

Supplementary Information File

Comparative systematic review and meta-analysis of reactogenicity, immunogenicity and efficacy of vaccines against SARS-CoV-2

Ian McDonald¹, Sam M Murray¹, Catherine J Reynolds¹, Daniel M Altmann^{2*} and
Rosemary J Boyton^{1,3*}

¹Department of Infectious Disease, Faculty of Medicine, Imperial College London, UK

²Department of Immunology and Inflammation, Faculty of Medicine, Imperial College London, UK

³Lung Division, Royal Brompton and Harefield Hospitals, London, UK

*Address for correspondence:

Prof. Rosemary Boyton, PhD, FRCP, FHEA

Lung Immunology Group, Adult Infectious Disease, Department of Infectious Disease, Faculty of Medicine, Room 8N22 Commonwealth Building, Hammersmith Hospital Campus,
Imperial College London, Du Cane Road, London W12 0NN, UK

Email: r.boyton@imperial.ac.uk

&

Prof. Daniel Altmann, PhD

Department of Immunology and Inflammation, Faculty of Medicine,
Imperial College London, Du Cane Road, London W12 0NN, UK

Email: d.altmann@imperial.ac.uk

Supplementary Figure 1: Heat map and table showing countries where HCoV pre-clinical and clinical studies were conducted

Supplementary Figure 2: Percent of Grade 3 adverse events (AE) recorded in human trials

Supplementary Figure 3: Human (n=25) and NHP (n=23) studies; comparative analysis of immunological readouts

Supplementary Table 1: Database Search Strategy: Search terms, phrases and limits related to HCoV vaccine research used in accordance with PRISMA guidelines

Supplementary Table 2: Inclusion and exclusion criteria

Supplementary Table 3: Characteristics of the human studies

Supplementary Table 4: Characteristics of the NHP studies

Supplementary Table 5. Summary of vaccine studies in NHP

Supplementary Table 6: Demographic characteristics of the human studies

Supplementary Table 7: Vaccine efficacy against COVID-19

Supplementary Table 8: NHP safety analysis

Supplementary Table 9. Interstudy analysis of individual local adverse events reported in vaccine group (excluding control group) of coronavirus vaccine studies.

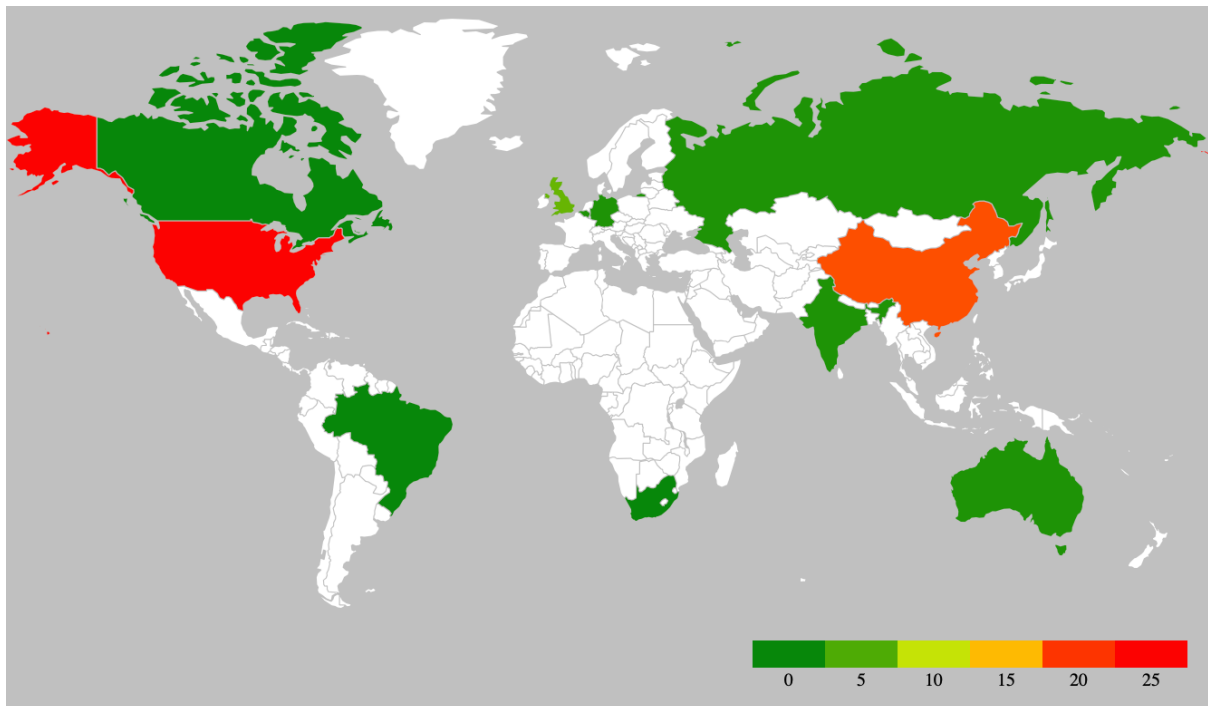
Supplementary Table 10: Interstudy analysis of individual systematic adverse events reported in vaccine group (excluding control group) of coronavirus vaccine studies.

Supplementary Table 11: Serious adverse events

Supplementary Table 12: Pre-existing anti-vector neutralising antibody titers recorded before vaccination and their correlation with anti-RBD seroconversion or SARS-CoV-2 neutralization in adenoviral vectored SARS-CoV-2 vaccines

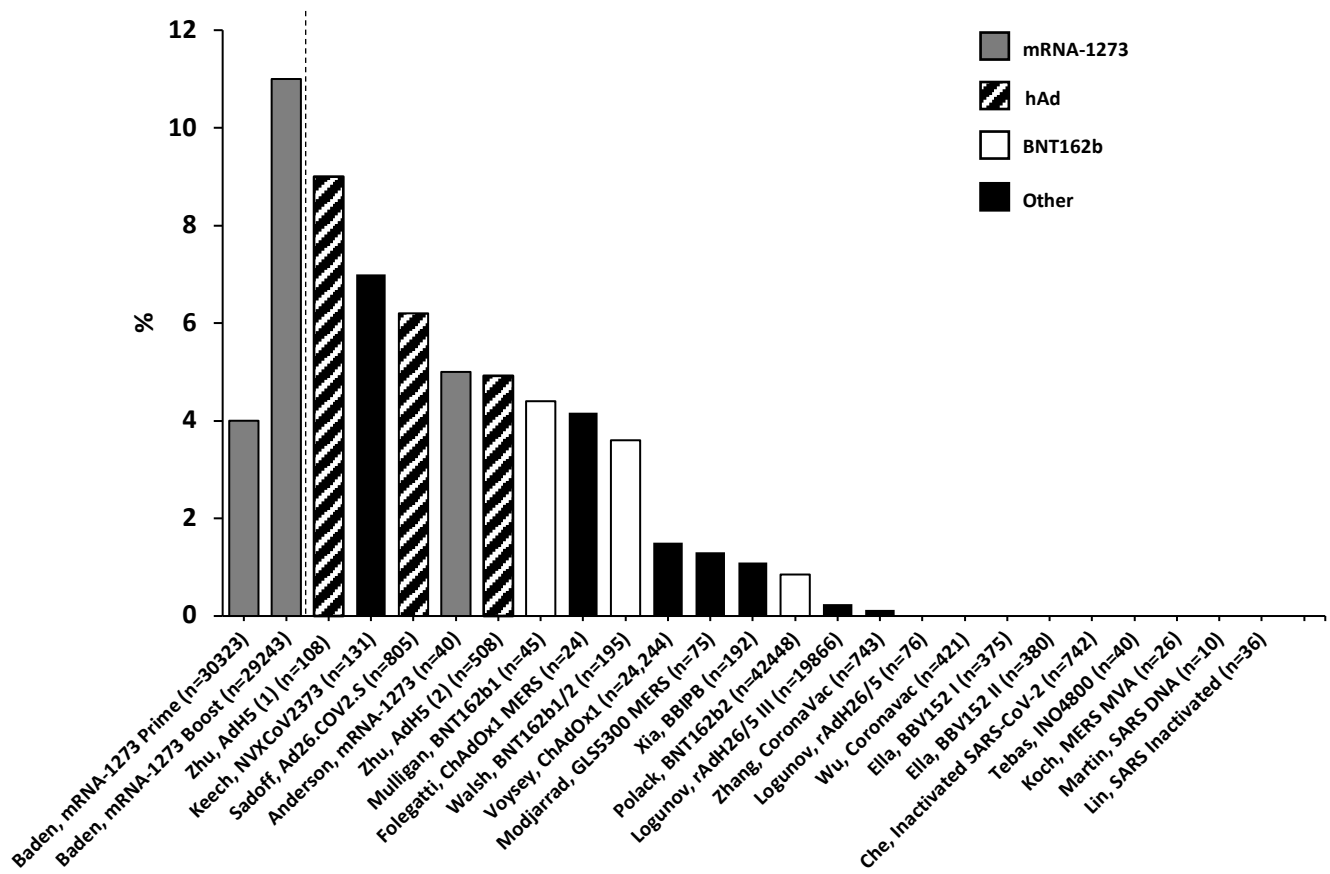
Supplementary Table 13. Human and NHP T cell analysis

Supplementary Figure 1: Heat map and table showing countries where HCoV pre-clinical and clinical studies were conducted

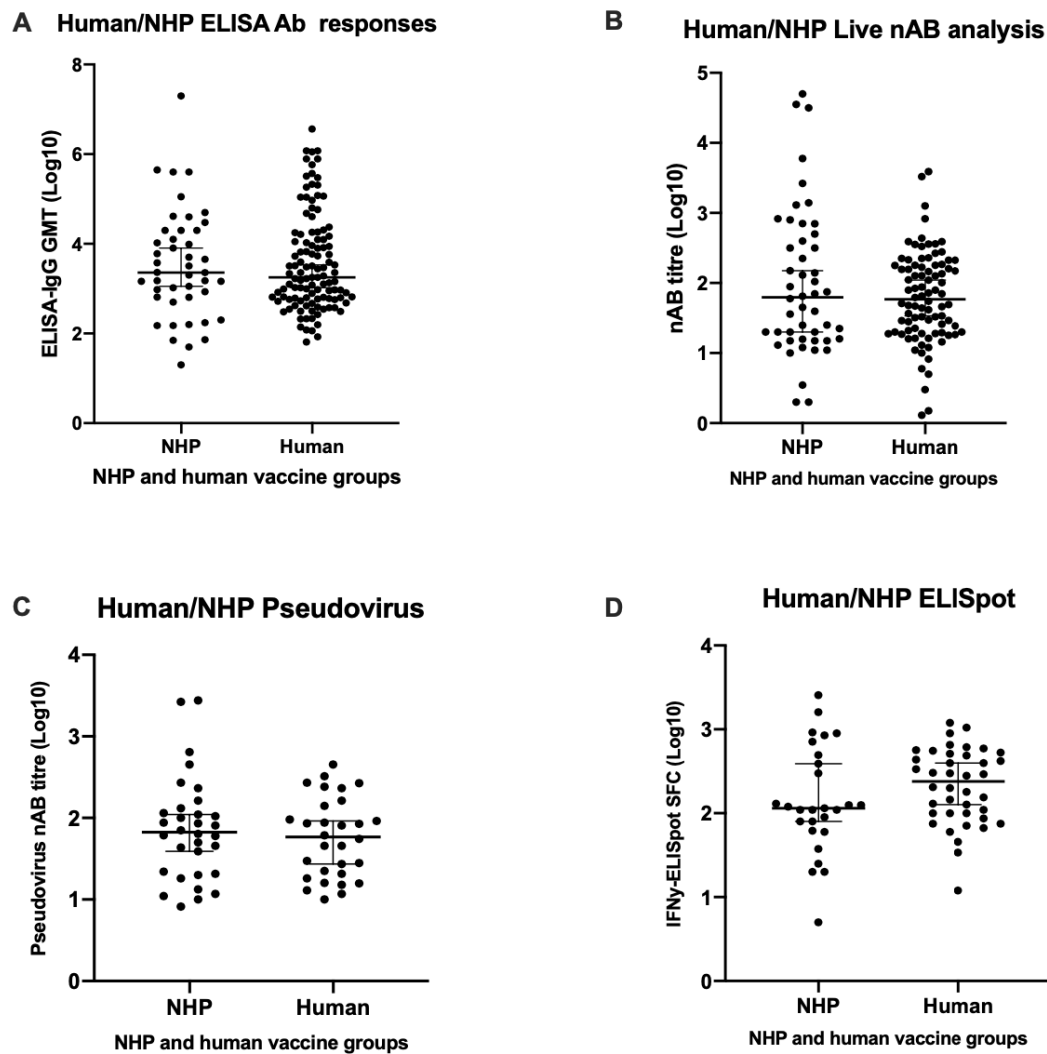


Country	Number
United States	21
China	18
United Kingdom	5
Belgium	2
Germany	2
India	2
Australia	2
Russia	2
Canada	1
Brazil	1
South Africa	1

Supplementary Figure 2. Percent of Grade 3 adverse events (AE) recorded in human trials. Grade 3 AE in both experimental and placebo groups are included in this analysis. First author, vaccine platform and number of participants in each study shown on the x-axis. Zhu, AdH5 (1): AdH5-SARS-CoV-2 phase 1 trial, Zhu, AdH5 (2): AdH5-SARS-CoV-2 phase 2 trial, Folegatti, ChAdOx1 (1): ChAdOx-MERS.



Supplementary Figure 3. Human (n=25) and NHP (n=23) studies; comparative analysis of immunological readouts: (A) ELISA-IgG, (B) Live neutralization antibody assay, (C) Pseudovirus neutralization antibody assay, (D) ELISpot T cell responses. Data are log transformed. Unpaired t-test of independence used to evaluate the statistical difference between human and NHP vaccine group responses ($p < 0.05$ was taken to indicate a significant difference)



Supplementary Table 1: Database Search Strategy: Search terms, phrases and limits related to HCoV vaccine research used in accordance with PRISMA guidelines.

Data base	Search strategy
PUBMED	(Coronavirus) OR ("sars"[All Fields]) OR ("middle east respiratory syndrome"[All Fields]) OR ("sars"[Title/Abstract]) OR ("mers"[Title/Abstract]) AND (Vaccin*) NOT (Review[Publication Type]) [Filter – Year of Publication – 2003-2021]
EMBASE	(coronaviridae OR 'severe acute respiratory syndrome' OR 'middle east respiratory syndrome coronavirus' OR 'sars' OR 'mers') AND (vaccin*) [Filter – Year of Publication – 2003-2021]

Supplementary Table 2: Inclusion and exclusion criteria

Inclusion Criteria

- Any study evaluating the safety, immunogenicity or efficacy of a coronavirus vaccine candidate in NHP or humans

Exclusion Criteria

- *In vitro* studies
- Other animal models
- Reviews, editorials, conference proceedings
- Unrelated to coronavirus vaccine development
- Duplicates

Note on exclusion of Pre-Prints from this analysis

- We have only included peer reviewed data in this analysis

Supplementary Table 3: Characteristics of the human studies

Study ID Location Ref No	Study Design, Length, Population (N), Age	Pathogen	Vaccine Platform	Antigen Insert	Group + Doses, Boosting, Route of Administration,	Measure of Ab Response	Measure of Cellular Response + Days
Ella et al, (16) 2021 India	Safety, immunogenicity Phase 1 double-blind, multi-center, randomized, placebo-controlled N=375 18-55y/o	SARS-CoV-2	BBV152	Inactivated whole virion	3ug with Algel-IMDG (N=100) 6ug with Algel-IMDG (N=100) 6ug with Algel (N=100) Placebo= Algel only (N=75) Boosted D14 IM	ELISA-IgG D0, 28 Microneutralization assay (MNT ₅₀) D0, D28 Plaque-reduction neutralization test (PRNT ₅₀)	ICS D0, 28 IFNγ ELISpot D0, 28
Richmond et al, (17) 2021 Australia	Safety, immunogenicity Phase 1, randomized, double-blind placebo-controlled N=151 18-54, 55-75y/o	SARS-CoV-2	S-Trimer (SCB-2019)	Trimer-Tag fused trimerized S protein	3ug w/o Adjuvant n=8 3ug AS03 N=16 3ug CpG/Alum N=16 9ug w/o Adjuvant N=8 9ug AS03 N=16 9ug CpG/Alum N=16 30ug w/o Adjuvant N=9 30ug AS03 N=16 30ug CpG/Alum N=16 Placebo N=30 All boosted D21 IM	ELISA-IgG D1,D22,D36,D50 ACE2-Competitive ELISA D1,D22,D36,D50 Authentic WT Neutralization D1,D22,D36,D50	ICS D1,D22,D36,D50
Logunov et al, (18) 2021 Russia	Safety, efficacy Phase 3, randomized, double-blind, placebo-controlled, multi-center N= 21,977 >18y/o	SARS-CoV-2	rAd26 and rAd5 Gam-COVID 'Sputnik'	Full-Length SARS-CoV-2 Spike GP	Vaccine N = 14964 Placebo N =4902 All boosted D21 IM	ELISA-IgG N=456 D42 TCID₅₀ N=100 D42	IFNγ ELISA n=58 D1, D28
Wu et al, (19) 2021 China	Safety, tolerability, immunogenicity Phase 1/2 randomized, double-blind, placebo-controlled Phase 1 N=72 18-59y/o Phase 2 N=350 \geq 60y/o	SARS-CoV-2	Virus Inactivated by β - Propiolactone (CoronaVac)	Inactivated SARS-CoV-2 Virus (CN02 Strain)	1.5ug Alum N=100 3ug Alum N=124 6ug Alum N= 124 Placebo N= 74 All boosted D28 IM	Microcytopathogenic Live nAb assay D0, D56	NA
Chu et al, (20) 2021 USA	Safety, immunogenicity Phase 2, randomized, observer-blind, placebo-controlled, multi-center N=600 18-55y/o (N=300), \geq 55y/o (N=300)	SARS-CoV-2	mRNA-1273 (LNP)	SARS-CoV-2 Spike S2-P	50ug N=200 100ug N=200 Placebo N=200 All boosted D29 IM	ELISA-IgG D0,29,43,57 Live virus microneutralization assay (MN ₅₀) D0,29,43,57	NA
Voysey et al, (21) 2021 UK/South Africa/Brazil	Immunogenicity, efficacy Pooled analysis of Phase 1/2 & 2/3(UK), Phase 3 (Brazil), Phase 2/3 SA N= 24,422 18-55, \geq 18, 18-65y/o	SARS-CoV-2	ChAdOx, MenACWY (Control)	Full-Length SARS-CoV-2 Spike GP	<u>Phase 1/2 UK</u> Vaccine N=544 Placebo N=533 <u>Phase 2/3 UK</u> Vaccine N=5593 Placebo N=5211 <u>Phase 3 Brazil</u> Vaccine N=5207 Placebo N=5209 <u>Phase 2/3 SA</u> Vaccine N=1064 Placebo N=1061 <u>Boost intervals:</u> <6 weeks N=7746 6-8 weeks N=2121 9-11 weeks N=1864 \geq 12 weeks N=2649 IM	ELISA-IgG D0, D56, D84, D112, D140, D182 (N=44), D28 after 2 nd dose (N=3337) Pseudotype nAb assay (IC ₅₀) D28 after 2 nd dose. (N=893)	NA
Ella et al, (22) 2021 India	Safety, immunogenicity Phase 2, double-blind, randomized, multi-center N= 380 12-65y/o	SARS-CoV-2	BBV152	Inactivated whole virion	3ug Algel-IMDG N=190 6ug Algel-IMDG N=190 Boosted D28 IM	ELISA-IgG D0, 28,42,56 Microneutralization assay (MNT ₅₀) D0, 56 Plaque-reduction neutralization test (PRNT ₅₀) D0, 56	Luminex ELISA for Th1/2 cytokines D0,42 FACS D0, 104
Sadoff et al, (23) 2021 Belgium/USA	Safety, immunogenicity Phase 1/2a, randomized, double-blind multi-center, placebo-controlled Ongoing N=805 >18y/o	SARS-CoV-2	rAd26.COVID.S	Full-length stabilized SARS-CoV-2 spike GP	Low dose = 5x10 ¹⁰ VP (N=323) High dose = 1x10 ¹¹ VP (N=318) Placebo=N=16 Boosted D57 IM	ELISA-IgG D15, 29,57,71 MNA₅₀ D15,29,57,71	ICS D1-15

Tebas et al (24) 2020 USA	Safety, tolerability, immunogenicity, Phase 1, open-label, multi-center, Ongoing N=40 18-50y/o	SARS-CoV-2	DNA (INO-4800)	SARS-CoV-2 spike GP	Low dose = 1mg High dose=2mg Boosted D28 ID with electroporation	ELISA IgG D7, 42 Authentic virus nAb assay D7, 42	IFNγ ELISpot D7, 42 ICS D7, 42
Baden et al (25) 2020 USA	Safety and Efficacy Phase 3 randomized, observer-blinded, placebo-controlled trial Ongoing N=30,420	SARS-CoV-2	mRNA-1273 (LNP)	SARS-CoV-2 Spike S2-P	Experimental = 100ug (N=15,181) All Boosted (D28) Placebo = Saline (N=15,170)	NA	NA
Polack et al (26) 2020 USA	Safety and Efficacy Multinational, observer blinded, placebo-controlled Phase 3 trial Ongoing N=43,448 >16 y/o	SARS-CoV-2	LNP mRNA BNT162b2	Prefusion stabilised full-length SARS-CoV-2 Spike GP	Experimental = 30ug (N=21720) Placebo = Saline (N=21728) All Boosted (D21) IM	NA	NA
Voysey et al (27) 2020 UK, Brazil, South Africa	Safety and Efficacy Blinded, randomized controlled trial Ongoing N=23,848 (11,636 included in analysis) $\geq 18y/o$	SARS-CoV-2	ChAdOx, MenACWY (Control)	Full-Length SARS-CoV-2 Spike GP	Experimental groups= 2.2 to 6.5x10 ¹⁰ (N=4440) Control groups= MenACWY (N=4455) Boost up to D84 IM	NA	NA
Ramasamy et al (28) 2020 UK	Safety and Immunogenicity Single blind, randomized Phase 2/3 trial Ongoing N=560 $\geq 18y/o$	SARS-CoV-2	ChAdOx, MenACWY (Control)	Full-Length SARS-CoV-2 Spike GP	Prime, low dose = 2.2x10 ¹⁰ vp (N=100) Prime, standard dose = 3.5-6.5x10 ¹⁰ vp (N=100) Prime-Boost, low dose = 2.2x10 ¹⁰ vp (N=195) Prime-Boost, standard dose = 3.5- 6.5x10 ¹⁰ vp (N=157)	ELISA-IgG D0-D28-D42-D56 SEAP Neutralization assay D0-D28-D42-D56 Microneutralization assay (MNA ₈₀) D0-D28-D42-D56	IFNγ Linked ELISpot D0-D14-D28-D42
Zhang et al 2020 (29) China	Safety, Tolerability and Immunogenicity Double-blind, placebo-controlled Phase 1 and 2 trial Ongoing Phase 1 - N=144 Phase 2 - N=600 18-59y/o	SARS-CoV-2	Virus Inactivated by β - Propiolactone (CoronaVac)	Inactivated SARS-CoV-2 Virus (CN02 Strain)	Phase 1 Low Dose = 3ug + Alum (N=48) High Dose = 6ug + Alum (N=48) Placebo = Alum (N=48) All Boosted D14 IM Phase 2 Low Dose = 3ug + Alum (N=237) High Dose = 6ug + Alum (N=237) Placebo = Alum (N=120) All Boosted D28 IM	ELISA-IgG/IgM D0-D28-D42-D56 Microcytopathogenic Live nAb Assay D0-D14-D28 Pseudovirus nAb assay D0-D14-D28	IFNγ Linked ELISpot D0-D14-D28 Flow cytometry/ICS D0-D14-D28
Che et al (30) 2020 China	Safety and Immunogenicity Double-blind, randomized phase 2 trial 7 weeks N=742 18-59y/o	SARS-CoV-2	Virus Inactivated by Formaldehyde and β - Propiolactone	Inactivated SARS-CoV-2 Virus (KMS-1 Strain)	Medium dose = 100 EU viral antigen + Alum= (N=300) High dose = 150 EU viral antigen + Alum (N=300) Placebo = Alum (N=150) All Boosted D14/ 28	ELISA-IgG D0-D14-D28 Live nAb Assay D0-D14-D28	NA
Xia et al (31) 2020 China	Safety and Immunogenicity Double-blind, randomized, placebo- controlled phase 1/2 trial Ongoing Phase 1 - N=192 Phase 2 - N=448	SARS-CoV-2	Virus Inactivated by β - Propiolactone (BBIBP-CorV)	Inactivated SARS-CoV-2 Virus (HB02 Strain)	Phase 1 Low dose = 2ug + Alum (N=48) Medium dose = 4ug + Alum (N=48) High Dose = 8ug + Alum (N=48) Placebo = Saline + Alum (N=47) All Boosted D28 Phase 2 Group 1 = 8ug + Alum (N=112) Group 2 = 4ug + Alum and placebo (N=112), Boosted D14 Group 3 = 4ug + Alum and placebo (N=112), Boosted D21 Group 4 = 4ug + Alum and placebo (N=112), Boosted D14-D28	Live nAb Assay D7-D14-D28-D32-42	NA

Walsh et al (32) 2020 USA	Safety and Immunogenicity Single-blinded, dose escalation, placebo-controlled phase 1 trial Ongoing N=195 18-55y/o, 65-85y/o	SARS-CoV-2	LNP mRNA BNT162b1 and BNT162b2	BNT162b1: Trimerized RBD BNT162b2: Membrane- anchored, full length, perfusion stabilized spike protein	BNT162b1 (18-55y/o) Group 1 =10ug (N=12) Group 2 =20ug (N=12) Group 3 =30ug (N=12) Group 4 =100ug (N=12) Group 5 = Placebo (N=12) BNT162b1 (65-85y/o) Group 1 =10ug (N=12) Group 2 =20ug (N=12) Group 3 =30ug (N=12) Group 4 = Placebo (N=9) BNT162b2 (18-55y/o) Group 1 =10ug (N=12) Group 2 =20ug (N=12) Group 3 =30ug (N=12) Group 4 = Placebo (N=9) BNT162b2 (65-85y/o) Group 1 =10ug (N=12) Group 2 =20ug (N=12) Group 3 =30ug (N=12) Group 4 = Placebo (N=9) All boosted D21 IM	WT serum neutralization assay D1-D21-D28-D35 S1 IgG direct Luminex immunoassay D1-D21-D28-D35 RBD IgG direct Luminex immunoassay D1-D21-D28-D35	NA
Sahin et al (33) 2020 Germany	Safety, tolerability and Immunogenicity Open label, dose escalation phase 1 trial 7 weeks N=60 18-85y/o	SARS-CoV-2	LNP mRNA BNT162b1	BNT162b1: Trimerized RBD	Group 1 =1ug (N=12) Group 2 =10ug (N=12) Group 3 =30ug (N=12) Group 4 =50ug (N=12) Group 5 =60ug (N=12) All Boosted D22 IM	RBD IgG direct Luminex immunoassay D1-D8-D22-D29-D43 VNT₅₀ D1-D8-D22-D29-D43 VSV-pseudovirus nAb assay D1-D8-D22-D29-D43	IFNγ Linked ELISpot D1-D29 Flow cytometry/ICS D1-D29
Anderson et al (34) 2020 USA	Safety and Immunogenicity Open-label, dose-escalation, phase 1 trial Ongoing N=40 >56y/o	SARS-CoV-2	mRNA-1273 (LNP)	SARS-CoV-2 Spike S2-P	56-70y/o Group 1 = 25ug (N=10) Group 2 = 100ug (N=10) $\geq 71y/o$ Group 3 = 25ug (N=10) Group 4 = 100ug (N=10) All Boosted D29 IM	ELISA-IgG D1-D15-D29-D36-D43-D57 Lentivirus Pseudovirus nAb assay D1-D15-D29-D36-D43-D57 HTNA D1-D29-D43 FRNT D1-D29-D43 PRNT D1-D29-D43	Flow Cytometry/ICS D1-D29-D43
Logunov et al (35) 2020 Russia	Safety and Immunogenicity Open label non-randomized phase 1/2 trial 7 weeks N=76 18-60y/o	SARS-CoV-2	rAd26 and rAd5 Gam-COVID 'Sputnik'	Full-Length SARS-CoV-2 Spike GP	Gam-COVID-Vac Group 1 = Ad26 (N=9) Group 2 = Ad5: (N=9) Group 3 = Ad26+Ad5: (N=20) Gam-COVID-Lyo Group 4 = Ad26: (N=9) Group 5 = Ad5: (N=9) Group 6 = Ad26+Ad5: (N=20) Dosage = 1x10 ¹¹ Group 3 and 6 boosted D21 IM	ELISA-IgG D0-D14-D21-D28-D42 MNA₅₀ D0-D14-D21-D28-D42	IFNγ Linked ELISpot D0-D14-D28 Flow cytometry/ICS D0-D14-D28
Keech et al (36) 2020 USA, Australia	Safety and Immunogenicity Randomized and placebo-controlled phase 1/2 trial Ongoing N=131 18-59y/o	SARS-CoV-2	Recombinant Nanoparticle NVX-CoV2373	Full-Length SARS-CoV-2 Spike GP	Group 1 = Placebo (N=23) Group 2 = 25ug (N=25) Group 3 = 5ug + 50ug Alum (N=26) Group 4 = 25ug + 50ug Alum (N=25) Group 5 = 25ug + 50ug Alum (N=26) Group 1/2/3/4 boosted D21 IM	ELISA-IgG D0-D7-D21-D28-D35 MNA₉₉ D0- D21-D35	Flow cytometry/ICS D0-D28

Xia et al (37) 2020 China	Safety and Immunogenicity Randomized, double-blind, placebo-controlled phase 1/2 trial Ongoing Phase 1: N=96 Phase 2: N=224 18-59y/o	SARS-CoV-2	Virus Inactivated by β- Propiolactone	Inactivated SARS-CoV-2 Virus (WIV04 Strain)	Phase 1 (D28,58 boost) Low dose= 2.5ug (N=24) Medium dose= 5ug (N=24) High dose= 10ug (N=24) Alum only= (N=24) Phase 2 (D14 boost) Medium dose= 5ug (N=84) Alum Only= (N=28) Phase 2 (D21 boost) Medium dose= 5ug (N=84) Alum Only= (N=28)	ELISA-IgG D4-D14-D21-D35-D56-D70 PRNT₅₀ D4-D14-D21	
Mulligan et al (38) 2020 USA	Safety, Tolerability and Immunogenicity Randomized, single-blind, dose escalation, placebo-controlled phase ⅓ trial Ongoing N=45 18-55y/o	SARS-CoV-2	LNP mRNA BNT162b1	BNT162b1: Trimerized RBD	Group 1= 10ug (N=12) Group 2= 30ug (N=12) Group 3= 100ug (N=12) Group 4 = Placebo (N=9) Group 1/2 boosted D21 IM	RBD IgG direct Luminex immunoassay D7-D21-D28-D35 VNT₅₀ D7-D21-D28-D35	NA
Zhu et al, (39) 2020 China	Safety, Tolerability and Immunogenicity. Open-Label, Dose-Escalation, Non-Randomized Phase 1 trial 4 Weeks N=108 18-60 y/o	SARS-CoV-2	AdH5	Full-Length SARS-CoV-2 Spike GP	Low Dose = 5x10 ¹⁰ vp (N=36) Intermediate Dose = 1x10 ¹¹ vp (N=36) High Dose = 1.5x10 ¹¹ vp (N=36) Not Boosted IM	ELISA-IgG D14-D28 Live nAb Assay D14-D28	IFNγ Linked ELISpot D0-D28 Flow cytometry/ICS D0-D28
Zhu et al, (40) 2020 China	Safety and Immunogenicity A randomized, double-blind, placebo-controlled trial Phase 2 4 Weeks N=508	SARS-CoV-2	AdH5	Full-Length SARS-CoV-2 Spike GP	Low dose = 1x10 ¹¹ vp (N=253) High Dose = 5x10 ¹⁰ vp (N=129) Placebo = Vaccine excipients (N=126) Not boosted IM	ELISA-IgG D0-D28 Live nAb assay D0-D28 VSV-pseudovirus nAb assay D0-D28	IFNγ-ELISpot D0-D28
Folegatti et al, (41) 2020 UK	Safety, Immunogenicity and efficacy Single blinded, multi-center, randomized, Phase1/2 Trial 8 Weeks N=1077 18=55y/o	SARS-CoV-2	ChAdOx, MenACWY (Control)	Full-Length SARS-CoV-2 Spike GP	Single dosage: 5x10 ¹⁰ vp Group 1: Single injection (N=44) + control (N=44) Group 2: Single Injection (N=489) + control (N=489) Group 3: Two injections (N=10) Group 4: Single injection (N=489) + control (N=489) Boosted D28 IM	ELISA-IgG D0-D56 Microneutralization assay (MNA_{50/80/90}) D0-D42 Lentivirus Pseudovirus nAb assay (IC₅₀) D0-D42 PRNT₅₀ D0-D28 Marburg nAb assay (IC₁₀₀) D0-D56 Multiplex Immunoassay D0-D42	IFNγ Linked ELISpot D0-D28
Jackson et al, (42) 2020 USA	Safety and Immunogenicity, Open-Label, Non-Randomized, Phase 1 trial 8 Weeks N=45 18-55 y/o	SARS-CoV-2	RNA mRNA-1273 (LNP)	SARS-CoV-2 Spike S2-P	Low Dose = 25ug (N=15) Intermediate = 100ug (N=15) High = 250ug (N=15) Boosted D29 IM	ELISA-IgG D1-D57 PRNT₈₀ D1-D43 Lentivirus Pseudovirus nAb assay (IC₅₀) D1-D57	Flow cytometry/ICS D1-D29
Folegatti et al, (43) 2020 UK	Safety and Immunogenicity, Open-Label, Dose-Escalation, Non-Randomized, Uncontrolled Phase 1 trial 52 Weeks N=24 18-55 y/o	MERS-CoV	ChAdOx1	Full-Length MERS-CoV Spike GP	Low Dose = 5x10 ⁹ vp (N=6) Intermediate Dose = 2.5x10 ¹⁰ vp (N=9) High Dose = 5x10 ¹⁰ vp (N=9) Not Boosted IM	ELISA-IgG D0-D364 Live nAb Assay D0-D28 HuH-7 Pseudotyped nAb Assay D0-D28	IFNγ Linked ELISpot D0-D364

Modjarrad et al, (44) 2019 USA	Safety and Immunogenicity, Open-Label, Dose-Escalation, Single-Arm Phase 1 trial 60 Weeks N=75 18-55 y/o	MERS-CoV	DNA Plasmid (GLS-5300)	Full-length MERS-CoV spike GP	Low Dose = 0.67mg (N=25) Intermediate Dose = 2mg (N=25) High Dose = 6mg (N=25) Boost: D28, D84 IM	ELISA-IgG D0-D420 Live nAb Assay D0-D420	IFN γ Linked ELISpot D0-D420 Flow cytometry/ICS D0-D98
Koch et al, (45) 2020 Germany	Safety and Immunogenicity, Open-Label, Non-Randomized, Phase 1 trial 24 Weeks N=26 18-55 y/o	MERS-CoV	MVA	Full-Length MERS-CoV Spike GP	Low Dose = 1x10 ⁷ PFU (N=14) High Dose = 1x10 ⁸ PFU (N=12) Control = Blood samples from healthy volunteers (N=6) Boost: D28 IM	ELISA-IgG D0-D180 Live nAb Assay D0-D180 PRNT ₈₀ D0-D180	IFN γ Linked ELISpot D0-D180 Flow cytometry/ICS D0-D42
Lin et al, (46) 2007 China	Safety and Immunogenicity, Randomized, Double-Blind, Placebo-Controlled Phase 1 Trial 30 Weeks N=36 21-40 y/o	SARS-CoV-1	Inactivated Virus β -Propiolactone	SARS-CoV-1 Virus	Low Dose - 16 SU (N=12) High Dose - 32 SU (N=12) Control = Saline/Alum (N=12) Boost: Day 28 IM	ELISA-IgG D0-D56 Live nAb Assay D0-D56	ND
Martin et al, (47) 2008 USA	Safety and Immunogenicity, Open-Label Phase 1 Trial 32 Weeks N=10 21-49 y/o	SARS-CoV-1	DNA Plasmid	Full-Length SARS-CoV-1 Spike GP	Experimental = 4mg (N=10) Boost: D28, D56 IM	ELISA-IgG D0-D224 PRNT D0-D224 Lentiviral Pseudotyped nAb Assay D0-D224	IFN γ Linked ELISpot D0-D224 Flow cytometry/ICS D0-D224

SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2, MERS-CoV: Middle east respiratory syndrome, SARS-CoV-1: Severe acute respiratory syndrome coronavirus 1, Ab: Antibody, nAb: Neutralizing antibody, AdHS: Recombinant human adenovirus 5, GP: Glycoprotein Vp: Viral particle, IM: Intramuscular, Enzyme-linked immunosorbent assay, IgG/A: Immunoglobulin G/A, IFN γ : Interferon gamma, ELISpot: Enzyme-linked immunospot, ICS: Intracellular staining, RT-PCR: Reverse transcription polymerase chain reaction, ChAdOx1: Replication-deficient simian adenovirus vaccine vector oxford 1, MenACWY: Meningococcal vaccine, MNA: Microneutralization assay, IC: Inhibitory concentration, VSV: Vesicular stomatitis virus, mRNA: Messenger ribonucleic acid, LNP: Lipid nanoparticle, S2-P: SARS-CoV-2 GP with a transmembrane anchor and intact S1-S2 cleavage site, ug: Microgram, PRNT: Plaque reduction neutralization assay, MVA: Recombinant Modified Vaccinia virus Ankara, PFU: Plaque forming units, mg: Milligrams, DNA: Deoxyribonucleic acid, HEK293T: Human embryonic kidney 293 cells, SU, SARS-CoV-1 units,, ND: Not defined

Supplementary Table 4: Characteristics of the NHP studies

Study ID	Study Outcomes, Duration, Population (N)	NHP Species Age (Years)	Pathogen	Vaccine Platform	Antigen Insert	Route	Vaccine Groups, Dose, Dose Intervals, Vaccine groups, Boost/No Boost	Measure of Ab Response	Measure of Cellular Response	Measure of Efficacy Strain, Dose
Sanchez-Felipe et al (48) 2020 Belgium	Immunogenicity, Protective Efficacy, 7 weeks N=12	Cynomolgus Macaques Male	SARS-CoV-2	Yellow fever 17D vector	SARS-CoV-2 Spike GP	IM	Experimental (n=6) Sham Control (n=6) 10 ⁶ PFU Boosted D7	IgG Indirect Immunofluorescence assay, HEK293T pseudovirus nAb assay, PRNT	IFN γ ELISpot Flow cytometry/ICS	RT-PCR, Radiology, Histology, ND, 1.5x10 ⁴ TCID ₅₀
Guebre-Xabier et al (49) 2020 USA	Immunogenicity, Protective Efficacy, 7 weeks N=12	Cynomolgus Macaques >3y/o	SARS-CoV-2	Recombinant Subunit and Matrix M Adjuvant NVX-CoV2373	SARS-CoV-2 Spike GP with perfusion stabilization	IM	Group 1 – 5ug + 50ug adjuvant (n=4) Group 2 - 25ug + 50ug adjuvant (n=4) Group 3 – 2.5ug + 25ug adjuvant (n=4) Boosted D21	ELISA-IgG Cytopathic effect assay (CPE)	NA	RT-PCR, Histology SARS-CoV-2 strain nCoV-WA1-2020, 1.1x10 ⁶ PFU
Zhang et al (50) 2020 China	Immunogenicity, 4 weeks N=30	Cynomolgus Macaques Adult Male/Female 3-6y/o	SARS-CoV-2	mRNA-LNP ARCoV	SARS-CoV-2 RBD	IM	Group 1 – 100ug (n=10) Group 2 - 1000ug (n=10) Group 3 – Placebo (n=10) Boosted D14	ELISA-IgG, Huh7.5 Pseudovirus nAb assay, PRNT	IFN γ ELISpot Flow cytometry/ICS	NA
Wang et al (51) 2020 China	Safety evaluation. Immunogenicity, Protective Efficacy, 5 weeks N=40	Rhesus Macaques 3-6y/o	SARS-CoV-2	Inactivated vaccine + Alum BBIBP-CorV	Inactivated SARS-CoV-2	IM/IP	Immunogenicity Group 1 – 2ug (n=10) Group 2 – 4ug (n=10) Group 3 – 8ug (n=10) Boosted D7-D14 Challenge Group 1 – 2ug (n=4) Group 2 – 8ug (n=4) Group 3 – Placebo (n=2) Boosted D14	Live nAb assay	NA	RT-PCR, Histology, Clinical evaluation, Biochemical analysis 10 ⁷ TCID ₅₀
Feng et al (52) 2020 China	Immunogenicity, Protective efficacy 9 weeks N=20	Rhesus Macaques Male/Female 6-14y/o	SARS-CoV-2	rAd-5 (Ad5-S-nb2)	SARS-CoV-2 Spike GP	IM/IN	Immunogenicity Group 1 - 1x10 ¹⁴ vp (n=4) Group 2 - 5x10 ¹⁴ vp (n=4) Group 3 - 1x10 ¹⁵ vp (n=4) Group 4 – Control 1x10 ¹⁴ vp (n=2) Challenge Group 5: Non-vaccinated (n=6)	ELISA-IgG, HEK293T pseudovirus nAb assay, Lentivirus pseudotyped assay, Microneutralization assay	IFN γ ELISpot	RT-PCR, Histology, PRNT, nAb assay ND 2x10 ⁷ TCID ₅₀ or 400 TCID ₅₀
Yang et al (53) 2020 USA	Immunogenicity, Protective efficacy 9 weeks N=32	Rhesus Macaques 5-9y/o	SARS-CoV-2	Recombinant subunit	SARS-CoV-2 RBD	IM	Immunogenicity Experimental - 40ug + Alum (n=10) Control – PBS + Alum (n=10) Boosted D7 Challenge Experimental – 40ug + Alum (n=4) Experimental – 20ug + Alum (n=3) Alum - (n=2) Control – PBS (n=3)	ELISA-IgG, VSV-pseudovirus nAb assay	NA	RT-PCR, ND, 10 ⁶ PFU
Ren et al (54) 2020 China	Immunogenicity 5 Weeks N=4	Rhesus Macaques 3-4y/o	SARS-CoV-2	CHO-expressed recombinant subunit vaccine and CFA, AD11.10 and AD20GOLD adjuvants	SARS-CoV-2 S1-Fc fusion protein	IM	Immunogenicity Experimental – (N=4) Boost D4-D9-D22-D26	ELISA-IgG, HEK293T pseudovirus nAb assay, Microdose cytopathogenic efficiency assay	NA	NA
Yu et al, (55) 2020 USA	Immunogenicity, Protective Efficacy, Safety (ADE), CoP Investigation, 6 Weeks, N=35	Rhesus Macaques, 6-12	SARS-CoV-2	DNA Plasmid	SARS-CoV-2 Spike GP Variants	IM	Immunogenicity S - (n=4) S.dCT - (n=4) S.dTM - (n=4) S1 - (n=4) RBD - (n=4) S.dTM.PP - (n=4) Sham Control - (n=10)	ELISA IgG, Live virus nAb Assay, HEK293T pseudovirus nAb assay	IFN γ ELISpot Flow cytometry/ICS	RT-PCR, ELISA IgG, Live virus nAb Assay, HEK293T pseudovirus nAb assay, Flow cytometry/ICS, Clinical observation, ND,

							5mg 0 and 3 rd week Boosted			1.2x10 ⁶ vp
Van Doremalen et al (56) 2020 UK	Immunogenicity, Protective Efficacy, Safety, 9 Weeks N=18	Rhesus Macaques 2-4yo	SARS-CoV-2	ChAdOx	SARS-CoV-2 Spike GP with tPA optimization	IM	Immunogenicity Prime – (n=6) Prime-Boost – (n=6) Control – (n=6) 2.5x10 ¹⁰ vp 0 and 4 th week Boosted	ELISA-IgG/IgM, Live virus nAb Assay,	IFN γ ELISpot Flow cytometry/ICS	RT-PCR, Histopathology, Clinical observation, SARS-CoV-2 strain nCoV- WA1-2020, 4x10 ⁷ TCID ₅₀
Gao et al, (57) 2020 China	Immunogenicity, Safety (ADE), Protective Efficacy, 4 Weeks, N=40	Rhesus Macaques, 3-4	SARS-CoV-2	Inactivated Virus By β - Propiolactone	Inactivated SARS-CoV-2	IM	<u>Immunogenicity/Vaccine Safety</u> High Dose - 6ug (n=10) Low Dose - 1.5ug (n=10) Sham (n=10) Placebo (n=10) 0, 1, 2 Week <u>Challenge</u> High Dose - 6ug (N=4) Medium Dose - 3ug (N=4) Sham - (N=4) Control - (N=4) 0, 1, 2 Week Boosted	ELISA IgG, Live virus nAb assay	ND	RT-PCR, ELISA IgG, Live virus nAb assay, Histopathology, Biochemical analysis, Flow cytometry/ICS, Clinical observation, SARS-CoV-2-CN1 1x10 ⁶ TCID ₅₀
Mercado et al., (58) 2020 USA	Immunogenicity, Safety (ADE), Protective Efficacy, 8 Weeks, N=52	Rhesus Macaques, 6-12	SARS-CoV-2	AdH26	SARS-CoV-2 Spike GP variants	IM	<u>Immunogenicity</u> tPA.S - (n=4) tPA.S.PP - (n=4) tPA.WT.S - (n=4) S - (n=4) S.dCT - (n=4) S.dTM.PP - (n=6) S.PP - (n=6) Sham - (20) 1x10 ⁶ vp Not Boosted	ELISA-IgG, Live virus nAb assay, Lentivirus pseudotyped assay, PFU assay	IL-4/IFN γ ELISpot Flow cytometry/ICS	RT-PCR, HEK293T pseudovirus nAb assay,
Erasmus et al, (59) 2020 USA	Immunogenicity, Safety, 14 Weeks, N=5	Pigtail Macaques, 3-6y/o	SARS-CoV-2	RNA LION/repRNA- CoV2S	SARS-CoV-2 Spike GP	IM	<u>Immunogenicity</u> Group 1 - 250ug (n=3) Group 2 - 50ug (n=2) Group 1 Not Boosted Group 2 Boosted Week 4	ELISA-IgG, MLV pseudotyped assay, Vero cell Pseudovirus nAb assay	IFN γ ELISpot Flow cytometry/ICS	ND
Corbett et al., (60) 2020 USA	Immunogenicity, Protective efficacy, 9 Weeks, N=24	Rhesus Macaques, 3-6y/o	SARS-CoV-2	DNA mRNA-1273 (LNP)	SARS-CoV-2 Spike S2-P	IM	<u>Immunogenicity</u> Low dose - 10ug (n=8) High dose - 100ug (n=8) Control - PBS (n=8) Week 0,4 Boosted	ELISA-IgG, Lentivirus pseudotyped assay, Live virus nAb assay	Flow cytometry/ICS	RT-PCR, Histopathology, SARS-CoV-2-USA- WA1/2020, 7.6x10 ⁹ PFU
Liu et al, (61) 2018 China	Immunogenicity, 7 Weeks, N=8	Rhesus Macaques, 2y/o	MERS-CoV	rVSV	MERS-CoV full- length Spike GP	IM/IN (Group 1) IN (Group 2)	<u>Immunogenicity</u> Group 1 - 2x10 ⁷ FFU (n=4) Group 2 - 2x10 ⁷ FFU (n=4) Week 0 Not Boosted	ELISA-IgG, Live Virus nAb Assay	IFN γ ELISpot	ND
Wang et al, (62) 2017 China	Immunogenicity, 8 Weeks, N=6	Rhesus Macaques, ND	MERS-CoV	Recombinant Baculovirus	MERS-CoV S, E, M proteins	IM	<u>Immunogenicity</u> Group 1: 250ug VLP + 250ug Alum (n=3) Control: PBS (n=3) 0,2,4,6 Weeks Boosted	ELISA-IgG, Live Virus nAb Assay	IFN γ and IL-4 ELISpot	ND
Lan et al, (63) 2015 China	Immunogenicity, Protective efficacy, 27 Weeks, N=9	Rhesus Macaques, ND	MERS-CoV	Subunit	MERS-CoV Spike GP: RBD	IM	<u>Immunogenicity</u> Low Dose = Prime - 50ug, Boost 1/2 – 100ug rRBD admix + 1mg Alum (n=3) High Dose = Prime - 200ug, Boost1/2 – 25ug rRBD admix + 1mg Alum (n=3) Mock Control = PBS (n=3) Week 0, 8, 25 Boosted	ELISA-IgG, Vero cell Pseudovirus nAb assay	IFN γ ELISpot	RT-PCR, Live nAb assay, Histopathology, Radiology, EMC-MERS-CoV, 6.5x10 ⁷ TCID ₅₀
Wang et al, (64) 2015 USA	Immunogenicity, 18 Weeks, N=18	Rhesus Macaques, 4.4y/o	MERS-CoV	DNA plasmid	MERS-CoV full- length Spike GP	IM	<u>Immunogenicity</u> DNA Group -1mg (n=6) Week 0, 4, 8 DNA-S1 Group -1mg (n=6) Week 0, 4, 8 Protein only group - 100mg S1 (n=6) Week 0, 8	ELISA-IgG, PRNT, Huh7.5 Pseudovirus nAb assay	ND	Clinical Observation, Radiology, JordanN3 MERS-CoV, 5x10 ⁶ vp

Challenge										
Group 1 - Unvaccinated (n=6)										
Group 2 - S-DNA/S1 Vaccinated (n=6)										
Group 3 -S1/S1 Vaccinated (n=6)										
Boosted										
Muthamani et al, (65) 2015 USA	Immunogenicity, Protective Efficacy, 12 weeks, N=12	Rhesus Macaques, ND	MERS-CoV	DNA Plasmid	MERS-CoV full-length Spike GP	IM	Immunogenicity Low dose group - 0.5mg (n=3) High dose group - 2mg (n=3) Control group - 2mg (Empty vector) (n=3) Week 0, 3, 7 Boosted	ELISA-IgG, HEK293T Pseudovirus nAB Assay, Live Virus nAb Assay	IFN γ ELISpot	RT-PCR, Radiological, Histopathology, Clinical Evaluation, EMC-2012-MERS-CoV, 7x10 ⁶ TCID ₅₀
Kobinger et al, (66) 2007 Canada	Immunogenicity, 38 Weeks, N=4	Rhesus Macaques, Adult	SARS-CoV-1	AdH5/AdC7	SARS-CoV-1 Spike ORF	IM	Immunogenicity Experimental - (n=4) 1x10 ¹⁰ vp AdH5 (1 st injection) 1x10 ¹² vp AdC7 (2 nd injection) Week 0, 13 Boosted	Live virus nAb assay	IFN γ ELISpot Flow cytometry/ICS	ND
Qin et al, (67) 2006 China	Immunogenicity, Safety (ADE), Protective efficacy, 14 Weeks, N=29	Cynomolgus Macaques, 4-5y/o	SARS-CoV-1	Inactivated Vero Cell With β -Propiolactone	Inactivated SARS-CoV-1 virion	IM	Immunogenicity Group 1 - Purified Vaccine + Alum 15ug (n=5) Group 2 - Purified Vaccine 15ug (n=5) Group 3 - Unpurified Vaccine 15ug (n=5) Group 4 - Control 15ug (n=5) Week 0, 1, 3, 7 Safety Group 1 - Purified inactivated 0.5ug (n=3) Group 2 - Purified inactivated 1ug (n=3) Group 3 - Purified inactivated 2ug (n=3) Week 0, 1 Challenge Group 2 - (n=4) Control - (n=4) Boosted	PRNT	ND	RT-PCR, PRNT, Histopathology, Biochemical analysis, Clinical observations Safety BJ-01 SARS-CoV-1, 7x10 ⁷ TCID ₅₀ Challenge GZ-01 SARS-CoV-1, 7x10 ⁷ TCID ₅₀
Chen et al, (68) 2005 USA	Immunogenicity, Protective Efficacy, 7 Weeks, N=8	Rhesus Macaques, ND	SARS-CoV-1	MVA	SARS-CoV-1 full-length Spike GP	IM	Immunogenicity Experimental - (n=4) 1x10 ⁸ TCID ₅₀ (1 st Injection) 3x10 ⁸ TCID ₅₀ (2 nd Injection) Control - (n=4) Week 0,4, Boosted	HEK293T pseudovirus nAB assay, Antibody Adsorption assay	ND	RT-PCR, Live Virus nAB assay, PUMC01-SARS-CoV-1, 1x10 ⁸ TCID ₅₀
Zhou et al, (69) 2005 China	Immunogenicity, Protective Efficacy, Safety, 7 Weeks, N=18	Rhesus Macaques, 2-5y/o	SARS-CoV-1	Inactivated Virus with formaldehyde	Inactivated SARS-CoV-1 virion	IM	Immunogenicity Group 1 - 0.5ug (n=4) Group 2 - 5ug (n=4) Group 3 - 50ug (n=4) Group 4 - 5000ug (n=2) Group 5 - PBS (n=2) Group 6 - PBS (n=2) Week 0, 2 Boosted	ELISA-IgG/IgA, Live virus nAb Assay	ELISA-IFN γ /IL-4, Flow cytometry/ICS	RT-PCR, ELISA-IgG, Clinical Observation, Histopathology, Biochemical analysis, Radiology, NS-1 SARS-CoV-1, 1x10 ⁸ PFU
Bukreyev et al, (70) 2004 USA	Immunogenicity, Protective Efficacy, 8 Weeks, N=8	African Green Monkeys, ND	SARS-CoV-1	Attenuated Parainfluenza Virus	SARS-CoV-1 full-length Spike GP	IN/IT	Immunogenicity Single Dose - (n=4) Control - (n=4) Week 0 Not Boosted	Live virus nAb assay	ND	RT-PCR, Live Virus nAB assay, ND, 1x10 ⁸ TCID ₅₀

SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2, MERS-CoV: Middle east respiratory syndrome, SARS-CoV-1: Severe acute respiratory syndrome coronavirus 1, Ab: Antibody, nAb: Neutralising antibody, ADE: Antibody dependent enhancement, CoP: Correlate of protection, ab: Antibody, nAb: Neutralising antibody, GP: Glycoprotein, IM: Intramuscular, IN: Intranasal, DNA: Deoxyribonucleic acid Vp: Virus particle, TCID₅₀: 50% tissue culture infective dose, S: Full length spike protein, S.dCT: Spike protein with a deletion of cytoplasmic tail, S.dTM: Spike protein with a deletion of transmembrane domain and cytoplasmic tail reflecting the soluble ectodomain, S1: S1 domain with a foldon trimerization tag, RBD: Receptor binding domain, S.dTM.PP: soluble ectodomain with a deleted furin cleavage site, with proline mutations and a foldon trimerization tag, ELISA: Enzyme-linked immunosorbent assay, IgG/A: Immunoglobulin G/A, IFN γ : Interferon gamma, ELISpot: Enzyme-linked immunospot, ICS: Intracellular staining, RT-PCR: Reverse transcription polymerase chain reaction, ChAdOx1: Replication-deficient simian adenovirus vaccine vector oxford 1, HEK293T: Human embryonic kidney 293 cells, AdH26: Recombinant human adenovirus-26, S.PP: Wild type leader sequence with full-length S GP with a mutation of the furin cleavage site and proline stabilizing mutations, tPA.S: Leader sequence with full length S, tPA.S.PP: Tissue plasminogen with full-length S with mutations of the furin cleavage site and two proline stabilization mutations, tPA.WT.S: Tandem tPA and wild type leader sequences with full-length S, sgRNA: Subgenomic ribonucleic acid, MLV: Murine Leukaemia virus, ND: Not defined, LNP: Lipid nanoparticle, S2-P: SARS-CoV-2 GP with a transmembrane anchor and intact S1-S2 cleavage site, PBS: Phosphate-buffered saline, AdH5: Human adenovirus vector 5, AdC7: Chimpanzee adenovirus 7, ORF: Open reading frame, PRNT: Plaque reduction neutralisation assay, ug: Microgram, IL-4: Interleukin 4, MVA: Recombinant modified Vaccinia virus Ankara, IT: Intratracheal, rVSV: Recombinant vesicular stomatitis virus, FFU: Focus forming units, E: Envelope protein, M: Membrane protein, VLP: Virus-Like Particle, RBD: Receptor binding domain, S1: Spike GP domain 1, Huh-7.5: hepatocyte derived cellular carcinoma cell line.

Supplementary Table 5. Vaccine studies in NHP

Candidate and Pathogen	Vaccine Platform	Description	Human	NHP
Unnamed DNA plasmid vaccine MERS-CoV (64)	DNA Plasmid	DNA plasmid expressing full-length spike or truncated S1 protein genes		<input checked="" type="checkbox"/>
Unnamed DNA Vaccine SARS-CoV-2 (55)	DNA	DNA vaccine encoding multiple optimized variations of the spike protein gene		<input checked="" type="checkbox"/>
repRNA-CoV2S SARS-CoV-2 (59)	RNA	Alphavirus derived replicating RNA vaccine expressing full-length spike protein gene in an inorganic lipid nanoparticle emulsion		<input checked="" type="checkbox"/>
Unnamed DNA plasmid vaccine MERS-CoV (65)	DNA Plasmid	DNA plasmid expressing full-length consensus spike protein		<input checked="" type="checkbox"/>
Unnamed adenovirus vaccine SARS-CoV-1 (66)	AdH5/AdC7	Human Adenovirus 5 and Chimpanzee adenovirus 7 vaccine regimen expressing spike protein		<input checked="" type="checkbox"/>
Unnamed inactivated virus vaccine SARS-CoV-1 (67)	Inactivated Virus (BJ-01 strain)	β -propiolactone Inactivated vaccine		<input checked="" type="checkbox"/>
Unnamed inactivated virus vaccine SARS-CoV-1 (69)	Inactivated Virus (NS-1 strain)	Formaldehyde inactivated vaccine		<input checked="" type="checkbox"/>
S1-Fc fusion SARS-CoV-2 (54)	Recombinant Protein	CHO-expressed S1-Fc fusion protein with CFA, AD11.10 and AD20GOLD adjuvants		<input checked="" type="checkbox"/>
ARCoV SARS-CoV-2 (50)	mRNA	mRNA vaccine encoding the RBD, encapsulated in a lipid nanoparticle.		<input checked="" type="checkbox"/>
rRBD-MERS-CoV MERS-CoV (63)	Recombinant subunit	Recombinant receptor binding domain protein vaccine administered with Alum adjuvant		<input checked="" type="checkbox"/>
YF-S SARS-CoV-2 (48)	Live-attenuated yellow fever virus	Yellow fever 17D: Single stranded, live attenuated virus vaccine		<input checked="" type="checkbox"/>
Unnamed live-attenuated vaccine SARS-CoV-1 (70)	Live attenuated Parainfluenza virus	Attenuated Parainfluenza virus vaccine expressing full length spike protein		<input checked="" type="checkbox"/>
Ad5-S-nb2 SARS-CoV-2 (52)	AdH5	Replication deficient adenovirus 5 vectored vaccine expressing codon optimized full-length spike protein.		<input checked="" type="checkbox"/>
Unnamed live-attenuated vaccine SARS-CoV-1 (68)	rMVA	Live-attenuated Modified Vaccinia Ankara (Poxvirus) expressing full-length spike protein		<input checked="" type="checkbox"/>
VSV Δ G-MERS MERS-CoV (61)	VSV	Vesicular stomatitis virus encoding the MERS-CoV S gene		<input checked="" type="checkbox"/>
MERS-CoV-VLP (62)	VLP	Recombinant Baculovirus expressing the spike, envelope and membrane genes		<input checked="" type="checkbox"/>

Polack, BNT162b2 (26)	43,448	52	19075	18631	-	31266	10543	3492	1608	855	409	76
Ramasamy, ChAdOx (28)	560	61.7	277	275	24.5	524	-	1	19	4	4	-
Jackson, mRNA-1273 (42)	45	33	22	23	25.3	40	6	2	1	-	2	1
Baden, mRNA-1273 (25)	30,420	51.4	15985	14366	29.3	24024	6235	3090	1382	636	637	67
Voysey, ChAdOx (27)	23,848	NA	10485	13260	24.8	17864	-	2394	825	2452	210	-
Sadoff, Ad26.COV2.S (23)	805	52.6	391	213	25	761	23	23	10	1	9	1
Tebas, DNA-INO-4800 (24)	40	35.3	22	18	-	33	0	2	5	-	-	-
Ella, BBV152 I (22)	375	NA	297	78	23.5	-	-	-	-	-	-	-
Logunov, rAdH26/5 III (18)	19866	45.3	12158	7708	26.75	19571	-	-	286	-	9	-
Wu, CoronaVac (19)	421	66.5	206	215	-	-	-	-	421	-	-	-
Chu, mRNA-1273 (20)	600	50.9	210	390	25.3	569	-	16	7	4	3	1
Richmond, SCB-2019 (17)	151	45.2	64	87	-	130	10	1	16	-	2	-
Ella, BBV152 II (16)	380	NA	285	95	25	-	-	-	-	-	-	-
Voysey, ChAdOx (21)	17178	NA	7482	9696	25.4	12975	-	1693	1210	1753	167	-
Total	142,958	42.7	50.6%	49.4%	24.9	72.78%	11.23%	7.17%	3.91%	3.80%	1.01%	0.10%

Zhu AdH5 (1): AdH5-SARS-CoV-2 phase 1 vaccine, Zhu AdH5 (2): AdH5-SARS-CoV-2 phase 2 vaccine, Folegatti ChAdOx (1): ChAdOx-MERS-CoV vaccine, Folegatti ChAdOx (2): ChAdOx-SARS-CoV-2 vaccine.

Supplementary Table 7: Vaccine efficacy against COVID-19

Vaccine Study	Number of study participants (n)	Efficacy End Point	Vaccine	Placebo	Vaccine efficacy (%)		
					(95% CI)		
			No of COVID-19 cases	No of COVID-19 cases			
Polack, BNT162b2 (26)	40137	COVID-19 infection 7 days after 2 nd vaccination in those with and without symptoms of infection.	9	169	94.6% (89.9-97.3)		
Baden, mRNA-1273 (25)	30352	Covid-19 Infection 14 days after the second injection with at least two of the following symptoms: fever (temperature $\geq 38^{\circ}\text{C}$), chills, myalgia, headache, sore throat, or new olfactory or taste disorder	11	185	94.1 (89.3-96.8)		
Voysey, ChAdOx (27)	11636	NAAT confirmed COVID-19 with a qualifying symptom (Fever, cough, anosmia, shortness of breath and ageusia)	30	101	70.4% (54.8-80.6)		
Logunov, rAd26/5 (18)	19866	Covid-19 Infection 21 days after first injection.	16	62	91.6% (85.6-95.2)		
Voysey, ChAdOx (21)	17178	Total Efficacy		84/8597	248/8581	66.7% (57.4-74.0)	
		Standard Dose/standard Dose	<6 weeks	Primary symptomatic Covid19 more than 14 days after first dose.	35/3890	76/3856	55.1% (33.0-69.9)
			6-8 weeks		20/1112	44/1009	59.9% (32.0-76.4)
			9-11 weeks		11/906	32/958	63.7% (28.0-81.7)
			≥ 12 weeks		8/1293	45/1356	81.3% (60.3-91.2)
		Low Dose/Standard dose			10/1396	51/1402	80.7% (62.1-90.2)
		Single Standard dose		Primary symptomatic Covid19, 22-90 days after dose.	17/9257	71/9237	76.0% (59.3-85.9)
		Standard Dose/standard Dose	<6 weeks	Asymptomatic COVID-19 cases more than 14 days after second dose	9/728	8/733	-11.8% (-189.5-56.8)
			6-8 weeks		14/528	7/476	-74.2% (-330.3-29.5)
			9-11 weeks		6/599	11/666	39.9% (-62.3-77.8)
			≥ 12 weeks		12/837	16/876	22.8% (-63.3-63.5)
		Standard Dose/standard Dose	<6 weeks	Any NAAT-positive COVID-19 cases more than 14 days after second dose	51/3890	94/3856	47.1% (25.6-62.4)
			6-8 weeks		39/1112	51/1009	32.6% (-2.2- 55.5)
			9-11 weeks		18/906	50/958	61.9% (34.8-77.8)
			≥ 12 weeks		24/1293	63/1356	59.9% (35.8-75.0)

Supplementary Table 8: NHP safety analysis

First author, Vaccine platform, Pathogen	Type of analysis	Summary
Zhou, 2005(69) Inactivated virus, SARS-CoV-1	Clinical signs, biochemical and hematological parameters	<ul style="list-style-type: none"> • No fluctuations in hematological or biochemical parameters • High dose vaccine caused mild induration in one subject
Qin, 2006(67) Inactivated virus, SARS-CoV-1	ADE, Clinical signs, biochemical and haematological parameters	<ul style="list-style-type: none"> • No evidence of ADE • No change in biochemical or haematological measures
Gao, 2020(57) Inactivated virus, SARS-CoV-2	ADE/Th2, Clinical signs, hematological and biochemical parameters. Histopathology	<ul style="list-style-type: none"> • No evidence of ADE even in the presence low nAB titer in some vaccine groups • No Th2 pathology registered • No change in biochemical, histopathological, or hematological parameters
Erasmus, 2020(59) RNA, SARS-CoV-2	Clinical signs, biochemical and hematological parameters	<ul style="list-style-type: none"> • No fluctuations in biochemical, hematological or biochemical parameters
Yu, 2020(55) DNA, SARS-CoV-2	ADE	<ul style="list-style-type: none"> • No Th2 skewing and no evidence of ADE
Corbett, 2020(60) mRNA-1273, SARS-CoV-2	Histopathology Lung inflammation assessment Th2 responses	<ul style="list-style-type: none"> • Inflammation mild in low dose group • No Inflammation in high dose group • No vaccine associated lung immunopathology • No Th2 responses
Wang, 2020 (51) BBIBP-CorV SARS-CoV-2	ADE, Clinical signs, biochemical and Hematological parameters	<ul style="list-style-type: none"> • Local injection site inflammation in all groups observed at D25 • No significant clinical abnormalities • No change in pathological indicators or lymphocyte subsets

Supplementary Table 9. Interstudy analysis of individual local adverse events reported in vaccine group (excluding control group) of coronavirus vaccine studies. Data represent % of patients in experimental group reporting any grade of symptomatic adverse event.

Study (% Patients)	Injection site pain	Redness	Swelling	Induration	Pruritus	Tenderness	Warmth	Bruising
Zhu, AdH5 (Phase 1) (n=108)	54.0	4.0	7.0	4.0	5.0	-	-	-
Zhu, AdH5 (Phase 2) Low Dose (n=129)	56.0	1.0	4.0	2.0	4.0	-	-	-
Zhu, AdH5 (Phase 2) High Dose (n=253)	57.0	2.0	4.0	10.0	5.0	-	-	-
Logunov AdH26/5-Vac (n=38)	55.3	-	2.6	-	2.6	-	5.3	-
Logunov AdH26/5-Lyo (n=38)	63	-	0.0	-	0	-	2.6	-
Sadoff, Ad26.COVS.2.S (n=805)	55.0	2.5	2.8	-	-	-	-	-
Ramasamy ChAdOx Prime (n=128)	29.6	1.9	0.9	0.2	5.0	53.1	4.9	-
Ramasamy ChAdOx Boost (n=128)	19.9	2.3	1.5	0.4	5.0	44.0	5.9	-
Folegatti, ChAdOx (Phase 1/2) (n=543)	65.6	2.9	4.1	3.1	7.0	82.1	24.5	-
Baden, mRNA-1273 Prime (n=15,210)	83.7	2.8	6.1	-	-	10.2	-	-
Baden, mRNA-1273 Boost (n=15,210)	88.2	8.6	12.2	-	-	14.2	-	-
Jackson mRNA-1273 Prime (n=45)	86.7	6.7	10.7	-	-	-	-	-
Jackson mRNA-1273 Boost (n=45)	91.7	11.0	9.7	-	-	-	-	-
Anderson mRNA-1273 Prime (n=40)	62.5	0.0	-	2.5	-	-	-	-
Anderson mRNA-1273 Boost (n=40)	75.0	17.5	-	20.0	-	-	-	-
Chu mRNA-1273 Prime (n=600)	74.5	3	4	-	-	-	-	-
Chu mRNA-1273 Boost (n=600)	82.5	6.5	8.5	-	-	-	-	-
Polack, BNT162b2 Prime (n=21,720)	77.0	5.0	6.5	-	-	-	-	-
Polack, BNT162b2 Boost (n=21,720)	72.0	6.5	6.5	-	-	-	-	-
Mulligan BNT162b1 Prime (n=36)	86.0	15.0	18.3	-	-	-	-	-
Mulligan BNT162b1 Boost (n=24)	90.0	7.5	11.0	-	-	-	-	-
Walsh BNT162b1 Prime (n=84)	79.2	2.8	12.5	-	-	-	-	-
Walsh BNT162b1 Boost (n=72)	82.0	5.5	13.8	-	-	-	-	-
Walsh BNT162b2 Prime (n=72)	65.3	1.3	2.8	-	-	-	-	-
Walsh BNT162b2 Boost (n=72)	63.7	0.0	0.0	-	-	-	-	-
Che inactivated SARS-COV-2 (n=600)	14.0	0.5	0.0	-	2.0	-	-	-
Xia BBIPB Phase I (n=144)	24.0	0.5	0.5	2.5	1.0	-	-	-
Xia BBIPB Phase II (n=336)	16.0	1.0	2.0	-	1.0	-	-	-
Zhang CoronaVac (n=570)	16.1	1.0	0.8	0.5	0.5	-	-	-
Wu, Coronavac I/II (n=421)	10.3	0.9	0.6	-	0.9	-	-	-
Ella, BBV152 Prime I (n=300)	3.7	-	0.0	-	-	-	-	-
Ella, BBV152 Boost I (n=300)	1.3	-	0.0	-	-	-	-	-
Ella, BBV152 II (n=380)	7	1	-	-	-	-	-	-
Keech NVX-CoV2373 Prime (n=102)	42.2	1.0	-	0.0	-	48.7	-	-
Keech NVX-CoV2373 Boost (n=76)	47.2	6.1	-	4.7	-	60.6	-	-
Tebas, INO-4800 Prime (n=40)	5.0	2.5	-	0.0	-	-	-	-
Tebas, INO-4800 Boost (n=40)	2.5	0.0	-	0.0	-	-	-	-
Richmond, SCB-2019 Prime (n=121)	28.3	3.3	3.3	-	-	-	-	-
Richmond, SCB-2019 Boost (n=121)	32.5	10.8	10.0	-	-	-	-	-
Koch MERS MVA (n=26)	65.0	42.0	38.0	38.0	-	-	-	27.0
Martin SARS DNA (n=10)	100.0	40.0	20.0	-	-	-	-	-
Lin SARS Inactivated (n=24)	29.2	8.4	-	-	4.2	-	-	-
Modjarrad GLS-5300 MERS (n=75)	92.0	6.7	-	2.7	-	84.0	-	1.3
Folegatti, ChAdOx 1 MERS (n=24)	80	20	0	-	21.0	-	20	-

Supplementary Table 11: Serious adverse events. Summary of events related to SARS-CoV-2 vaccine or placebo reported in humans studies. Vaccine study, population (n), number of serious adverse events and description of these events.

Vaccine Study	N	Description	Treatment Group
Baden, mRNA-1273 (25)	30420	(1) Autonomic nervous system imbalance (2) Paraesthesia (3) Dyspnoea (4) Pulmonary embolism (5) Nausea (6) Vomiting (7) Rheumatoid arthritis (8) Polymyalgia rheumatica (9) Swelling face (10) Edema peripheral (11) Feeling hot (12) Immunization anxiety-related reaction (13) Procedural haemorrhage	(1) Vaccine (2) Placebo (3) Vaccine (4) Placebo (5) Vaccine (6) Vaccine (7) Vaccine (8) Placebo (9) 1 Case Placebo, 2 Cases Vaccine (10) Vaccine (11) Placebo (12) Placebo (13) Placebo
Polack, BNT162b2 (26)	43488	(1) Shoulder injury related to vaccination (2) Right axillary lymphadenopathy (3) Paroxysmal ventricular arrhythmia (4) Right leg paraesthesia	All vaccine
Voysey, ChAdOx (27)	23848	(1) Hemolytic anemia (2) Transverse Myelitis (3) Fever	(1) Placebo (2) Vaccine (3) Vaccine
Sadoff, Ad26.COV2.S (23)	805	(1) Pyrexia	(1) Vaccine
Folegatti, ChAdOx (41)	1077	(1) Haemolytic anaemia	(1) Placebo
Logunov, rAd26/5 (18)	21862	-	-

Supplementary Table 12: Pre-existing anti-vector neutralizing antibody titers recorded before vaccination and their correlation with anti-RBD seroconversion or SARS-CoV-2 neutralization in adenoviral vectored SARS-CoV-2 vaccines. n= number of patients with pre-existing neutralizing antibody titer available.

Vaccine group	n	No. participants with nAb titer = 0	No. participants with nAb titer 0<N≤200	No. participants with >200 nAb titer	Regression analysis: Vector nAb: Anti-RBD/SARS-CoV-2 nAb.	Summary
Zhu, AdH5 (Phase 1) Low dose (39)	36	NA	16(44%)	20(56%)	-1.67 (p=0.0003)	High levels of AdH5 nAbs at baseline. Significantly less nAb after vaccination in those with pre-existing AdH5 nAb.
Zhu, AdH5 (Phase 1) Middle dose (39)	36	NA	17(47%)	19(53%)		
Zhu, AdH5 (Phase 1) High dose (39)	36	NA	20(56%)	16(44%)		
Zhu, AdH5 (Phase 2) Low dose (40)	129	NA	54(42%)	75(58%)	-1.24 (p<0.0001)	High pre-existing AdH5 neutralizing antibody titer associated with reduced antibody responses, especially in those 55 years and older.
Zhu, AdH5 (Phase 2) High dose (40)	253	NA	127(50%)	126(50%)		
Folegatti, ChAdOx (Phase 2) (41)	98	79(81%)	18(18%)	1(1%)	No relationship	No association between pre-existing antibodies to the ChAdOx vector and antibody responses to SARS-CoV-2.
Logunov AdH26/5-Vac rAd26 (35)	38	32(84%)	3(8%)	3(8%)	0.07 (p=0.77)	No significant correlation between nAb titers to the adenoviral vector and the titer of RBD-specific IgG. No nAb cross reactivity between AdH5 and AdH26 adenoviral vectors.
Logunov AdH26/5-Vac rAd5 (35)	38	27(81%)	6(16%)	5(13%)	-0.2 (p=0.39)	
Logunov AdH26/5-Lyo rAd26 (35)	38	31(82%)	5(13%)	2(5%)	-0.44 (p=0.06)	
Logunov AdH26/5-Vac rAd5 (35)	38	29(76%)	5(13%)	4(11%)	-0.44 (p=0.06)	
Ramasamy ChAdOx (28)	552	522(100%)	0	0	NA	Anti-ChAdOx nAb titer increased following prime vaccination. No increase after boosting. Small negative correlation between Anti-ChAdOx nAb titre before boosting and anti-Spike IgG titer after boosting.
Sadoff rAd26.COVS.S (23)	303	303(99.4%)	2(0.6%)	0	-0.13 (NS)	No significant relationship between pre-existing neutralizing antibody titer and SARS-CoV-2 nAb induction. No relationship apparent after boost.

Supplementary Table 13. Human and NHP T cell analysis. *data from trial was estimated using graphical representations, **responses too low to extract.

Study Title Vaccine Group	Pathogen, Platform	Study Subjects	Polyfunctionality	T cell subsets	Effector Function, Cytokine Proportion (Mean, %)	Peptides	Summary
Ella, 2021 (16)	SARS-CoV-2 BBV152	Human	Yes – Week 7	<ul style="list-style-type: none"> CD4+ IFNγ, IL-2, and TNFα (Th1) IL-5, IL-10, and IL-13 (Th2) Effector Memory CD4+CD45RO+ CD4+CD45RO+CD27+ 	<ul style="list-style-type: none"> NA 	Overlapping Spike GP peptide pools covering the RBD protein	<ul style="list-style-type: none"> Th1 bias observed on day 42 Minimal Th2 responses observed in all vaccine groups Memory T cell response observed on day 104 in all vaccine and control groups
Richmond, 2021 (17)	SARS-CoV-2 S-Timer	Human	NA	<ul style="list-style-type: none"> CD4 IFNγ and/or IL-2+ (Th1) IL-4 and/or IL-5 (Th2) IL-17 (Th17) 	<ul style="list-style-type: none"> NA 	Spike GP peptide pools	<ul style="list-style-type: none"> Th1 bias recorded in the adjuvanted vaccine groups No T cell responses in the non-adjuvanted group. Dose dependant increase in IFNγ and IL-2-positive CD4+ T-cells No Th2 or Th17 responses were observed in any vaccine group.
Zhu, 2020 (39)* Phase 1 trial Low Dose	SARS-CoV-2 AdH-5	Human	Yes – Week 2	<ul style="list-style-type: none"> CD4+ IFNγ+, TNFα+, IL-2+ (Memory) CD8+ IFNγ+, TNFα+, IL-2+ (Memory) 	<ul style="list-style-type: none"> CD4 IFNγ+ = 0.18% TNFα+ = 0.06% IL-2+ = 0.16% CD8 IFNγ+ = 0.2% TNFα+ = 0.018% IL-2+ = 0.011% 	Overlapping Spike GP peptide pools	<ul style="list-style-type: none"> Higher polyfunctionality proportion in CD4+ memory T cells than CD8+ T cells IL-2 higher in CD4+ T cells than CD8+ T cells TNFα expression in CD4/CD8 lowest in low dose group (Highest = High dose) Higher polyfunctionality phenotypes associated with higher doses
Zhu, 2020 (39)* Phase 1 trial Inter Dose					<ul style="list-style-type: none"> CD4 IFNγ+ = 0.19% TNFα+ = 0.06% IL-2+ = 0.17% CD8 IFNγ+ = 0.18% TNFα+ = 0.012% IL-2+ = 0.005% 		
Zhu, 2020 (39)* Phase 1 trial High Dose					<ul style="list-style-type: none"> CD4 IFNγ+ = 0.11% TNFα+ = 0.055% IL-2+ = 0.11% CD8 IFNγ+ = 0.14% TNFα+ = 0.0125% IL-2+ = 0.004% 		
Anderson, 2020 (42) Low Dose 56-70yo	SARS-CoV-2 mRNA-1273	Human	Yes – Week 6	<ul style="list-style-type: none"> CD4+ IFNγ+, TNFα+, IL-2+, IL-4+, IL-13+ CD8+ IFNγ+, TNFα+, IL-2+ 	<ul style="list-style-type: none"> CD4 IFNγ+ = 0.108% TNFα+ = 0.224% IL-2+ = 0.204% IL-4+ = 0.01% IL-13+ = 0.019% CD8 IFNγ+ = 0.088% TNFα+ = 0.061% IL-2+ = 0.047% 	Overlapping Spike GP peptide pools	<ul style="list-style-type: none"> Strong CD4+ response in both 100ug groups and the 56-70yo 25ug group Effector function hierarchy: TNFα>IL-2>IFNγ Th2 response was minimal across all groups Lowest response was found in the 25ug >71y/o group CD8+ responses to S-2p were low after 2nd
Anderson, 2020 (42)					<ul style="list-style-type: none"> CD4 IFNγ+ = 0.031% 		

Low Dose ≥71yo				<ul style="list-style-type: none"> CD8+ IFNγ+, TNFα+, IL-2+ 	TNF α + = 0.085% IL-2+ = 0.065% IL-4+ = 0.005% IL-13+ = 0.013% <ul style="list-style-type: none"> CD8 IFNγ+ = 0.031% TNFα+ = 0.018% IL-2+ = 0.008% 		vaccination in the 100ug groups
Anderson, 2020 (42) High Dose 56-70yo				<ul style="list-style-type: none"> CD4+ IFNγ+, TNFα+, IL-2+, IL-4+, IL-13+ CD8+ IFNγ+, TNFα+, IL-2+ 	<ul style="list-style-type: none"> CD4 IFNγ+ = 0.148% TNFα+ = 0.296% IL-2+ = 0.224% IL-4+ = 0.021% IL-13+ = 0.018% CD8 IFNγ+ = 0.058% TNFα+ = 0.036% IL-2+ = 0.029% 		
Anderson, 2020 (42) High Dose ≥71yo				<ul style="list-style-type: none"> CD4+ IFNγ+, TNFα+, IL-2+, IL-4+, IL-13+ CD8+ IFNγ+, TNFα+, IL-2+ 	<ul style="list-style-type: none"> CD4 IFNγ+ = 0.164% TNFα+ = 0.295% IL-2+ = 0.214% IL-4+ = 0.015% IL-13+ = 0.015% CD8 IFNγ+ = 0.126% TNFα+ = 0.087% IL-2+ = 0.056% 		
Tebas, INO-4800 (24) High Dose	SARS-CoV-2	Human	Yes- Week 6	<ul style="list-style-type: none"> CD4+ IFNγ+, TNFα+, IL-2+, IL-4+, CD45RA+, CCR7- (Effector) CD45RA-, CCR7- (Effector memory) CD45RA-, CCR7+ (Central Memory) CD8+ IFNγ+, TNFα+, IL-2+, IL-4+, CD45RA+, CCR7- (Effector) CD45RA-, CCR7- (Effector memory) CD45RA-, CCR7+ (Central Memory) 	<ul style="list-style-type: none"> CD4 TNFα+: 0.02% CD8 IFNγ/IL-2/TNFα+: 0.11% 	Overlapping Spike GP peptide pools.	<ul style="list-style-type: none"> Largest responses in the high dose group. No significant Th2 responses. High CD8+polyfunctionality responses recorded. CD8+ responses were balanced among effector, effector memory and central memory, while the CD4+ population were mostly central memory. In the low dose group, CD8+ response were IFNγ+ monofunctional. CD4+ response were polyfunctional (IFNγ+ /IL-2+/TNFα+) in both dose groups.
Sadoff, 2021 (23) Low dose	SARS-CoV-2 Ad26.COV.2.S	Human	Yes- Week 2	<ul style="list-style-type: none"> CD4+ IFNγ+, IL-2+, IL-4+, IL-5+, IL-13+, CD40L+ CD8+ IFNγ+ and IL-2+ 	<ul style="list-style-type: none"> CD4 IFNγ/IL-2+: 0.08% IFNγ/IL-2+: 0.09% (≥65yo cohort) CD8 IFNγ+ and IL-2+: 0.07% IFNγ+ and IL-2+: 0.06% (≥65yo cohort) 	Overlapping Spike GP peptide pools.	<ul style="list-style-type: none"> Polyfunctionality was skewed towards Th1 responses. Two participants in this trial recorded a measurable Th2 response. Lower CD8+ responses were found in older adults than younger adults.
Sadoff, 2021 (23) High dose			<ul style="list-style-type: none"> CD4+ IFNγ+, IL-2+, IL-4+, IL-5+, IL-13+, CD40L+ CD8+ IFNγ+ and IL-2+ 	<ul style="list-style-type: none"> CD4 IFNγ/IL-2+: 0.11% IFNγ/IL-2+: 0.11% (≥65yo cohort) CD8 IFNγ+ and IL-2+: 0.09% IFNγ+ and IL-2+: 0.02% (≥65yo cohort) 			
Logunov, 2020 (35)	SARS-CoV-2 AdH26-AdH5- Vac	Human	NA	<ul style="list-style-type: none"> CD4+ and CD8+ 	<ul style="list-style-type: none"> CD4+ = 2.5% CD8+ = 1.3% 	NA	<ul style="list-style-type: none"> Higher CD4+ and CD8+ responses in the frozen

	SARS-CoV-2 AdH26-AdH5- Lyo			<ul style="list-style-type: none"> CD4+ and CD8+ 	<ul style="list-style-type: none"> CD4+ = 1.3% CD8+ = 1.1% 		formulation compared to the lyophilised formulation
Keech, 2020 (36) All dosage groups	SARS-CoV-2 NVX- CoV2373	Human	Yes- Week 4 Adjuvanted Vaccine groups	<ul style="list-style-type: none"> CD4+ IFNγ, TNFα, IL-2, IL-5, IL-13 CD8+ IFNγ, TNFα, IL-2+ 	<ul style="list-style-type: none"> NA 	NA	<ul style="list-style-type: none"> Strong Th1 responses Minimal Th2 responses Adjuvanted groups induced highest polyfunctional CD4+ responses
Sahin, 2020 (33) All dosage groups	SARS-CoV-2 BNT162b1	Human	Yes – D29	<ul style="list-style-type: none"> CD4+ IFNγ, IL-2+, IL-4+, IL-13+ CD8+ IFNγ, IL-2+ 	<ul style="list-style-type: none"> NA 	Overlapping peptide pool of vaccine encoded full length RBD	<ul style="list-style-type: none"> Strong functional and proinflammatory Th1 responses induced Minimal Th2 responses
Xia, 2020 (37)	SARS-CoV-2 Inactivated	Human	No	<ul style="list-style-type: none"> CD4+ IFNγ, IL-2+, IL-4+, IL-5+, IL-10+, IL-12+, IL-13+, TNFα, IL-17+, IL-21+ 	<ul style="list-style-type: none"> NA 	<ul style="list-style-type: none"> NA 	<ul style="list-style-type: none"> No changes in T cell population subset functionality
Jackson, 2020* (42) Low Dose	SARS-CoV-2 mRNA-1273	Human	Yes – D43 (W6)	<ul style="list-style-type: none"> CD4+CD3+ IFNγ, TNFα, IL-2+, IL-4+, IL-13+ 	<ul style="list-style-type: none"> S1 peptide pool CD4+ Th1 response = 0.09% CD4+ Th2 response = ** S2 peptide pool CD4+ Th1 response = 0.2% CD4+ Th2 response = ** 	Overlapping peptide pool of Spike 1 and 2 peptides (S1/2 separate analysis)	<ul style="list-style-type: none"> Low and intermediate-dose elicited CD4+ responses. Th1 bias observed. Effector function hierarchy: TNFα>IL-2>IFNγ Boost required for any notable polyfunctionality Low CD8 responses: responses achieved only after boost injection Minimal Th2 responses overall
Jackson, 2020* (42) Intermediate dose				<ul style="list-style-type: none"> CD8+CD3+ IFNγ, TNFα, IL-2+ 	<ul style="list-style-type: none"> S1 peptide pool CD4+ Th1 response = 0.1% CD4+ Th2 response = ** S2 peptide pool CD4+ Th1 response = 0.22% CD4+ Th2 response = ** 		
Koch, 2020 (45) Low Dose	MERS-CoV MVA	Human	NA IFN γ only assessed	<ul style="list-style-type: none"> CD4+ CD3+CD4+IFNγ CD8 CD3+CD8+IFNγ 	<ul style="list-style-type: none"> NA 	Overlapping Spike GP peptide pools	<ul style="list-style-type: none"> Higher responses in the low dose group compared to the high dose group
Modjarrad, 2019*(44) All Doses (Low, Inter, High)	MERS-COV DNA	Human	Yes - D98	<ul style="list-style-type: none"> CD4+CD3+ IFNγ, TNFα, IL-2+, IL-4+, IFNγ TNFα, IFNγ and/or TNFα, IFNγ and/or TNFα and/or IL-2 CD8+CD3+ IFNγ, TNFα, IL-2+, IL-4+, IFNγ TNFα, IFNγ and/or TNFα, IFNγ and/or TNFα and/or IL-2 	<ul style="list-style-type: none"> CD4 IFNγ = 0.14% TNFα = 0.05% IL-2+ = 0.04 IL-4+ = 0.025% IFNγ TNFα = 0.03% IFNγ and/or TNFα = 0.175% IFNγ and/or TNFα and/or IL-2 = 0.18% CD8 IFNγ = 0.17% TNFα = 0.1% IL-2+ = 0.2% IL-4+ = 0.045% IFNγ TNFα = 0.075% IFNγ and/or TNFα = 0.19% IFNγ and/or TNFα and/or IL-2 = 0.27% 	Overlapping peptide pool of entire spike GP	<ul style="list-style-type: none"> CD4+ and CD8+ polyfunctionality recorded 2 weeks following 3rd vaccination
Martin, 2008 (47)* Experimental	SARS-CoV-1 DNA	Human	NA	<ul style="list-style-type: none"> CD4+CD3+ IFNγ, IL-2+ CD8+CD3+ IFNγ, IL-2+ 	<ul style="list-style-type: none"> CD4 IFNγ = 0.11% CD8 IFNγ = - 	Vaccine insert specific peptide pools	<ul style="list-style-type: none"> CD4+ responses higher in magnitude and frequency than CD8+ response CD8+ only registered in 2 study subjects
Yu, 2020 (55) All groups	SARS-CoV-2 DNA	NHP	Yes – D3-5 (W5)	<ul style="list-style-type: none"> CD4+CD3+ IFNγ, IL-4+ CD8+CD3+ IFNγ, IL-4+ 	<ul style="list-style-type: none"> NA 	Overlapping peptide pool of Spike 1 and 2 peptides	<ul style="list-style-type: none"> CD8/4+IFNγ responses stimulated CD4/8+ IL-4 responses minimal S1/RBD groups recorded the lowest responses.

							<ul style="list-style-type: none"> Results suggestive of a Th1 bias response
Muthumani, 2015*(65) Low dose	MERS-CoV DNA	NHP	Yes – D70 (W10)	<ul style="list-style-type: none"> CD3+CD4+ IFNγ+, TNFα+, IL-2+ (Memory) 	<ul style="list-style-type: none"> CD3+CD4+ IFNγ+ = 0.03% TNFα+ = 0.15% IL-2+ = 0.015% 	6 peptide pools of entire Spike GP	<ul style="list-style-type: none"> High dose group produced highest polyfunctionality, followed by low dose group Cytokine hierarchy = IFNγ>TNFα>IL-2
Muthumani, 2015*(65) High dose				<ul style="list-style-type: none"> CD3+CD8+ IFNγ+, TNFα+, IL-2+ (Memory) 	<ul style="list-style-type: none"> CD3+CD4+ IFNγ+ = 0.125% TNFα+ = 0.12% IL-2+ = 0.024% 		
Erasmus, (2020) (59)	SARS-CoV-2	NHP	NA	<ul style="list-style-type: none"> IFNγ+, IL-2+, IL-17a+, TNFα+, MIP8, Granzyme b/CD107a 	NA	NA	<ul style="list-style-type: none"> A non-significant increase of IFNγ producing CD4+CD8+ t cells. Slight increase in S-specific effector memory CD8+ T cells
Corbett, 2020* (60) Low dose	SARS-CoV-2 mRNA-1273	NHP	Yes – D56 (W8)	<ul style="list-style-type: none"> CD3+CD4+ IFNγ+, TNFα+, IL-2+ (Th1 memory response) CD40L (B-Cell activation) 	<ul style="list-style-type: none"> Th1 = 0.02% Th2 = - CD40L = 0.04% Tfh = 0.05% 	Overlapping peptide pool of Spike 1, 2 and NP	<ul style="list-style-type: none"> Highest Th1 response in high dose group Dose-dependent increase in Th1 responses following 2nd vaccination Minimal to undetectable Th2/CD8 responses.
Corbett, 2020 (60)* High dose				<ul style="list-style-type: none"> CD3+CD8+ IL-4, IL-13 (Th2 memory response) IL-21 (Tfh central memory response) 	<ul style="list-style-type: none"> Th1 = 0.1% Th2 = - CD40L = 0.1% Tfh = 0.2% 		
Mercado, 2020 (58)	SARS-CoV-2 AdH26	NHP	Yes - D28 (W4)	<ul style="list-style-type: none"> CD3+CD4+ IFNγ+, TNFα+ CD3+CD8+ IFNγ+, TNFα+ 	<ul style="list-style-type: none"> NA 	Overlapping Spike GP peptide pools	<ul style="list-style-type: none"> Higher IFNγ+ CD8 responses compared to IFNγ+CD4 responses Minimal IL-4 responses suggesting Th1 responses
Kobinger, 2007 (66) Experimental	SARS-CoV-1 AdC7/H5	NHP	NA IFN γ only assessed	<ul style="list-style-type: none"> CD4+ IFNγ+ CD8+ IFNγ+ 	<ul style="list-style-type: none"> NA 	5 peptide pools of spike GP	<ul style="list-style-type: none"> CD8+IFNγ+ was the predominant cellular response

SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2, MERS-CoV: Middle east respiratory syndrome, SARS-CoV-1: Severe acute respiratory syndrome coronavirus 1, AdH5: Recombinant human adenovirus 5, CD3/4/8: Cluster of differentiation 3/4/5, TNF α : Tumour necrosis factor alpha, IFN γ : Interferon gamma, IL-2/4/13: Interleukin-2/4/13, GP: Glycoprotein, MVA: Recombinant modified Vaccinia virus Ankara, DNA: Deoxyribonucleic acid, S1: Spike domain 1, S2: Spike domain 2, Th1: T helper type 1, Th2, T helper type 2, mRNA: messenger ribonucleic acid, NHP: Non-human primate, AdC7: Recombinant chimpanzee adenovirus-7, CD40L: Cluster of differentiation 40 ligand, Tfh: T follicular helper cell, AdH26: Recombinant human adenovirus-26, NP: Nucleoprotein