May 2021

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

Hold the Needles and the Ice

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VAXART

UNLOCKING THE FULL POTENTIAL OF ORAL VACCINES

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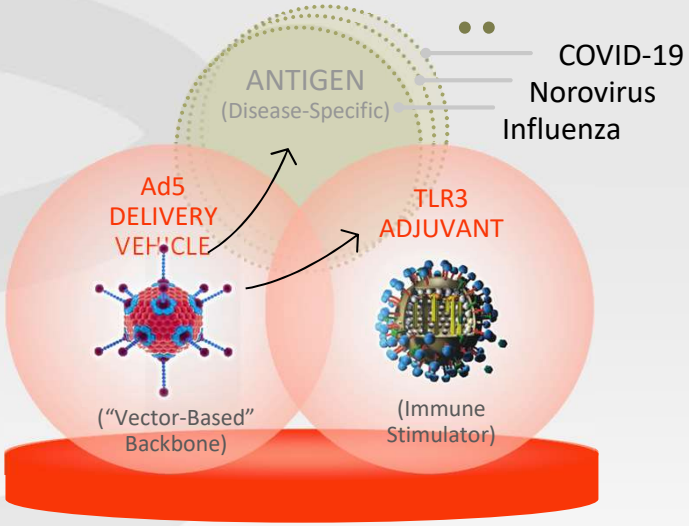
Proprietary Oral Vaccine Platform : Vaccine Tablets

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

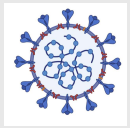
COVID Vaccines – Where are we now?

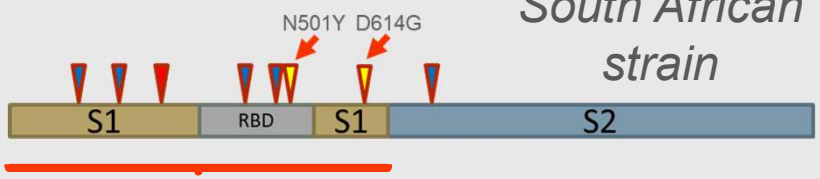
- Vaccine developers have made advanced candidates at incredible speed
- Several needle-based vaccines have completed Phase 3
  - Expression of the S protein in people leads to substantial protection (symptomatic illness) against matched strains (Moderna, Pfizer, Astrazeneca, Janssen)
  - S Protein vaccine also protective (Novavax)
  - Drop-off in efficacy noted when the vaccine strain doesn't match the circulating strain
- Roll out >3M vaccinations a day in the US under EUA
- 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

VAXART

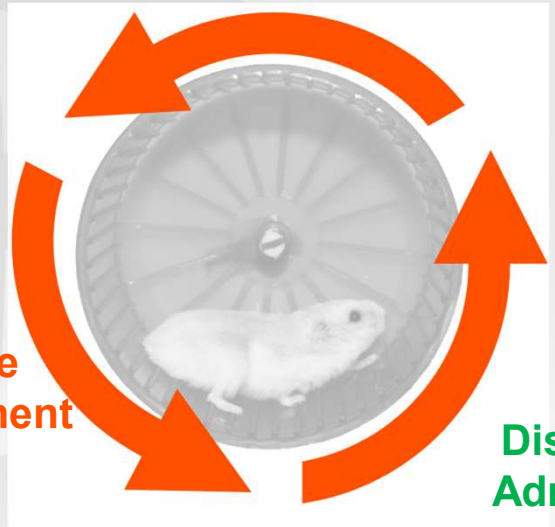
Rapid Emergence of new SARS-CoV-2 strains





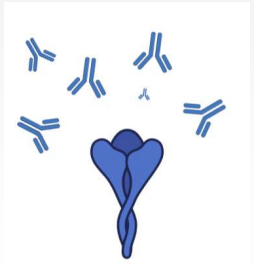
South African strain

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

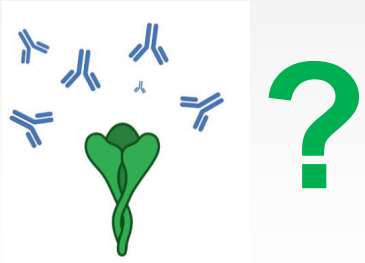


Vaccine Development

Distribution & Administration



Current vaccine strain



Future SARS-CoV-2 variants

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

An Important Step is the time for injecting large populations: Vaxart Takes Away the Needles

Rapid Emergence of new SARS-CoV-2 strains

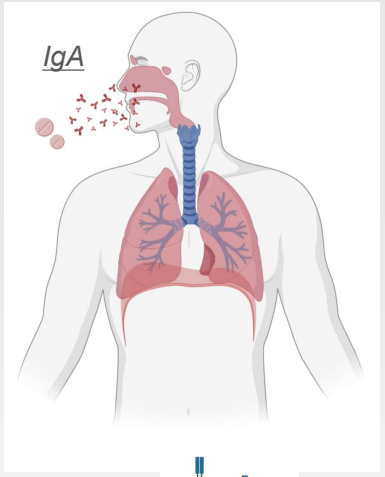
Vaccine Development

Rapid Distribution & Administration

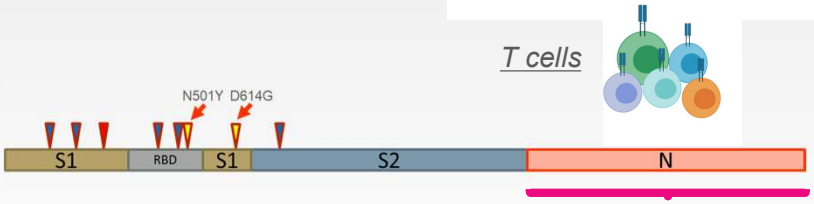
Get Off The Wheel – Shorten the Time to Herd Immunity

Vaxart's solution

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



T cells



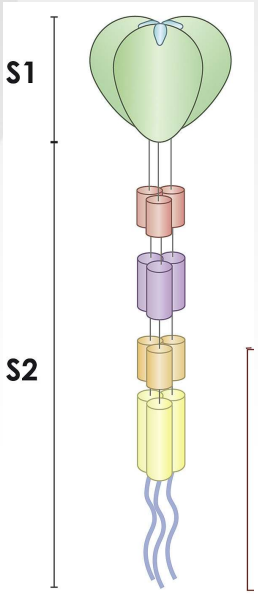
- More conserved across strains
- Strong target for T cells

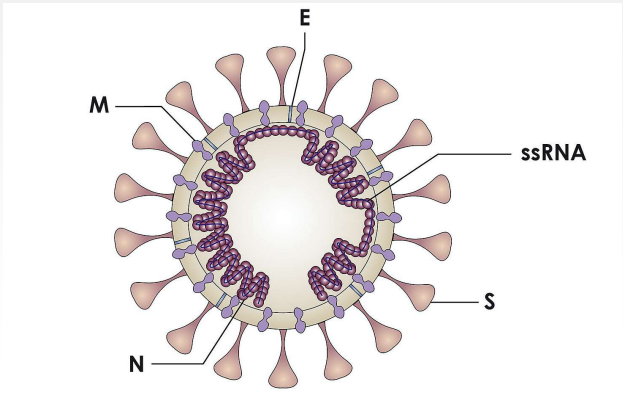
Dutta, et al, JV, 2020

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

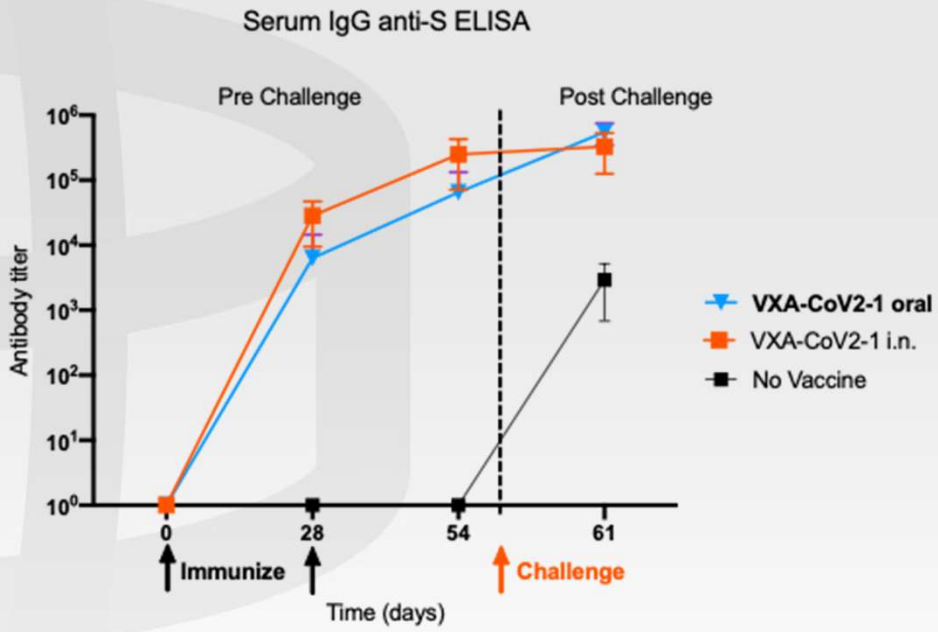
Candidate VXA-CoV2-1

- 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
- Goal is to make cross-strain reactive vaccine
  - address more than simply the original SARS-CoV-2 parental





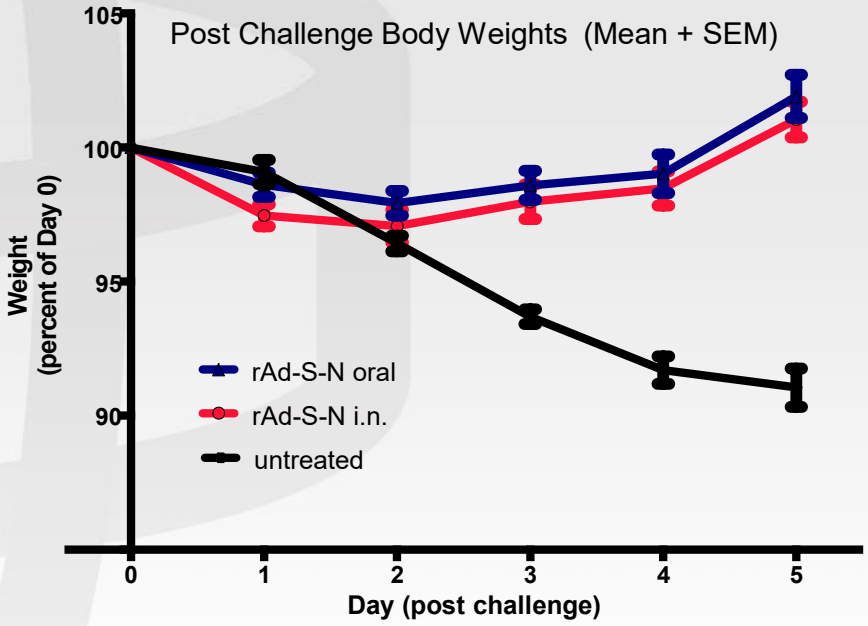
Oral COVID-19 vaccine candidate induces potent antibody responses in hamsters



- 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 candidate protects against a key clinical outcome, weight loss, in a hamster challenge model

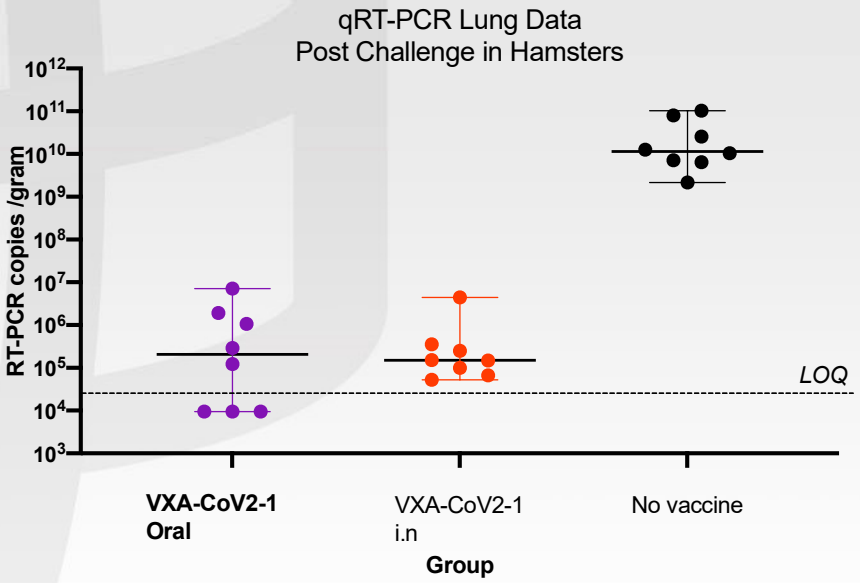


- The Syrian hamster is a very sensitive COVID-19 model
- Syrian hamsters have an ACE2 receptor that can bind SARS-CoV-2
- Hamsters challenged nasally with COVID-19 virus have similar disease as humans*
- Clinical symptoms of COVID-19 infection include weight loss

*Chan, et al, Oxford U Press, 2020

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**

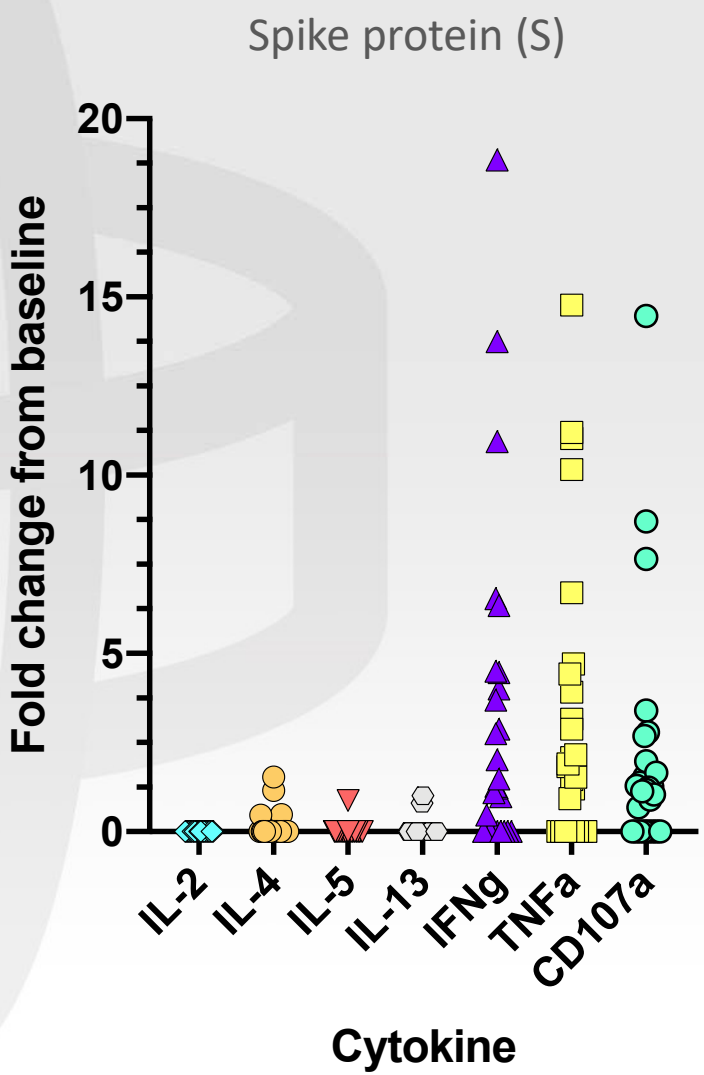
Treatment Group	Vaccine	Dose (±0.5 log)	No. of Doses	No. of Subjects
Cohort 1 (Sentinels)	VXA-CoV2-1	$1x10^{10}$ I.U.	2	5
	SMC Review of Safety Data through Day 8 Visit			
Cohort 2	VXA-CoV2-1	$1x10^{10}$ I.U.	1	15
Cohort 3	VXA-CoV2-1	$5x10^{10}$ I.U.	1	15
			Total	35

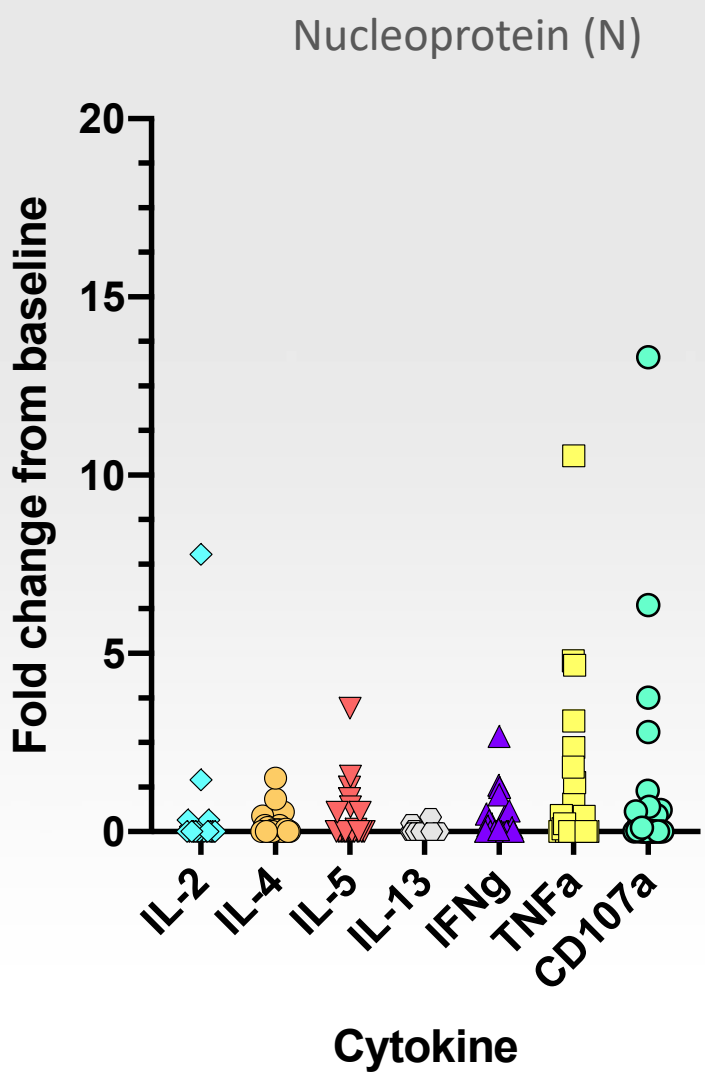
Solicited Symptoms Post Vaccination – Phase I

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 candidate shows preferential Th1 responses, inducing a strong CD8 cytotoxic response

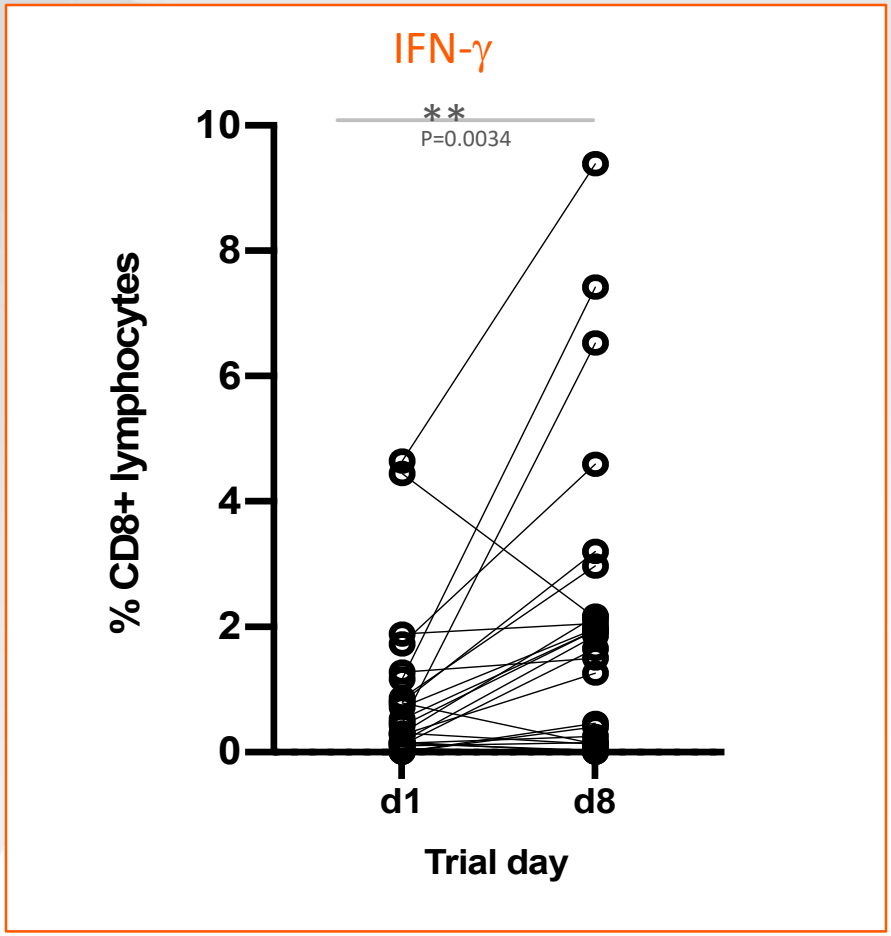


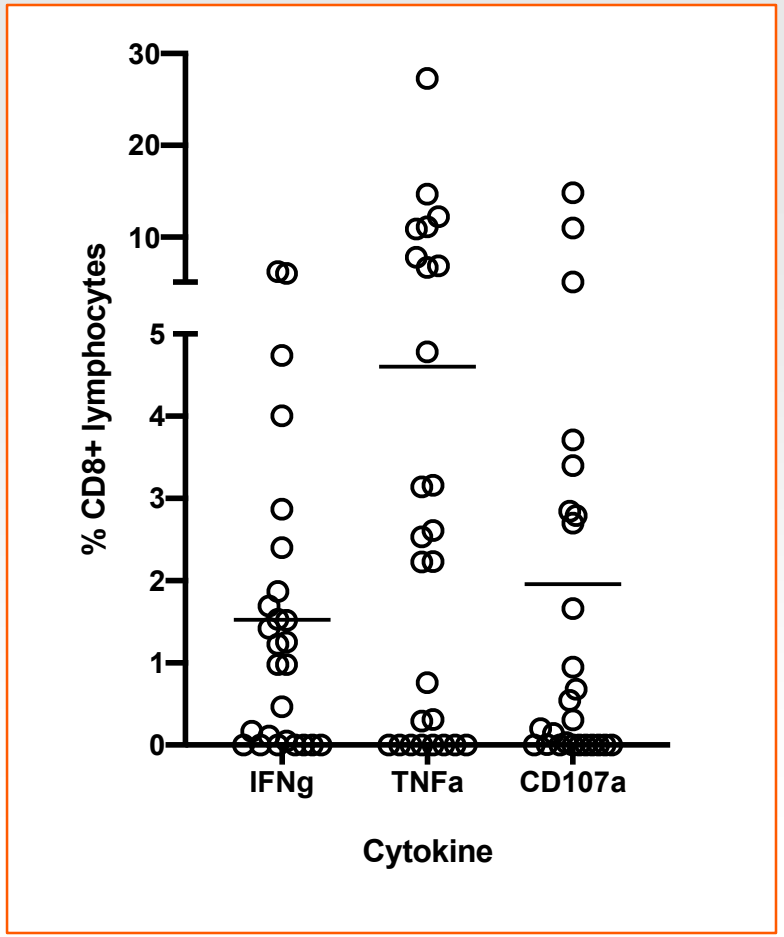


Restimulation with S or N peptide pools on PBMCs from pre and post vaccination. Th2 cytokines are CD4+ T cells, Th1 cytokines are CD8+ T cells. Fold change is calculated over the pre-vaccination sample.

Vaxart's Oral Vaccine candidate generates robust CD8 T cell responses

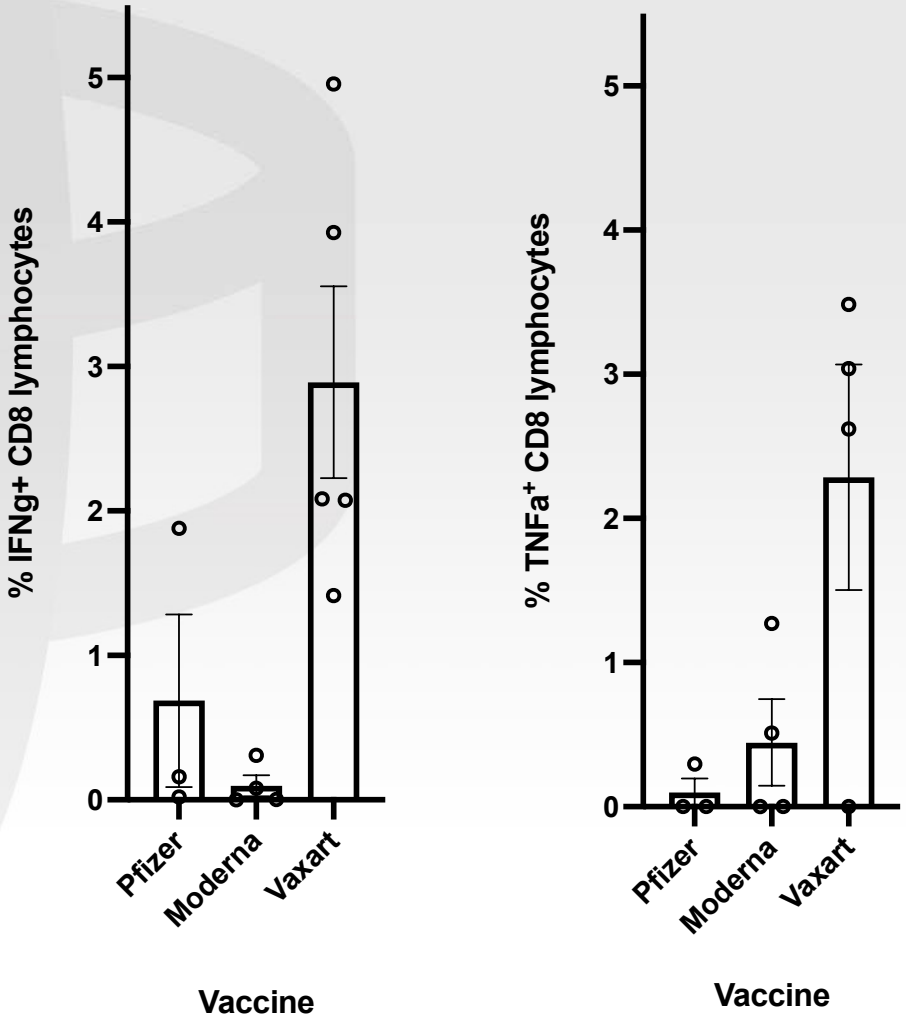
Vaxart's Oral Vaccine candidate generates high numbers of S specific IFN-γ, TNFα and CD107a producing T cells post immunization.





Vaxart's Oral Vaccine generates robust CD8 T cell responses – Compares favorably to the mRNA vaccines

Induction of T cells responses measured 7 days after the first dose. Increase over day 1 for IFN-g and TNF are shown



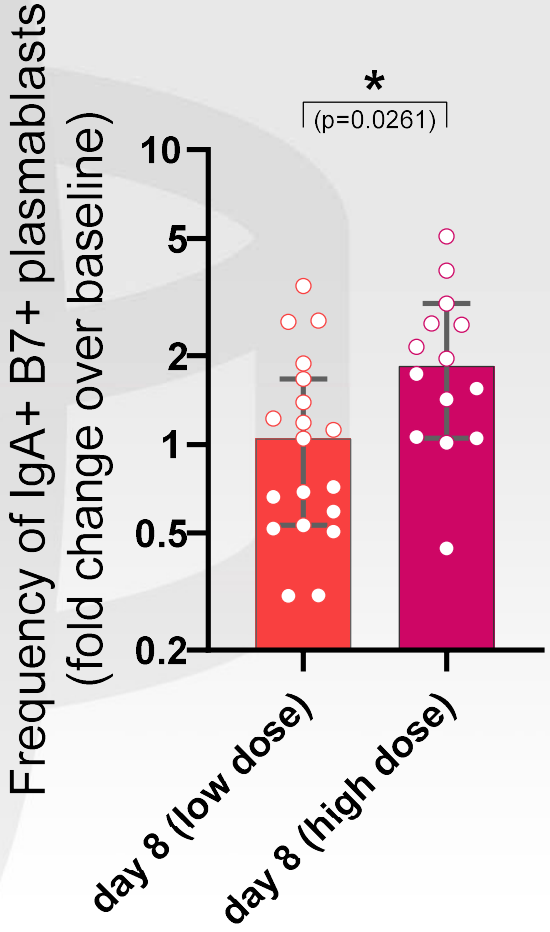
Frozen PBMC samples from Vaxart's Phase I trial were compared to PBMCs from volunteers that were immunized with the Pfizer or Moderna vaccines under EUA. Analysis was done at the same time points post immunization

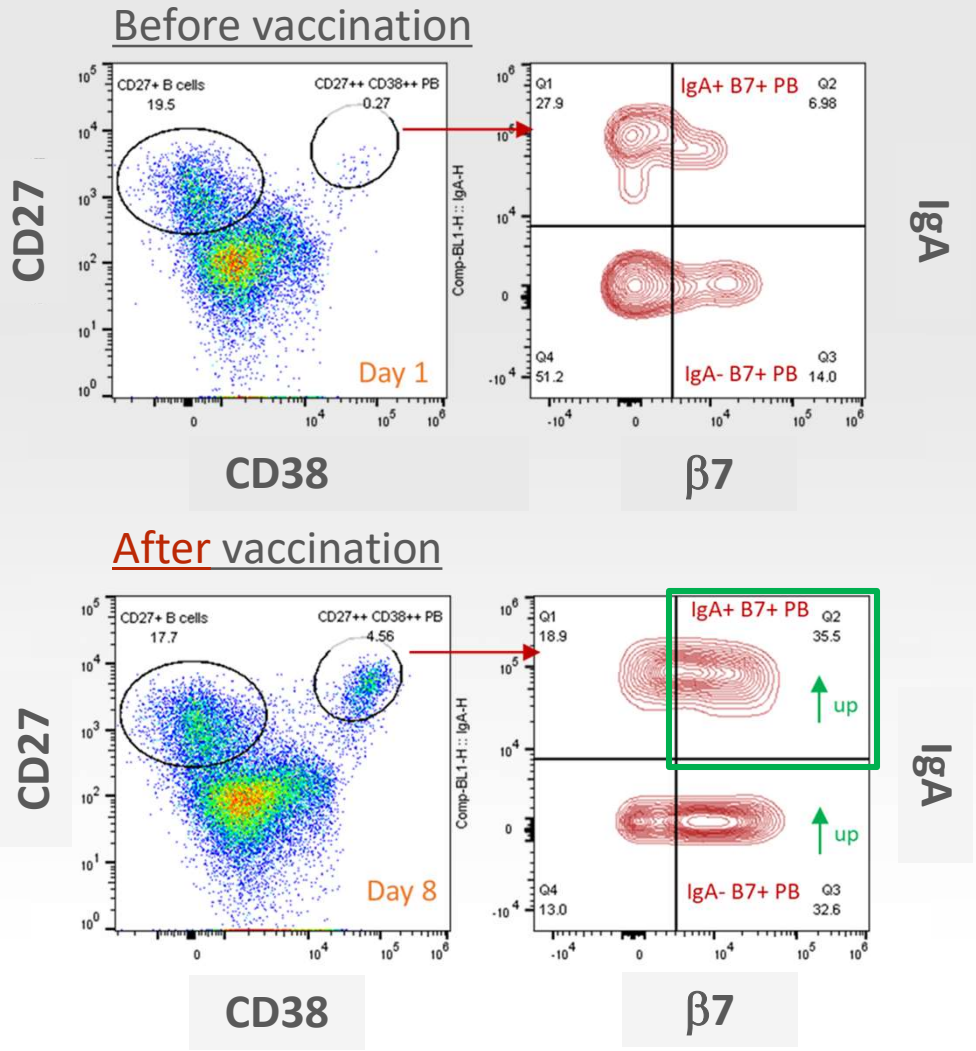
Preliminary data

Why T cells may be important for COVID

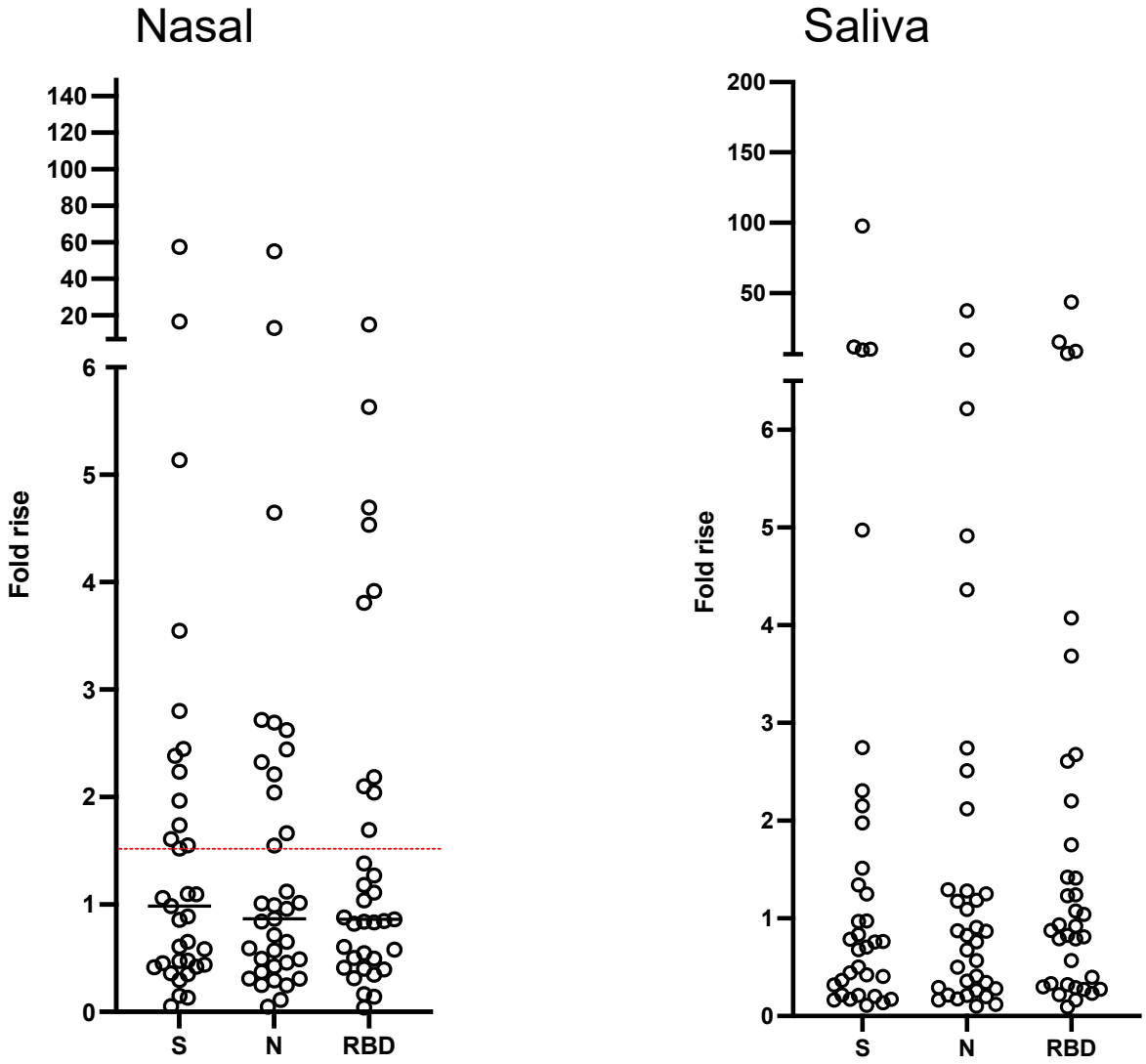
- Cross-protective and long-lasting
  - N protein responses to SARS-CoV-1 last 17 years after infection and cross-react to SARS-CoV-2 (Hellerstein, et al, Vaccine, 2020)
- People with agammaglobulinemia don't die of COVID and have a mild course of infection (Quinti, et al, J Allergy Clin Immunol, 2020)
- 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)

Vaccine-induced plasmablasts preferentially express IgA and upregulate the Mucosal Homing Receptor α4β7, particularly at higher dose



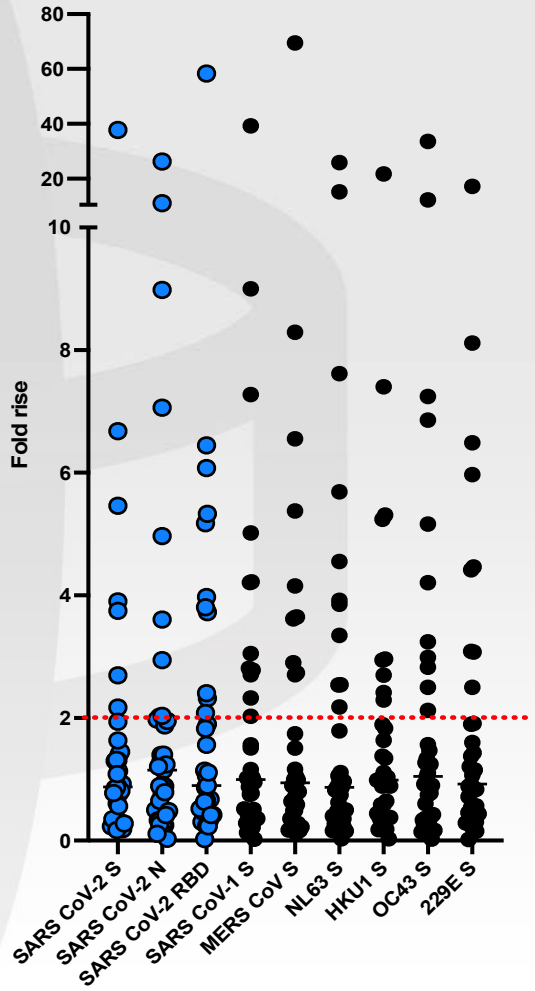


Vaxart oral vaccine candidate induces an increase in SARS-COV-2 specific mucosal IgA



Updated May 2021. Data is normalized to total IgA

Vaxart immunized subjects have increased cross-reactive nasal IgA response to other coronaviruses



Increased IgA antibodies to SARS-Cov-2 also leads to increased antibody responses to the S protein of other coronaviruses including SARS-CoV-1, MERS, and endemic common cold viruses

Preliminary Data

Graph shows increase in nasal IgA at d29 over d1 sample, normalized for amounts of total IgA

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
  - Observed increased nasal IgA antibody responses including cross-reactive IgA against other coronaviruses
- 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
- Vaxart will continue to evaluate cross-reactivity of our current clinical candidate and explore more strain specific responses in research

Acknowledgements and Thanks

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