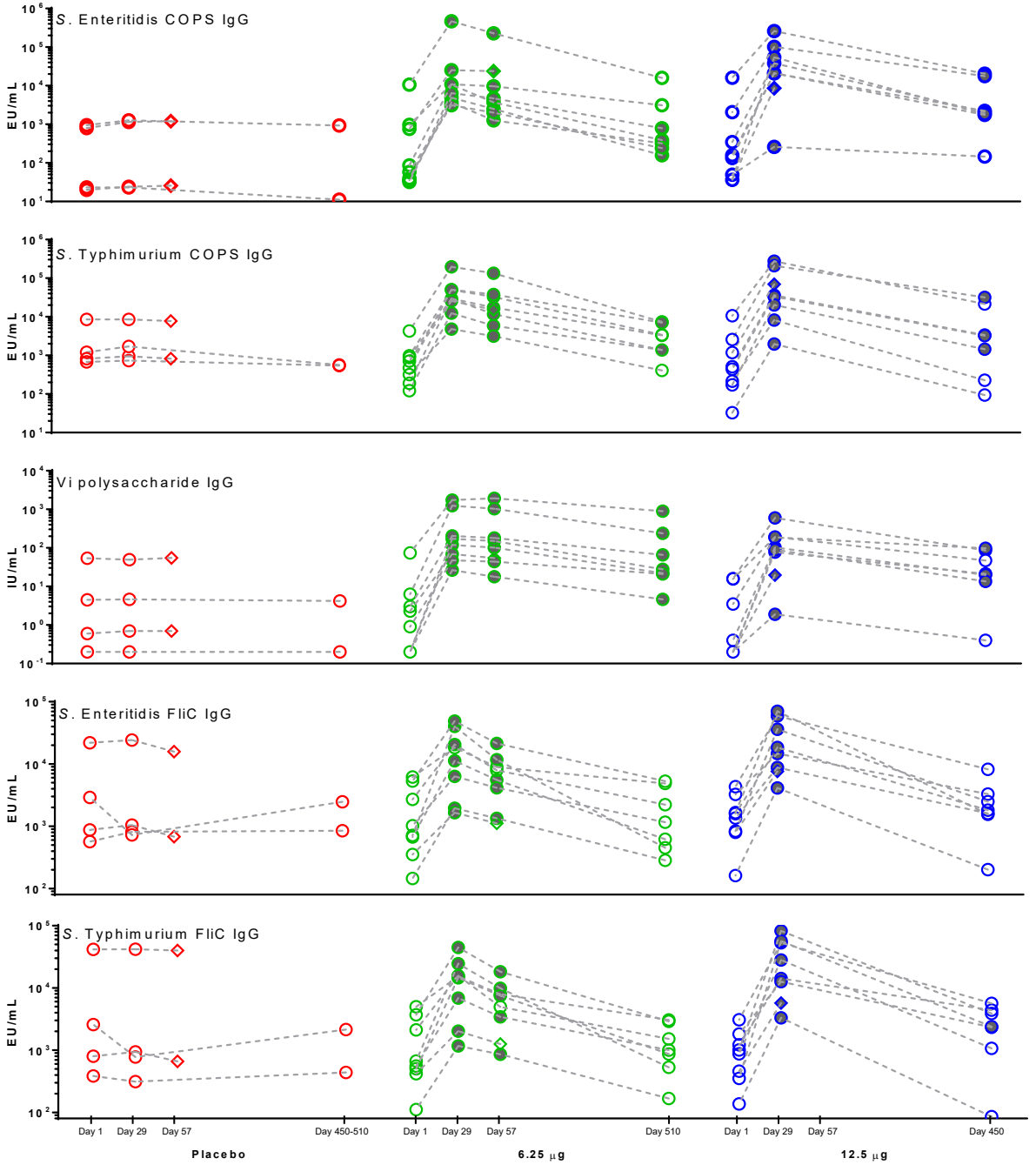


Phase 1 FIH: serum ELISA IgG

100% seroconversions† for all 5 antigens:

- SE COPS
- ST COPS
- Vi PS
- SE FliC
- ST FliC

† 4-fold or greater increase in titer, compared to baseline

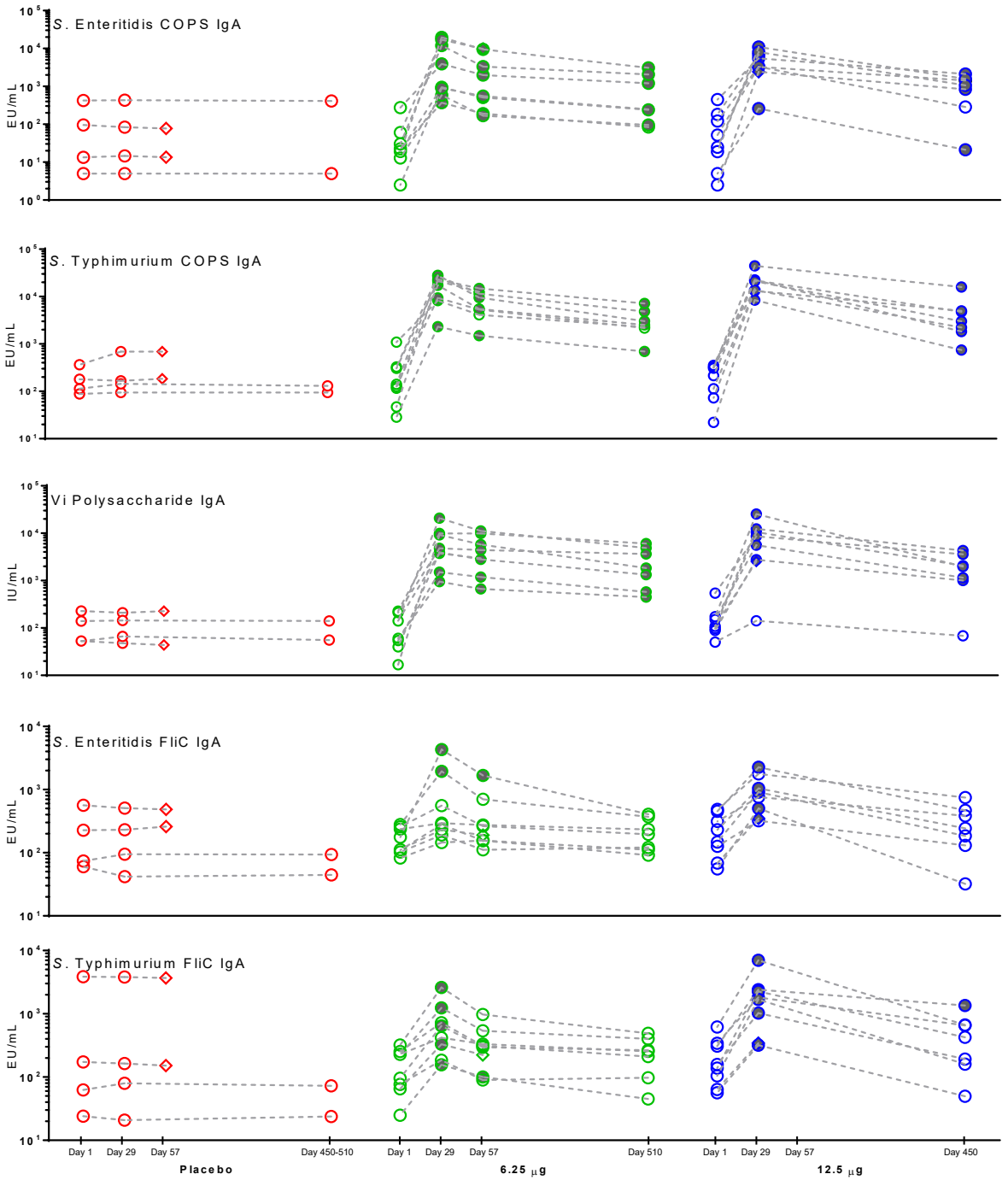


Phase 1 FIH: serum ELISA IgA

100% seroconversions† for 3 antigens:

- SE COPS
- ST COPS
- Vi PS

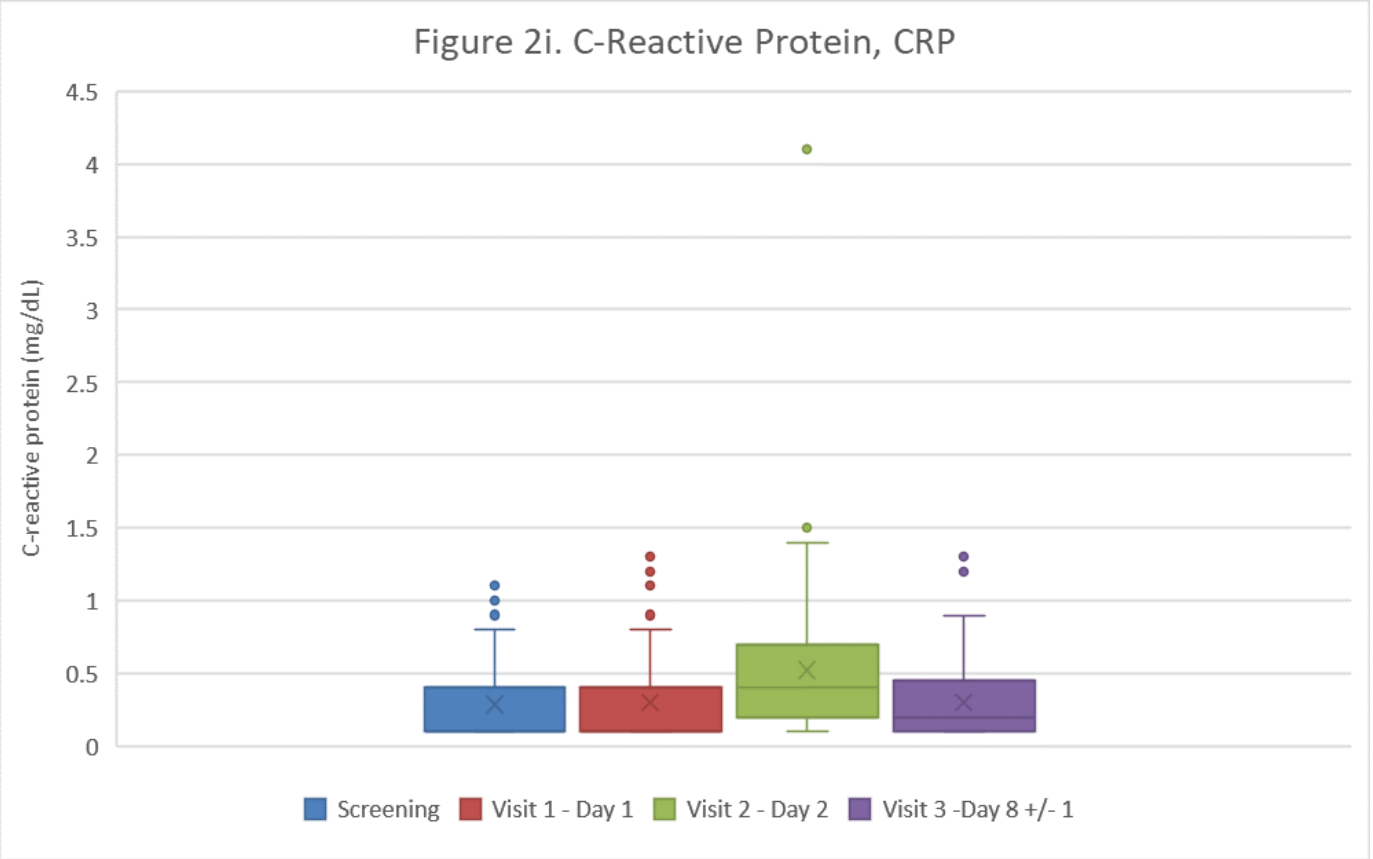
† 4-fold or greater increase in titer, compared to baseline



Phase 1/2a Bridging: Safety

(remains blinded)

- No SAEs
- No halting rules
- No safety concerns



Phase 2: Demographics for Steps 1A to 2B

- Cohort 1A - 05APR2023
- Cohort 1B - 29APR2023
- Cohort 1C – 23MAY2023
- Cohort 1D - 13JUNE2023
- Cohort 2A – 18JUL2023
- Cohort 2B – 07AUG2023

Total Enrolled	Cohort 1A 20-35 y	Cohort 1B 5-9 y	Cohort 1C 24-59m	Cohort 1D 16-23m	Cohort 2A 12-16m	Cohort 2B 8-11m
N	40	40	40	80	120	120
Gender						
No. male (%)	19 (47.5%)	21 (52.5%)	18 (45%)	38 (47.5%)	76 (63.3%)	65 (54.2%)
Ethnicity						
Bambara	12 (30.0%)	13 (32.5%)	14 (35.0%)	38 (47.5%)	47 (39.2%)	38 (31.7%)
Mandika/Malinke	17 (42.5%)	14 (35.0%)	10 (25.0%)	22 (27.5%)	29 (24.2%)	43 (35.8%)
Fula/Peuhl	5 (12.5%)	5 (12.5%)	8 (20.0%)	7 (8.8%)	13 (10.8%)	13 (10.8%)
Sarahule/Sarakole	1 (2.5%)	3 (7.5%)	4 (10.0%)	2 (2.5%)	9 (7.5%)	5 (4.2%)
Other	5 (12.5%)	5 (12.5%)	4 (10.0%)	11 (13.7%)	22 (18.3%)	21 (17.5%)

Study Design – Safety Review