



# VAXART

## **Evaluating Vaxart's oral bivalent GI.1/GII.4 norovirus vaccine in healthy lactating females and their nursing infants: VXA-NVV-108**

A phase I, multicenter, randomized, double-blind, placebo-controlled single dose, dose-ranging study to evaluate the safety, tolerability, and immunogenicity of orally administered bivalent GI.1/GII.4 norovirus vaccine in healthy lactating females  $\geq 18$  years old and their breast-feeding infants

Lam Nguyen, MD

IDWeek

October 19, 2024

# Forward looking statement

---

This presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, included in this presentation regarding Vaxart's strategy, prospects, plans and objectives, results from preclinical and clinical trials, commercialization agreements and licenses, beliefs and expectations of management are forward-looking statements. These forward-looking statements may be accompanied by such words as "believe," "could," "potential," "expect," "will" and other words and terms of similar meaning. Examples of such statements include, but are not limited to, statements relating to Vaxart's ability to develop and commercialize its product candidates; expected clinical results and trial data (including plans with respect to the proposed COVID-19 vaccine program); Vaxart's intention to continue its efforts to advance its oral tablet seasonal flu vaccine; Vaxart's expectations with respect to the important advantages it believes its oral vaccine platform can offer over injectable alternatives, particularly for mucosal pathogens such as norovirus, flu and RSV, as well as coronaviruses such as SARS, MERS and COVID-19; and Vaxart's expectations with regard to the vaccination market. Vaxart may not actually achieve the plans, carry out the intentions or meet the expectations or projections disclosed in the forward-looking statements and you should not place undue reliance on these forward-looking statements. Actual results or events could differ materially from the plans, intentions, expectations and projections disclosed in the forward-looking statements. Various important factors could cause actual results or events to differ materially from the forward-looking statements that Vaxart makes, including uncertainties inherent in research and development, including the ability to meet anticipated clinical endpoints, commencement and/or completion dates for clinical trials, regulatory submission dates, regulatory approval dates and/or launch dates, as well as the possibility of unfavorable new clinical data and further analyses of existing clinical data; the risk that clinical trial data are subject to differing interpretations and assessments by regulatory authorities; whether regulatory authorities will be satisfied with the design of and results from the clinical studies; decisions by regulatory authorities impacting labeling, manufacturing processes, and safety that could affect the availability or commercial potential of any product candidate, including the possibility that Vaxart's product candidates may not be approved by the FDA or non-U.S. regulatory authorities; that, even if approved by the FDA or non-U.S. regulatory authorities, Vaxart's product candidates may not achieve broad market acceptance; that a Vaxart collaborator may not attain development and commercial milestones; that Vaxart or its partners may experience manufacturing issues and delays due to events within, or outside of, Vaxart's or its partners control, including the recent outbreak of COVID-19; that Vaxart or its partners may not be able to obtain, maintain and enforce necessary patent and other intellectual property protection; that Vaxart's capital resources may be inadequate; Vaxart's ability to obtain sufficient capital to fund its operations on terms acceptable to Vaxart, if at all; the impact of government healthcare proposals and policies; competitive factors; and other risks described in the "Risk Factors" sections of Vaxart's Quarterly and Annual Reports filed with the SEC. Vaxart does not assume any obligation to update any forward-looking statements, except as required by law.

# Conflict of Interest Disclosure

---

I am a **Medical Director employed by Vaxart**. As such, I have a financial relationship with the company, which may present a conflict of interest in the context of this presentation.

# Norovirus is the leading cause of acute gastroenteritis worldwide

## Yearly Global Disease and Economic Burden

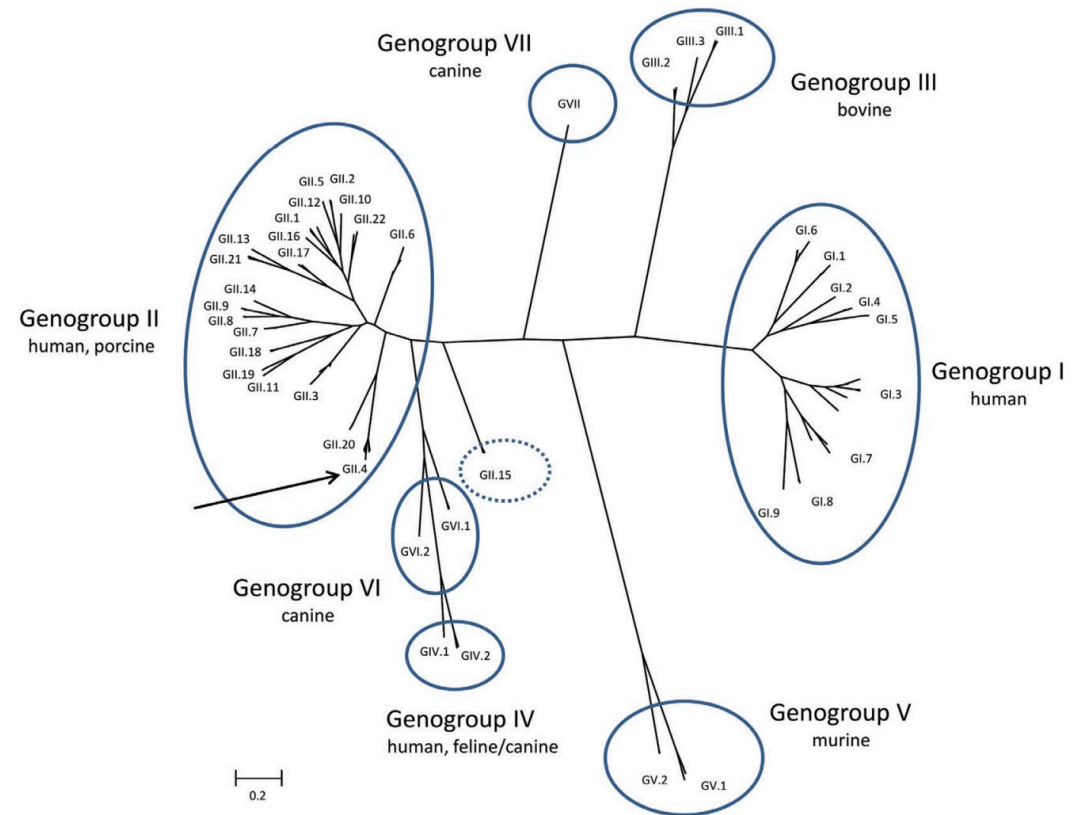
- 699 million norovirus infections
- 219,000 deaths
- \$4.2 billion in health system costs
- \$60.3 billion in societal costs annually

## Risk Groups

- Elderly, young children
- immunocompromised
- Food handlers, travelers and military

## Virology

- Several genogroups
  - GI and GII account for the majority of disease in humans
- Virus may be shed for > 4 weeks



Patel MM, Widdowson MA, Glass RI, Akazawa K, Vinjé J, Parashar UD. Systematic literature review of role of noroviruses in sporadic gastroenteritis. *Emerg Infect Dis.* 2008 Aug;14(8):1224-31. doi: 10.3201/eid1408.071114. PMID: 18680645  
Pires SM, Fischer-Walker CL, Lanata CF, et al. Aetiology-Specific Estimates Of The Global And Regional Incidence And Mortality Of Diarrhoeal Diseases Commonly Transmitted Through Food. *PLoS One* [Internet] 2015 Dec 3;10(12):e0142927 <https://www.cdc.gov/norovirus/data-research/index.html>

Image from Vinjé J. Advances in laboratory methods for detection and typing of norovirus. *J Clin Microbiol.* 2015 Feb;53(2):373-81. doi: 10.1128/JCM.01535-14. Epub 2014 Jul 2. PMID: 24989606; PMCID: PMC4298492.

# Vaxart Oral Vaccine Solution

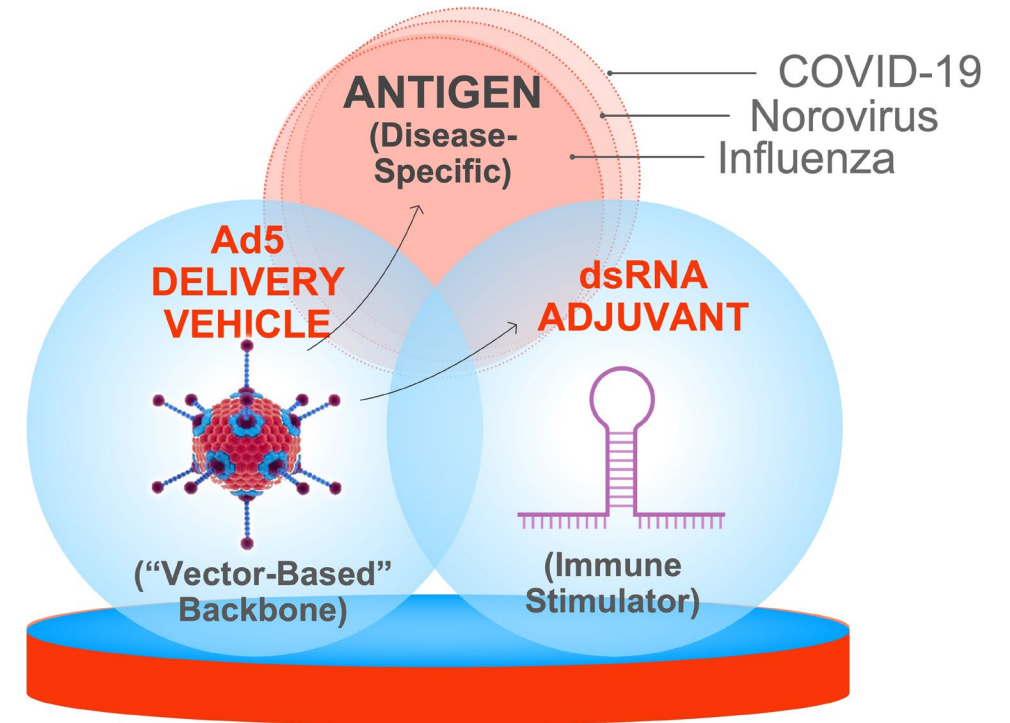
## Vector-Adjuvant-Antigen Standardized Technology (VAAST™)

- Modular, Scalable and Standardized Vaccine Creation
- Self Administered Oral Vaccine
- Room temperature stable
- Immunogenic at mucosal surfaces
- Rapidly deployed in a pandemic/outbreak
- Well tolerated and safe
  - 445 subjects exposed to any Vaxart Norovirus vaccine candidate

## Vaxart bivalent GI.1/GII.4 norovirus vaccine

- VXA-G1.1-NN: Norovirus GI.1 Norwalk VP1
- VXA-G2.4-NS: Norovirus GII.4 Sydney VP1

### Proprietary Oral Vaccine Platform: VAAST™



# Background Studies

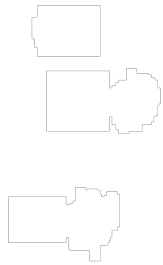
---

- Labayo et al.<sup>1</sup> Norovirus-specific immunoglobulin A in breast milk for protection against norovirus-associated diarrhea among infants
  - What is the protective role of NV specific IgA (NV-IgA) in breast milk?
    - Mothers with high positivity rates and titers of NV-IgA in breast milk had NV infected infants with reduced diarrheal symptoms.
- Vaxart, Dr. Stephanie Langel, and Duke University colleagues<sup>2</sup>
  - Oral immunization of lactating ferrets with Vaxart vaccine can provide substantial breast milk antibodies (IgA and IgG) to the vaccine's target disease.

1. Labayo HKM, Pajuelo MJ, Tohma K, Ford-Siltz LA, Gilman RH, Cabrera L, Mayta H, Sanchez GJ, Cornejo AT, Bern C, Dapat C, Nochi T, Parra GI, Oshitani H, Saito M. Norovirus-specific immunoglobulin A in breast milk for protection against norovirus-associated diarrhea among infants. *EClinicalMedicine*. 2020 Oct 5;27:100561. doi: 10.1016/j.eclinm.2020.100561. PMID: 33043286; PMCID: PMC7536734.

2. Langel, et al, unpublished data

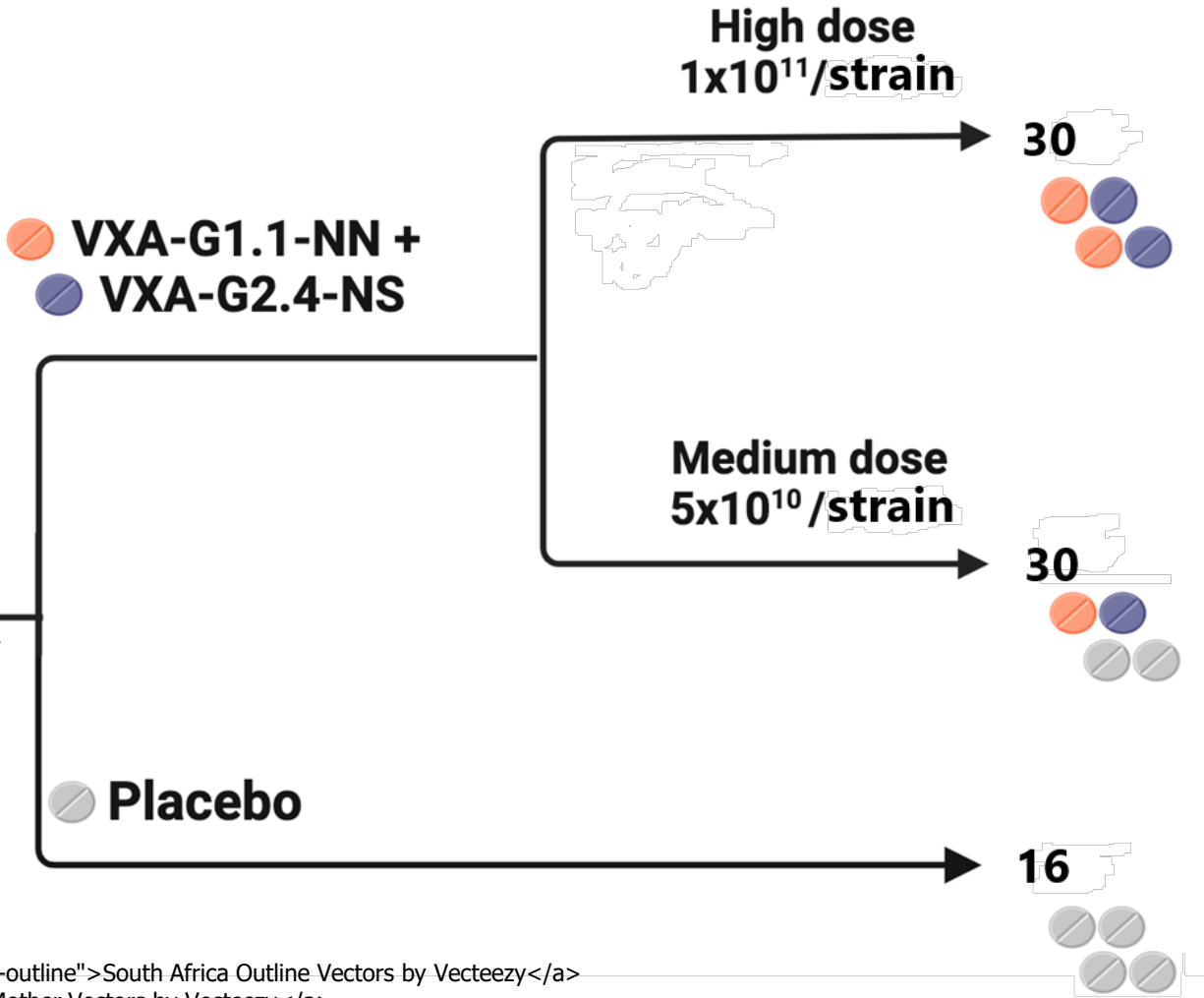
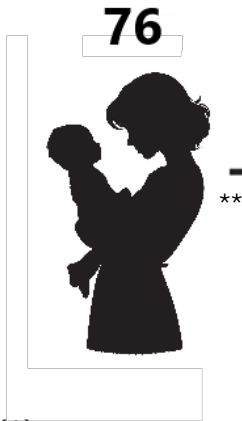
# VXA-NVV-108 Study Design: Phase 1 multi-center, double-blind, placebo-controlled single dose, dose ranging study to evaluate the bivalent vaccine safety and immunogenicity



Subjects  $\geq$  18 y.o. & Nursing infants >30 days to 11 months of age.

### Demographics

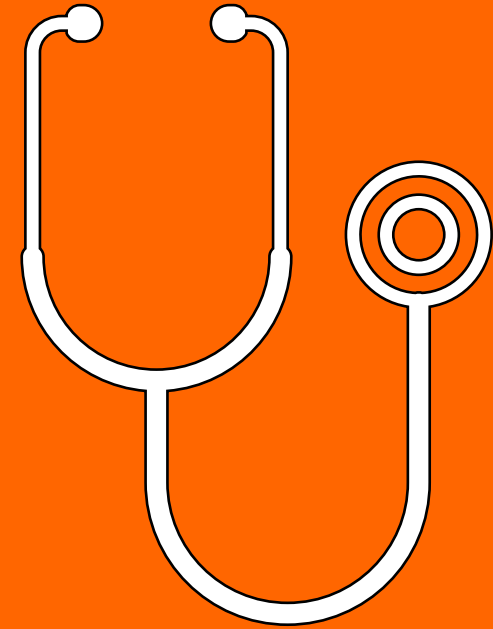
- 18-43 yo
- BMI 17.5-54.4 kg/m<sup>2</sup>
- Race
  - Black/AA (71)
  - Others (5)
    - South African Colored (1)
    - Colored (4)



\*Image is from <https://www.vecteezy.com/free-vector/south-africa-outline> South Africa Outline Vectors by Vecteezy

\*\*Image is from <https://www.vecteezy.com/free-vector/mother> Mother Vectors by Vecteezy

# Safety Analysis





# Vaxart's oral bivalent GI.1/GII.4 norovirus vaccine is well tolerated

## VXA-NVV-108 Summary of Solicited Adverse Events of Reactogenicity Post-Vaccination (Day 1-Day 8)

	SSx Severity by Treatment Arm						Cumulative SSx by Treatment Arm			All Arms	
	Med Dose N=30		High Dose N=30		Placebo N=16		Med Dose	High Dose	Placebo		
Severity	1	2	1	2	1	2	All (n %)	All (n %)	All (n %)	All	(n %)
Subjects with ≥1 symptom with maximal severity of grades 1-4	15	1	8	5	5	1	16 (53.3%)	13 (43.3%)	6 (37.5%)	35	46.1%
Headache	6	0	4	4	3	1	6 (20.0%)	8 (26.7%)	4 (25.0%)	18	23.7%
Nausea	5	0	5	1	1	0	5 (16.7%)	6 (20.0%)	1 (6.3%)	12	15.8%
Diarrhea	4	0	3	1	1	0	4 (13.3%)	4 (13.3%)	1 (6.3%)	9	11.8%
Malaise/Fatigue	2	0	2	1	2	0	2 (6.7%)	3 (10.0%)	2 (12.5%)	7	9.2%
Abdominal Pain	1	0	1	1	2	0	1 (3.3%)	2 (6.7%)	2 (12.5%)	5	6.6%
Myalgia	2	1	1	1	0	0	3 (10.0%)	2 (6.7%)	0	5	6.6%
Fever	2	0	2	0	0	0	2 (6.7%)	2 (6.7%)	0	4	5.3%
Anorexia	0	0	2	0	1	0	0	2 (6.7%)	1 (6.3%)	3	3.9%
Vomiting	1	0	0	0	0	0	1 (3.3%)	0	0	1	1.3%
Total# of SSx by severity/arm	23	1	20	9	10	1	24	29	11	64	

Severity Grading 1-4: Mild = 1; Moderate = 2; Severe = 3 and Life-Threatening = 4.

There were no solicited symptoms with severity grading of severe or life-threatening.

Percentages were calculated using the number of enrolled subjects in the designated arm as the denominator.

\*22/35 subjects reported 1 solicited symptom

# Vaxart's oral bivalent GI.1/GII.4 norovirus vaccine is well tolerated

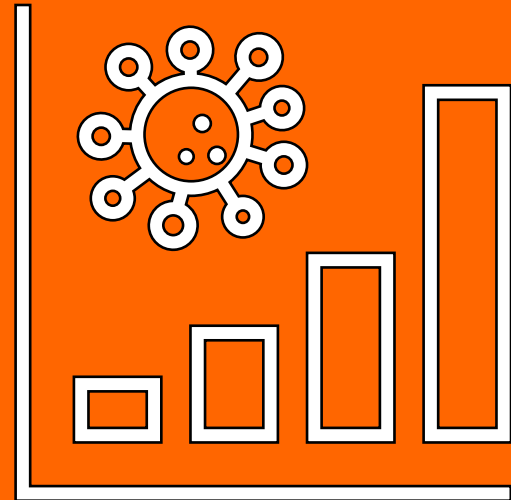
## VXA-NVV-108 Summary of Unsolicited Treatment Emergent Adverse Event (Day1-Day 29)

Cohort	Subject	Active Period N=76	Severity	Causality
Medium Dose n=3.3%	1	DIARRHEA	Moderate	Not related
	2	UPPER RESPIRATORY TRACT INFECTION	Mild	Not related
	3	DIARRHEA	Mild	Potential
High Dose n=3.3%	4	BLOODY DISCHARGE FROM RIGHT NIPPLE	Mild	Not related
	5	MYALGIA (LOCALIZED - RIGHT LEG)	Mild	Unlikely
		SORE THROAT	Mild	Unlikely
		DIARRHEA	Mild	Potential
6	FATIGUE	Mild	Unlikely	
Placebo n=12.5%	7	INTERMITTENT HEADACHE	Mild	Potential
	8	HEADACHE	Mild	Potential

The medium dose and high dose arms had 30 subjects each; the placebo arm had 16 subjects. "n" is calculated by the number of subjects in the arm with related AEs divided by the number of subjects enrolled in the designated arm.

- To date, there have been no SAEs, AESIs, NOCIs, TEAEs leading to study discontinuation or withdrawal, severe adverse reactions, or safety signals.

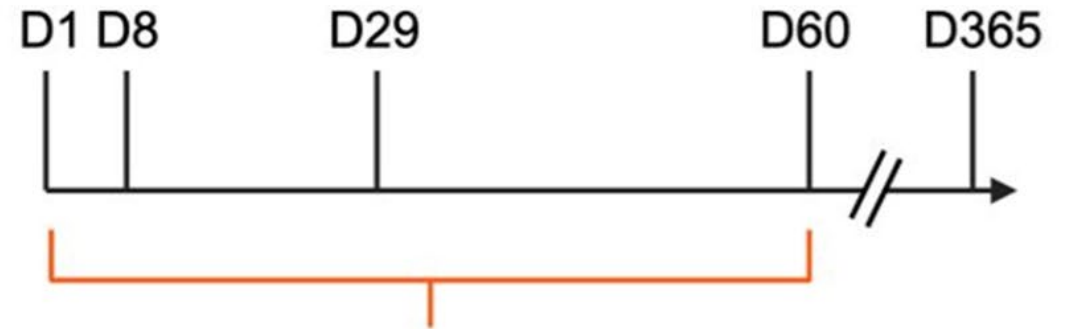
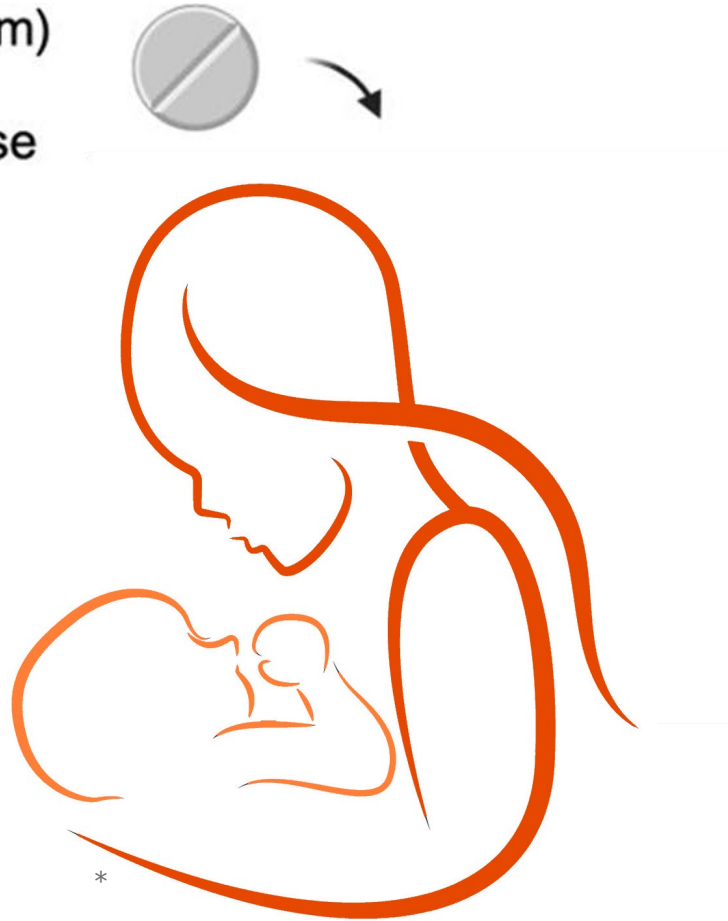
# Immunogenicity



# Immunogenicity Endpoints: Mucosal and Serum Antibodies

## Study Overview:

$5 \times 10^{10}$  IU (medium)  
 $1 \times 10^{11}$  IU (high)  
per strain per dose



### Breastmilk

- VP1 specific (GI.1, GII.4) IgA

### Serum

- VP1 specific (GI.1, GII.4) IgA, IgG
- Norovirus Blocking Antibody Assay (NBAA)

### Fecal

- VP1 specific (GI.1, GII.4) IgA

\*Image taken from <https://www.vecteezy.com/free-vector/feeding> Feeding Vectors by Vecteezy and modified

# Serum immune response to oral bivalent GI.1/GII.4 norovirus vaccine

---

**Antibodies in serum remain above baseline through D29**

IgA

IgG

Mean +/- SEM

# Serum immune response to oral bivalent GI.1/GII.4 norovirus vaccine

---

**Norovirus Blocking Antibody Assay (NBAA): surrogate assay to measure functionality of serum antibodies**

Mean +/- SEM

# Breast milk immune response to oral bivalent GI.1/GII.4 norovirus vaccine

---

**IgA in breast milk increases through D29 post vaccination and remains above baseline through D60**

# Breast milk immune response to oral bivalent GI.1/GII.4 norovirus vaccine

---

**Breast milk IgA induction is not impacted by time of vaccination post birth**

GI.1

GII.4

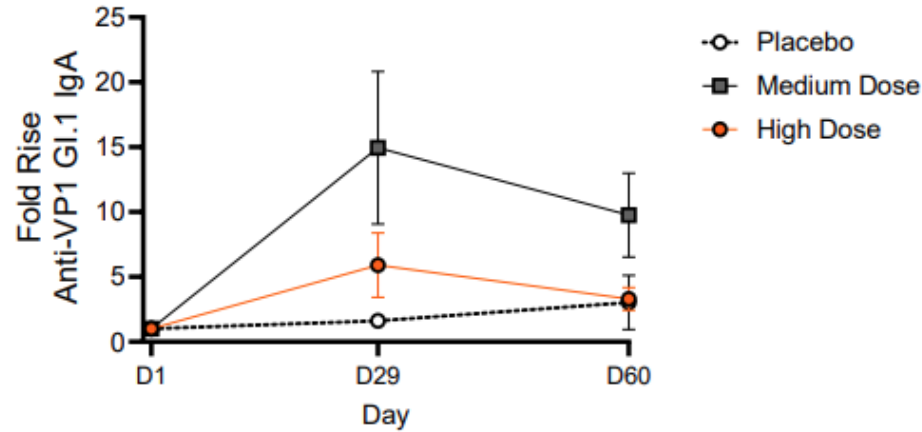
Mean +/- SEM



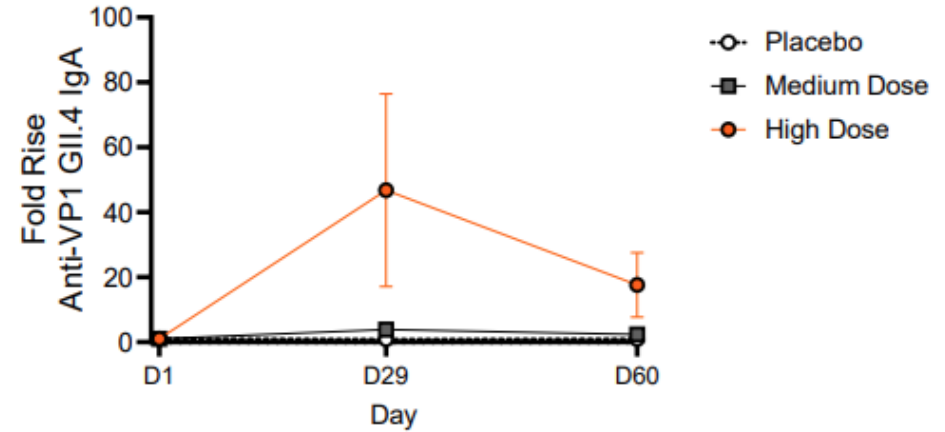
# Infant response to breastmilk norovirus antibody

**Infant fecal IgA increases through D29 post vaccination and remains above baseline through D60**

### Infant Stool IgA GI.1

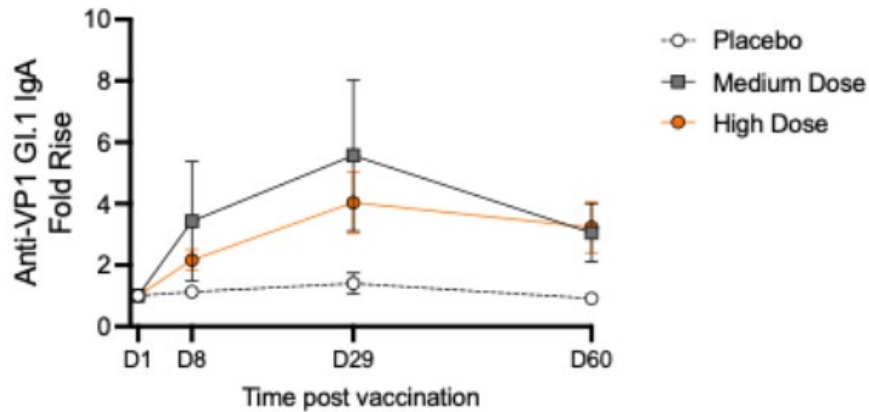


### Infant Stool IgA GII.4

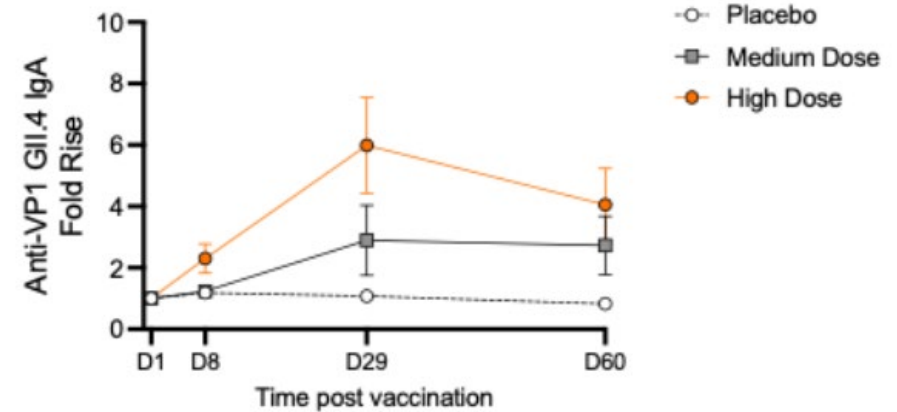


**Infant fecal IgA increase mirrors Breastmilk IgA increase**

### Breast Milk IgA GI.1



### Breast Milk IgA GII.4



# VXA-NVV-108 Summary

---

- **Safety**

- Vaxart's Bivalent Norovirus GI.1/GII.4 Vaccine side effect profile is similar to placebo and is well tolerated in post-partum, lactating subjects.
  - Solicited and unsolicited AEs are not dose dependent and are similar between active treatment and placebo arms.
  - To date, there have been no SAEs, AESIs, NOCIs, TEAEs leading to study discontinuation, or safety signals.
- The safety profile aligns with Vaxart's previous clinical trials, which enrolled healthy male and female adult subjects and exposed them to anti-infective candidates built on the VAAST platform.
  - There were no related SAEs, AESIs, NOCIs, TEAEs leading to study discontinuation, or safety signals in all of the completed studies.

# VXA-NVV-108 Summary

---

- Immunogenicity

- First description of Vaxart's oral tablet vaccine showing immunogenicity in an emerging economy and in breast milk
- Immunization of lactating women can
  - induce norovirus-specific breast milk IgA
    - Breastmilk IgA remained detectable above baseline through D60
    - Induction of breastmilk IgA responses was not impacted by time post-partum
  - induce norovirus-specific and functional serum antibodies
    - IgA and IgG remained detectable above baseline through D29
    - Induction of functional antibodies was observed to both GI.1 and GII.4
  - induce norovirus-specific fecal IgA in breastfeeding infants
    - Infant fecal IgA remained detectable above baseline through D60
    - The infant fecal IgA trend mirrors the lactating subjects' breastmilk IgA trend

# VXA-NVV-108 Summary

---

- Pending
  - Breast milk and serum immunogenicity through D181 – durability of the immune response
  - Nasal and saliva IgA responses
  - Safety followed through D365
- In conclusion, these results are an important step in the development of a norovirus vaccine that is safe and immunogenic in lactating females with the potential to decrease disease severity in their breastfeeding infants.

# Acknowledgments

---



James F. Cummings, MD  
Sean N. Tucker, PhD  
Susan N. Greco, MD MPH  
Becca A. Flitter, PhD MPH  
Molly R. Braun, PhD  
Darreann Carmela M. Hailey, MS  
Colin A. Lester  
Nick D'Amato, MS

BILL & MELINDA  
GATES *foundation*

Grant number: INV-051351

Omar Vandal, PhD