COVIVAXX

Virus-like particle (VLP) vaccine designed against COVID 19

16 December 2020

SERUM INSTITUTE OF INDIA PVT. LTD.
Cyrus Poonawalla Group

Bilthoven Biologicals
Cyrus Poonawalla Group

VPM
Volkzine Projekt Management GmbH

Companies involved in the product development

SERUM INSTITUTE OF INDIA PVT. LTD.
Cyrus Poonawalla Group

→ Drug development and manufacture of drug substance

Bilthoven Biologicals
Cyrus Poonawalla Group

→ Drug product manufacture and QP certification

VPM
Vakzine Projekt Management GmbH
Cyrus Poonawalla Group

→ Sponsorship and overall project management

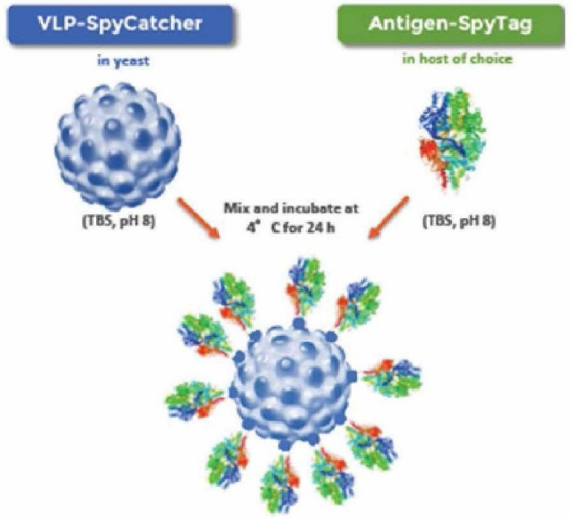
Objectives

- To develop a safe, efficacious and cost-effective vaccine against COVID-19 which will provide the protection of **children**, **adolescents** and **adults**
- To play a key role in disease elimination for public health benefit by **blocking the transmission** of novel corona virus
- To manufacture and distribute **billions of doses** in a cost-effective manner within a short period of time
- **Unique concept:**
  - Conjugate of Receptor Binding Domain (RBD) and Virus Like Particles (VLP)
  - Stronger immunogen using SpyCatcher-SpyTag Technology (**RBD on VLP**) with efficient display and presentation for enhanced immunogenicity

COVIVAXX – product and technology

- COVIVAXX comprises a conjugate of the Receptor Binding Domain (RBD) of the spike protein of SARS-CoV-2 and the established and reliable technology of virus like particles (**VLP**)
- Better immunogenicity through effective surface presentation of the antigen
- SpyCatcher-SpyTag technology is a yeast based production and it is
  - Well established
  - Reliable
  - Easily scalable

→ Proof of concept was already demonstrated for a malarial antigen by inducing a higher antibody response



Advantages of VLP display

- VLPs displaying T-cell epitopes are capable of eliciting efficient TH1 and CTL responses.
- VLPs have the ability to be cross-presented and enter the major histocompatibility class I (MHC-I) pathway.

  This ability is owed to their particulate nature which allows the VLPs to be efficiently taken up by APCs and enter the MHC-I pathway.
- SpyTag and SpyCatcher react spontaneously upon mixing to form an amide bond. This bond formation is irreversible.
- Conjugation process is a simple mixing step without the use of any organic solvent and hazardous chemicals.

Immunogenicity studies

	Animal species, quantity & strain	Volume/ Route	Dose in µg/mL/animal	Serum dilutions for ELISA	Sero-converted animals	Antibody titer / Day (Dilution based)
1	Rabbit 01 Male & 01 Female (Species: New Zealand white)	0.5 mL/IM	20 µg/ 0.5 mL/Rabbit	1:10 to 1:3200	02/02	1:>3200 (Day 18)
2	Guinea Pig 03 Male (Species: Dunkin Hartley)	0.5 mL/IP	20 µg/ 0.5 mL/Guinea pig	1:10 to 1:3200	03/03	1:3200 (Day 28)
3	Mice 10 Male (Species: NIH Ola/Hsd)	0.5 mL/IP	20 µg/ 0.5 mL/Mouse	1:10 to 1:3200	10/10	1:3200 (Day 28)

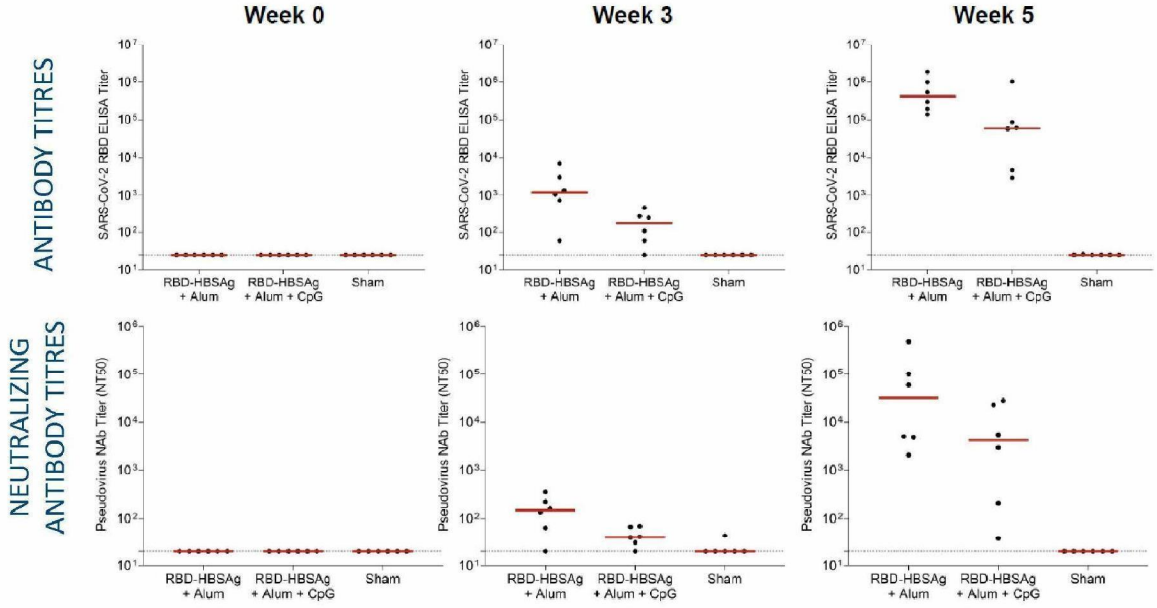
Seroconversion was shown in all analysed species during preliminary studies

Repeated dose Immunogenicity (rats)

IgG Titres Day 30				
Group	Group Name	Dose (µg/rat)	anti-RBD	PRNT50 (neutralization assay)
G2	Low Dose	10	8,000 to 128,000	326 - 2560
G3	High Dose	50	48,000 to 384,000	1,221 – 3,019

Dose dependent induction of anti-RBD antibodies (IgG) and neutralizing antibodies

Challenge studies in non-human primates



Performed at Dr. Dan Barouchs lab, Harvard with support from Gates foundation

The ongoing challenge study results show an excellent response in terms of IgG antibodies and neutralizing antobodies when immunised with 5 µg of RBD-HBsAg protein. Viral load is currently being estimated.

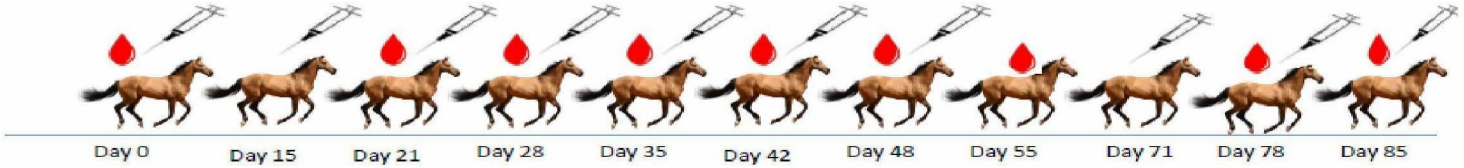
Immunogenicity Comparision between RBD-HBsAg VLP and Whole Virus

Animal Model	Route	PRNT50 for Inactivated Whole Virus	PRNT50 for RBD HBsAg
BALB/c Mice	s.c.	< 40- 175	250-275
Guinea pig	s.c.	2273	11200
New zealand white Rabbit	s.c.	2470-4077	12350-13872

- Small animals were immunized with COVID-19 inactivated whole virus antigen and Serum institute's RBD-HBsAg VLP conjugate. Plasma obtained from these animals were tested for PRNT50 titres.
- PRNT50 titre obtained from animal plasma immunized with RBD-HBsAg conjugate is significantly higher than animals immunized with COVID-19 inactivated whole virus antigen.

Immunogenicity studies in equines

		Plasma			Purified concentrated bulk (RBD-HBsAg VLP)	
Sr. No.	Batch No.	RBD ELISA titre	PRNT 50		RBDELISA titre	PRNT 50
1	ICOB20001	>512000	6331282		>1024000	12088331
2	ICOB20002	>512000	2226748		>1024000	9232838
3	ICOB20003	>512000	2357098		~1024000	6681868



Equines (Indian Horse) were immunized with RBD-HBsAg VLP conjugate mixed with Freund's adjuvant via the subcutaneous route. Purification was performed with a new unique method of manufacturing and purified F(ab)2 obtained. The purified hyper immune sera F(ab)2 would be clinically evaluated for therapeutic application.

Toxicity studies

Single dose toxicity study in rats

- RBD SARS-CoV-2 HBsAg VLP vaccine did not induce any adverse or other effects in the treated rats, when administered by intramuscular injections at the doses of 10 µg or 40 µg per rat.
- RBD SARS-CoV-2 HBsAg VLP vaccine was well tolerated at the injection sites in rats.

Repeated dose toxicity and immunogenicity study in rats

- RBD SARS-CoV-2 HBsAg VLP vaccine when injected to rats by three i.m. injections, each of 10 µg or 50 µg per rat, did not induce any systemic toxicity in the treated rats.
- RBD SARS-CoV-2 HBsAg VLP vaccine did not induce any adverse local tissue reaction and was well tolerated at the injection sites in rats.
- The no-observed-adverse-effect level (NOAEL) in rats was found to be greater than 50 µg per rat.
- The vaccine induced the production of antibodies in a dose dependent fashion.

COVIVAXX – CMC highlights

- The drug substance is produced at Serum Institute of India

  Production capacity: **100 - 200 million doses / month**

- The drug product is manufactured at Bilthoven Biologicals (The Netherlands)
- Vaccine formulation with reduced aluminium content for intradermal administration is under development
- Vaccine formulation with CpG adjuvant (produced by Dynavax) is under development for use in immunodeficient individuals and elderly)

Overall manufacturing capacities

- SIIPL's motto of supplying life saving vaccines cost effectively is supported by its huge manufacturing capacities
- SIIPL has more than five decades of experience in manufacturing and commercializing vaccines across the globe and more than two decades of expertise in yeast based product manufacturing
- Distributed more than 1.6 billion doses per annum
- State of the art facilities identified for the production of COVIVAX (up to 200 million doses per month)

COVIVAXX – Clinical highlights

- COVIVAXX was shown to be safe and well tolerated in the Phase I trial
- All subjects from Phase II clinical studies in Australia have received first dose of the vaccine without any safety findings
- Phase III pivotal trial is planned in Europe (start in Q2 2021)
- Clinical evaluation in **children, adolescents, adults and elderly** (4 years and above)
- Phase III study will assess immunogenicity, safety and efficacy of COVIVAXX administered intramuscularly and intradermally

COVIVAXX – Salient Features

- The COVIVAXX candidate has RBD as the target antigen and hence is envisaged to block transmission of the virus.
- Being a protein subunit based vaccine with time tested adjuvant viz; alum, the vaccine can be administered to children, adolescents, adults and geriatric populations without any safety concerns.
- The vaccine will offer significant public health benefits as it can be administered to school going children who are the primary carriers of the virus and thus highest transmitters to the more susceptible geriatric population.
- The vaccine is highly safe as it does not use any unproven adjuvant. Alum as an adjuvant has more than five decades of proven safety in billions of subjects.
- The vaccine can be stored and transported at 2-8 deg Celsius and also expected to be thermo stable making it easily deployable in mass vaccination campaigns.
- SIIPL plans to use a unique multidose vial adapter that allows multiple withdrawals from a multidose vial (preservative free) without disturbing the integrity of the vial and providing sterility assurance.

Thank you!

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