

Feb 2021

Vaxart's Oral Vaccine Candidate for Prevention of Covid-19

Hold the Needles and the Ice



VAXART

UNLOCKING THE FULL POTENTIAL OF ORAL VACCINES

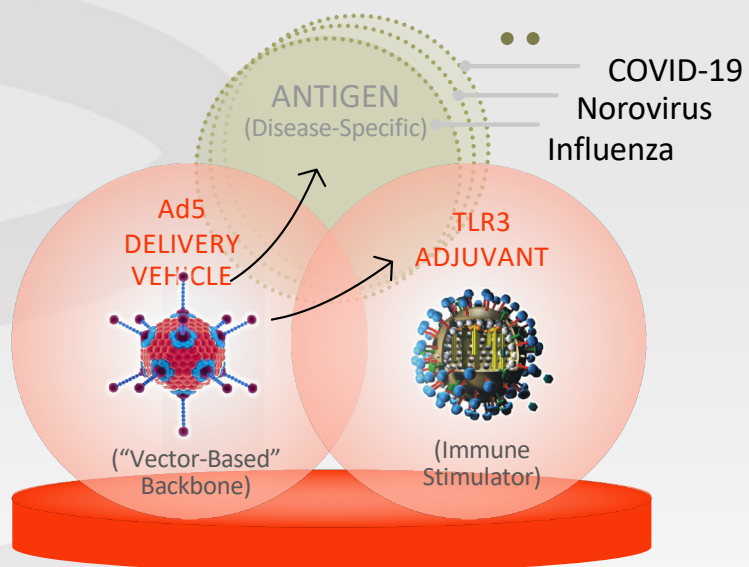
Forward-Looking Statement



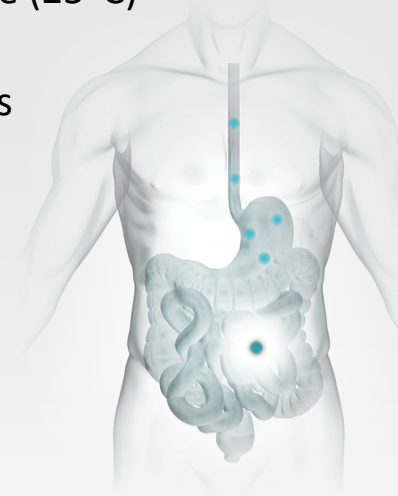
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Proprietary Oral Vaccine Platform : Vaccine Tablets

Intestinal Delivery + Targeted Immune Activation



Platform: Room-temperature (25°C)
stable
enteric-coated tablets



VAAST™: Vector-Adjuvant-Antigen Standardized Technology

Manufacturing
Standardized

Adjuvant & Antigen are Co-expressed:
Potential Safety, Efficacy Benefits

Patents with Broad Composition of
Matter and Method Claims

Platform has been tested in humans for a different respiratory pathogen



Double-Blind, Placebo-Controlled - with Active Comparator (Fluzone)

- **Funded by HHS/ASPR/BARDA¹ as innovative approach to develop more effective influenza vaccines**
- **Three Groups received a one-time administration of:**
 - **Vaxart Tablet:** Vaxart tablet vaccine + placebo IM injection
 - **Active Comparator:** Fluzone IM injection + oral placebo tablet
 - **Placebo:** Placebo IM injection + oral placebo tablet
- **Challenge at Day 90-120 post-randomization with A/CA/2009/pH1N1'**
 - **Target 2:2:1 ratio (Vaccine groups vs placebo)**



READ-OUTS

- **Primary endpoint:**
 - Number and % of Vaxart subjects protected against **influenza illness** following challenge as compared to placebo and Fluzone
- **Secondary endpoint:**
 - Number and % of Vaxart subjects protected against **influenza infection**, as measured by qRT-PCR in nasal swabs following challenge as compared to placebo and Fluzone

1) HHS/ASPR/BARDA: U.S. Department of Health and Human Services Office of the Assistant Secretary for Preparedness and Response / Biomedical Advanced Research and Development Authority, Contract no.: HHSO 100201500034C

Favorable Safety and Tolerability Profile Observed

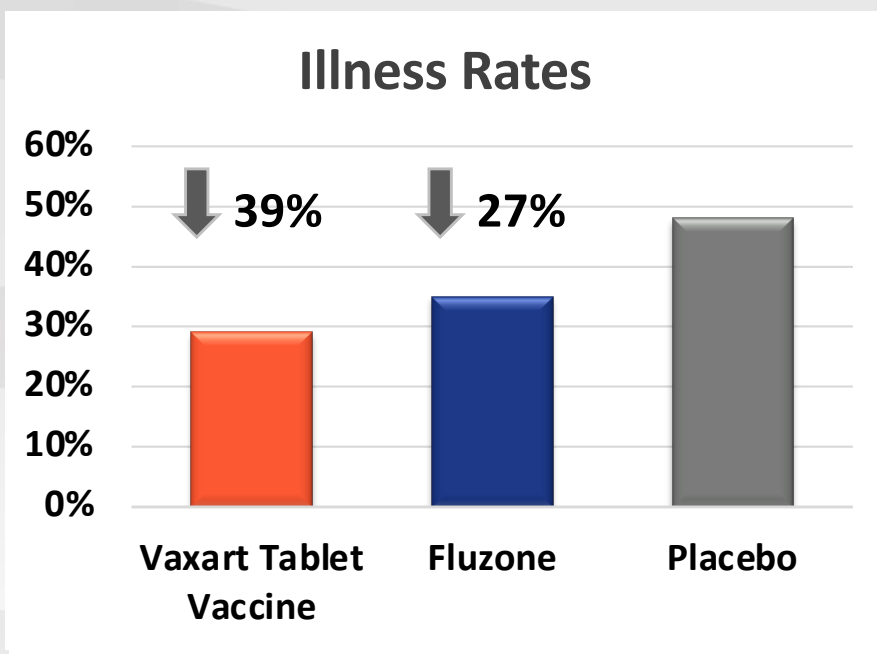
Solicited Symptom	Placebo	VXA-A1.1	Fluzone
	(n=36)	(n=70)	(n=72)
Number of Subjects with Solicited Symptom TEAEs	15 (42%)	20 (29%)	26 (36%)
General Disorders and Nervous System Disorders			
Malaise/Fatigue	5 (14%)	3 (4%)	5 (7%)
Headache	7 (19%)	5 (7%)	6 (8%)
Myalgia/body aches	1 (3%)	1 (1%)	0
Fever	0	2 (3%)	0
Gastrointestinal Disorders			
Diarrhea	5 (14%)	4 (6%)	0
Abdominal Pain	1 (3%)	0	1 (1%)
Nausea	1 (3%)	4 (6%)	3 (4%)
Vomiting	0	0	1 (1%)
Local Symptoms			
Pain at injection site	1 (2.8%)	2 (2.9%)	10 (13.9%)
Tenderness at injection site	1 (2.8%)	3 (4.3%)	19 (26.4%)

Reduction in Illness and Infection Rates Similar to Fluzone

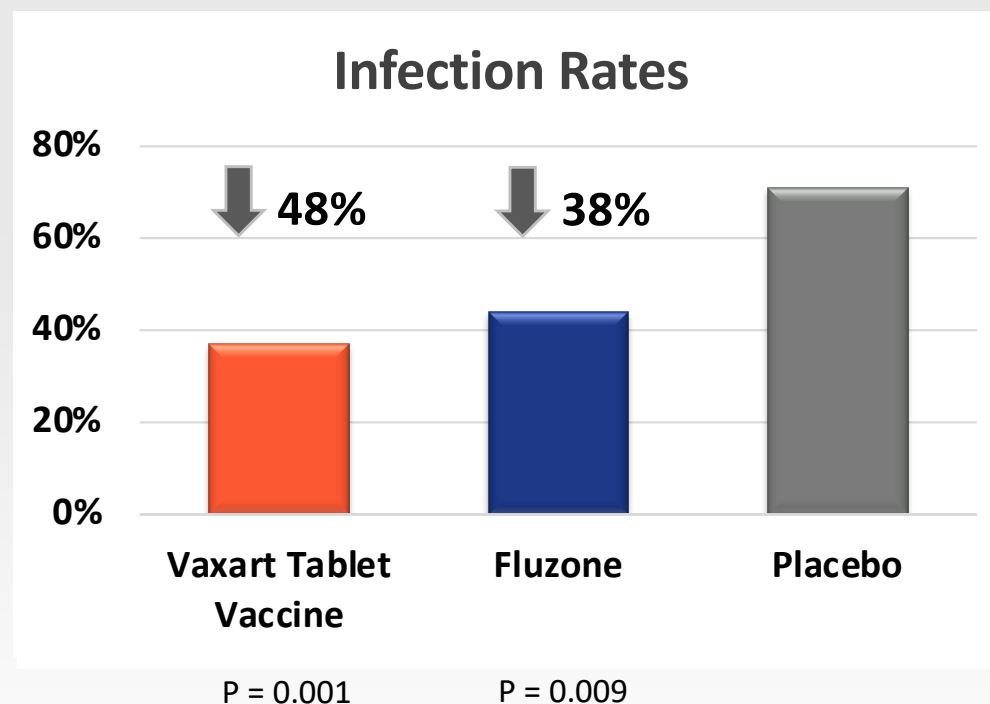
Reduction in Illness and Infection Rates Trended Superior to Fluzone



Protection Against Illness



Protection Against Infection



Defined by % of subjects shedding 36 hours post challenge to remove pass-through virus

Vaxart Tablet Vaccine: Protection Highly Correlated With Mucosal Response

Liebowitz, et al, Lancet ID, 2020

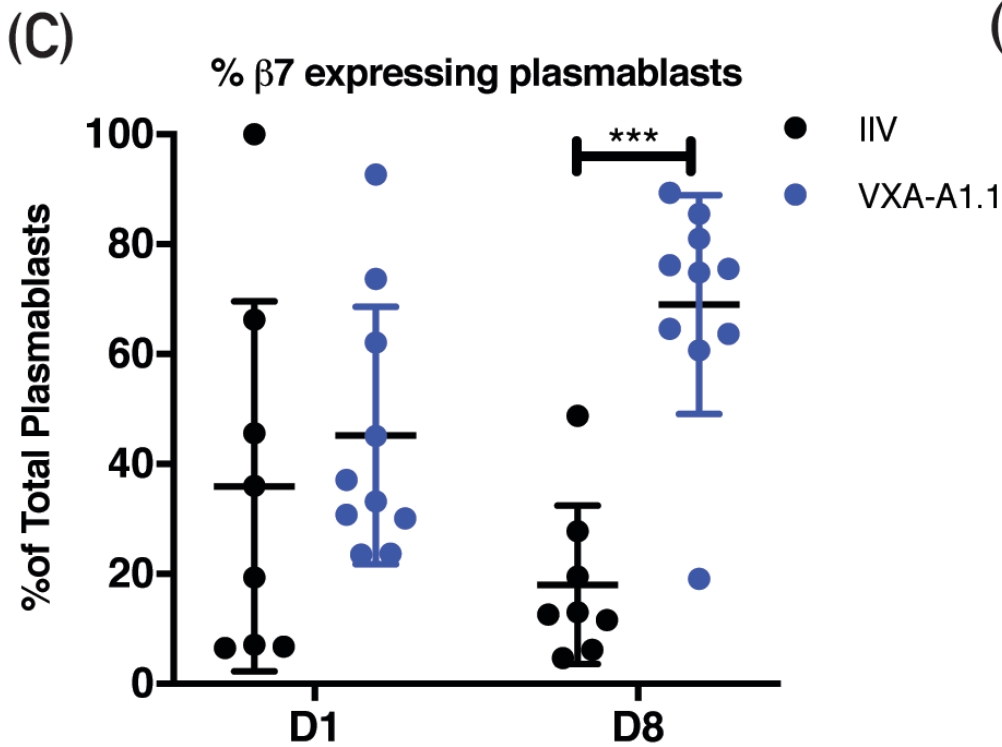
IgA ASC was the most important immune parameter to predict protection from oral immunization



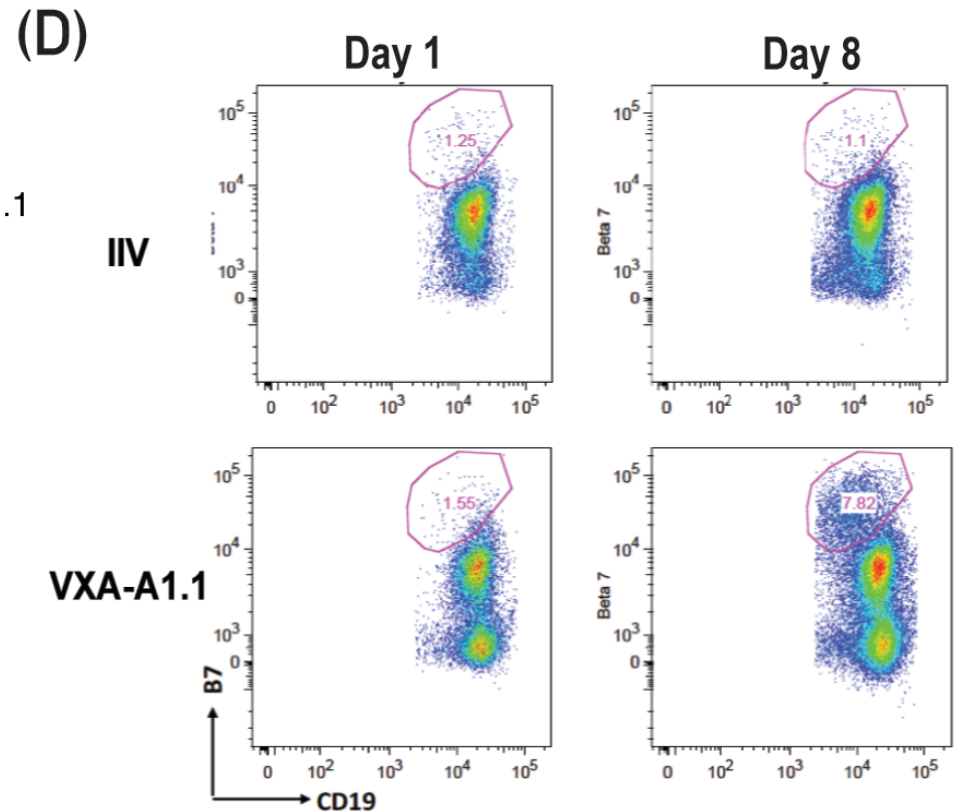
- Random Forest Analysis
 - IgA ASC most important immunological feature for protection against shedding for the Oral Vaccine
 - HAI most important feature for protection against shedding for the QIV vaccine
- Logistic fit analysis (rough correlation between IgA ASC Counts and predicted protection rate for the oral influenza vaccine)

IgA ASC Count per 1e6	Predicted Protection Rate
2.3	50%
55.4	75%
108.4	90%
144.5	95%

Vaxart Vaccine Specifically Elicits Increased Expression of Mucosal Homing Receptor $\alpha 4\beta 7$ on Activated Plasmablasts



*** P<0.0001



Liebowitz, et al, Lancet ID, 2020

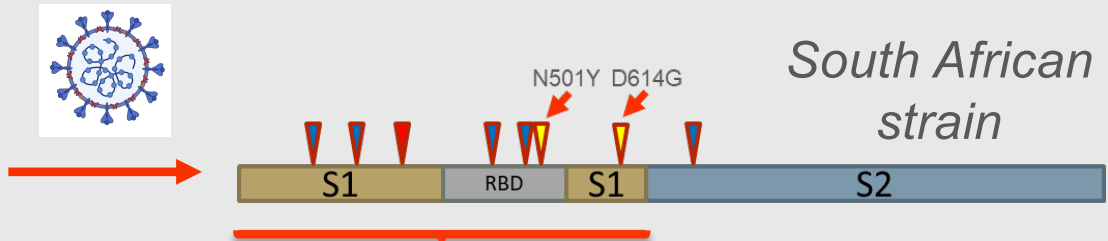
COVID Vaccines – Where are we now?

- Vaccine developers have made advanced candidates at incredible speed
- Several needle-based vaccines have completed Phase 3
 - Expression of the S protein in people leads to substantial protection (symptomatic illness) against matched strains (Moderna, Pfizer, Astrazeneca, Janssen)
 - S Protein vaccine also protective (Novavax)
 - Drop-off in efficacy noted when the vaccine strain doesn't match the circulating strain
- Roll out >1.2M vaccinations a day in the US under EUA
 - 8 months to immunize 300 M people, 16 months to immunize 600M people
- Coronavirus S mutations are showing up without vaccine selective pressure, including mutations in the RDB
- Discussion about building new vaccine strains that match the new coronavirus mutants

COVID-19 Vaccine Development and Distribution Efforts are Being Outpaced by Rapidly Emergent Strains

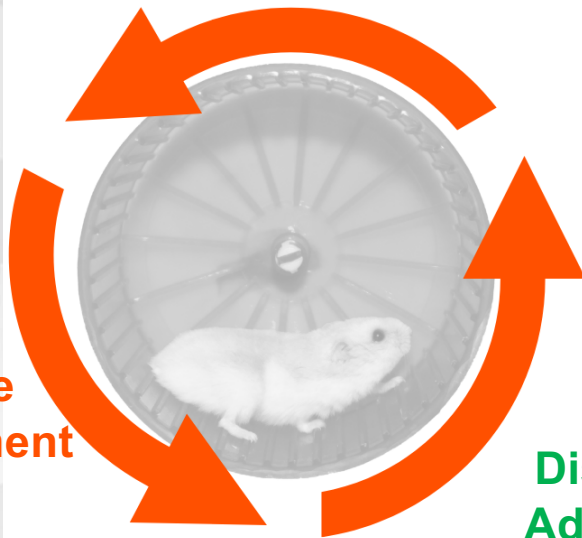


Rapid Emergence of new SARS-CoV-2 strains

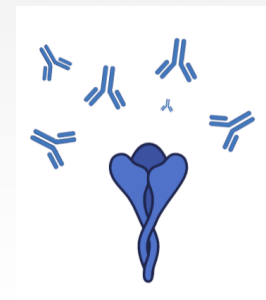


- New mutations are starting to accumulate in the S1/RBD domain, where neutralizing antibodies generated by current vaccines bind

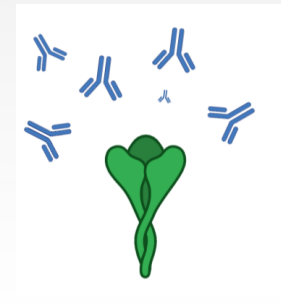
Vaccine Development



Distribution & Administration



Current vaccine strain



Future SARS-CoV-2 variants



- We are currently chasing the virus with vaccines like a hamster on a wheel

Rate Limiting Step is the time for injected large populations: Vaxart Takes Away the Needles



Rapid Emergence of new SARS-CoV-2 strains

Vaccine Development



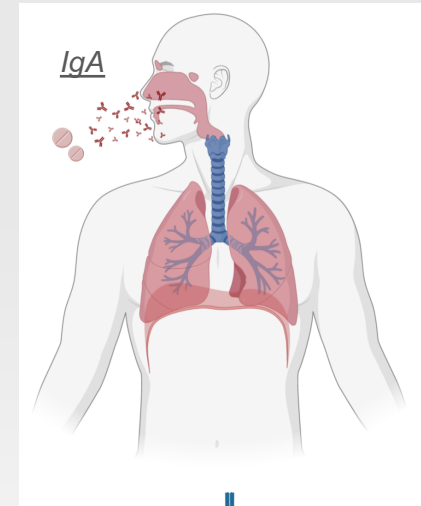
Rapid Distribution & Administration

Get Off The Wheel – Shorten the Time to Herd Immunity

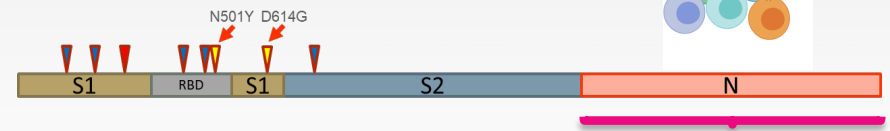


Vaxart's solution

- Room temperature stable tablet, easy to produce, distribute, and administer



T cells

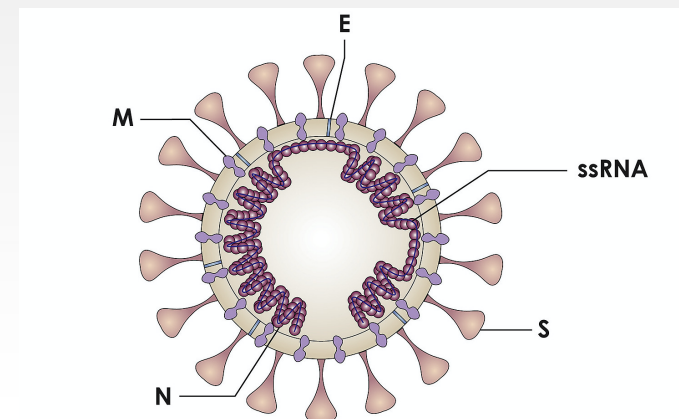
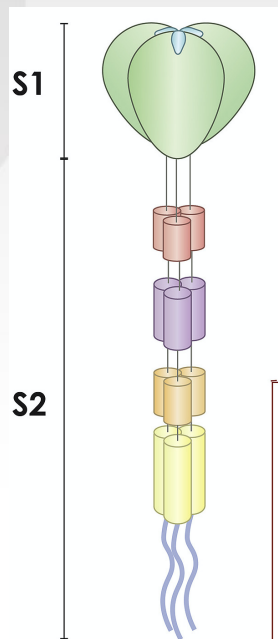


- More conserved across strains
- Strong target for T cells

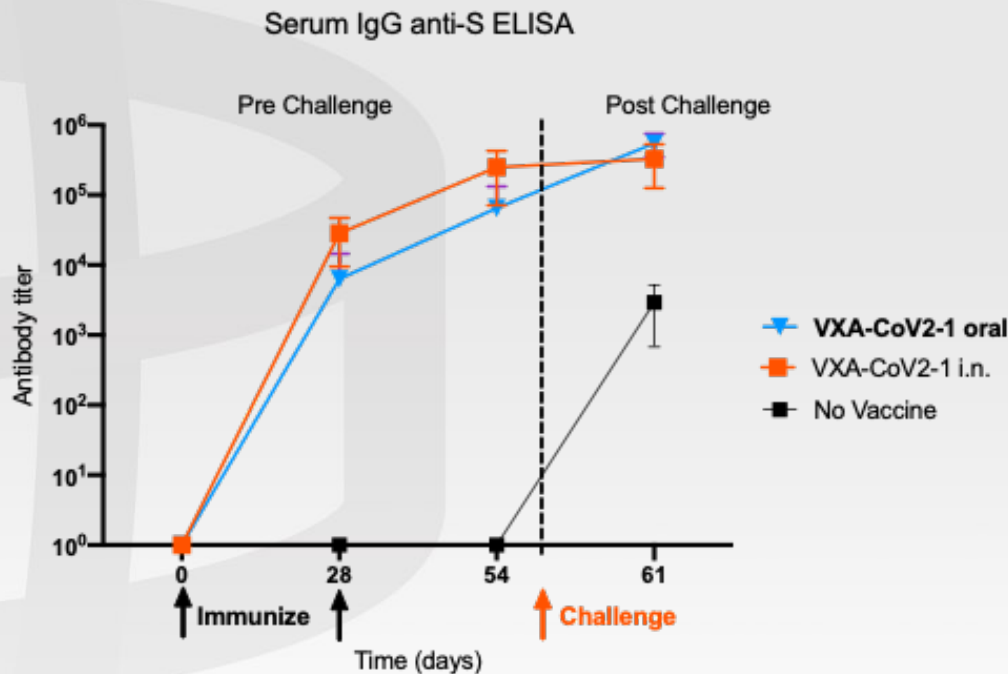
Goal: Drive CD8 T cell responses and mucosal responses with our Covid-19 vaccine candidate

Candidate VXA-CoV2-1

- Expressing both S and N proteins
 - S is good antibody target, but also has a lot of T cell epitopes
 - N is more conserved and a good target for T cell responses
- Made several different vaccine candidates
 - Chose construct that made highest lung IgA responses in mice
- rAd + TLR3 should drive T cell responses toward Th1



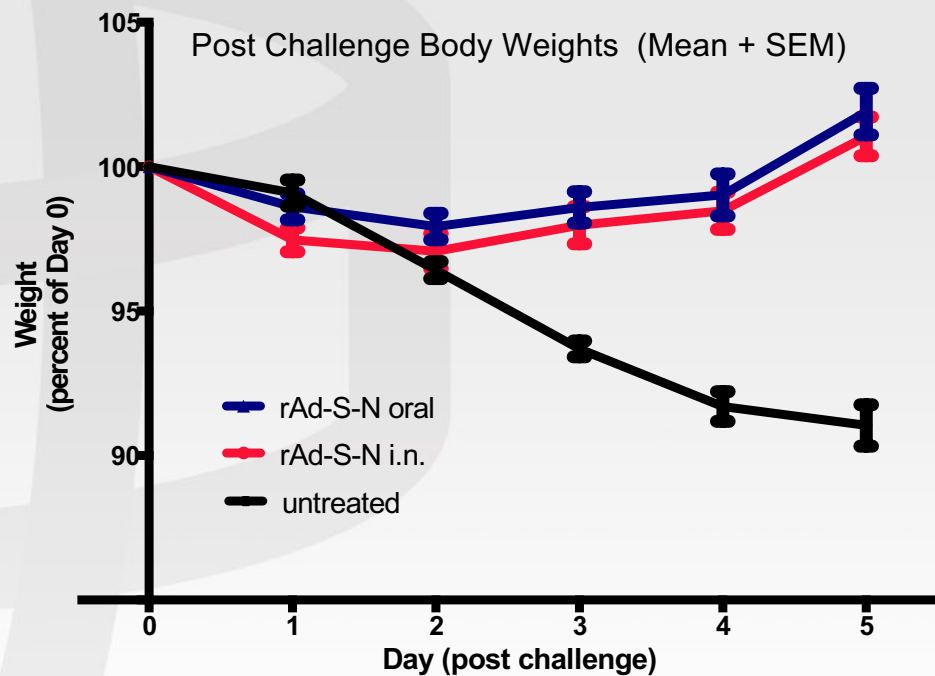
Oral COVID-19 vaccine candidate induces potent antibody responses in hamsters



- Oral administration induced specific antibody titers above 10,000 over background
- Oral administration performed as well as intranasal

- Vaxart rAd vaccine candidate expressing the S and N protein used at 1:10/1:100 of the human dose
- Two doses given, 0 and 4 weeks. rAd given at 1e9 IU. Challenge at week 8.
- Administered orally and intranasally (i.n.)

Oral COVID-19 vaccine protects against a key clinical outcome, weight loss, in a hamster challenge model

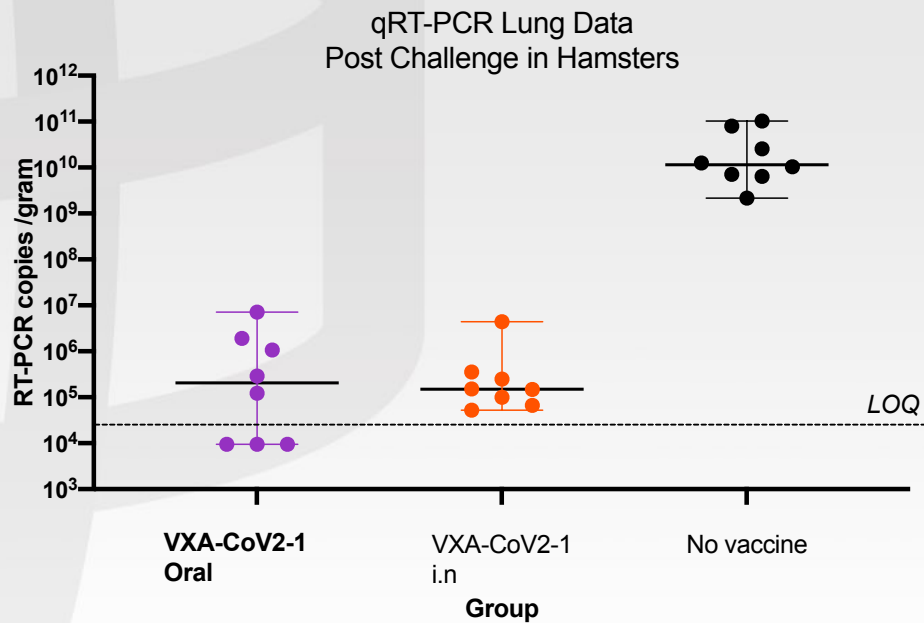


- The Syrian hamster is a very sensitive COVID-19 model
- Syrian hamsters have an ACE2 receptor that can bind SARS-CoV-2
- Hamsters challenged nasally with COVID-19 virus have similar disease as humans
- Clinical symptoms of COVID-19 infection include weight loss

Orally vaccinated hamsters protected against lung COVID-19 infection as measured by qRT-PCR



4-5 logs reduction in lung viral load in hamsters that received two oral vaccine doses as compared to non-vaccinated animals



Oral administration performed as well as intranasal vaccination after intranasal viral challenge as assessed by several different quantitative measures of COVID disease and infection

VXA-COV2-101 Phase 1 Study Design and Schema

- Single Dose, Oral Tablet Study at Low and Medium Doses
- Small Sentinel Cohort that was boosted
- **Primary (Safety) and Secondary (Immunogenicity) Endpoints Met**

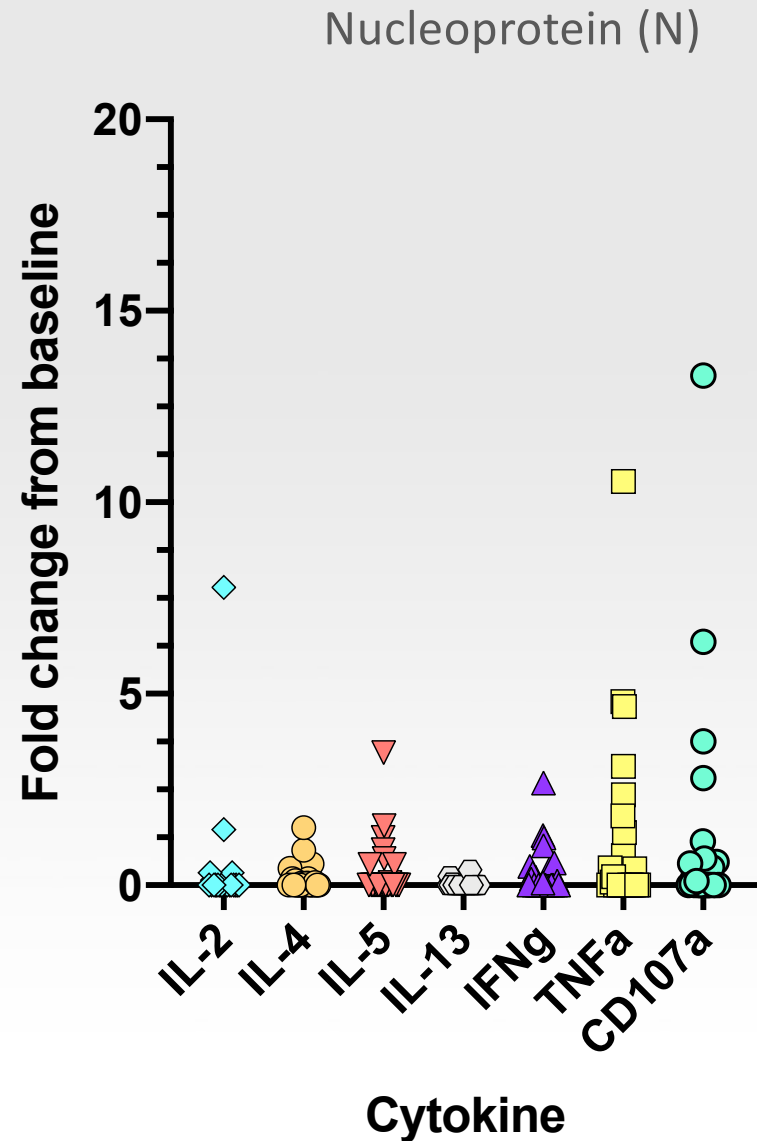
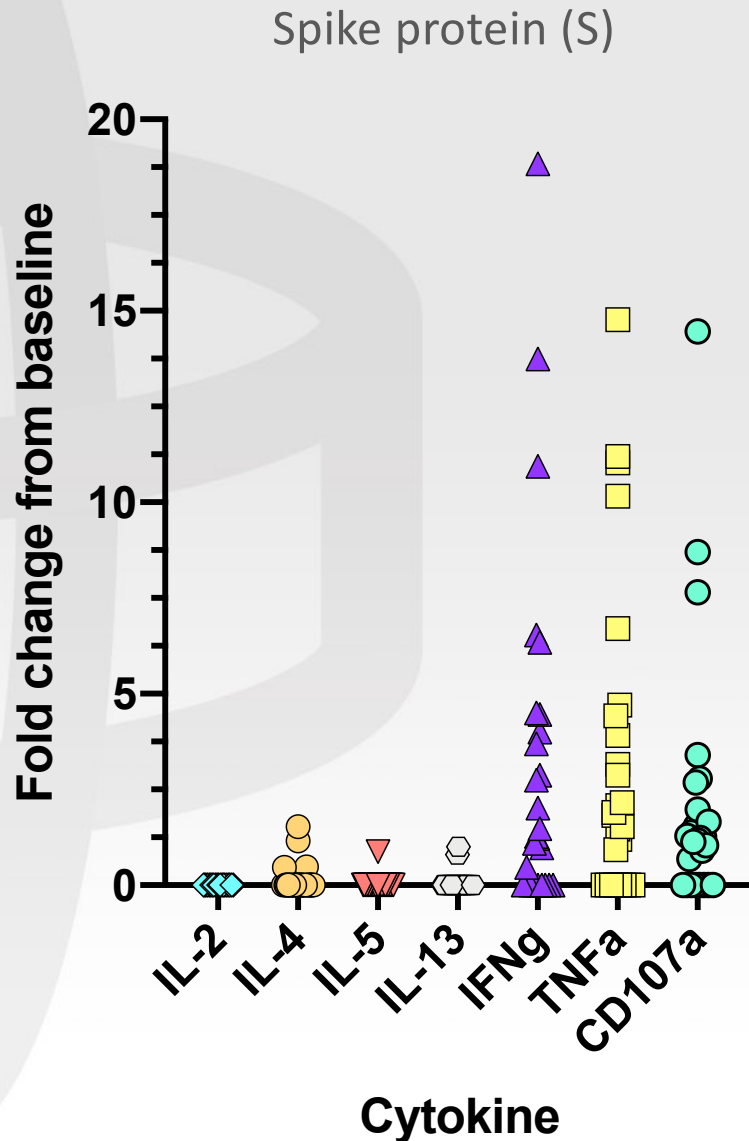
Treatment Group	Vaccine	Dose (± 0.5 log)	No. of Doses	No. of Subjects
Cohort 1 (Sentinels)	VXA-CoV2-1	1×10^{10} I.U.	2	5
	SMC Review of Safety Data through Day 8 Visit			
Cohort 2	VXA-CoV2-1	1×10^{10} I.U.	1	15
Cohort 3	VXA-CoV2-1	5×10^{10} I.U.	1	15
			Total	35

Solicited Symptoms Post Vaccination

Solicited Symptom Days (1 – 8)	Low Dose (n=20)	High Dose (n=15)
No. (%) with Solicited Symptoms	4 (20)	10 (66.7)
Gastrointestinal Symptoms		
Diarrhea	0 (00)	4 (26.7)
Nausea	0 (00)	5 (33.3)
Vomiting	0 (00)	0
Abdominal Pain	1 (5.0)	2 (13.3)
General Symptoms		
Malaise/Fatigue	2 (10)	2 (13.3)
Myalgia (Muscle Pain)	1 (5.0)	1 (6.7)
Anorexia	0 (00)	2 (13.3)
Headache	3 (15)	2 (13.3)
Fever	0 (00)	1 (6.7)

- Most Solicited Adverse Events mild and transient; few moderates @ Days 2 to 6
- 6 Mild unsolicited AEs: sore throat, epistaxis, chills, dry sinus, back pain & testicular pain
- No SAEs or MAAEs reported to date

Vaxart's oral vaccine shows preferential Th1 responses, inducing a strong CD8 cytotoxic response



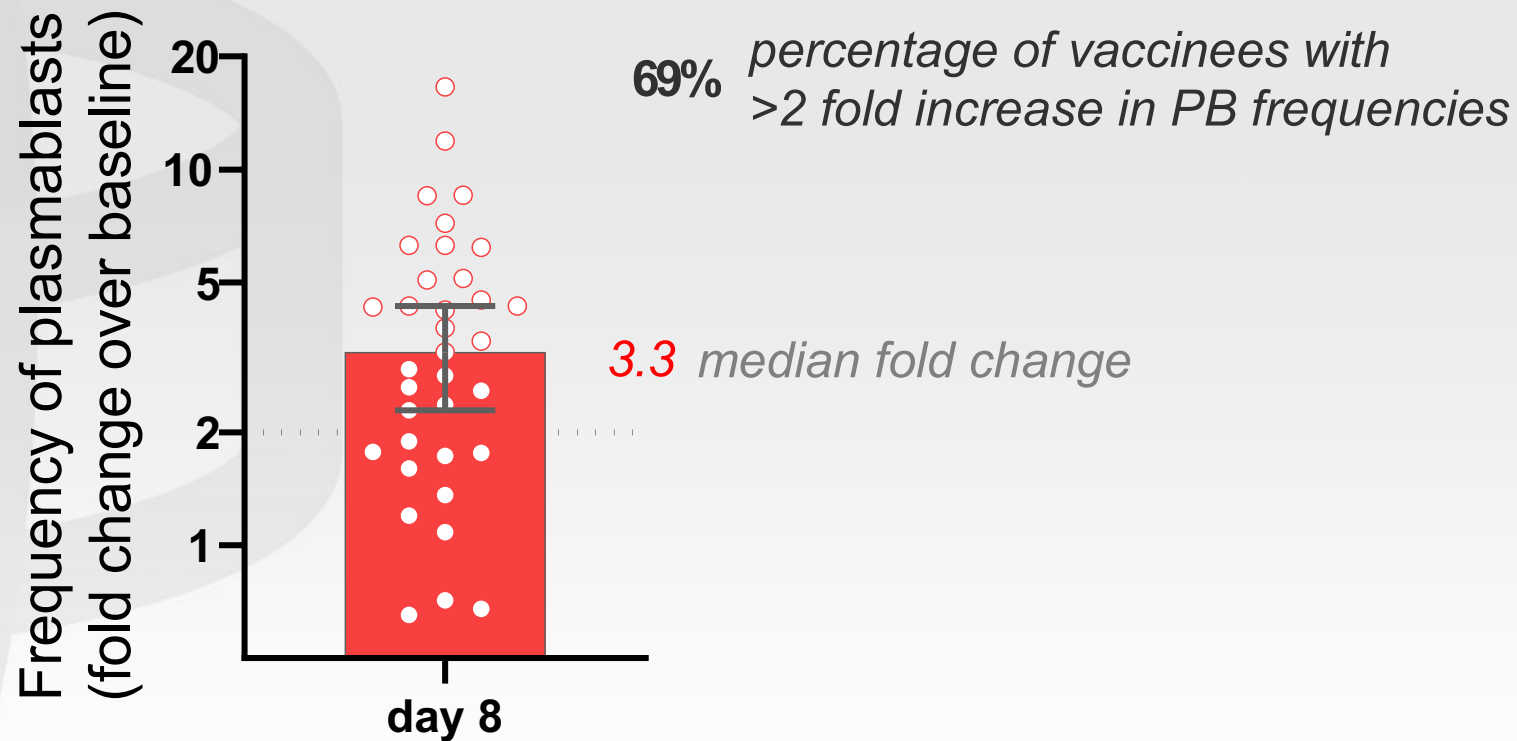
Restimulation with S or N peptide pools on PBMCs from pre and post vaccination. Th2 cytokines are CD4+ T cells, Th1 cytokines are CD8+ T cells. Fold change is calculated over the pre-vaccination sample.

Why T cells may be important for COVID

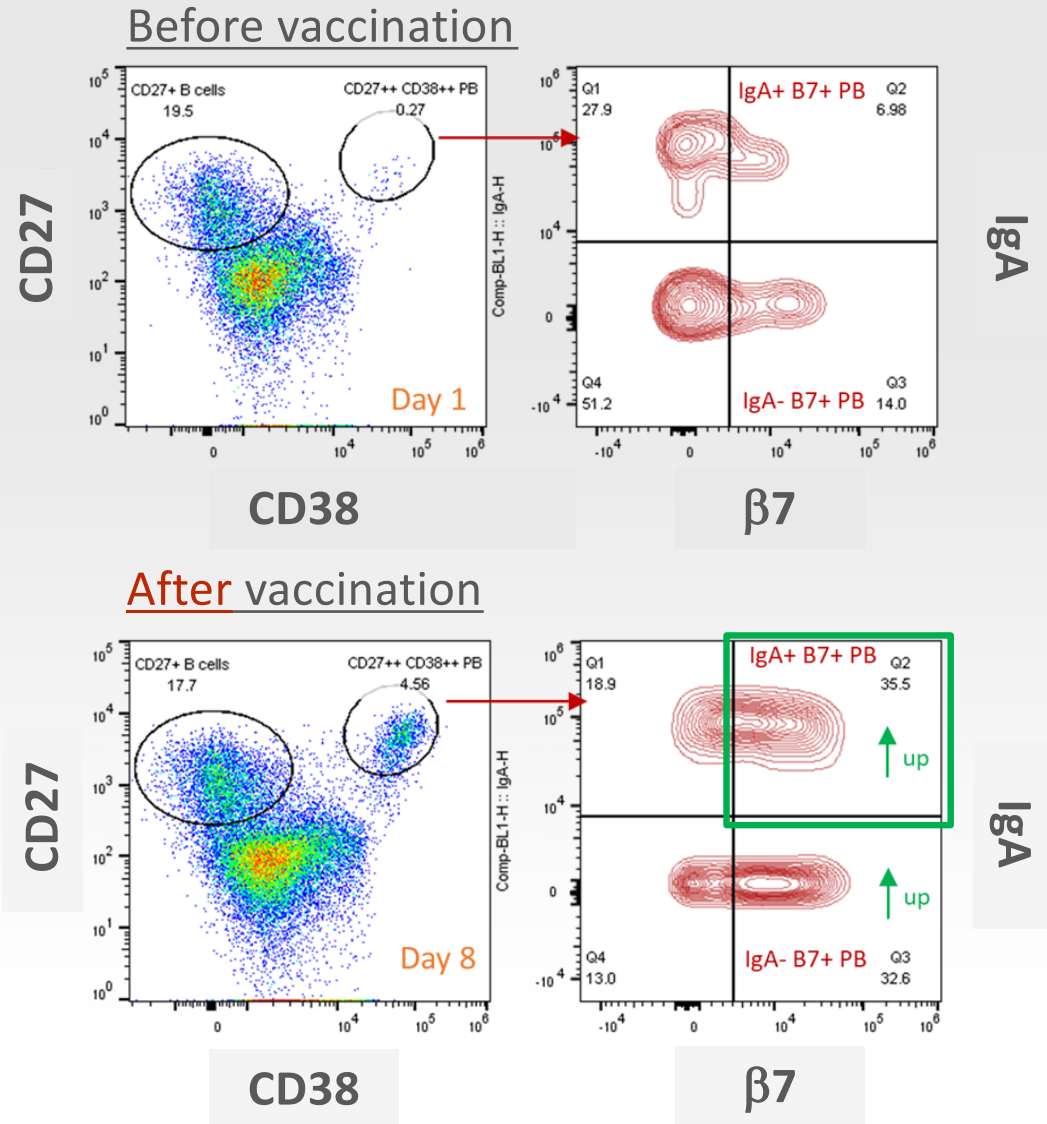
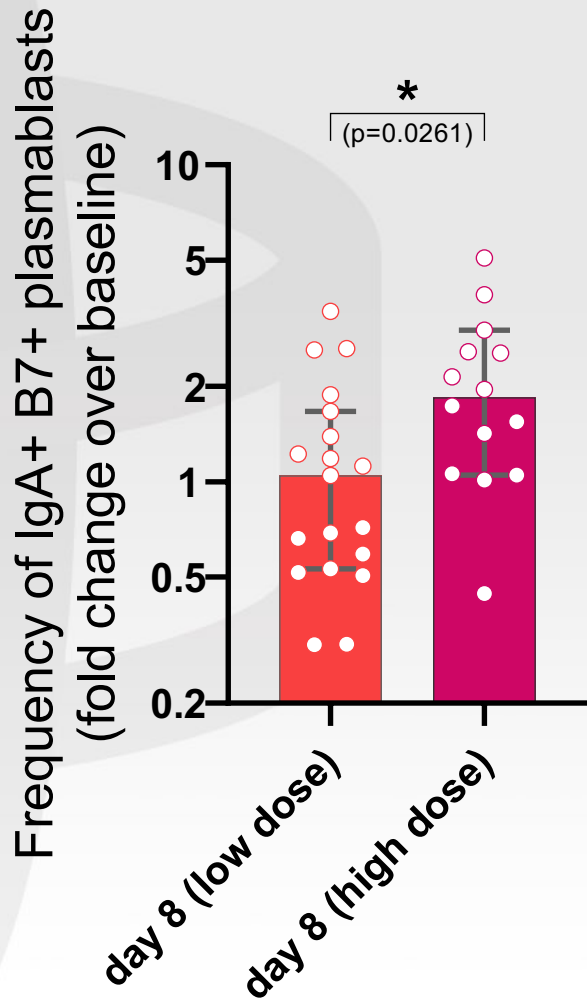
- Cross-protective
- Long-lasting
- Reduces severity and length of the infection
- Mucosal T cells may be capable of blocking shedding and transmission
- Higher T cell responses correlated to protection against COVID disease in in prospective study of first responders (Wylie, et al, Medrxiv, 2020)
- Broader antigenic repertoire than antibody responses - T cell responses recognize at least 30-40 epitopes in each donor, as measured in 99 subjects. (Tarke, Cell Reports Medicine, Jan 21)

B cell Responses to Oral Immunization

Sharp increase in plasmablast frequencies on day 8 after vaccination



Vaccine-induced plasmablasts preferentially express IgA and upregulate the Mucosal Homing Receptor $\alpha 4\beta 7$, particularly at higher dose



52% of participants showed 2-fold or above increase in specific IgA to RDB, S, or N

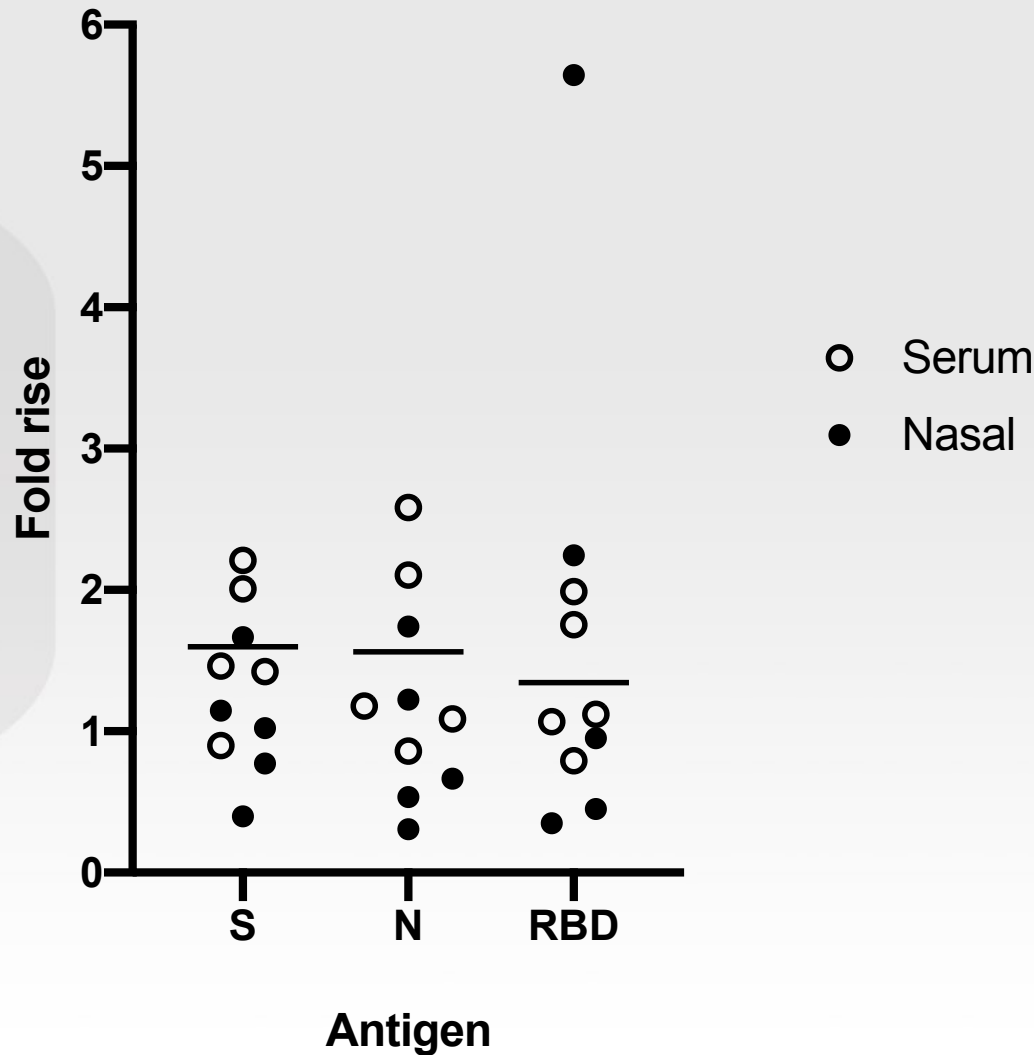


RBD responses	S responses	N responses	Any response
16/35	11/35	13/35	18/35

Preliminary Data

Responses calculated as a 2 or higher fold increase at d29 above pre-vaccination baseline measured in nasal, saliva, or serum samples.

100% of participants given two doses had an increase in specific IgA in one or more compartments



Preliminary Data

Fold rise d1 to d57 in serum and nasal IgA. 100% had a fold rise above 1.5 times pre-vaccination levels in at least one of serum or nasal samples.

Vaxart Strategy for COVID

Summary for VXA-CoV2-1

- Met Primary and Secondary Endpoints
 - Well-tolerated
 - Easy to distribute and administer (Tablets)
 - Highly immunogenic on eliciting T cells
 - Dose dependent responses observed with B cells
- Formulation and dosing will be evaluated in subsequent clinical studies to increase antibody responses

US will be immunized in 6 months

- Next generation vaccine approaches will need to be able to boost prior immunized people
- Evaluate cross-reactivity and potentially building new vaccines that address emerging escape mutants