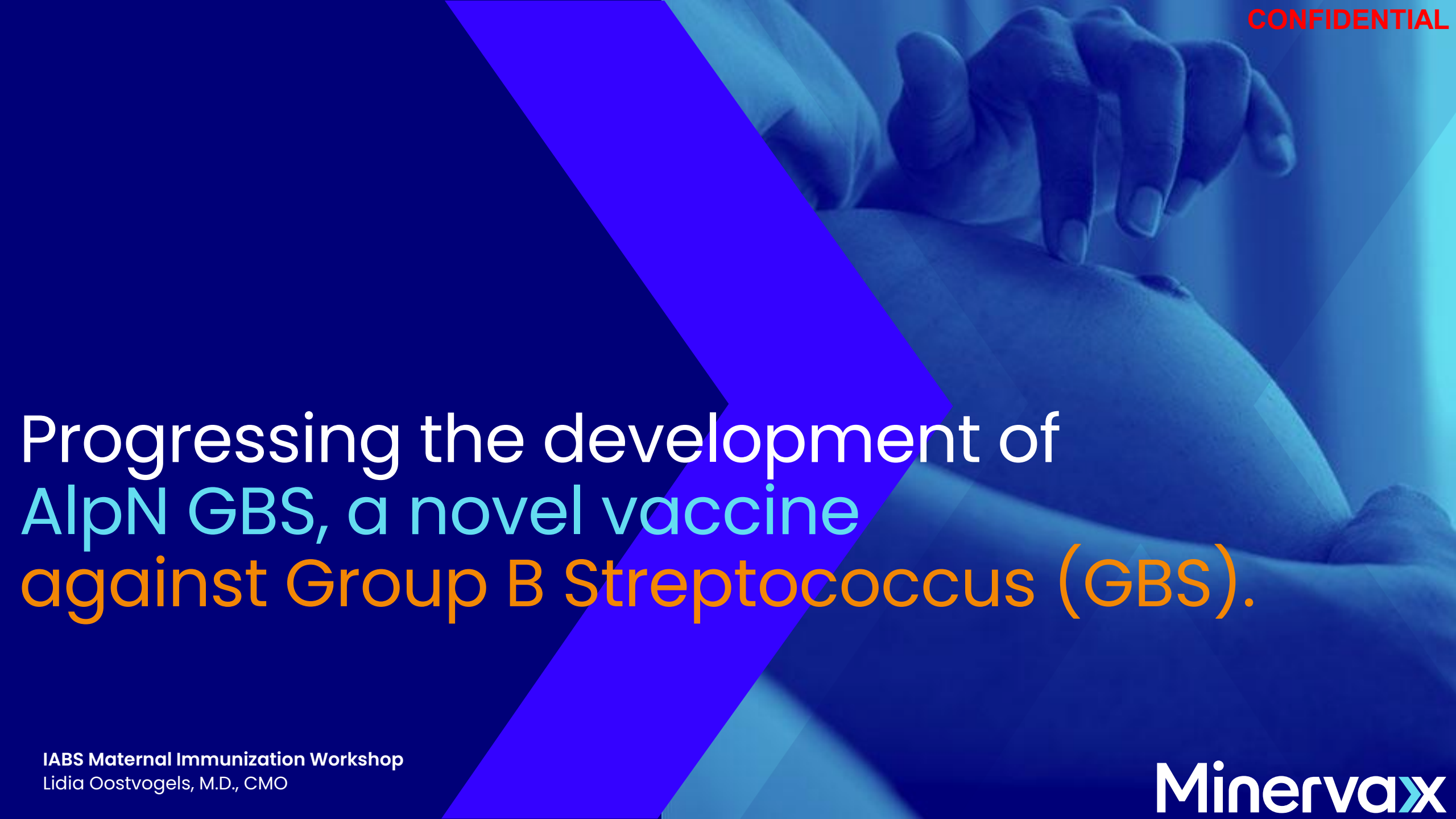

Progressing the development of AlpN GBS, a novel vaccine against Group B Streptococcus (GBS).

IABS Maternal Immunization Workshop
Lidia Oostvogels, M.D., CMO

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GBS is a WHO-Recognized Global Health Priority

Supported by International Health Organizations & Funders

Pregnant Women

Adverse pregnancy Outcomes such as Premature Births, Stillbirths & Maternal Invasive Disease

Newborn Babies

A Leading Threat to Newborn Health causing Pneumonia, Sepsis, Meningitis & Impaired Development

Older Adults

Affecting growing Older Adult population with Diabetes & Cardio-vascular Co-morbidities causing Sepsis & Death

WHO · Gavi The Vaccine Alliance · CDC · GOV.UK · Gates Foundation · EDCTP · European Investment Bank · AFRICA CDC Centres for Disease Control and Prevention Safeguarding Africa's Health

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GROUP B STREPTOCOCCUS (GBS)

Up to 25% of individuals have non-symptomatic colonisation of the gastrointestinal tract or urogenital tract

Group B streptococcus colonisation in pregnant persons can be responsible for:

- Adverse pregnancy outcomes
  - Stillbirths and pre-term births
- Neonatal infections during first three months of life
  - Sepsis, pneumonia, meningitis
  - Global incidence of 0.49 in 1,000 live births
  - 50% of neonatal infections and 80% of meningitis <2 months of age

319,000	0–3.5 million	90,000	57,000
Neonatal infections	Preterm births	Newborn deaths	Stillbirths

Madrid et al. Clin Infect Dis. 2017;65(suppl2):S160-S172. doi: 10.1093/cid/cix656; Prasad et al. Lancet Reg Health Am. 2025;47:101120. doi: 10.1016/j.lana.2025.101120; Seale et al. Clin Infect Dis. 2017;65(suppl2):S200-S219. doi: 10.1093/cid/cix664; Seale et al. Clin Infect Dis. 2017;65(suppl2):S125-S132. doi: 10.1093/cid/cix585;

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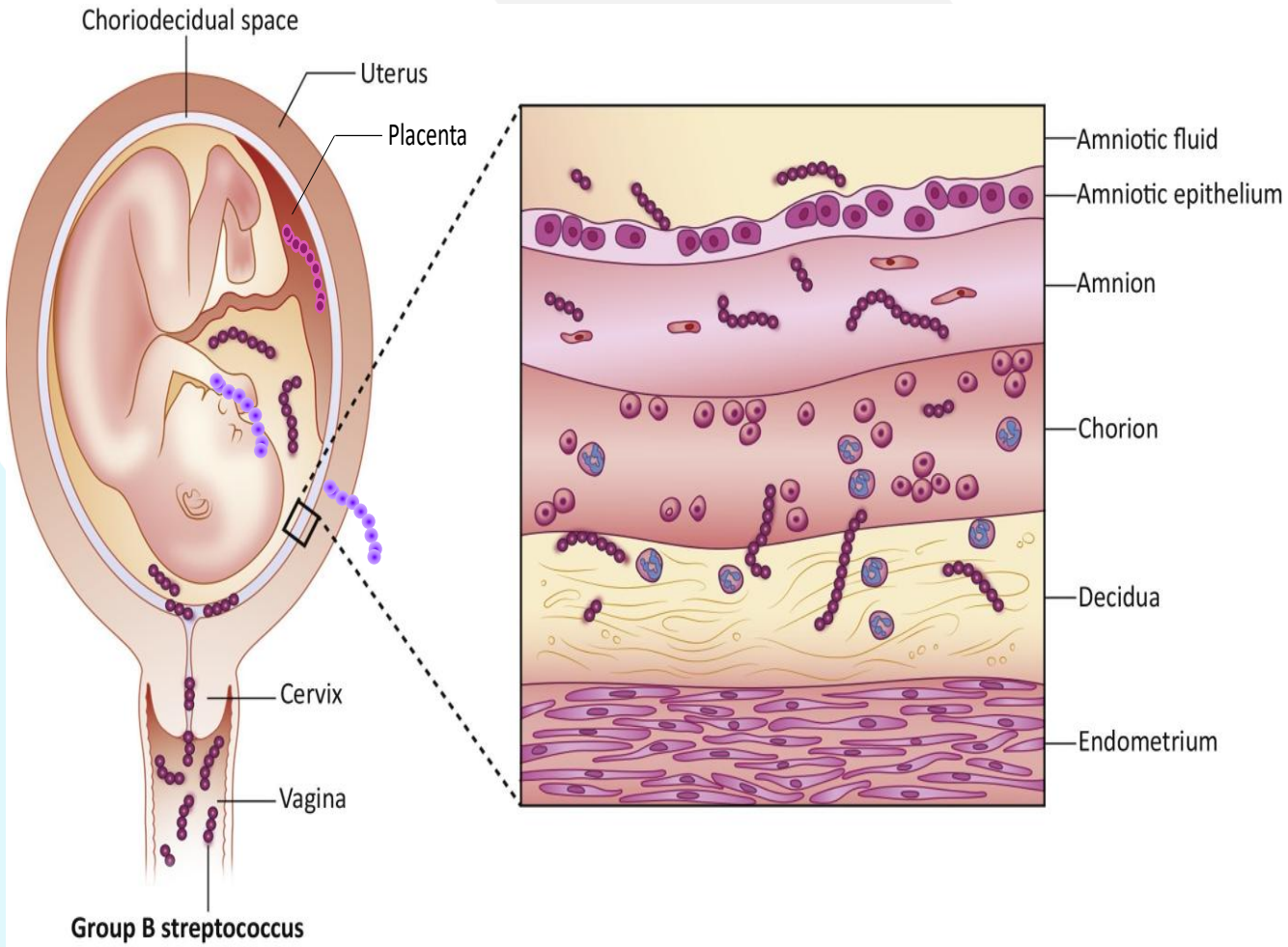
OUTCOMES OF ASCENDING GBS INFECTION

- Placental Colonization
  - Small for gestational age
- Chorioamnionitis
  - Preterm Delivery
- Foetal infection
  - Abortion
  - Stillbirth
  - Early Onset Neonatal Disease



Trends in Microbiology

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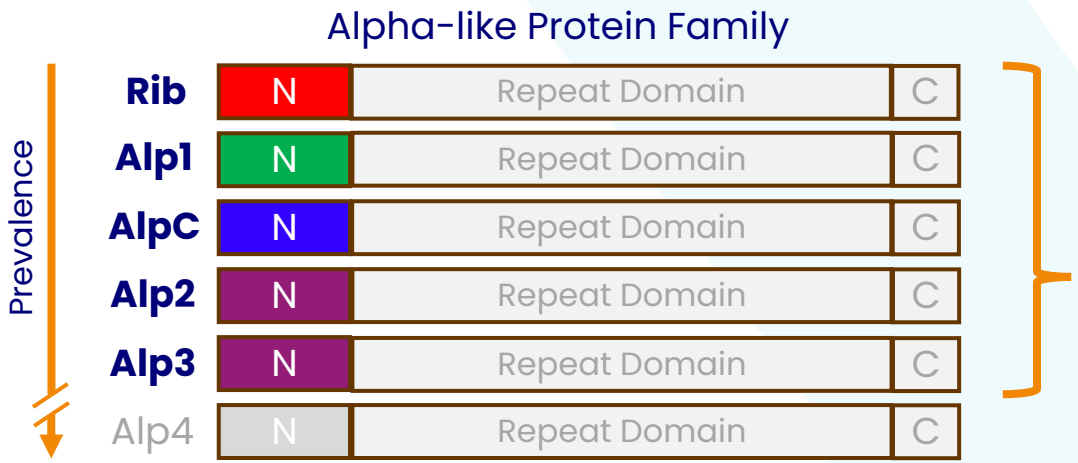
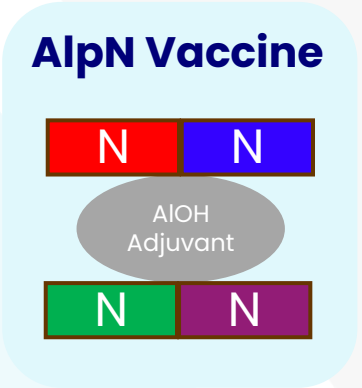
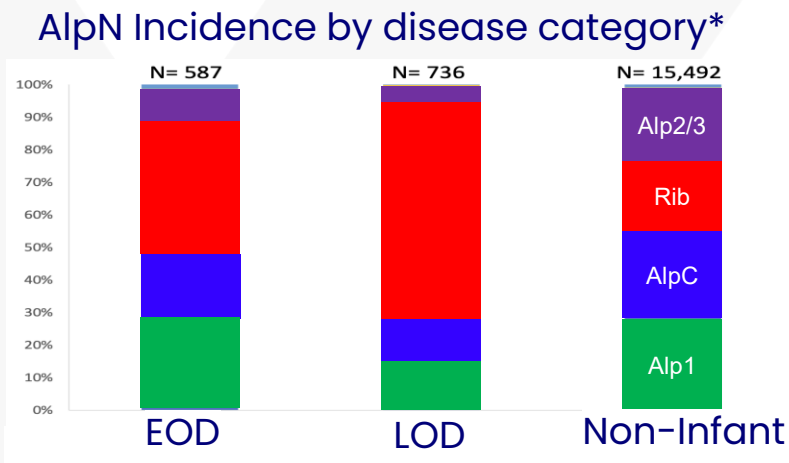
ALPN GBS IS PROTEIN-BASED VACCINE WITH 99% COVERAGE







Vaccine Target

- **N-terminal domain** of Alpha-like GBS surface protein family, AlpN
- Highly conserved, with **limited antigenic drift**

Vaccine Composition

- **Two fusion proteins**, GBS-NN and GBS-NN2
- Simple **manufacturing** at high yields in *E.coli.*
- AlOH adjuvant already used in Tdap for pregnant women

Functional Antibodies

- AlpN antibodies killing GBS via **opsono-phagocytosis**
- And **block entry** of GBS across epithelial cell barriers

Placental Transfer

- Induction of **IgG1** that are actively transported across placenta during pregnancy
- **Long half-life** of transferred antibodies protects newborn infants for 3 mths

*) US CDC data, ABC network

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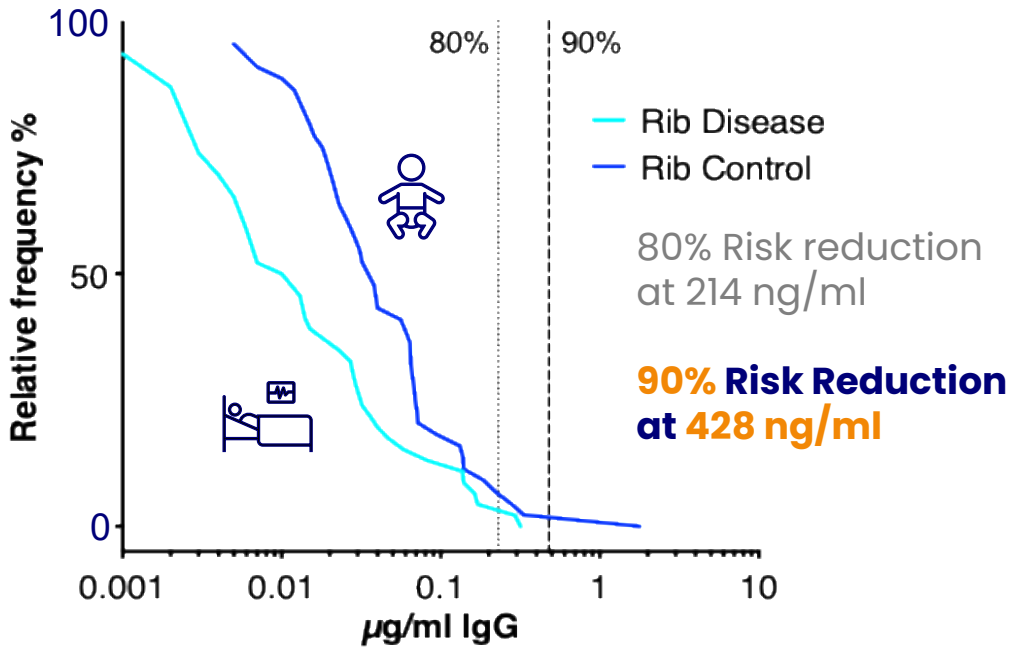
NATURAL ALPN ANTIBODIES CORRELATE WITH LOWER RISK OF INVASIVE NEONATAL GBS DISEASE

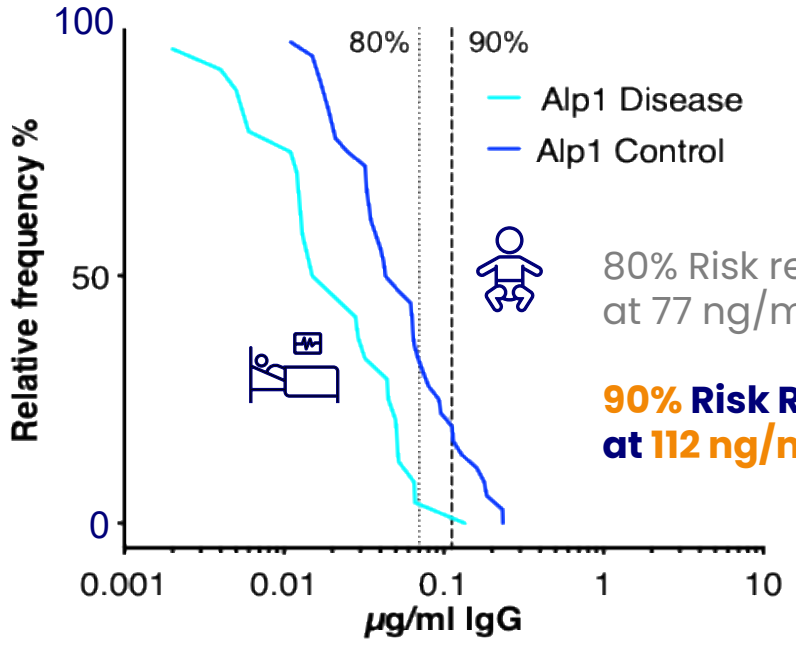
Anti-RibN Antibodies



80% Risk reduction at 214 ng/ml

90% Risk Reduction at 428 ng/ml

Anti-Alp1N Antibodies



80% Risk reduction at 77 ng/ml

90% Risk Reduction at 112 ng/ml

Paves the way for developing a validated **Surrogate Efficacy Marker (SEM)** from large-scale sero-epi studies which may be used for **Licensure**

* Dangor, et al. 2023

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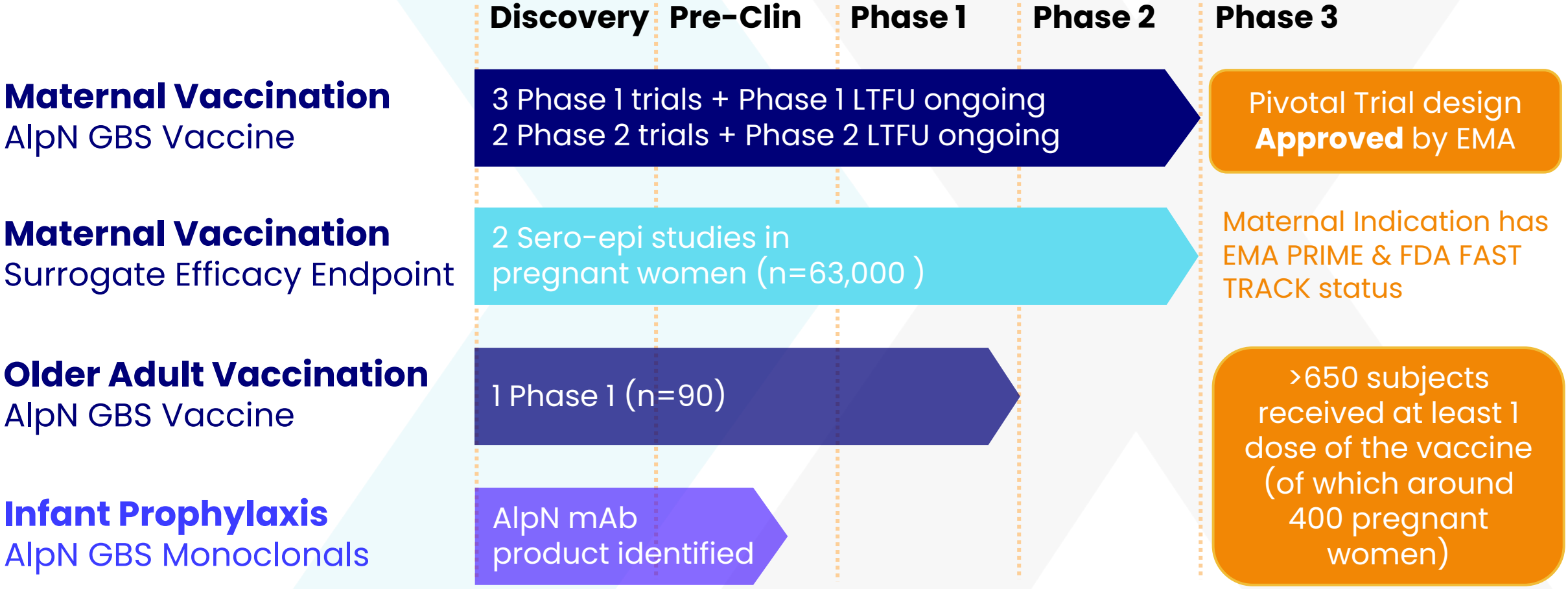
DEVELOPMENT PROGRAM SUPPORTS UNMET NEEDS IN PREGNANT WOMEN, PRETERM BABIES AND OLDER ADULTS



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Phase 2 trial
MVX0004

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MVX0004 PHASE 2 TRIAL
269 HEALTHY PREGNANT WOMEN (DK, UK & SA)

Trial design:

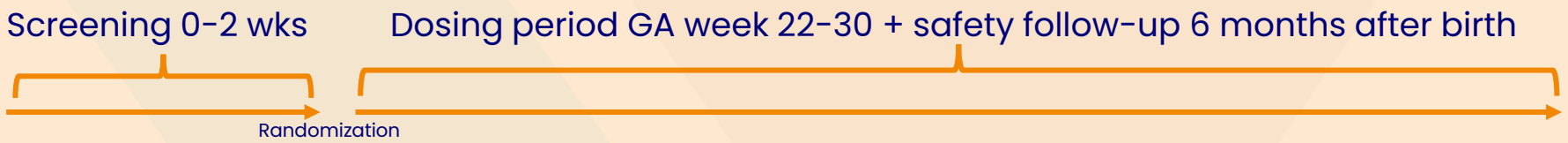
Randomised, parallel group, observer-blind, placebo-controlled

Inclusion criteria:

- Healthy pregnant women
- ~ 20 weeks GA
- Singleton pregnancy
- GBS vaccine naïve

Objectives:

- Safety
- AlpN IgG
- AlpN OPkA



Gestational Age (wks):	22	26	30	Delivery
Group 1 (n=61)	P	A	A	2 doses late, 4 wks apart
Group 2 (n=59)	A	A	P	2 doses early, 4 wks apart
Group 3 (n=59)	A	P	A	2 doses early/late , 8 wks apart
Group 4 (n=60)	P	A	P	Single dose early
Group 5 (n=30)	P	P	P	Placebo

ClinicalTrials.gov ID NCT05154578

GA: Gestational Age

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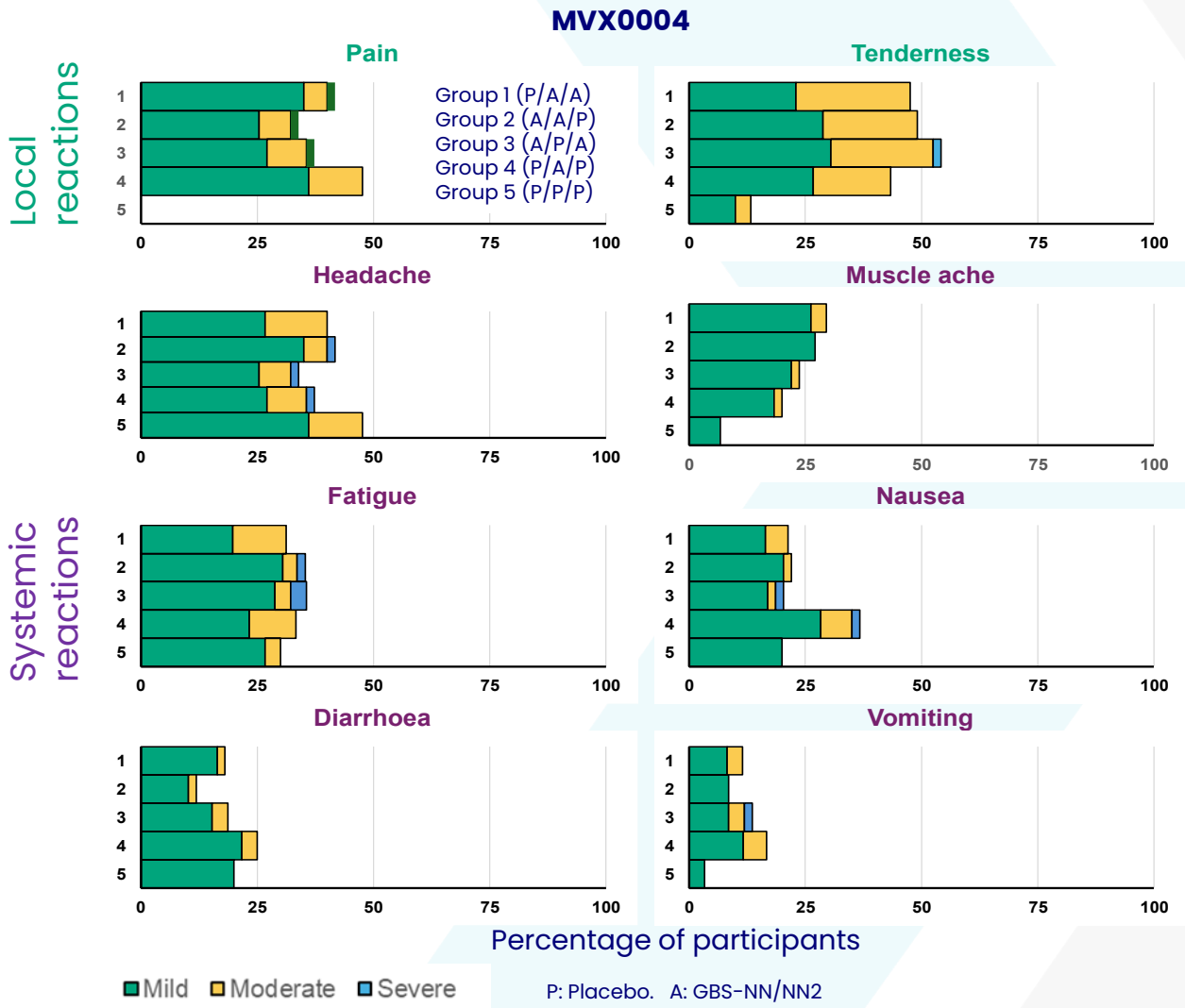
ALPN GBS VACCINE HAS AN ACCEPTABLE SAFETY PROFILE



MVX0004	Group 1 (n=61)	Group 2 (n=59)	Group 3 (n=59)	Group 4 (n=60)	Group 5 (n=30)
Any treatment-emergent adverse event	56 (92%)	54 (92%)	57 (97%)	56 (93%)	26 (87%)
Any vaccine-related treatment-emergent adverse event	8 (13%)	9 (15%)	3 (5%)	9 (15%)	3 (10%)
Any severe treatment-emergent adverse event	17 (28%)	10 (17%)	17 (29%)	23 (38%)	13 (43%)
Any vaccine-related severe treatment-emergent adverse event	0	0	0	0	0
Any serious treatment-emergent adverse event	23 (38%)	12 (20%)	20 (34%)	25 (42%)	14 (47%)
Any vaccine-related serious treatment-emergent adverse event	0	0	0	0	0
Any treatment-emergent adverse event of special interest	1 (2%)	3 (5%)	2 (3%)	5 (8%)	4 (13%)
Any treatment-emergent adverse event leading to withdrawal	2 (3%)	1 (2%)	3 (5%)	0	1 (3%)
Any treatment-emergent adverse event leading to death	0	0	0	0	0

- Mostly mild injection site reactions
- Very low levels of redness or swelling
- Very low levels of fever reported
  - Similar patterns seen after each dose
- **Post hoc** analysis of combining with 2nd Phase 2 trial showed **40% reduction of stillbirth and preterm** delivery

Heath et al. 2025

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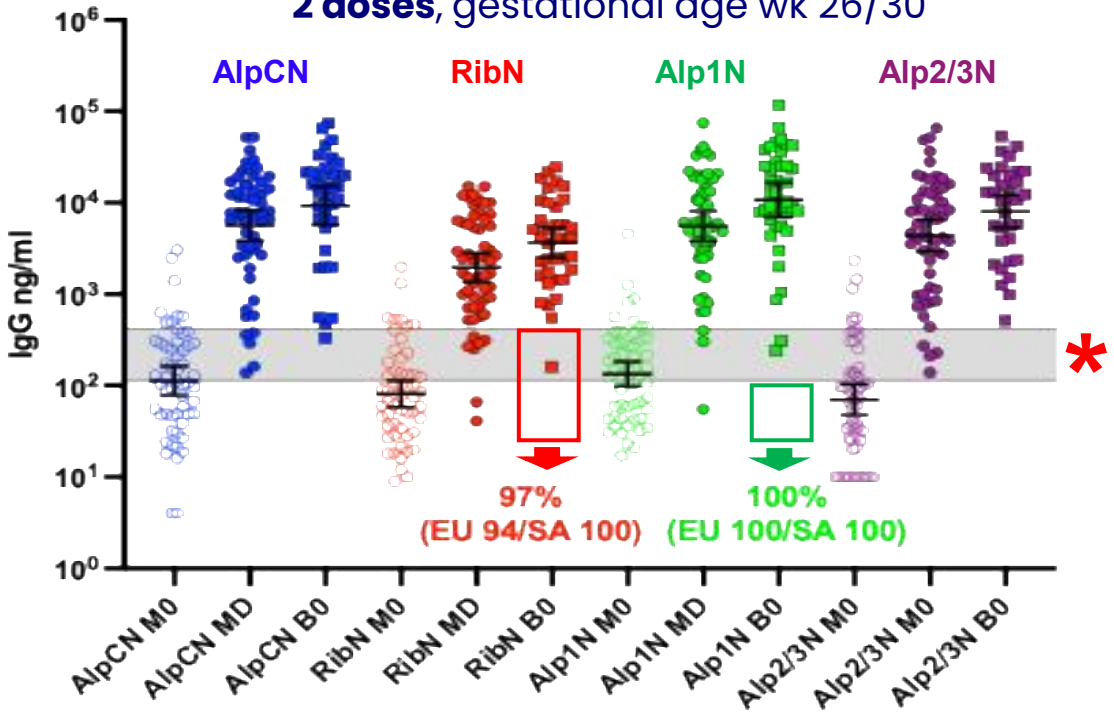
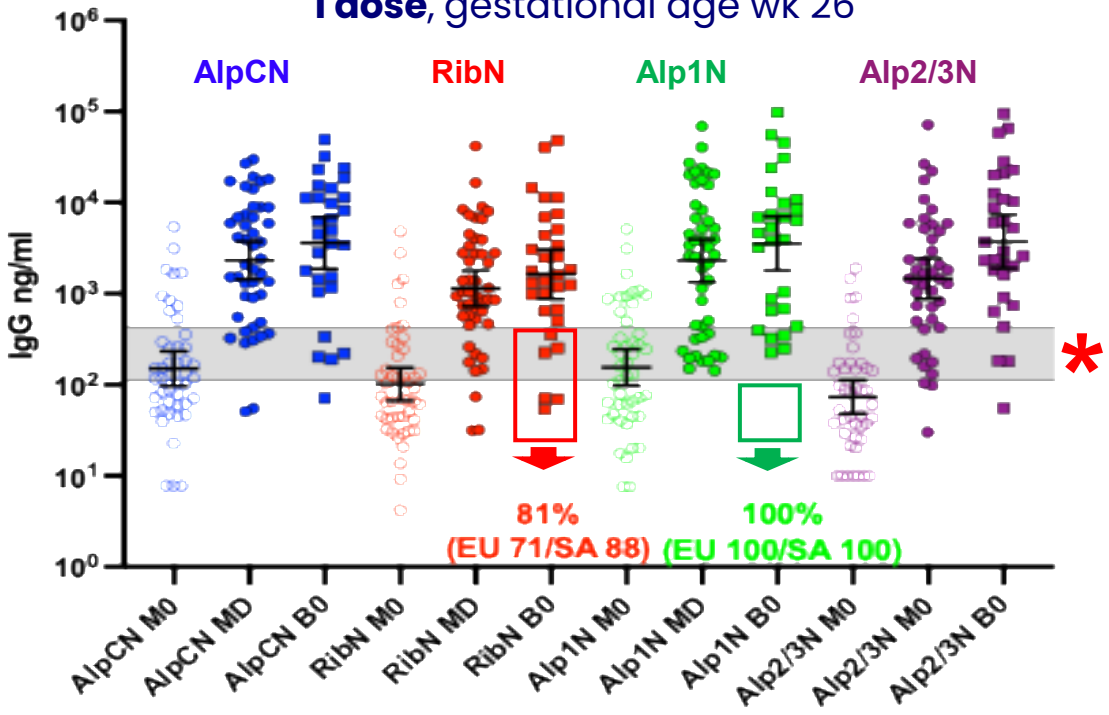
ALPN GBS VACCINATION OF PREGNANT WOMEN RESULTS IN HIGH LEVELS OF INFANT ALPN ANTIBODIES

MVX0004 IgG

Group 1 (post hoc)
2 doses, gestational age wk 26/30



Group 4 (post hoc)
1 dose, gestational age wk 26



Consistent responses in women with HIV (MVX0005 only) and without HIV

M0 = Mother Delivery; MD = Mother Delivery; B0 = Baby Cord

*) Upper boundary of grey area represents preliminary 90% protection threshold for RibN IgG and lower boundary the 90% protection threshold for Alp1N IgG, Dangor, et al. 2023

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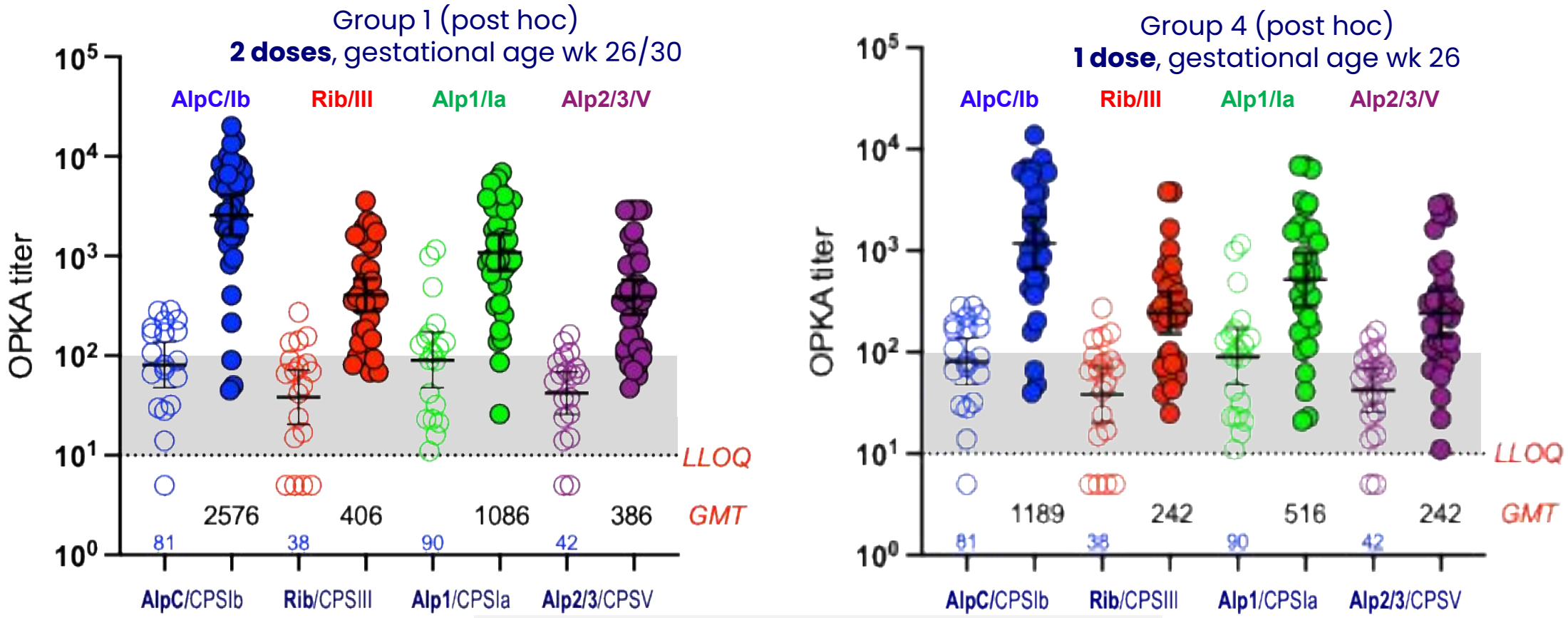
ALPN GBS VACCINATION OF PREGNANT WOMEN RESULTS IN HIGH LEVELS OF INFANT OPKA KILLING TITRES

MVX0004 OPkA



Gray area is arbitrarily set to OPkA titres <1/100

Open circles are infants born to pregnant women receiving placebo. **Closed circles** are infants born to pregnant women receiving active
Infants with OPkA titres **below LLOA** are assigned a value of **50% of LLOQ**

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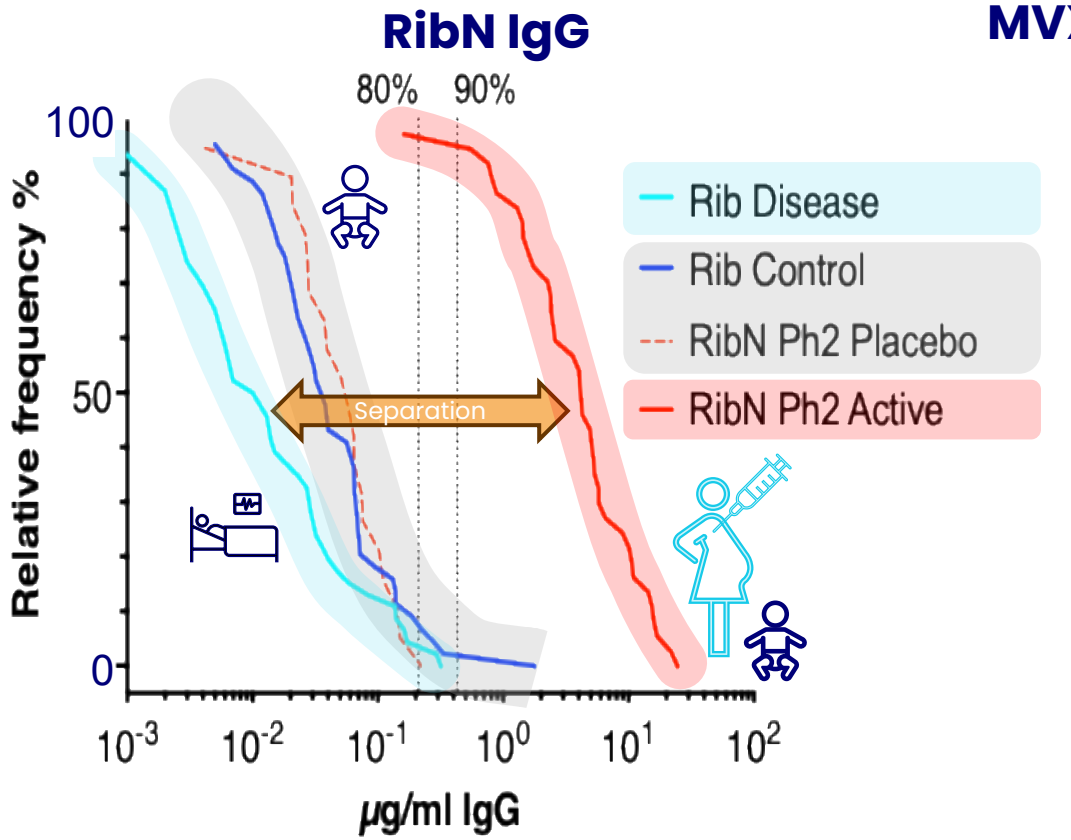
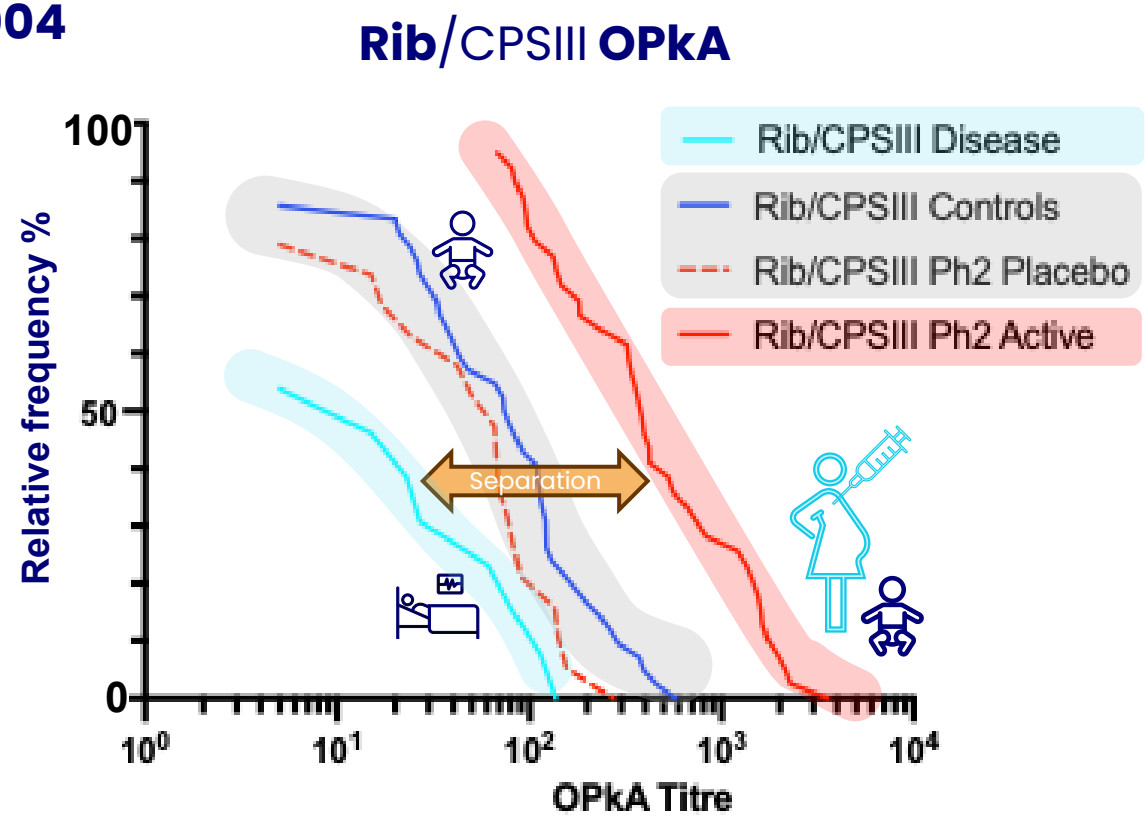
HIGH ALPN IgG & OPkA IN 'VACCINE INFANTS' COMPARED TO PLACEBO AND INFANTS WITH INVASIVE GBS DISEASE

MVX0004





Infant cord from mother receiving **placebo overlap nicely with non-disease controls**

 RibN IgG Disease and Control data are from Dangor et al 2023 – Rib/CPSIII OPkA Disease and Control Data are from preliminary analysis if new SEM samples

AlpN GBS clinical development Maternal vaccination

Safety oversight ongoing and planned trials

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ALPN GBS VACCINE: ONGOING AND PLANNED MATERNAL VACCINATION TRIALS

- **MVX0008 (ongoing)**
  - Follow-up trial of MVX0004, assessing:
    - Persistence of the immune response
    - Safety and immunogenicity of AlpN GBS booster dose during a subsequent pregnancy

- **MVX010 (under preparation)**
  - Pivotal trial for registration, assessing safety, reactogenicity and immunogenicity in pregnant participants and their infants

MOTIVATION TRIAL

MOTHER TO INFANT PROTECTION BY VACCINATION

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SAFETY OVERSIGHT

- **Safety Review Team (SRT)**
  - Safety monitoring by the internal SRT in a blinded way to support safety signal detection at any time during the trial.
- **Data Safety Monitoring Board (DSMB)**
  - An unblinded DSMB will closely monitor the safety of maternal and infant participant.
  - Consisting of independent consultants, including a statistician and physicians necessary to interpret the clinical trial data.
  - Review:
    - Predefined timepoints for data review meetings (as per the DSMB Charter).
    - Ad-hoc Meetings (if required, that may be triggered by the review of individual safety events).

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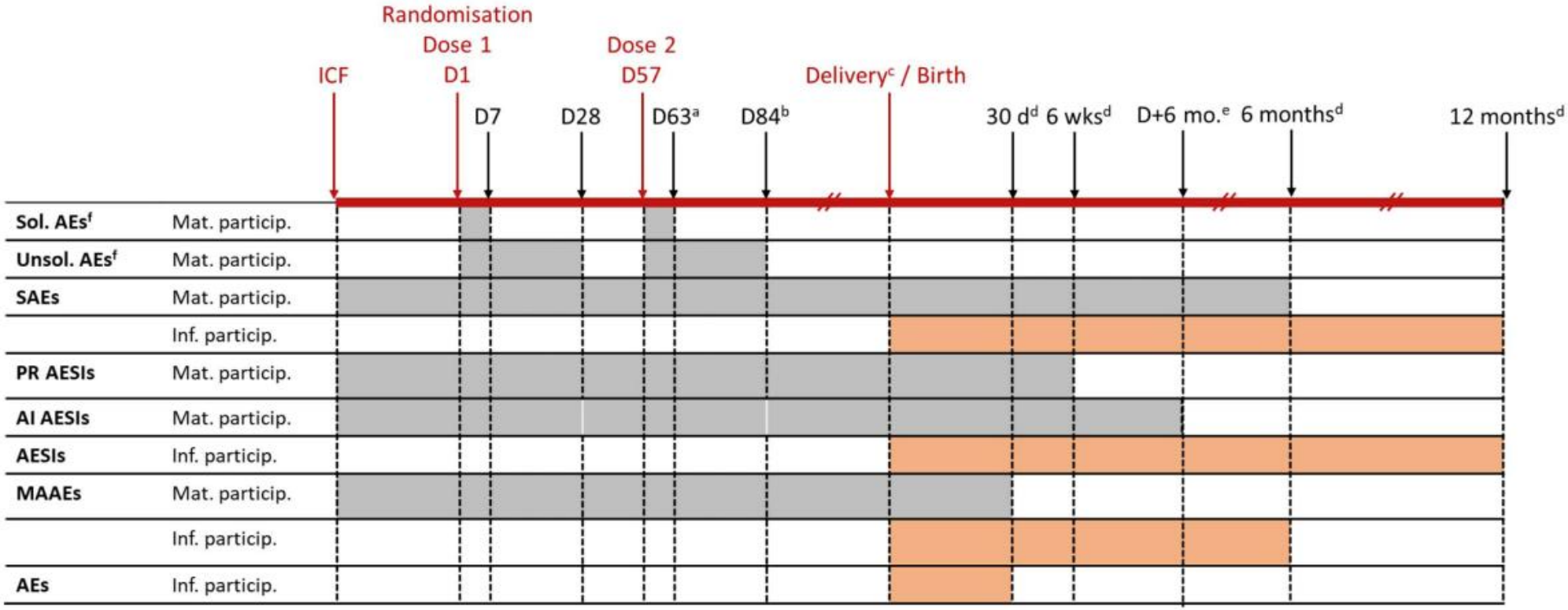
SAFETY REPORTING IN MATERNAL VACCINATION TRIALS

- **Maternal participants**
  - Reactogenicity up to D7 post each dose (local and systemic solicited Adverse Events (AE))
  - Unsolicited AE up to D28 post each dose
  - Serious AE (SAE) up to 6 months post delivery/ pregnancy termination
  - Medically Attended AE up to up to 1 month post delivery/ pregnancy termination
  - AE of Special Interest (AESI):
    - Pregnancy related (up to 6 weeks post delivery/pregnancy termination)
    - Auto-immune related (up to 6 months post last dose)
- **Infant participants**
  - AE up to 1 month of life
  - SAE and AESI up to 12 months of life
  - Medically Attended AE up to 6 months of life

SAFETY REPORTING PERIODS

Figure 2 Safety Reporting Periods Over the Entire Trial



Note: grey and orange boxes represent safety reporting periods for maternal and infant participants, respectively.
AE: adverse event; AESI: adverse event of special interest; AI: auto-immune; D/d: day; ICF: informed consent form; inf.: infant; MAAE: medically-attended adverse event; mat.: maternal; mo.: months; particip.: participant; PR: pregnancy-related; SAE: serious adverse event; sol.: solicited; unsol.: unsolicited; wks: weeks

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ADVERSE EVENTS OF SPECIAL INTEREST

Maternal participants:

- Pregnancy-related AESIs will be recorded from signing the informed consent up to 6 weeks after delivery or pregnancy termination. Cases to be ascertained according to GAIA recommendations, as described per protocol
  - Maternal death related to pregnancy
  - Pre-term delivery (PTD) : infant born before 37+0 weeks of pregnancy
  - Stillbirth (SB) : death after 22+0 weeks of pregnancy (before or during birth).
  - Confirmed iGBSd
  - Chorioamnionitis, Foetal distress, Hypertensive disorder of pregnancy (including preeclampsia and/or eclampsia and HELLP (haemolysis, elevated liver enzymes, and low platelets) syndrome), Foetal growth restriction
- Immune-mediated disorders, up to 6 months post last vaccination

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ADVERSE EVENTS OF SPECIAL INTEREST

Infant participants:

- To be recorded from birth until 12 months of age
- Cases ascertainment standardized as per protocol:
  - Neonatal death and infant death
  - Preterm birth, referring to an infant born before 37+0 weeks of pregnancy have been completed
  - Neonatal infections and infant confirmed iGBSd
  - Small for GA
  - Low birth weight
  - Congenital anomalies

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KEY FEATURES OF THE ALPN GBS VACCINE

› Four-valent AlpN vaccine **cover ALL invasive and colonizing GBS isolates**

› **Simple manufacturing** process enabling affordable vaccine for LICs

› **Surrogate Efficacy based on function**/OPKA

› **Dual Mode of Action** – Killing and Blocking Entry

› **Flexible dosing regimen during pregnancy**

- Two doses boosts IgG & OPkA responses in subjects not responding well to a single dose => lifts the immune response in those most in need
- Single-dose, especially if given later, likely sufficient in certain geographical areas
- Two-doses, with 1st given early and 2nd given late likely optimal for efficacy against
  - Adverse pregnancy outcomes
  - iGBSd in term and preterm babies

› **Target population** – **Infants (maternal vaccination)** and Older/At Risk Adults

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ACKNOWLEDGEMENTS

Maternal vaccination trials:

- MVX0004 Investigators
  - Prof. Paul Heath, PI
  - + investigators and staff
- MVX0005 Investigators
  - Prof. Shabir Mahdi
  - + investigators and staff
- The trial participants

- My MinervaX colleagues

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