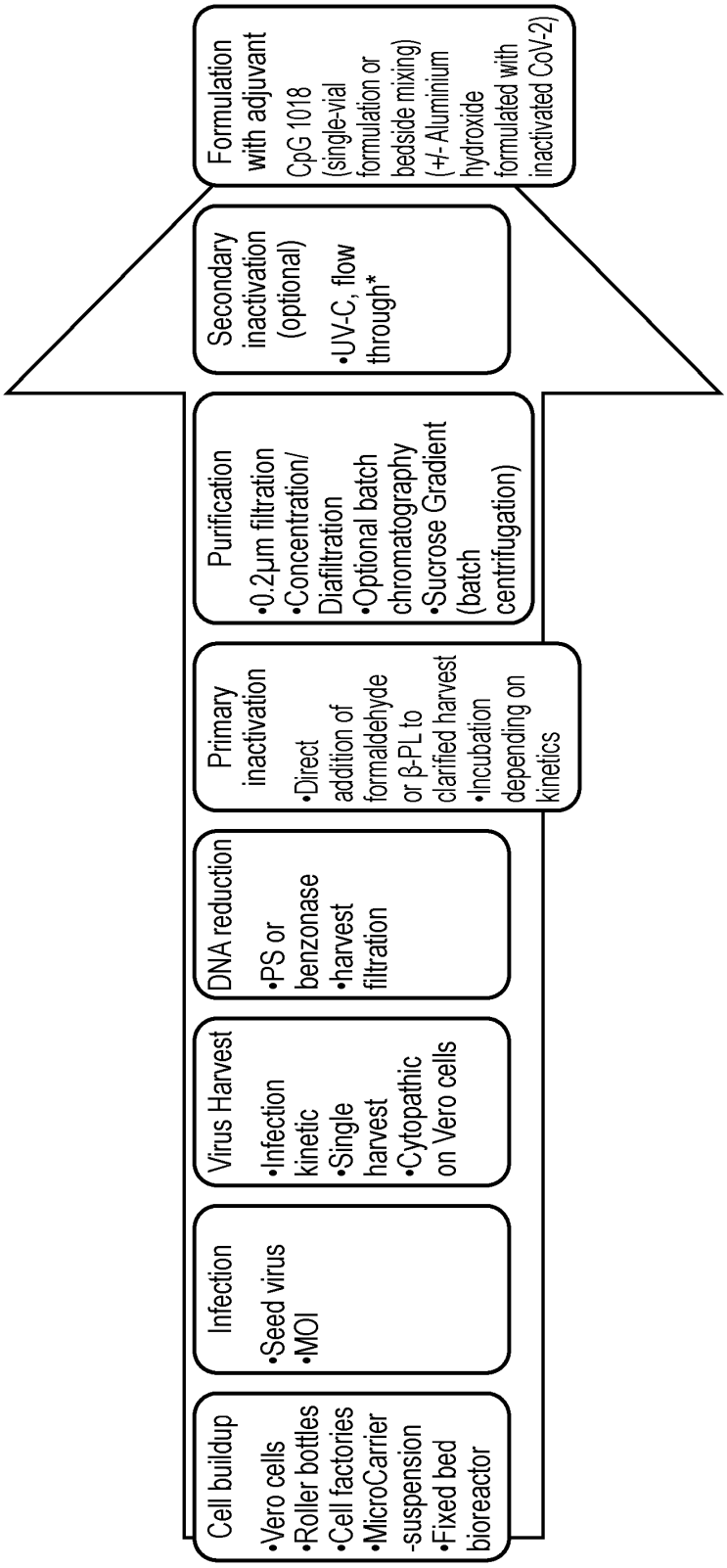

Cell buildup
•Vero cells
•Roller bottles
•Cell factories
•MicroCarrier -suspension
•Fixed bed bioreactor
Infection
•Seed virus
•MOI
Virus Harvest
•Infection kinetic
•Single harvest
•Cytopathic on Vero cells
DNA reduction
•PS or benzonase
•harvest filtration
Primary inactivation
•Direct addition of formaldehyde or β-PL to clarified harvest
•Incubation depending on kinetics
Purification
•0.2µm filtration
•Concentration/ Diafiltration
•Optional batch chromatography
•Sucrose Gradient (batch centrifugation)
Secondary inactivation (optional)
•UV-C, flow through*
Formulation with adjuvant
CpG 1018 (single-vial formulation or bedside mixing)
(+/- Aluminium hydroxide formulated with inactivated CoV-2)

FIG. 1

Isolate	GenBank accession number**			Locality
	Genome	orf1ab polyprotein	s protein	
Severe acute respiratory syndrome coronavirus 2*	MN908947 (SEQ ID NO: 1)	QHD43415 (SEQ ID NO: 2)	QHD43416 (SEQ ID NO: 3)	China
SARS-CoV-2/Hu/DP/Kng/19-020	LC528232	BCA87360	BCA87361	Japan
SARS-CoV-2/Hu/DP/Kng/19-027	LC528233	BCA87370	BCA87371	Japan
TKYE6182_2020	LC529905	BCB15089	BCB15090	Japan
From Wuhan outbreak patient 2019-12-26	LR757995	-	-	China:Wuhan
From Wuhan outbreak patient 2020-01-01	LR757996	-	-	China:Wuhan
From Wuhan outbreak patent 2019-12-26	LR757998	-	-	China:Wuhan
2019-nCoV_HKU-SZ-002a_2020	MN938384	QHN73794	QHN73795	China:Shenzhen
2019-nCoV_HKU-SZ-005b_2020	MN975262	QHN73809	QHN73810	China
2019-nCoV/USA-WA1/2020	MN985325	QHO60603	QHO60594	USA:WA
2019-nCoV WHU01	MN988668	QHO62106	QHO62107	China
2019-nCoV WHU02	MN988669	QHO62111	QHO62112	China
2019-nCoV/USA-IL1/2020	MN988713	QHO62876	QHO62877	USA:IL
2019-nCoV/USA-CA1/2020	MN994467	QHQ71962	QHQ71963	USA:CA
2019-nCoV/USA-CA2/2020	MN994468	QHQ71972	QHQ71973	USA:CA
WIV02	MN996527	QHR63249	QHR63250	China:Wuhan
WIV04	MN996528	QHR63259	QHR63260	China:Wuhan
WIV05	MN996529	QHR63269	QHR63270	China:Wuhan
WIV06	MN996530	QHR63279	QHR63280	China:Wuhan
WIV07	MN996531	QHR63289	QHR63290	China:Wuhan
2019-nCoV/USA-AZ1/2020	MN997409	QHQ82463	QHQ82464	USA:AZ
Australia/VIC01/2020	MT007544	QHR84448	QHR84449	Australia:Victoria
SARS-CoV-2/29/human/2020/IND	MT012098	QHS34545	QHS34546	India:Kerala State

FIG. 2

SUBSTITUTE SHEET (RULE 26)

Isolate	GenBank accession number**			Locality
	Genome	orf1ab polyprotein	s protein	
BetaCoV/Wuhan/IPBCAMS-WH-01/2019	MT019529	QHU36823	QHU36824	China:Wuhan
BetaCoV/Wuhan/IPBCAMS-WH-02/2019	MT019530	QHU36833	QHU36834	China:Wuhan
BetaCoV/Wuhan/IPBCAMS-WH-03/2019	MT019531	QHU36843	QHU36844	China:Wuhan
BetaCoV/Wuhan/IPBCAMS-WH-04/2019	MT019532	QHU36853	QHU36854	China:Wuhan
BetaCoV/Wuhan/IPBCAMS-WH-05/2020	MT019533	QHU36863	QHU36864	China:Wuhan
2019-nCoV/USA-WA1-A12/2020	MT020880	QHU79193	QHU79194	USA:WA
2019-nCoV/USA-WA1-F6/2020	MT020881	QHU79203	QHU79204	USA:WA
2019-nCoV/USA-CA3/2020	MT027062	QHW06038	QHW06039	USA:CA
2019-nCoV/USA-CA4/2020	MT027063	QHW06048	QHW06049	USA:CA
2019-nCoV/USA-CA5/2020	MT027064	QHW06058	QHW06059	USA:CA
HZ-1	MT039873	QHZ00357	QHZ00358	China:Hangzhou
2019-nCoV/USA-WI1/2020	MT039887	QHZ00388	QHZ00389	USA:WI
2019-nCoV/USA-MA1/2020	MT039888	QHZ00398	QHZ00399	USA:MA
SNU01	MT029890	QHZ00378	QHZ00379	South Korea
2019-nCoV/USA-CA6/2020	MT044258	QHZ87591	QHZ87592	USA:CA
SARS-CoV-2/Yunnan-01/human/2020/CHN	MT049951	QIA20042	QIA20043	China:Yunnan
SARS-CoV-2/2166/human/2020/IND	MT050493	QIA98582	QIA98583	India:Kerala State
SARS-CoV-2/INMI1/human/2020/ITA	MT066156	QIA98553	QIA98554	Italy
SARS-CoV-2/NTU01/2020/TWN	MT066175	QIA98595	QIA98596	Taiwan
SARS-CoV-2/NTU02/2020/TWN	MT066176	QIA98605	QIA98606	Taiwan
SARS-CoV-2/01/human/2020/SWE	MT093571	QIC53203	QIC53204	Sweden
SARS-CoV-2/WH-09/human/2020/CHN	MT093631	QIC53222	QIC53213	China
2019-nCoV/USA-CA7/2020	MT106052	QID21047	QID21048	USA:CA

FIG. 2 (Continued)

Isolate	GenBank accession number**			Locality
	Genome	orf1ab polyprotein	s protein	
2019-nCoV/USA-CA8/2020	MT106053	QID21057	QID21058	USA:CA
2019-nCoV/USA-TX1/2020	MT106054	QID21067	QID21068	USA:TX
2019-nCoV/USA-CA9/2020	MT118835	QID98793	QID98794	USA:CA
SARS-CoV-2/SH01/human/2020/CHN	MT121215	QII57165	QII57161	China:Shanghai
SARS-CoV-2/IQTC01/human/2020/CHN	MT123290	QIE07450	QIE07451	China:Guangzhou
SARS-CoV-2/IQTC02/human/2020/CHN	MT123291	QIE07460	QIE07461	China:Guangzhou
SARS-CoV-2/IQTC04/human/2020/CHN	MT123292	QIE07470	QIE07471	China:Guangzhou
SARS-CoV-2/IQTC03/human/2020/CHN	MT123293	QIE07480	QIE07481	China:Guangzhou
SARS-CoV-2/SP02/human/2020/BRA	MT126808	QIG55993	QIG55994	Brazil
SARS-CoV-2/2105/human/2020/CHN	MT135041	QIH45022	QIH45023	China:Beijing
SARS-CoV-2/2231/human/2020/CHN	MT135042	QIH45032	QIH45033	China:Beijing
SARS-CoV-2/2233/human/2020/CHN	MT135043	QIH45042	QIH45043	China:Beijing
SARS-CoV-2/2235/human/2020/CHN	MT135044	QIH45052	QIH45053	China:Beijing
SARS-CoV-2/WA2/human/2020/USA	MT152824	QIH55220	QIH55221	USA:WA
2019-nCoV/USA-CruiseA-7/2020	MT159705	QII57167	QII57168	USA
2019-nCoV/USA-CruiseA-8/2020	MT159706	QII57177	QII57178	USA
2019-nCoV/USA-CruiseA-10/2020	MT159707	QII57187	QII57188	USA
2019-nCoV/USA-CruiseA-11/2020	MT159708	QII57197	QII57198	USA
2019-nCoV/USA-CruiseA-12/2020	MT159709	QII57207	QII57208	USA
2019-nCoV/USA-CruiseA-9/2020	MT159710	QII57217	QII57218	USA
2019-nCoV/USA-CruiseA-13/2020	MT159711	QII57227	QII57228	USA
2019-nCoV/USA-CruiseA-14/2020	MT159712	QII57237	QII57238	USA
2019-nCoV/USA-CruiseA-15/2020	MT159713	QII57247	QII57248	USA

FIG. 2 (Continued)

Isolate	GenBank accession number**			Locality
	Genome	orf1ab polyprotein	s protein	
2019-nCoV/USA-CruiseA-16/2020	MT159714	QII57257	QII57258	USA
2019-nCoV/USA-CruiseA-17/2020	MT159715	QII57267	QII57268	USA
2019-nCoV/USA-CruiseA-18/2020	MT159716	QII57277	QII57278	USA
2019-nCoV/USA-CruiseA-1/2020	MT159717	QII57287	QII57288	USA
2019-nCoV/USA-CruiseA-2/2020	MT159718	QII57297	QII57297	USA
2019-nCoV/USA-CruiseA-3/2020	MT159719	QII57307	QII57308	USA
2019-nCoV/USA-CruiseA-4/2020	MT159720	QII57317	QII57318	USA
2019-nCoV/USA-CruiseA-5/2020	MT159721	QII57327	QII57328	USA
2019-nCoV/USA-CruiseA-6/2020	MT159722	QII57337	QII57338	USA
SARS-CoV-2/WA3-UW1/human/2020/USA	MT163716	QII87780	QII87781	USA:WA
SARS-CoV-2/WA4-UW2/human/2020/USA	MT163717	QII87792	QII87793	USA:WA
SARS-CoV-2/WA6-UW3/human/2020/USA	MT163718	QII87804	QII87805	USA:WA
SARS-CoV-2/WA7-UW4/human/2020/USA	MT163719	QII87816	QII87817	USA:WA
2019-nCoV/USA-CruiseA-19/2020	MT184907	QIJ96462	QIJ96463	USA
2019-nCoV/USA-CruiseA-21/2020	MT184908	QIJ96472	QIJ96473	USA
2019-nCoV/USA-CruiseA-22/2020	MT184909	QIJ96482	QIJ96483	USA
2019-nCoV/USA-CruiseA-23/2020	MT184910	QIJ96492	QIJ96493	USA
2019-nCoV/USA-CruiseA-24/2020	MT184911	QIJ96502	QIJ96503	USA
2019-nCoV/USA-CruiseA-25/2020	MT184912	QIJ96512	QIJ96513	USA
2019-nCoV/USA-CruiseA-26/2020	MT184913	QIJ96522	QIJ96523	USA
USA/MN3-MDH3/2020	MT188339	QIK02943	QIK02944	USA:MN
USA/MN2-MDH2/2020	MT188340	QIK02953	QIK02954	USA:MN
USA/MN1-MDH1/2020	MT188341	QIK02963	QIK02964	USA:MN

FIG. 2 (Continued)

Isolate	GenBank accession number**			Locality
	Genome	orf1ab polyprotein	s protein	
SARS-CoV-2/CGMH-CGU-01/human2020/TWN	MT192759	QIK50416	QIK50417	Taiwan
SARS-CoV-2/PC00101P/human/2020/USA	MT192765	QIK50426	QIK50427	USA:CA
SARS-CoV-2/nCoV-19-01S/human/2020/VNM	MT192772	QIK50437	QIK50438	Vietnam:Ho Chi Minh City
SARS-CoV-2/nCoV-19-02S/human/2020/VNM	MT192773	QIK50447	QIK50448	Vietnam:Ho Chi Minh City
SARS-CoV-2/KMS1/human/2020/CHN	MT226610	QIO04366	QIO04367	China
SARS-CoV-2/Valencia5/human/2020/ESP	MT233519	QIQ08789	QIQ08790	Spain:Valencia
SARS-CoV-2/Valencia7/human/2020/ESP	MT233522	QIQ08819	QIQ08820	Spain:Valencia
SARS-CoV-2/Valencia8/human/2020/ESP	MT233523	QIQ08829	QIQ08830	Spain:Valencia
SARS-CoV-2/Gilgit1/human/2020/PAK	MT240479	QIQ22758	QIQ22759	Pakistan:Gilgit
SARS-CoV-2/WA-UW192/human/2020/USA	MT246449	QIQ49761	QIQ49762	USA:WA
SARS-CoV-2/WA-UW193/human/2020/USA	MT246450	QIQ49771	QIQ49772	USA:WA
SARS-CoV-2/WA-UW194/human/2020/USA	MT246451	QIQ49781	QIQ49782	USA:WA
SARS-CoV-2/WA-UW195/human/2020/USA	MT246452	QIQ49791	QIQ49792	USA:WA
SARS-CoV-2/WA-UW196/human/2020/USA	MT246453	QIQ49801	QIQ49802	USA:WA
SARS-CoV-2/WA-UW197/human/2020/USA	MT246454	QIQ49811	QIQ49812	USA:WA
SARS-CoV-2/WA-UW198/human/2020/USA	MT246455	QIQ49821	QIQ49822	USA:WA
SARS-CoV-2/WA-UW199/human/2020/USA	MT246456	QIQ49831	QIQ49832	USA:WA
SARS-CoV-2/WA-UW200/human/2020/USA	MT246457	QIQ49841	QIQ49842	USA:WA
SARS-CoV-2/WA-UW201/human/2020/USA	MT246458	QIQ49851	QIQ49852	USA:WA
SARS-CoV-2/WA-UW202/human/2020/USA	MT246459	QIQ49861	QIQ49862	USA:WA
SARS-CoV-2/WA-UW203/human/2020/USA	MT246460	QIQ49871	QIQ49872	USA:WA
SARS-CoV-2/WA-UW204/human/2020/USA	MT246461	QIQ49881	QIQ49882	USA:WA
SARS-CoV-2/WA-UW205/human/2020/USA	MT246462	QIQ49891	QIQ49892	USA:WA

FIG. 2 (Continued)

Isolate	GenBank accession number**			Locality
	Genome	orf1ab polyprotein	s protein	
SARS-CoV-2/WA-UW207/human/2020/USA	MT246464	QIQ49911	QIQ49912	USA:WA
SARS-CoV-2/WA-UW209/human/2020/USA	MT246466	QIQ49931	QIQ49932	USA:WA
SARS-CoV-2/WA-UW210/human/2020/USA	MT246467	QIQ49941	QIQ49942	USA:WA
SARS-CoV-2/WA-UW211/human/2020/USA	MT246468	QIQ49951	QIQ49952	USA:WA
SARS-CoV-2/WA-UW212/human/2020/USA	MT246469	QIQ49961	QIQ49962	USA:WA
SARS-CoV-2/WA-UW213/human/2020/USA	MT246470	QIQ49971	QIQ49972	USA:WA
SARS-CoV-2/WA-UW214/human/2020/USA	MT246471	QIQ49981	QIQ49982	USA:WA
SARS-CoV-2/WA-UW215/human/2020/USA	MT246472	QIQ49991	QIQ49992	USA:WA
SARS-CoV-2/WA-UW216/human/2020/USA	MT246473	QIQ50001	QIQ50002	USA:WA
SARS-CoV-2/WA-UW217/human/2020/USA	MT246474	QIQ50011	QIQ50012	USA:WA
SARS-CoV-2/WA-UW218/human/2020/USA	MT246475	QIQ50021	QIQ50022	USA:WA
SARS-CoV-2/WA-UW219/human/2020/USA	MT246476	QIQ50031	QIQ50032	USA:WA
SARS-CoV-2/WA-UW220/human/2020/USA	MT246477	QIQ50041	QIQ50042	USA:WA
SARS-CoV-2/WA-UW221/human/2020/USA	MT246478	QIQ50051	QIQ50052	USA:WA
SARS-CoV-2/WA-UW222/human/2020/USA	MT246479	QIQ50061	QIQ50062	USA:WA
SARS-CoV-2/WA-UW223/human/2020/USA	MT246480	QIQ50071	QIQ50072	USA:WA
SARS-CoV-2/WA-UW224/human/2020/USA	MT246481	QIQ50081	QIQ50082	USA:WA
SARS-CoV-2/WA-UW225/human/2020/USA	MT246482	QIQ50091	QIQ50092	USA:WA
SARS-CoV-2/WA-UW227/human/2020/USA	MT246484	QIQ50111	QIQ50112	USA:WA
SARS-CoV-2/WA-UW228/human/2020/USA	MT246485	QIQ50121	QIQ50122	USA:WA
SARS-CoV-2/WA-UW229/human/2020/USA	MT246486	QIQ50131	QIQ50132	USA:WA
SARS-CoV-2/WA-UW230/human/2020/USA	MT246487	QIQ50141	QIQ50142	USA:WA
SARS-CoV-2/WA-UW231/human/2020/USA	MT246488	QIQ50151	QIQ50152	USA:WA

FIG. 2 (Continued)

Isolate	GenBank accession number**			Locality
	Genome	orf1ab polyprotein	s protein	
SARS-CoV-2/WA-UW232/human/2020/USA	MT246489	QIQ50161	QIQ50162	USA:WA
SARS-CoV-2/WA-UW233/human/2020/USA	MT246490	QIQ50171	QIQ50172	USA:WA
SARS-CoV-2/WA-UW236/human/2020/USA	MT251972	QIQ68463	QIQ68464	USA:WA
SARS-CoV-2/WA-UW237/human/2020/USA	MT251973	QIQ68473	QIQ68474	USA:WA
SARS-CoV-2/WA-UW238/human/2020/USA	MT251974	QIQ68483	QIQ68484	USA:WA
SARS-CoV-2/WA-UW239/human/2020/USA	MT251975	QIQ68493	QIQ68494	USA:WA
SARS-CoV-2/WA-UW240/human/2020/USA	MT251976	QIQ68503	QIQ68504	USA:WA
SARS-CoV-2/WA-UW234/human/2020/USA	MT251977	QIQ68513	QIQ68514	USA:WA
SARS-CoV-2/WA-UW235/human/2020/USA	MT251978	QIQ68523	QIQ68524	USA:WA
SARS-CoV-2/WA-UW241/human/2020/USA	MT251979	QIQ68533	QIQ68534	USA:WA
SARS-CoV-2/WA-UW242/human/2020/USA	MT251980	QIQ68543	QIQ68544	USA:WA
SARS-CoV-2/HZ-162/human/2020/CHN	MT253696	QIQ68553	QIQ68554	China:Hangzhou
SARS-CoV-2/HZ-178/human/2020/CHN	MT253697	QIQ68563	QIQ68564	China:Hangzhou
SARS-CoV-2/HZ-185/human/2020/CHN	MT253698	QIQ68573	QIQ68574	China:Hangzhou
SARS-CoV-2/HZ-477/human/2020/CHN	MT253699	QIQ68583	QIQ68584	China:Hangzhou
SARS-CoV-2/HZ-481/human/2020/CHN	MT253700	QIQ68593	QIQ68594	China:Hangzhou
SARS-CoV-2/HZ-48/human/2020/CHN	MT253701	QIQ68603	QIQ68604	China:Hangzhou
SARS-CoV-2/HZ-49/human/2020/CHN	MT253702	QIQ68613	QIQ68614	China:Hangzhou
SARS-CoV-2/HZ-551/human/2020/CHN	MT253703	QIQ68623	QIQ68624	China:Hangzhou
SARS-CoV-2/HZ-576/human/2020/CHN	MT253704	QIQ68633	QIQ68634	China:Hangzhou
SARS-CoV-2/HZ-60/human/2020/CHN	MT253705	QIQ68643	QIQ68644	China:Hangzhou
SARS-CoV-2/HZ-62/human/2020/CHN	MT253706	QIQ68653	QIQ68654	China:Hangzhou
SARS-CoV-2/HZ-638/human/2020/CHN	T253707	QIQ68663	QIQ68664	China:Hangzhou

FIG. 2 (Continued)

Isolate	GenBank accession number**			Locality
	Genome	orf1ab polyprotein	s protein	
SARS-CoV-2/HZ-79/human/2020/CHN	MT253708	QIQ68673	QIQ68674	China:Hangzhou
SARS-CoV-2/HZ-90/human/2020/CHN	MT253709	QIQ68683	QIQ68684	China:Hangzhou
SARS-CoV-2/HZ-91/human/2020/CHN	MT253710	QIQ68693	QIQ68694	China:Hangzhou
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/England/ex-SA/2021, EVAg Ref-SKU:004V-04071 (SA_P2) complete genome. South-African B.1.351 lineage	SA_P2_t0.9_q20 (SEQ ID NO: 18)		SA_P2_gp02 (SEQ ID NO: 19)	UK
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/GHA/n-mimr-SARS-CoV-2-TRA-143/2021, complete genome. South-African B.1.351 lineage	MW598408.1		QRN78215.1	Ghana
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/GHA/n-mimr-SARS-CoV-2-TRA-186/2021, complete genome. South-African B.1.351 lineage	MW598413.1		QRN78275.1	Ghana
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/GHA/n-mimr-SARS-CoV-2-TRA-201/2021, complete genome. South-African B.1.351 lineage	MW598419.1		QRN78347.1	Ghana

FIG. 2 (Continued)

Isolate	GenBank accession number**			Locality
	Genome	orf1ab polyprotein	s protein	
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/USA/MA-Broad_CR-SP-00844/2021, complete genome. South-African B.1.351 lineage	MW617734.1		QRU93410.1	USA
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/USA/MD-MDH-0862/2021, complete genome. South-African B.1.351 lineage	MW621453.1		QRV12312.1	USA
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/USA/SC-COV-ID21-0037/2021 ORF1ab polyprotein (ORF1ab) gene, complete cds; ORF1a polyprotein (ORF1ab) gene, partial cds; surface glycoprotein (S), ORF3a protein (ORF3a), and envelope protein (E) genes, complete cds; membrane glycoprotein (M) and ORF7b (ORF7b) genes, partial cds; and ORF8 protein (ORF8), nucleocapsid phosphoprotein (N), and ORF10 protein (ORF10) genes, complete cds. South-African B.1.351 lineage	MW517347.1		QQW56090.1	USA

FIG. 2 (Continued)

Isolate	GenBank accession number**			Locality
	Genome	orf1ab polyprotein	s protein	
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human /USA/SC-CDC-LC0003421/2021 ORF1ab polyprotein (ORF1ab) gene, complete cds; ORF1a polyprotein (ORF1ab) gene, partial cds; surface glycoprotein (S), ORF3a protein (ORF3a), envelope protein (E), membrane glycoprotein (M), ORF6 protein (ORF6), and ORF7a protein (ORF7a) genes, complete cds; ORF7b (ORF7b) and nucleocapsid phosphoprotein (N) genes, partial cds; and ORF10 protein (ORF10) gene, complete cds. South-African B.1.351 lineage	MW548962.1		QRA20125.1	USA
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/GHA/WACCBIP_nCoV-_GS73/2021 ORF1ab polyprotein (ORF1ab), ORF1a polyprotein (ORF1ab), surface glycoprotein (S), ORF3a protein (ORF3a), envelope protein (E), membrane glycoprotein (M), ORF6 protein (ORF6), ORF7a protein (ORF7a), ORF7b (ORF7b), ORF8 protein (ORF8), nucleocapsid phosphoprotein (N), and ORF10 protein (ORF10) genes, complete cds. South-African B.1.351 lineage	MW571126.1		QRG27673.1	Ghana

FIG. 2 (Continued)

Isolate	GenBank accession number**			Locality
	Genome	orf1ab polyprotein	s protein	
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/USA/MD-MDH-0830/2021 ORF1ab polyprotein (ORF1ab), ORF1a polyprotein (ORF1ab), surface glycoprotein (S), ORF3a protein (ORF3a), envelope protein (E), membrane glycoprotein (M), ORF6 protein (ORF6), ORF7a protein (ORF7a), ORF7b (ORF7b), ORF8 protein (ORF8), nucleocapsid phosphoprotein (N), and ORF10 protein (ORF10) genes, complete cds. South-African B.1.351 lineage	MW580573.1		QRI43422.1	USA
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human /USA/MD-MDH-0831/2021, complete genome. South-African B.1.351 lineage	MW580574.1		QRI43434.1	USA
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human /USA/MD-MDH-0833/2021, complete genome. South-African B.1.351 lineage	MW580576.1		QRI43458.1	USA
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/USA/MN-MDH-2399/2021, complete genome. Brazilian P1 lineage	MW520923.1 (SEQ ID NO: 20)		QQX12069.1 (SEQ ID NO: 21)	USA

FIG. 2 (Continued)

Isolate	GenBank accession number**			Locality
	Genome	orf1ab polyprotein	s protein	
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human /USA/MN-MDH-2575/2021, complete genome. Brazilian P1 lineage	MW558281.1		QRD95445.1	USA
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/USA/OK-USAF-SAM-S0004/2021 ORF1ab polyprotein (ORF1ab), ORF1a polyprotein (ORF1ab), surface glycoprotein (S), ORF3a protein (ORF3a), envelope protein (E), membrane glycoprotein (M), ORF6 protein (ORF6), ORF7a protein (ORF7a), ORF7b (ORF7b), ORF8 protein (ORF8), nucleocapsid phosphoprotein (N), and ORF10 protein (ORF10) genes, complete cds. Brazilian P1 lineage	MW559120.1		QRE01802.1	USA
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human /USA/MD-MDH-0841/2021, complete genome. Brazilian P1 lineage	MW621433.1		QRV12072.1	USA

FIG. 2 (Continued)

Isolate	GenBank accession number**			Locality
	Genome	orf1ab polyprotein	s protein	
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/England/MIG457/2020, EVAg Ref-SKU:004V-04032, complete genome. UK B 1.1.7 lineage	UK_MIG457 (SEQ ID NO: 22)		MIG457_gp02 (SEQ ID NO: 23)	UK
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/USA/CO-CD-PHE-2100156850/2020, complete genome. UK B 1.1.7 lineage	MW422256.1		QQH18545.1	USA
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human /DOM/-CDC-9KZX-8454/2020, complete genome. UK B 1.1.7 lineage	MW494127.1		QQV26699.1	Dominican Republic
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/USA/-CA-CDC-STM-A100427/2021, complete genome. UK B 1.1.7 lineage	MW519625.1		QQX03098.1	USA
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human /USA/MN-MDH-2415/2021, complete genome. UK B 1.1.7 lineage	MW520939.1		QQX12261.1	USA

FIG. 2 (Continued)

Isolate	GenBank accession number**			Locality
	Genome	orf1ab polyprotein	s protein	
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human /USA/MN-MDH-2416/2021, complete genome. UK B 1.1.7 lineage	MW520940.1		QQX12273.1	USA
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/USA/-CA-CDC-STM-A100377/2021, complete genome. UK B 1.1.7 lineage	MW523787.1		QQX30401.1	USA
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/USA/-FL-CDC-STM-0000013-F08/2021, complete genome. UK B 1.1.7 lineage	MW524888.1		QQX33678.1	USA
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/USA/-CA-CDC-STM-0000025-C04/2021, complete genome. UK B 1.1.7 lineage	MW525027.1		QQX35346.1	USA
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human /USA/MI-CDC-STM-0000013-E10/2021, complete genome. UK B 1.1.7 lineage	MW525061.1		QQX35754.1	USA

FIG. 2 (Continued)

Isolate	GenBank accession number**			Locality
	Genome	orf1ab polyprotein	s protein	
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human /USA/MN-CDC-STM-0000013-A10/2021, complete genome. UK B 1.1.7 lineage	MW525074.1		QQX35910.1	USA
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/BGD/G039392/2021, complete genome. UK B 1.1.7 lineage	MW531680.1		QQX99439.1	Bangladesh
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human /USA/MN-MDH-2501/2021, complete genome. UK B 1.1.7 lineage	MW549866.1		QRA60361.1	USA
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/USA/-CA-QDX-4373/2021, complete genome. UK B 1.1.7 lineage	MW560781.1		QRF69855.1	USA
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/hu-man/USA/MD-MDH-0745/2021, complete genome. UK B 1.1.7 lineage	MW565850.1		QRG21605.1	USA

FIG. 2 (Continued)

Isolate	GenBank accession number**			Locality
	Genome	orf1ab polyprotein	s protein	
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human /USA/MD-MDH-0749/2021, complete genome. UK B 1.1.7 lineage	MW565853.1		QRG21641.1	USA
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human /USA/MD-MDH-0750/2021, complete genome. UK B 1.1.7 lineage	MW565854.1		QRG21653.1	USA
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human /USA/MD-MDH-0751/2021, complete genome. UK B 1.1.7 lineage	MW565855.1		QRG21665.1	USA
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human /USA/MD-MDH-0814/2021, complete genome. UK B 1.1.7 lineage	MW580558.1		QRI43243.1	USA
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human /USA/MD-MDH-0815/2021, complete genome. UK B 1.1.7 lineage	MW580559.1		QRI43255.1	USA

FIG. 2 (Continued)

Isolate	GenBank accession number**			Locality
	Genome	orf1ab polyprotein	s protein	
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human /USA/MD-MDH-0817/2021, complete genome. UK B 1.1.7 lineage	MW580561.1		QRI43279.1	USA
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/USA/OH-UHTL-2/2020, complete genome. UK B 1.1.7 lineage	MW584988.1		QRJ69803.1	USA
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/USA/-CA-CDC-STM-000002976/2021, complete genome. UK B 1.1.7 lineage	MW586592.1		QRK23526.1	USA
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/USA/-CA-CDC-STM-000002933/2021, complete genome. UK B 1.1.7 lineage	MW586593.1		QRK23538.1	USA
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/hu-man/USA/NC-CDC-STM-000002954/2021, complete genome. UK B 1.1.7 lineage	MW586597.1		QRK23586.1	USA

FIG. 2 (Continued)

Isolate	GenBank accession number**			Locality
	Genome	orf1ab polyprotein	s protein	
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/USA/-FL-CDC-STM-0000030354/2021, complete genome. UK B 1.1.7 lineage	MW586603.1		QRK23658.1	USA
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/USA/-FL-CDC-STM-0000030373/2021, complete genome. UK B 1.1.7 lineage	MW586613.1		QRK23778.1	USA
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/USA/NJ-CDC-STM-0000030010/2021, complete genome. UK B 1.1.7 lineage	MW586623.1		QRK23898.1	USA
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/USA/-FL-CDC-STM-0000036618/2021, complete genome. UK B 1.1.7 lineage	MW586670.1		QRK24462.1	USA
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/USA/-FL-CDC-STM-0000036556/2021, complete genome. UK B 1.1.7 lineage	MW586671.1		QRK24474.1	USA

FIG. 2 (Continued)

Isolate	GenBank accession number**			Locality
	Genome	orf1ab polyprotein	s protein	
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/USA/-FL-CDC-STM-0000003509/2021, complete genome. UK B 1.1.7 lineage	MW586673.1		QRK24498.1	USA
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/USA/-FL-CDC-STM-0000003537/2021, complete genome. UK B 1.1.7 lineage	MW586679.1		QRK24570.1	USA
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/USA/-FL-CDC-STM-0000003592/2021, complete genome. UK B 1.1.7 lineage	MW586680.1		QRK24582.1	USA
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/USA/-FL-CDC-STM-0000003574/2021, complete genome. UK B 1.1.7 lineage	MW586681.1		QRK24594.1	USA
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/USA/-CA-LACPHL-AF00368/2021, complete genome. UK B 1.1.7 lineage	MW587778.1		QRL06527.1	USA

FIG. 2 (Continued)

Isolate	GenBank accession number**			Locality
	Genome	orf1ab polyprotein	s protein	
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/USA/N-MDOH-2021013232/2021, complete genome. [Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)]. Californian B.1.427 lineage	MW493681.1 (SEQ ID NO: 24)		QQV21856.1 (SEQ ID NO: 25)	USA
Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/USA/-CA-CZB-12872/2020, complete genome. [Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)] Californian B.1.429 lineage	MW306426.1 (SEQ ID NO: 26)		QPJ72086.1 (SEQ ID NO:L 27)	USA

* Wu, F., et al. A new coronavirus associated with human respiratory disease in China (2020) Nature 579:265-269.
**All genome sequences are ss-RNA sequences wherein thymine (i.e. t or T) stands for uracil (as it is a RNA) in order to simplify the presentation (no difference made in the sequences between DNA and RNA). Info re ssRNA can be found in the header row of the Genebank entry.

FIG. 2 (Continued)

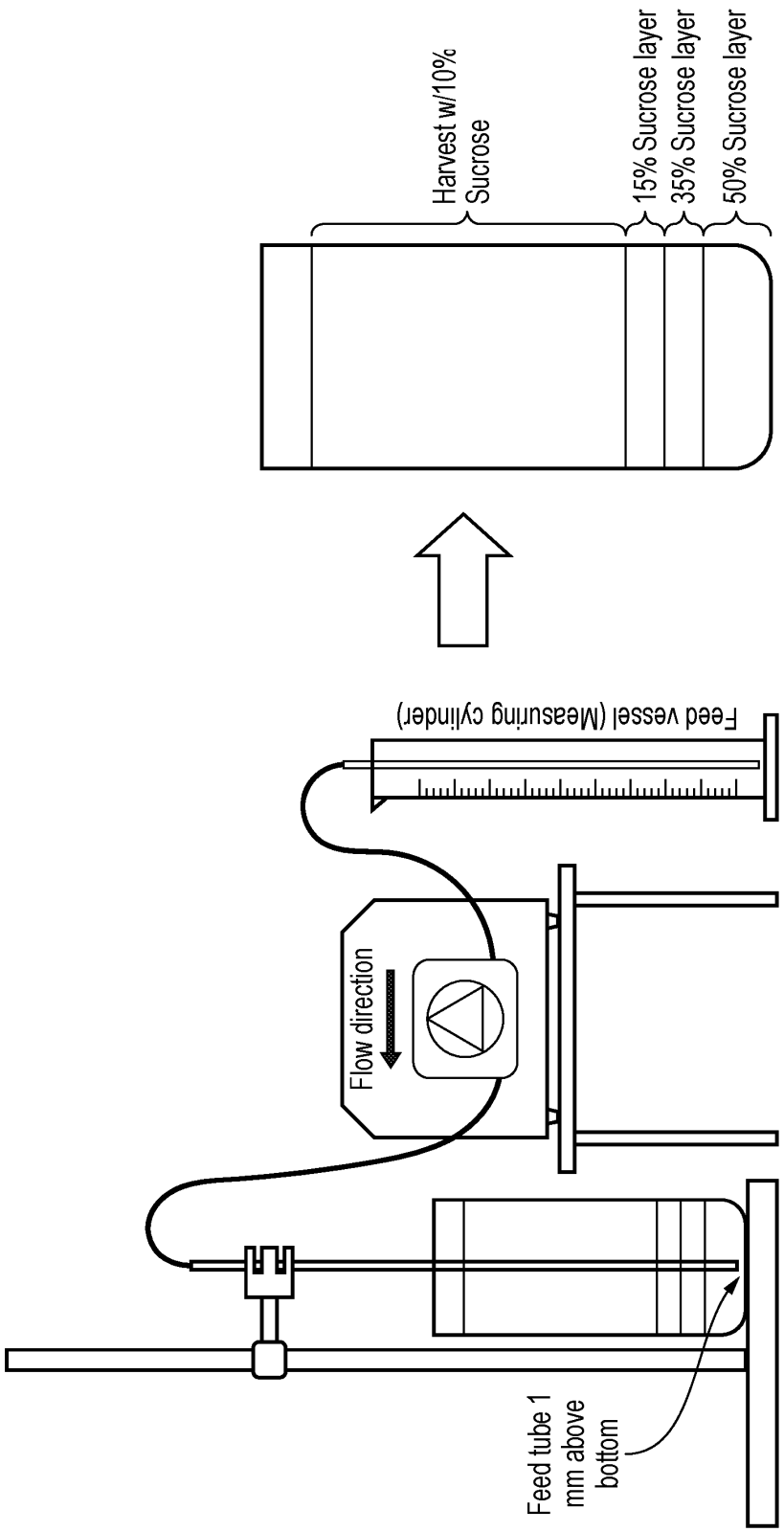

Harvest w/10% Sucrose
15% Sucrose layer
35% Sucrose layer
50% Sucrose layer
Feed vessel (Measuring cylinder)
Flow direction
Feed tube 1 mm above bottom

FIG. 3

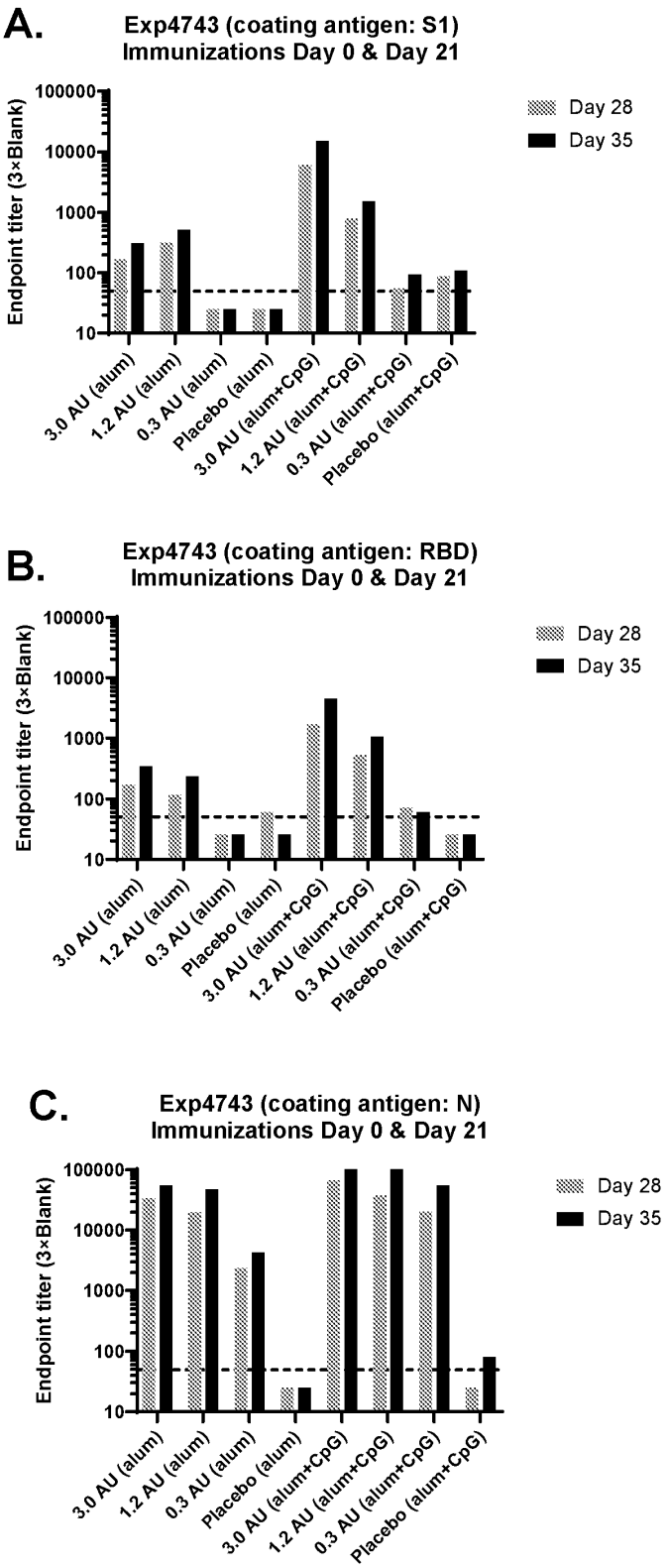

A.
Exp4743 (coating antigen: S1)
Immunizations Day 0 & Day 21
Endpoint titer (3×Blank)
100000
10000
1000
100
10
Day 28
Day 35
3.0 AU (alum)
1.2 AU (alum)
0.3 AU (alum)
Placebo (alum)
3.0 AU (alum+CpG)
1.2 AU (alum+CpG)
0.3 AU (alum+CpG)
Placebo (alum+CpG)
B.
Exp4743 (coating antigen: RBD)
Immunizations Day 0 & Day 21
Endpoint titer (3×Blank)
100000
10000
1000
100
10
Day 28
Day 35
3.0 AU (alum)
1.2 AU (alum)
0.3 AU (alum)
Placebo (alum)
3.0 AU (alum+CpG)
1.2 AU (alum+CpG)
0.3 AU (alum+CpG)
Placebo (alum+CpG)
C.
Exp4743 (coating antigen: N)
Immunizations Day 0 & Day 21
Endpoint titer (3×Blank)
100000
10000
1000
100
10
Day 28
Day 35
3.0 AU (alum)
1.2 AU (alum)
0.3 AU (alum)
Placebo (alum)
3.0 AU (alum+CpG)
1.2 AU (alum+CpG)
0.3 AU (alum+CpG)
Placebo (alum+CpG)

FIG. 4

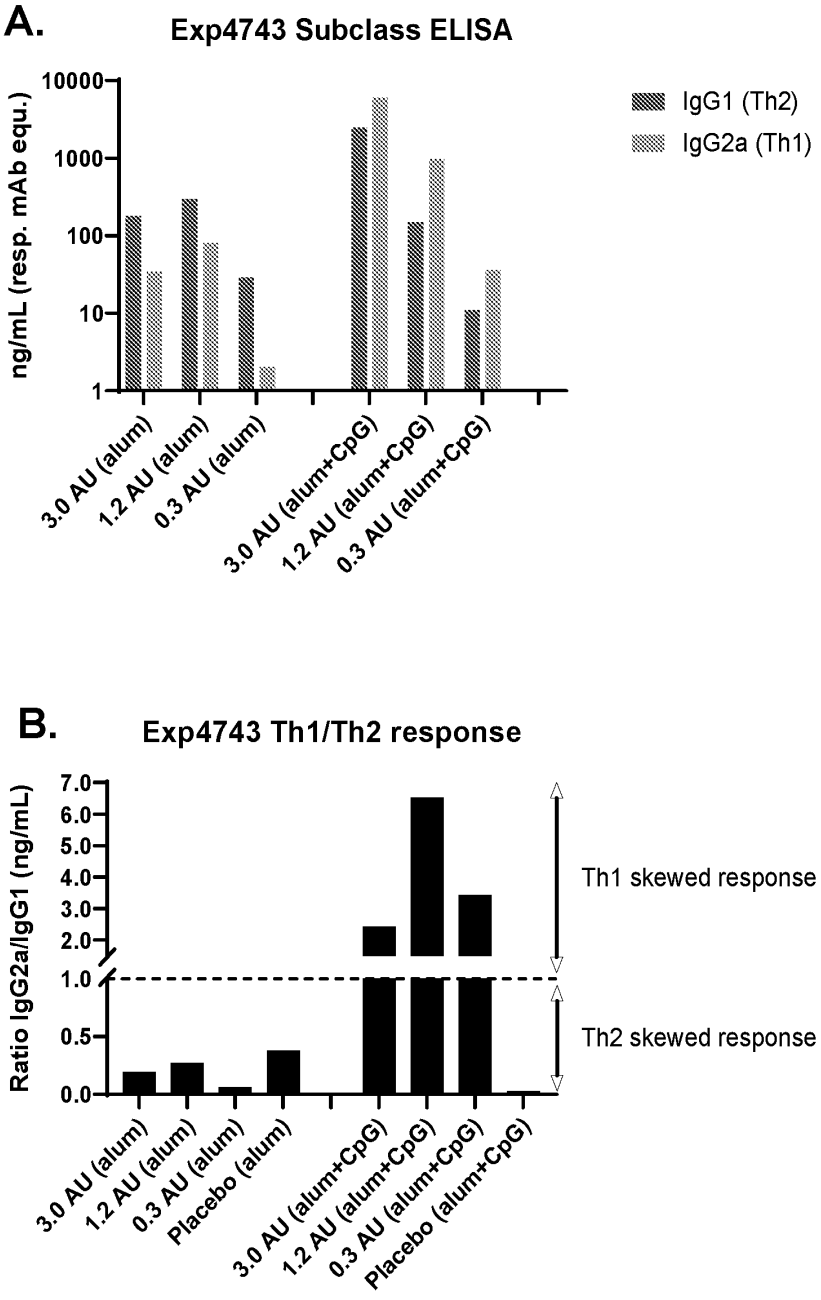

A.
Exp4743 Subclass ELISA
ng/mL (resp. mAb equ.)
10000
1000
100
10
1
IgG1 (Th2)
IgG2a (Th1)
3.0 AU (alum)
1.2 AU (alum)
0.3 AU (alum)
3.0 AU (alum+CpG)
1.2 AU (alum+CpG)
0.3 AU (alum+CpG)
B.
Exp4743 Th1/Th2 response
Ratio IgG2a/IgG1 (ng/mL)
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.5
0.0
Th1 skewed response
Th2 skewed response
3.0 AU (alum)
1.2 AU (alum)
0.3 AU (alum)
Placebo (alum)
3.0 AU (alum+CpG)
1.2 AU (alum+CpG)
0.3 AU (alum+CpG)
Placebo (alum+CpG)

FIG. 5

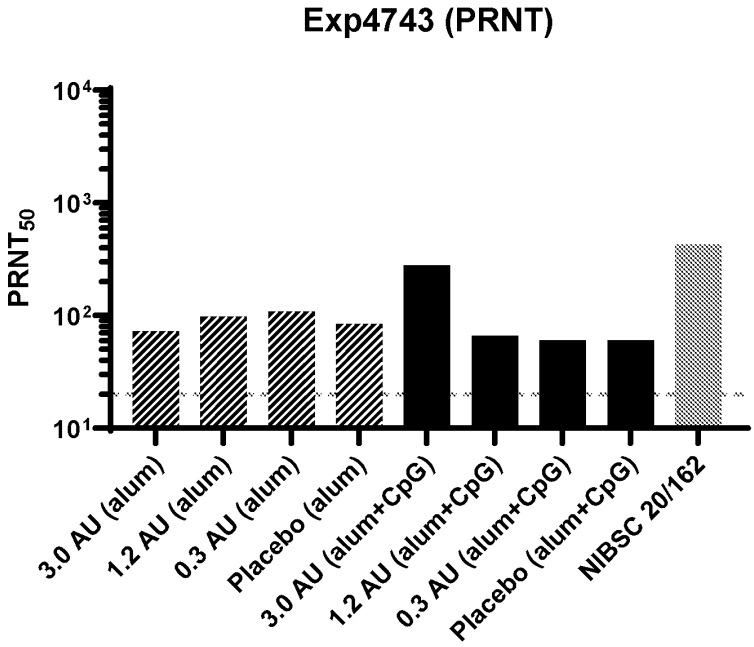

Exp4743 (PRNT)
PRNT50
10^4
10^3
10^2
10^1
3.0 AU (alum)
1.2 AU (alum)
0.3 AU (alum)
Placebo (alum)
3.0 AU (alum+CpG)
1.2 AU (alum+CpG)
0.3 AU (alum+CpG)
Placebo (alum+CpG)
NIBSC 20/162

FIG. 6

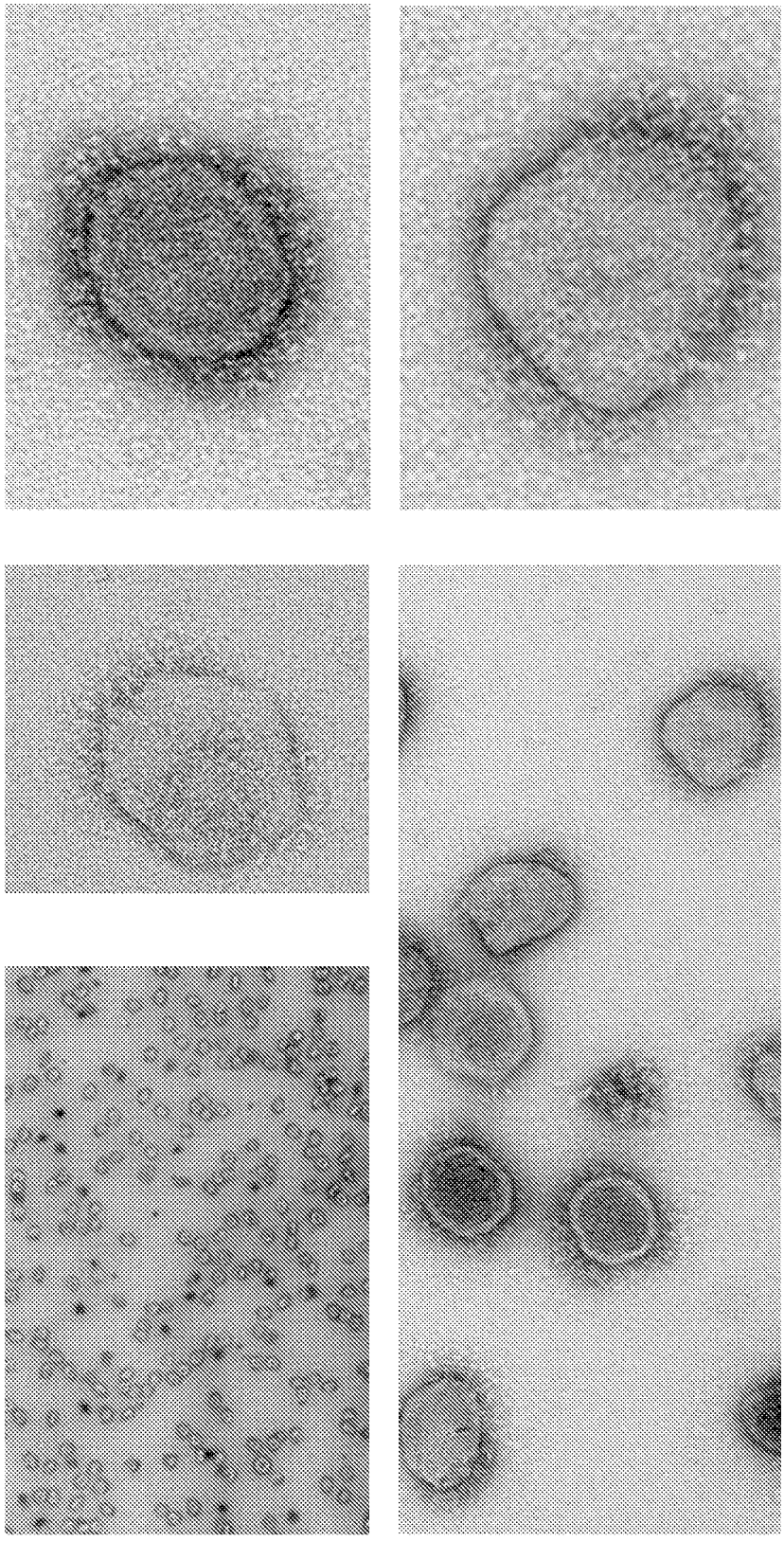


FIG. 7

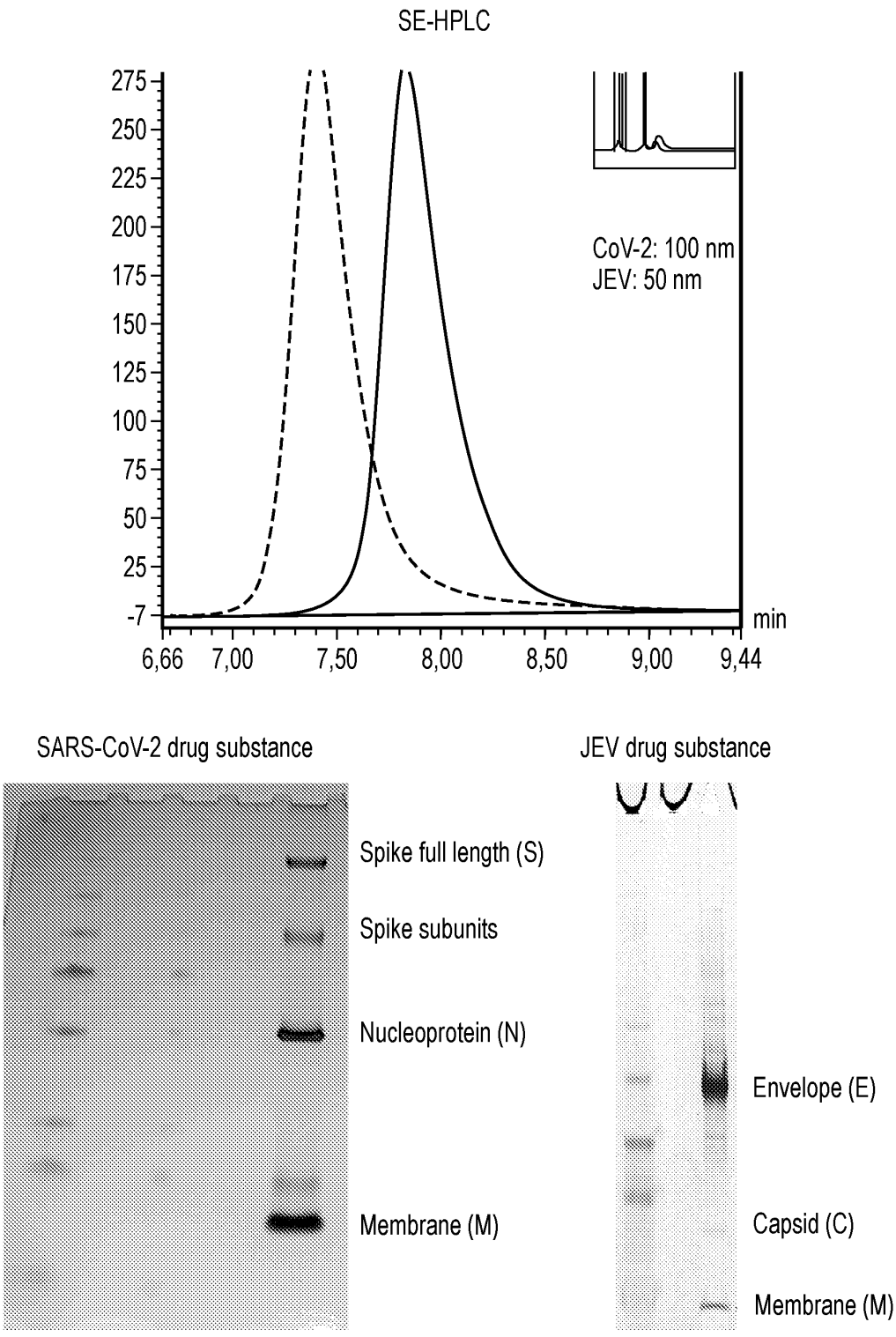

SE-HPLC
275
250
225
200
175
150
125
100
75
50
25
-7
min
6,66
7,00
7,50
8,00
8,50
9,00
9,44
CoV-2: 100 nm
JEV: 50 nm
SARS-CoV-2 drug substance
JEV drug substance
Spike full length (S)
Spike subunits
Nucleoprotein (N)
Membrane (M)
Envelope (E)
Capsid (C)
Membrane (M)

FIG. 8

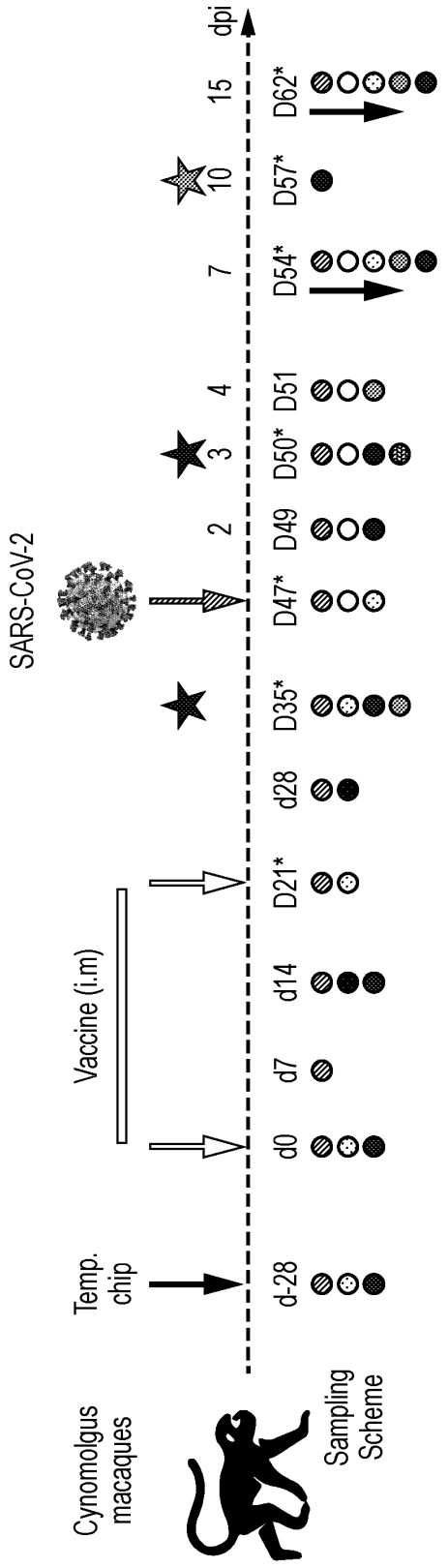

Cynomolgus macaques
Temp. chip
Vaccine (i.m)
SARS-CoV-2
Sampling Scheme
d-28
d0
d7
d14
D21*
d28
D35*
D47*
D49
D50*
D51
D54*
D57*
D62*
2
3
4
7
10
15
dpi

FIG. 9

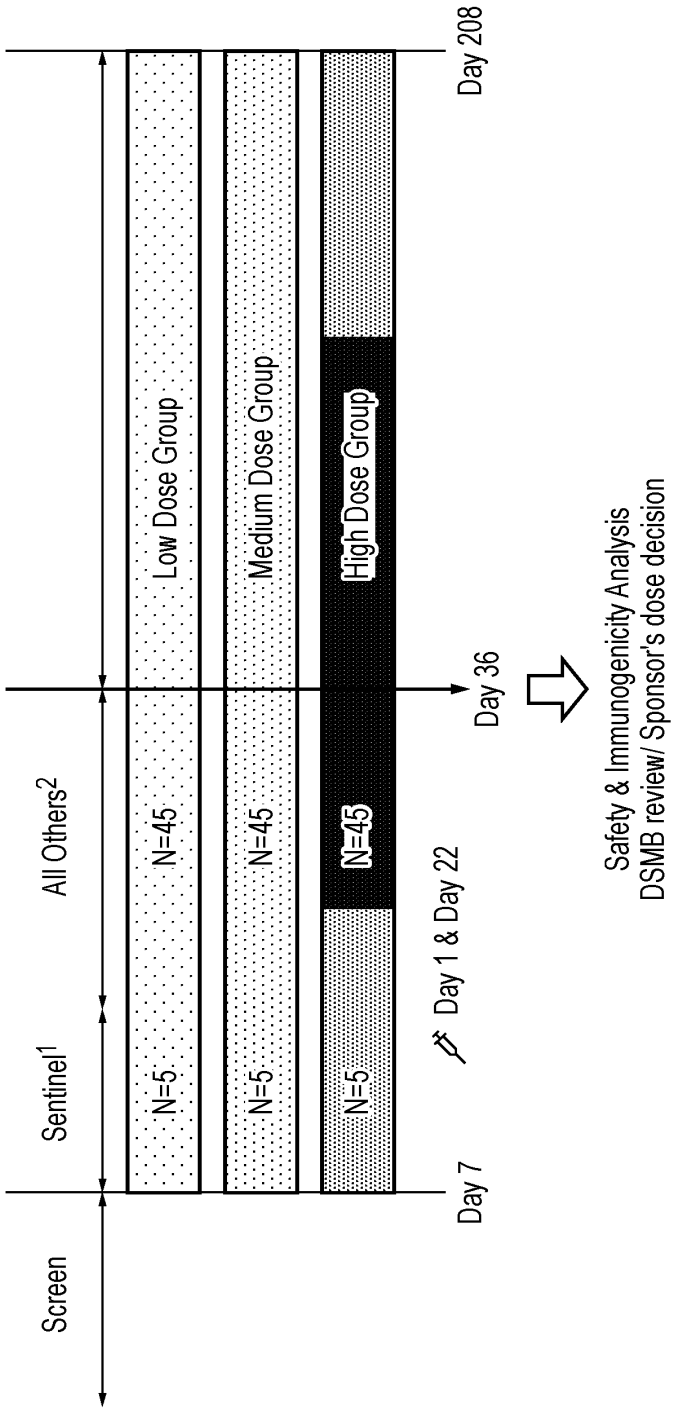

Screen
Sentinel[1]
All Others[2]
N=5
N=45
Low Dose Group
N=5
N=45
Medium Dose Group
N=5
N=45
High Dose Group
Day 7
Day 1 & Day 22
Day 36
Day 208
Safety & Immunogenicity Analysis
DSMB review/ Sponsor's dose decision
[1] Open-label, dose-escalation design
[2] Randomized, blinded design

FIG. 10

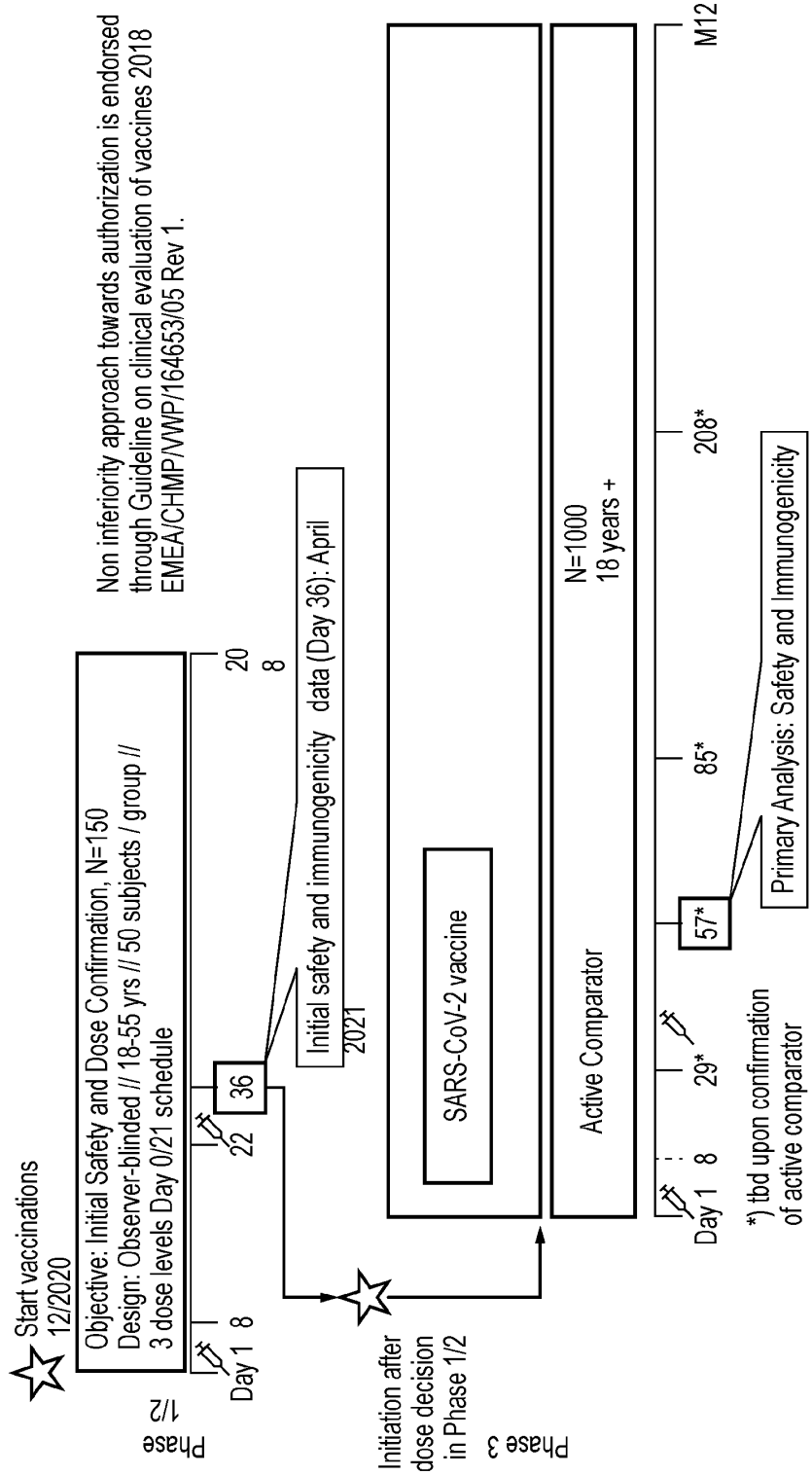

Start vaccinations
12/2020
Objective: Initial Safety and Dose Confirmation, N=150
Design: Observer-blinded // 18-55 yrs // 50 subjects / group //
3 dose levels Day 0/21 schedule
Phase 1/2
Day 1 8
22
36
20
8
Initial safety and immunogenicity data (Day 36): April 2021
Initiation after dose decision in Phase 1/2
Phase 3
SARS-CoV-2 vaccine
Active Comparator
N=1000
18 years +
Day 1 8
29*
57*
85*
208*
M12
Primary Analysis: Safety and Immunogenicity
*) tbd upon confirmation of active comparator
Non inferiority approach towards authorization is endorsed through Guideline on clinical evaluation of vaccines 2018 EMEA/CHMP/VWP/164653/05 Rev 1.

FIG. 11

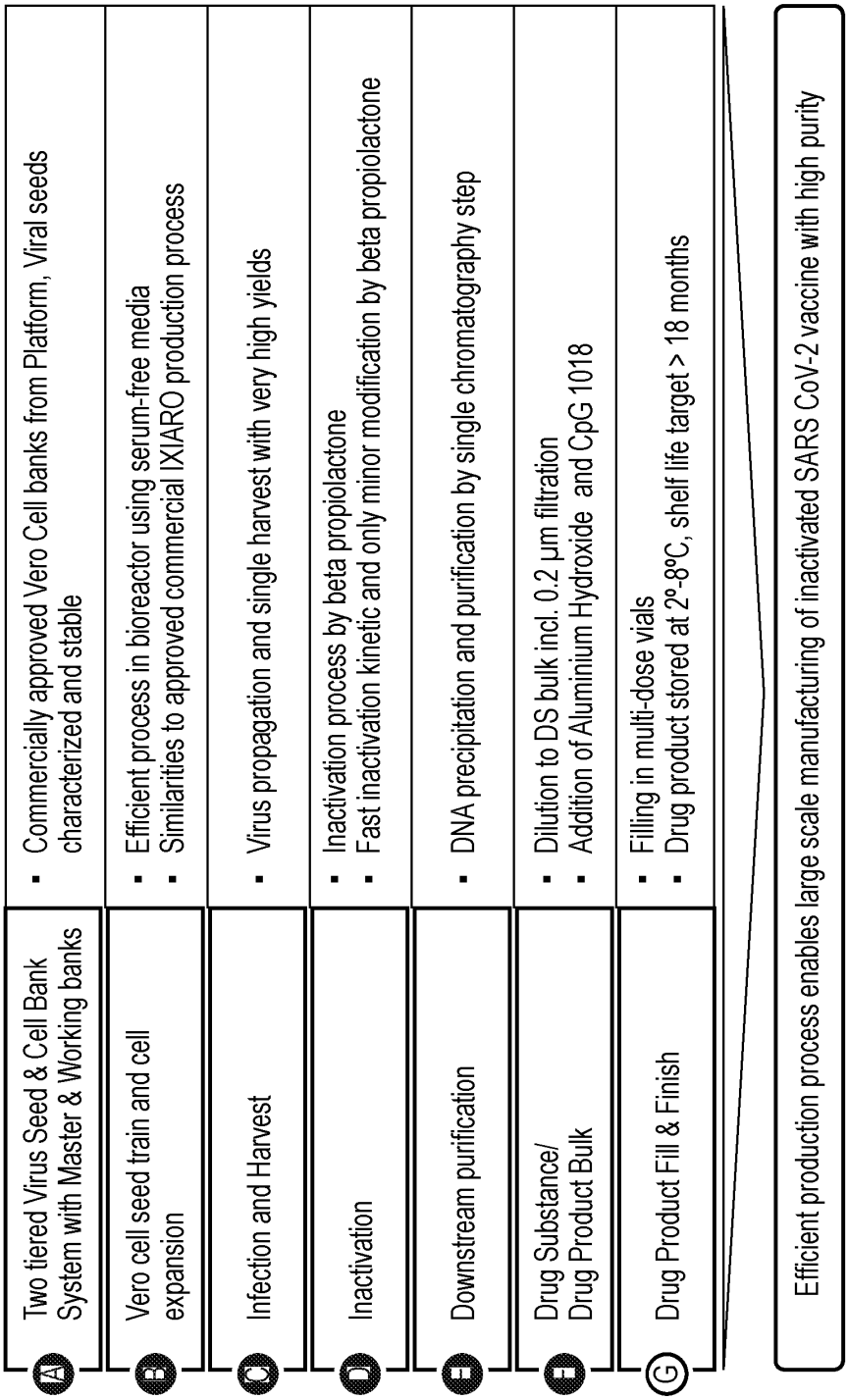

A
Two tiered Virus Seed & Cell Bank System with Master & Working banks
Commercially approved Vero Cell banks from Platform, Viral seeds characterized and stable
B
Vero cell seed train and cell expansion
Efficient process in bioreactor using serum-free media
Similarities to approved commercial IXIARO production process
C
Infection and Harvest
Virus propagation and single harvest with very high yields
D
Inactivation
Inactivation process by beta propiolactone
Fast inactivation kinetic and only minor modification by beta propiolactone
E
Downstream purification
DNA precipitation and purification by single chromatography step
F
Drug Substance/ Drug Product Bulk
Dilution to DS bulk incl. 0.2 µm filtration
Addition of Aluminium Hydroxide and CpG 1018
G
Drug Product Fill & Finish
Filling in multi-dose vials
Drug product stored at 2°-8°C, shelf life target > 18 months
Efficient production process enables large scale manufacturing of inactivated SARS CoV-2 vaccine with high purity

FIG. 12

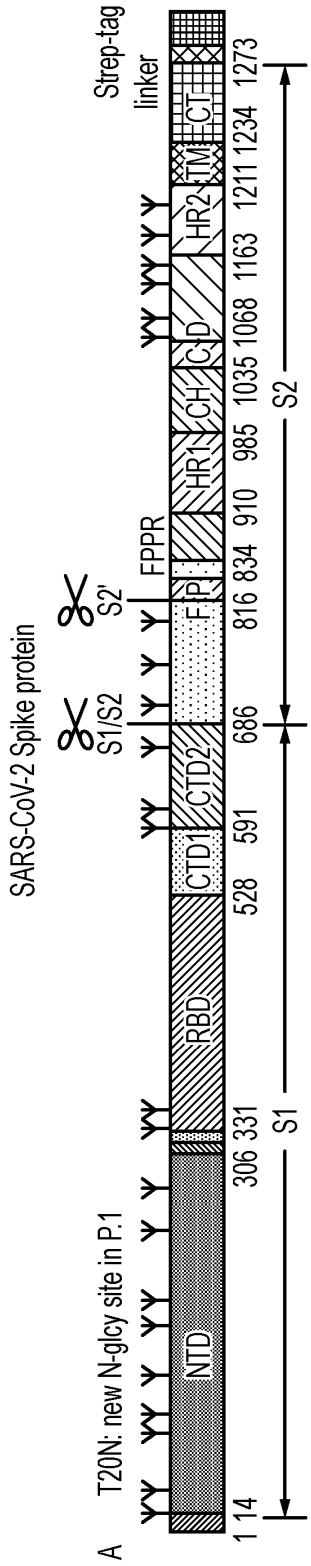

SARS-CoV-2 Spike protein
A
T20N: new N-glcy site in P.1
NTD
RBD
CTD1
CTD2
S1/S2
S2'
FPPR
FP
HR1
CH
CD
HR2
TM
CT
Strep-tag
linker
1
14
306
331
528
591
686
816
834
910
985
1035
1068
1163
1211
1234
1273
S1
S2

FIG. 13

				Total	Cluster						
				33	13	4	10	2	1	3	
B.1.1.7	B.1.351	P.1	Domain	Weight	A	B	C	D	E	N	Ref aa
	x	x	S-NTD	0	0	0	0	0	0	0	L18
		x	S-NTD	0	0	0	0	0	0	0	T20
		x	S-NTD	0	0	0	0	0	0	0	P26
x			S-NTD	0	0	0	0	0	0	0	H69
x			S-NTD	0	0	0	0	0	0	0	V70
	x		S-NTD	0	0	0	0	0	0	0	D80
			S-NTD	1	0	0	0	0	0	1	A123
		x	S-NTD	0	0	0	0	0	0	0	D138
			S-NTD	1	0	0	0	0	0	1	F140
			S-NTD	1	0	0	0	0	0	1	G142
x			S-NTD	3	0	0	0	0	0	3	Y144
x			S-NTD	1	0	0	0	0	0	1	Y145
			S-NTD	1	0	0	0	0	0	1	H146
			S-NTD	1	0	0	0	0	0	1	K147
			S-NTD	1	0	0	0	0	0	1	K150
			S-NTD	1	0	0	0	0	0	1	W152
			S-NTD	1	0	0	0	0	0	1	F157
			S-NTD	1	0	0	0	0	0	1	R158
			S-NTD	1	0	0	0	0	0	1	N164
		x	S-NTD	0	0	0	0	0	0	0	R190
	x	x	S-NTD	0	0	0	0	0	0	0	D215
	x		S-NTD	0	0	0	0	0	0	0	L242
	x		S-NTD	0	0	0	0	0	0	0	A243
	x		S-NTD	0	0	0	0	0	0	0	L244
			S-NTD	1	0	0	0	0	0	1	H245
	x		S-NTD	1	0	0	0	0	0	1	R246
			S-NTD	1	0	0	0	0	0	1	S247
			S-NTD	1	0	0	0	0	0	1	Y248
			S-NTD	1	0	0	0	0	0	1	L249
			S-RBD	1	0	0	0	0	1	0	N334
			S-RBD	1	0	0	0	0	1	0	L335
			S-RBD	1	0	0	0	0	1	0	P337

Listed are residues which are within the footprint of neutralizing mAbs and/or which are lineage defining mutation positions for B.1.1.7, B.1.351 or P.1 (marked 'x')

FIG. 13 (continued)

				Total	Cluster						
				33	13	4	10	2	1	3	
B.1.1.7	B.1.351	P.1	Domain	Weight	A	B	C	D	E	N	Ref aa
			S-RBD	1	0	0	0	0	1	0	G339
			S-RBD	1	0	0	0	0	1	0	E340
			S-RBD	1	0	0	0	0	1	0	N343
			S-RBD	0	0	0	0	0	0	0	A344
			S-RBD	3	0	0	1	1	1	0	T345
			S-RBD	6	0	0	4	1	1	0	R346
			S-RBD	1	0	0	1	0	0	0	F347
			S-RBD	0	0	0	0	0	0	0	A348
			S-RBD	1	0	0	1	0	0	0	S349
			S-RBD	1	0	0	1	0	0	0	Y351
			S-RBD	0	0	0	0	0	0	0	A352
			S-RBD	1	0	0	0	0	1	0	K356
			S-RBD	1	0	0	0	0	1	0	R357
			S-RBD	1	0	0	0	0	1	0	S359
			S-RBD	1	0	0	0	0	1	0	N360
			S-RBD	1	0	0	0	0	1	0	C361
			S-RBD	4	0	4	0	0	0	0	Y369
			S-RBD	2	0	2	0	0	0	0	N370
			S-RBD	1	0	1	0	0	0	0	S371
			S-RBD	2	0	2	0	0	0	0	A372
			S-RBD	1	0	1	0	0	0	0	S373
			S-RBD	2	0	2	0	0	0	0	F374
			S-RBD	3	0	3	0	0	0	0	S375
			S-RBD	2	0	2	0	0	0	0	T376
			S-RBD	4	0	4	0	0	0	0	F377
			S-RBD	4	0	4	0	0	0	0	K378
			S-RBD	4	0	4	0	0	0	0	C379
			S-RBD	3	0	3	0	0	0	0	Y380
			S-RBD	2	0	2	0	0	0	0	G381
			S-RBD	2	0	2	0	0	0	0	V382
			S-RBD	4	0	4	0	0	0	0	S383

Listed are residues which are within the footprint of neutralizing mAbs and/or which are lineage defining mutation positions for B.1.1.7, B.1.351 or P.1 (marked 'x')

FIG. 13 (continued)

				Total	Cluster						
				33	13	4	10	2	1	3	
B.1.1.7	B.1.351	P.1	Domain	Weight	A	B	C	D	E	N	Ref aa
			S-RBD	4	0	4	0	0	0	0	P384
			S-RBD	4	0	4	0	0	0	0	T385
			S-RBD	2	0	2	0	0	0	0	K386
			S-RBD	1	0	1	0	0	0	0	N388
			S-RBD	1	0	1	0	0	0	0	L390
			S-RBD	2	0	2	0	0	0	0	F392
			S-RBD	10	10	0	0	0	0	0	R403
			S-RBD	7	6	1	0	0	0	0	D405
			S-RBD	1	1	0	0	0	0	0	E406
			S-RBD	1	0	1	0	0	0	0	V407
			S-RBD	5	3	2	0	0	0	0	R408
			S-RBD	2	2	0	0	0	0	0	Q409
			S-RBD	1	0	1	0	0	0	0	A411
			S-RBD	3	0	3	0	0	0	0	P412
			S-RBD	2	0	2	0	0	0	0	G413
			S-RBD	3	0	3	0	0	0	0	Q414
			S-RBD	11	11	0	0	0	0	0	T415
			S-RBD	11	11	0	0	0	0	0	G416
	x	x	S-RBD	11	10	0	1	0	0	0	K417
			S-RBD	10	10	0	0	0	0	0	D420
			S-RBD	11	11	0	0	0	0	0	Y421
			S-RBD	2	0	2	0	0	0	0	D427
			S-RBD	2	0	2	0	0	0	0	D428
			S-RBD	2	0	2	0	0	0	0	F429
			S-RBD	1	0	1	0	0	0	0	T430
			S-RBD	1	0	1	0	0	0	0	N437
			S-RBD	1	0	0	1	1	0	0	S438
			S-RBD	1	0	0	1	1	0	0	N439
			S-RBD	2	0	0	1	1	0	0	N440
			S-RBD	4	0	0	1	1	1	0	L441
			S-RBD	1	0	0	0	0	0	0	D442

Listed are residues which are within the footprint of neutralizing mAbs and/or which are lineage defining mutation positions for B.1.1.7, B.1.351 or P.1 (marked 'x')

FIG. 13 (continued)

				Total	Cluster						
				33	13	4	10	2	1	3	
B.1.1.7	B.1.351	P.1	Domain	Weight	A	B	C	D	E	N	Ref aa
			S-RBD	4	0	0	4	0	0	0	K444
			S-RBD	2	1	0	1	0	0	0	V445
			S-RBD	9	2	0	7	0	0	0	G446
			S-RBD	2	0	0	2	0	0	0	G447
			S-RBD	4	0	0	4	0	0	0	N448
			S-RBD	11	2	0	8	1	0	0	Y449
			S-RBD	4	0	0	4	0	0	0	N450
			S-RBD	1	0	0	1	0	0	0	Y451
			S-RBD	4	0	0	4	0	0	0	L452
			S-RBD	12	10	0	1	1	0	0	Y453
			S-RBD	15	12	0	2	1	0	0	L455
			S-RBD	15	12	0	2	1	0	0	F456
			S-RBD	11	11	0	0	0	0	0	R457
			S-RBD	11	11	0	0	0	0	0	K458
			S-RBD	4	4	0	0	0	0	0	S459
			S-RBD	11	11	0	0	0	0	0	N460
			S-RBD	0	0	0	0	0	0	0	I468
			S-RBD	1	0	0	1	0	0	0	T470
			S-RBD	0	0	0	0	0	0	0	I472
			S-RBD	12	11	0	1	0	0	0	Y473
			S-RBD	7	7	0	0	0	0	0	Q474
			S-RBD	14	12	0	2	0	0	0	A475
			S-RBD	13	12	0	1	0	0	0	G476
			S-RBD	12	11	0	1	0	0	0	S477
			S-RBD	2	2	0	0	0	0	0	T478
			S-RBD	2	0	0	2	0	0	0	N481
			S-RBD	2	0	0	2	0	0	0	G482
			S-RBD	4	0	0	4	0	0	0	V483
	x	x	S-RBD	9	0	0	8	1	0	0	E484
			S-RBD	9	1	0	7	1	0	0	G485
			S-RBD	18	12	0	5	1	0	0	F486

Listed are residues which are within the footprint of neutralizing mAbs and/or which are lineage defining mutation positions for B.1.1.7, B.1.351 or P.1 (marked 'x')

FIG. 13 (continued)

				Total	Cluster						
				33	13	4	10	2	1	3	
B.1.1.7	B.1.351	P.1	Domain	Weight	A	B	C	D	E	N	Ref aa
			S-RBD	16	13	0	3	0	0	0	N487
			S-RBD	2	0	0	2	0	0	0	C488
			S-RBD	17	12	0	4	1	0	0	Y489
			S-RBD	8	1	0	62	1	0	0	F490
			S-RBD	3	0	0	2	1	0	0	L492
			S-RBD	15	10	0	4	1	0	0	Q493
			S-RBD	10	4	0	5	1	0	0	S494
			S-RBD	9	9	0	0	0	0	0	Y495
			S-RBD	7	6	0	1	0	0	0	G496
			S-RBD	10	7	0	31	0	0	0	Q498
			S-RBD	3	1	0	1	1	0	0	P499
			S-RBD	9	8	0	1		0	0	T500
x	x	x	S-RBD	13	12	0	1	0	0	0	N501
			S-RBD	10	10	0	0	0	0	0	G502
			S-RBD	3	2	1	0	0	0	0	V503
			S-RBD	14	13	0	1	0	0	0	Y505
			S-RBD	1	0	0	1	0	0	0	R509
			S-RBD	0	0	0	0	0	0	0	F515
			S-RBD	0	0	0	0	0	0	0	E516
			S-RBD	2	0	2	0	0	0	0	L517
x			S-CDT1	0	0	0	0	0	0	0	A570
x	x	x	S-CDT2	0	0	0	0	0	0	0	D614
		x	S-CDT2	0	0	0	0	0	0	0	H655
x			S-nearCLY	0	0	0	0	0	0	0	P681
	x		S-S2	0	0	0	0	0	0	0	A701
x			S-S2	0	0	0	0	0	0	0	T716
x			S-HR1	0	0	0	0	0	0	0	S982
		x	S-CH	0	0	0	0	0	0	0	T1027
x			S-CD	0	0	0	0	0	0	0	D1118
		x	S-HR2	0	0	0	0	0	0	0	V1176

Listed are residues which are within the footprint of neutralizing mAbs and/or which are lineage defining mutation positions for B.1.1.7, B.1.351 or P.1 (marked 'x')

FIG. 13 (continued)

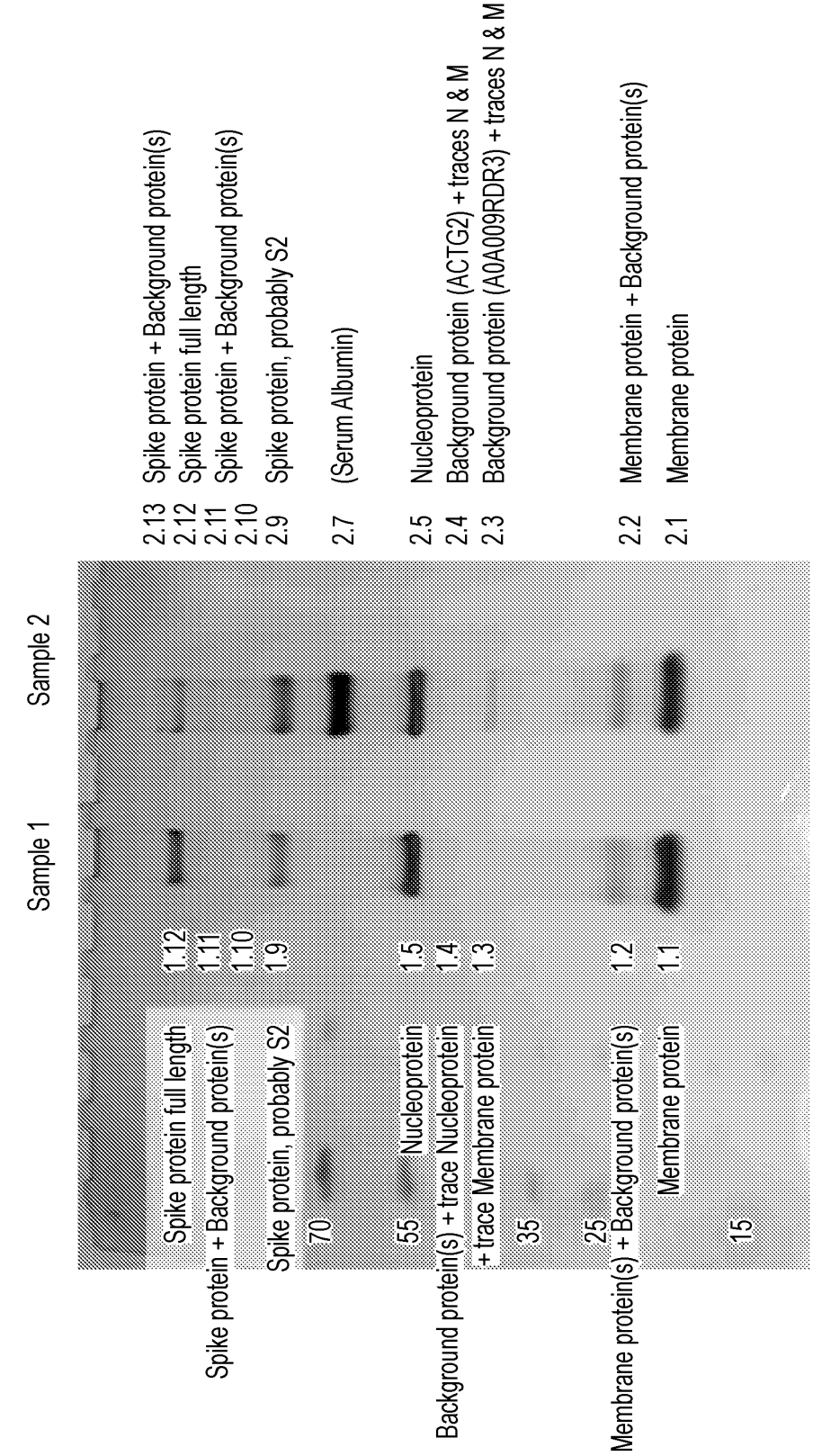

Sample 1
Sample 2
Spike protein full length
Spike protein + Background protein(s)
Spike protein, probably S2
Nucleoprotein
Background protein(s) + trace Nucleoprotein + trace Membrane protein
Membrane protein(s) + Background protein(s)
Membrane protein
70
55
35
25
15
1.12
1.11
1.10
1.9
1.5
1.4
1.3
1.2
1.1
2.13 Spike protein + Background protein(s)
2.12 Spike protein full length
2.11 Spike protein + Background protein(s)
2.10
2.9 Spike protein, probably S2
2.7 (Serum Albumin)
2.5 Nucleoprotein
2.4 Background protein (ACTG2) + traces N & M
2.3 Background protein (A0A009RDR3) + traces N & M
2.2 Membrane protein + Background protein(s)
2.1 Membrane protein

FIG. 14

SUBSTITUTE SHEET (RULE 26)

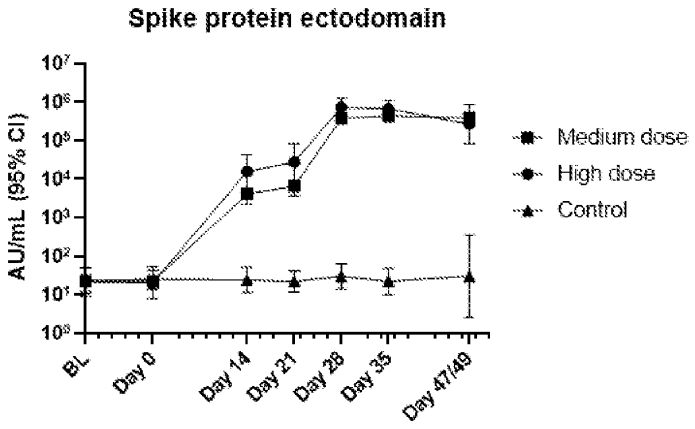
UK	UK_MIG457 Human nCoV19 isolate/England/MIG457/2020 (lineage B.1.1.7), EVAg Ref-SKU: 004V-04032
SA	Human nCoV19 isolate/England ex-SA/2021 (lineage B.1.351), EVAg Ref-SKU: 004V-04071, (SA_P2)

no change vs Wuhan-1
changed vs Wuhan-1

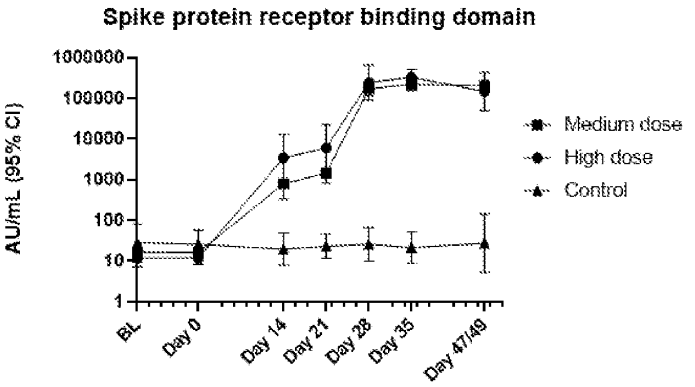
	Nucleotide				Amino acids			
Gene	nt Position	CHN Wuhan	UK MIG457	SA SA P2	aa Position	CHN Wuhan	UK B.1.1.7 MIG457	SA B.1.315 SA P2
S (21563..25384	21614-21616	CTT	CTT	CTT	18	Leu	Leu	Leu
	21765-21770	aTACATGtc	deleted (Ile restored)		69-70del	His-Val	(deleted)	His-Val
	21801	A	A	C	80	Asp	Asp	Ala
	21991 or 21994	TTA	deleted	TTA	144 or 145	Tyr	(deleted)	Tyr
	22206	A	A	G	215	Asp	Asp	Gly
	22282-22291	aCTTTACTTGct	(same)	NNNNNN	240,241-243	Thr-Leu-Leu-Ala	Thr-Leu-Leu-Ala	Thr, (Leu-Leu-Ala)del
	22298-22300	AGA	AGA	AGA	246	Arg	Arg	Arg
	22661	G	G	G	367	Val	Val	Val
	22813	G	G	T	417	Lys	Lys	Asn
	23012	G	G	A	484	Glu	Glu	Lys
	23063	A	T	T	501	Asn	Tyr	Tyr
	23271	C	A	C	570	Ala	Asp	Ala
	23403	A	G	G	614	Asp	Gly	Gly
	23604	C	A	C	681	Pro	His	Pro
	23664	C	C	T	701	Ala	Ala	Val
	23687	A	A	A	709	Asn	Asn	Asn
	23709	C	T	C	716	Thr	Ile	Thr
	24506	T	G	T	982	Ser	Ala	Ser
	24621	C	C	C	1020	Ala	Ala	Ala
	24914	G	C		1118	Ala	His	Ala

FIG. 15

A


Spike protein ectodomain
AU/mL (95% CI)
Medium dose
High dose
Control
BL
Day 0
Day 14
Day 21
Day 28
Day 35
Day 47/49

B


Spike protein receptor binding domain
AU/mL (95% CI)
Medium dose
High dose
Control
BL
Day 0
Day 14
Day 21
Day 28
Day 35
Day 47/49

C

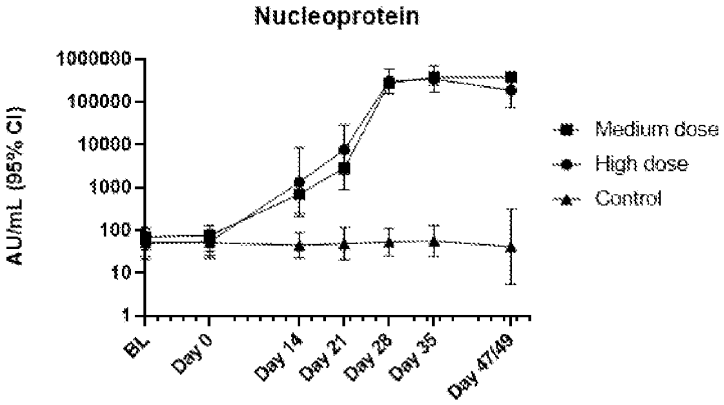

Nucleoprotein
AU/mL (95% CI)
Medium dose
High dose
Control
BL
Day 0
Day 14
Day 21
Day 28
Day 35
Day 47/49

FIG. 16

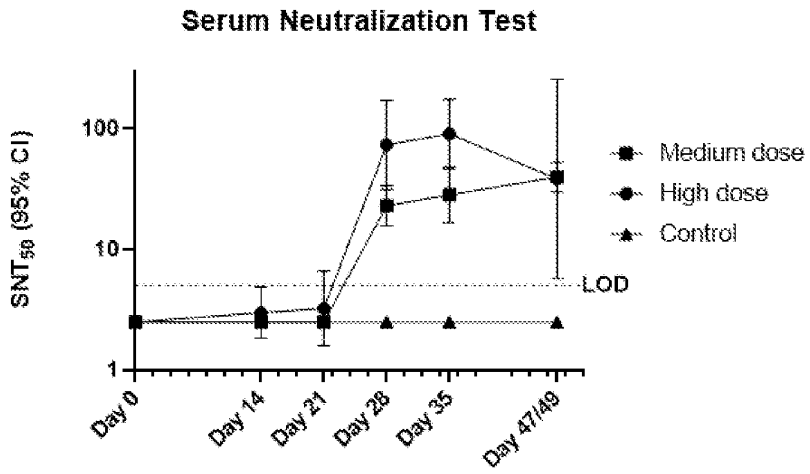

Serum Neutralization Test
SNT50 (95% CI)
100
10
1
LOD
Day 0
Day 14
Day 21
Day 28
Day 35
Day 47/49
Medium dose
High dose
Control

FIG. 17

A

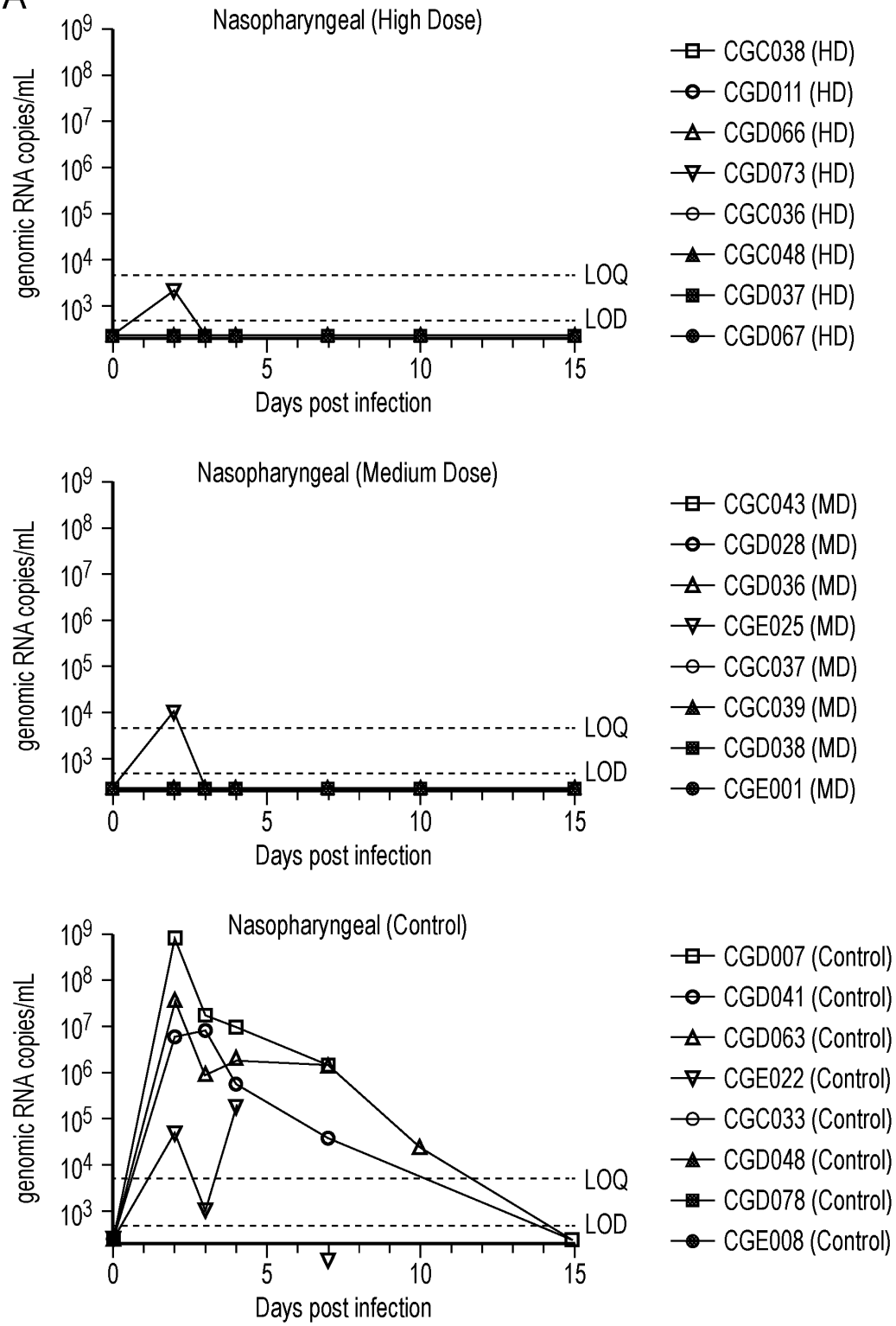

Nasopharyngeal (High Dose)
genomic RNA copies/mL
10^9
10^8
10^7
10^6
10^5
10^4
10^3
LOQ
LOD
0
5
10
15
Days post infection
CGC038 (HD)
CGD011 (HD)
CGD066 (HD)
CGD073 (HD)
CGC036 (HD)
CGC048 (HD)
CGD037 (HD)
CGD067 (HD)
Nasopharyngeal (Medium Dose)
genomic RNA copies/mL
LOQ
LOD
Days post infection
CGC043 (MD)
CGD028 (MD)
CGD036 (MD)
CGE025 (MD)
CGC037 (MD)
CGC039 (MD)
CGD038 (MD)
CGE001 (MD)
Nasopharyngeal (Control)
genomic RNA copies/mL
LOQ
LOD
Days post infection
CGD007 (Control)
CGD041 (Control)
CGD063 (Control)
CGE022 (Control)
CGC033 (Control)
CGD048 (Control)
CGD078 (Control)
CGE008 (Control)

FIG. 18

B

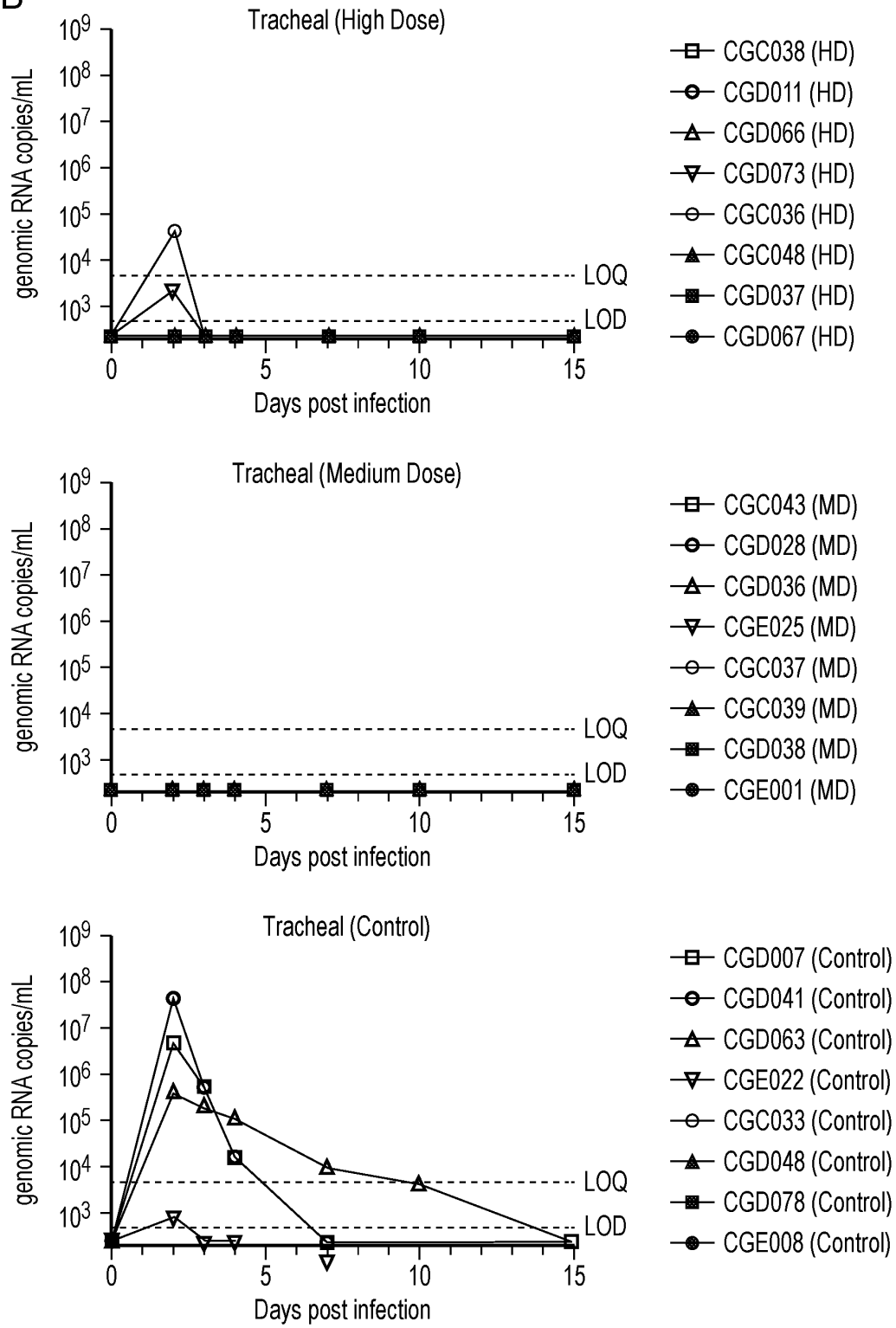


FIG. 18 (Continued)

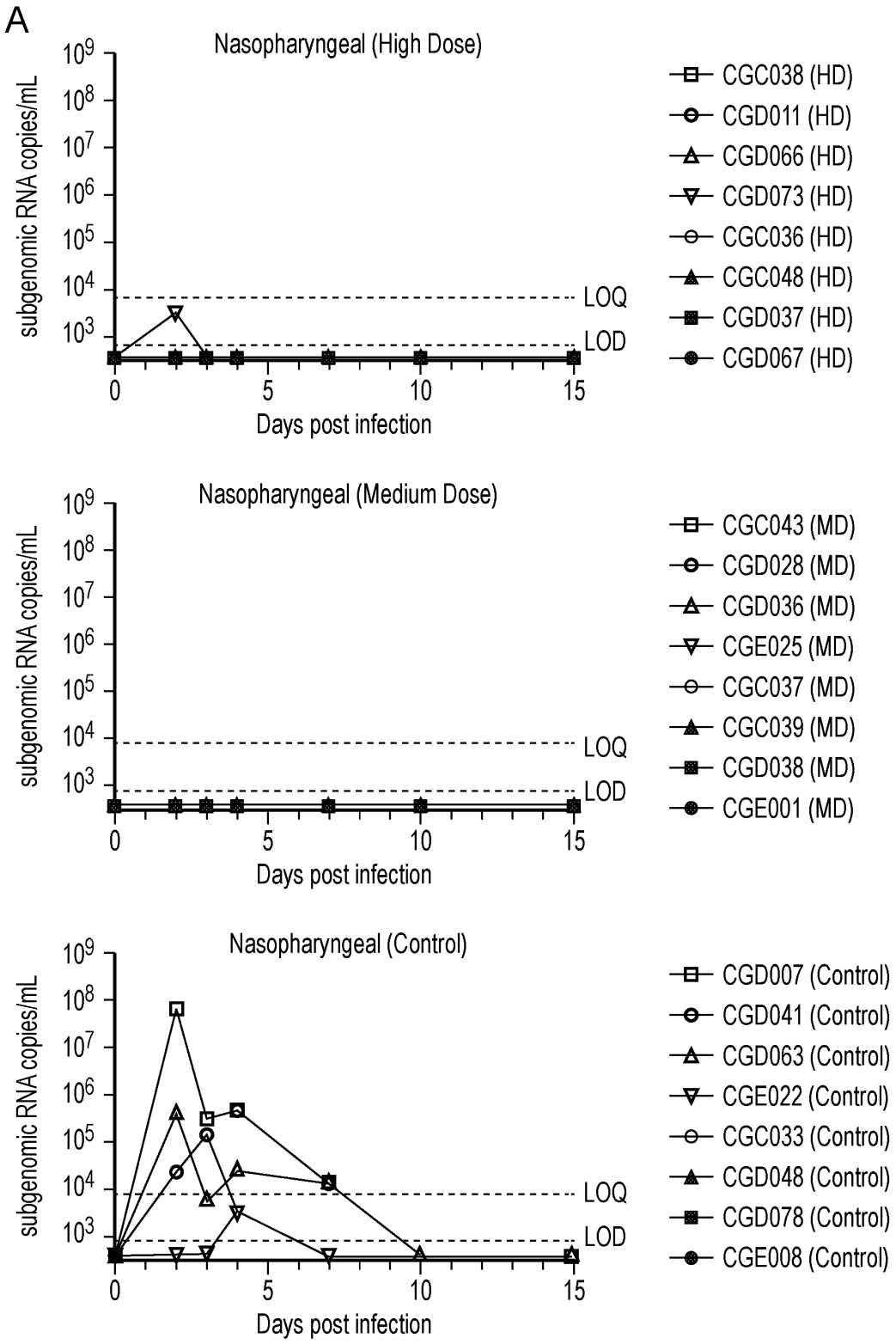

A
Nasopharyngeal (High Dose)
subgenomic RNA copies/mL
10^9
10^8
10^7
10^6
10^5
10^4
10^3
LOQ
LOD
0
5
10
15
Days post infection
CGC038 (HD)
CGD011 (HD)
CGD066 (HD)
CGD073 (HD)
CGC036 (HD)
CGC048 (HD)
CGD037 (HD)
CGD067 (HD)
Nasopharyngeal (Medium Dose)
subgenomic RNA copies/mL
LOQ
LOD
Days post infection
CGC043 (MD)
CGD028 (MD)
CGD036 (MD)
CGE025 (MD)
CGC037 (MD)
CGC039 (MD)
CGD038 (MD)
CGE001 (MD)
Nasopharyngeal (Control)
subgenomic RNA copies/mL
LOQ
LOD
Days post infection
CGD007 (Control)
CGD041 (Control)
CGD063 (Control)
CGE022 (Control)
CGC033 (Control)
CGD048 (Control)
CGD078 (Control)
CGE008 (Control)

FIG. 19

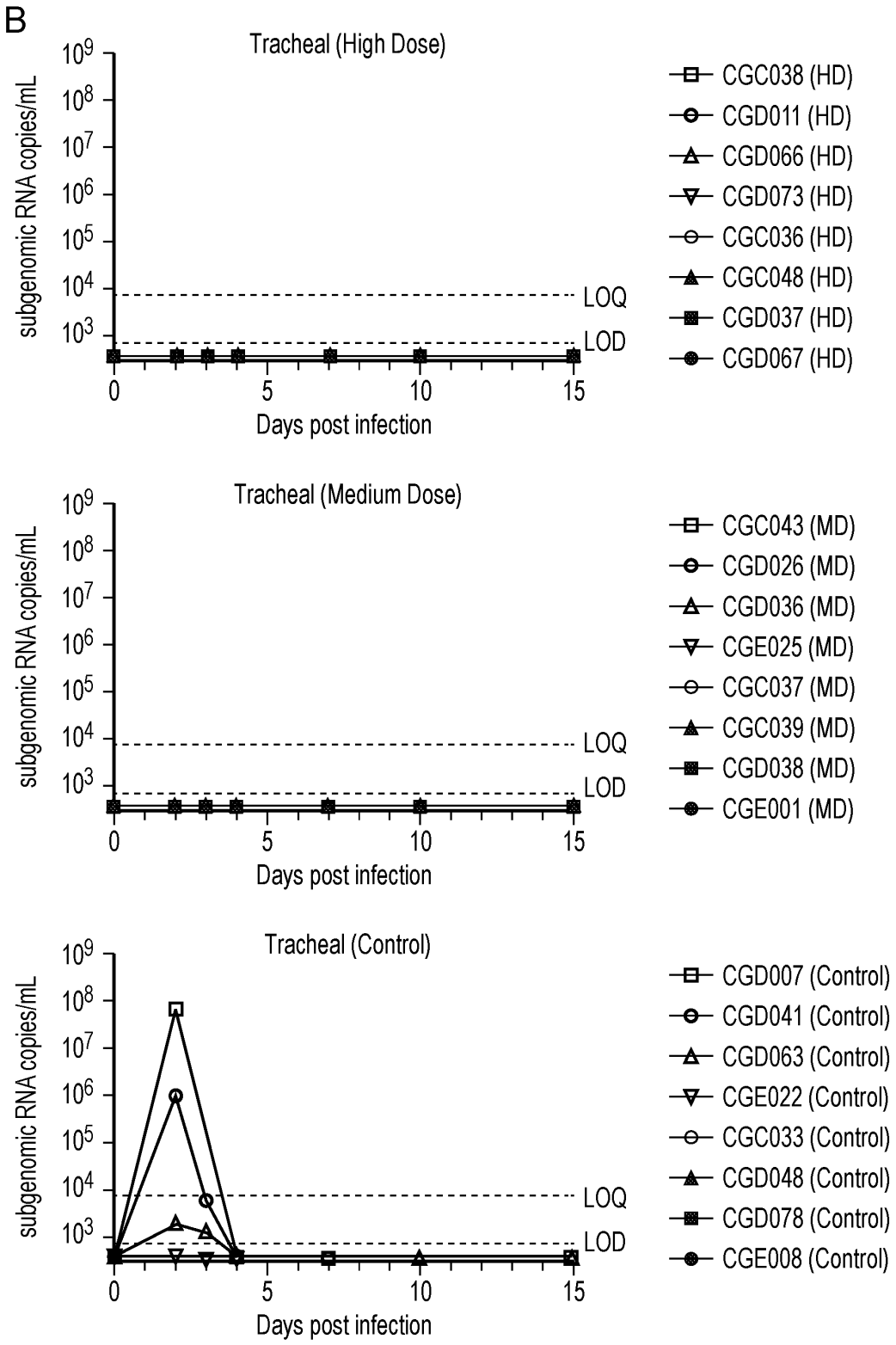


FIG. 19 (Continued)

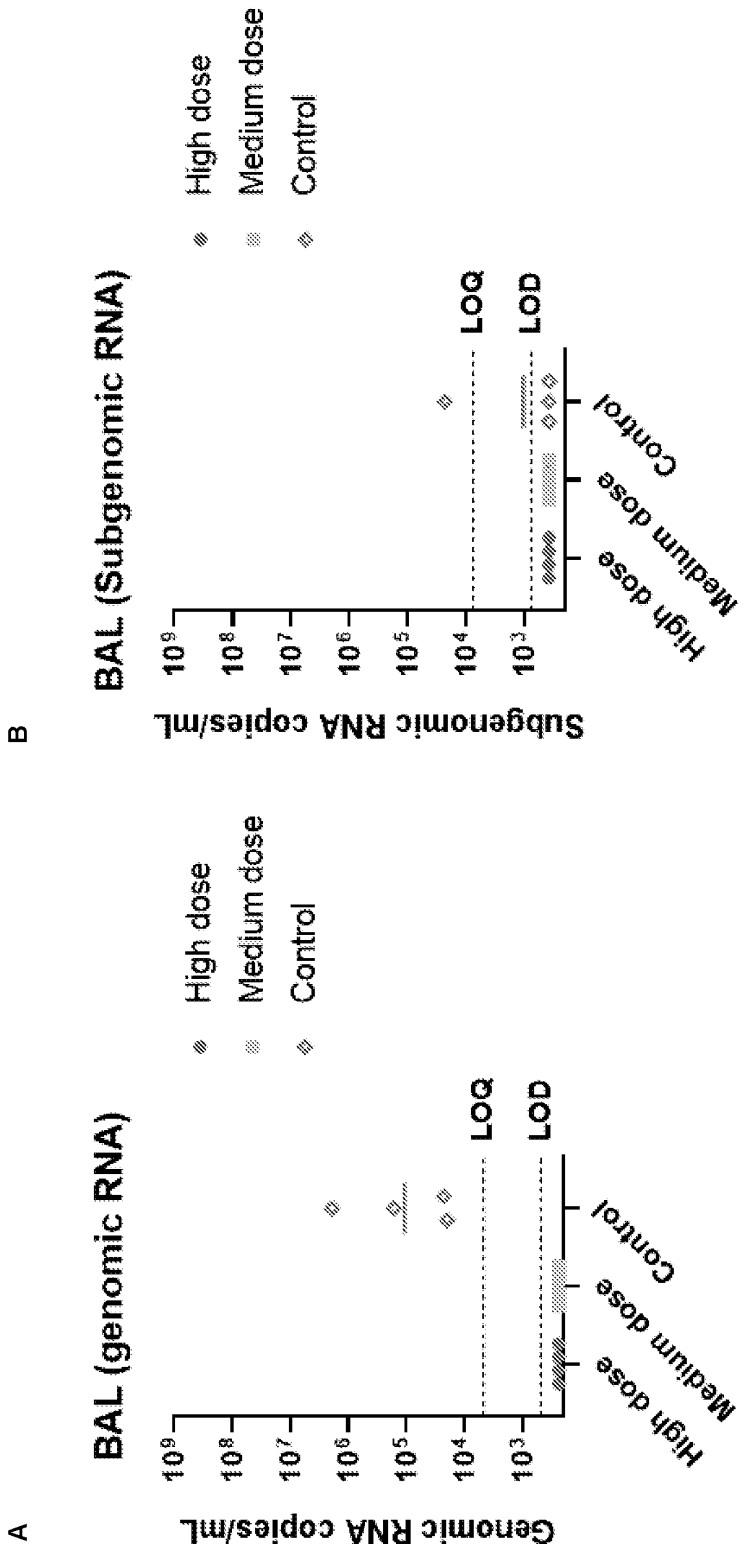

A
BAL (genomic RNA)
Genomic RNA copies/mL
10^9
10^8
10^7
10^6
10^5
10^4
10^3
LOQ
LOD
High dose
Medium dose
Control
B
BAL (Subgenomic RNA)
Subgenomic RNA copies/mL
10^9
10^8
10^7
10^6
10^5
10^4
10^3
LOQ
LOD
High dose
Medium dose
Control

FIG. 20

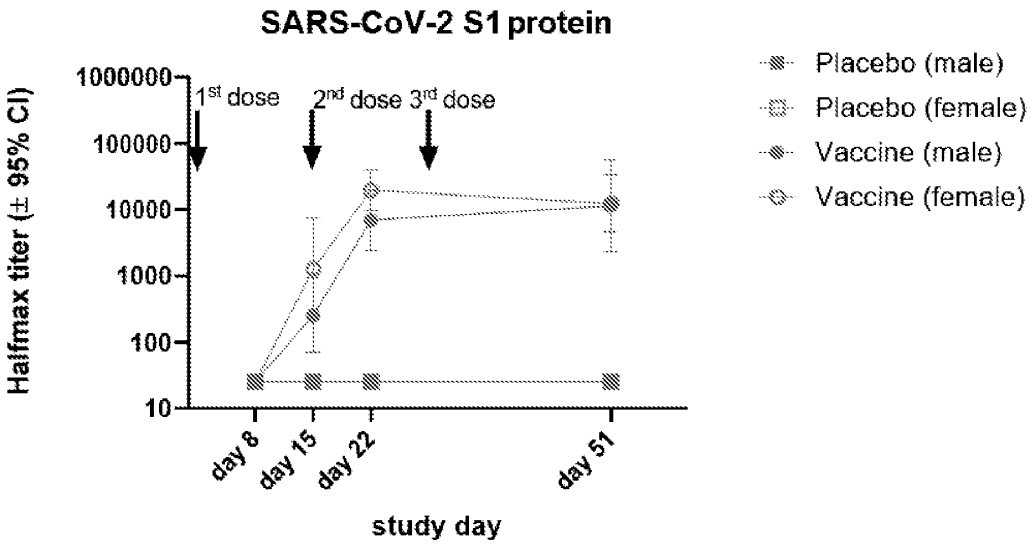

SARS-CoV-2 S1 protein
Halfmax titer (± 95% CI)
1000000
100000
10000
1000
100
10
1st dose
2nd dose
3rd dose
day 8
day 15
day 22
day 51
study day
Placebo (male)
Placebo (female)
Vaccine (male)
Vaccine (female)

FIG. 21

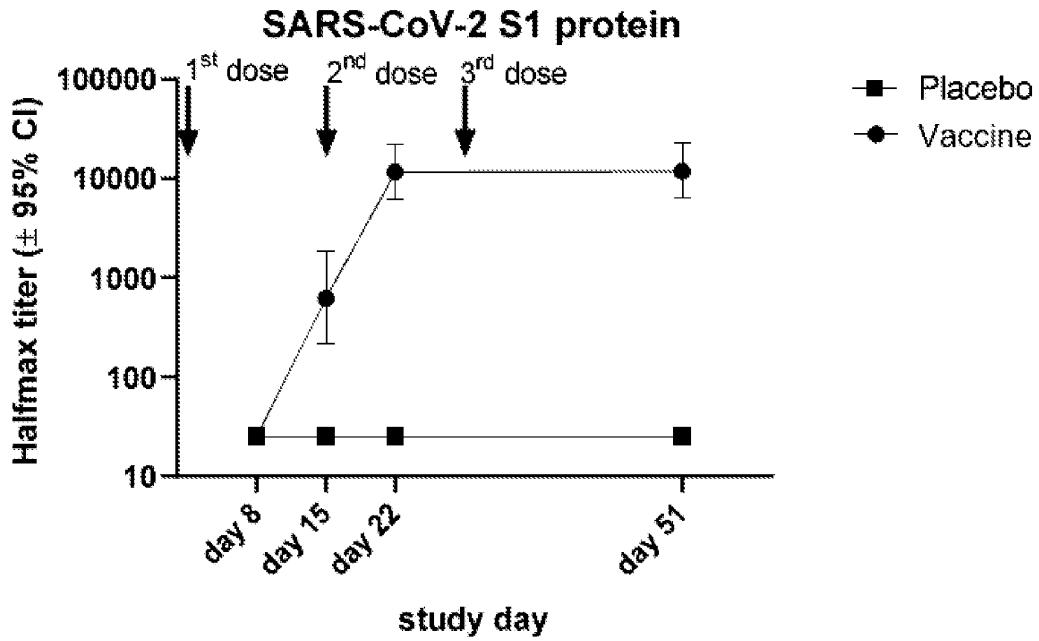

SARS-CoV-2 S1 protein
Halfmax titer (± 95% CI)
100000
10000
1000
100
10
1st dose
2nd dose
3rd dose
day 8
day 15
day 22
day 51
study day
Placebo
Vaccine

FIG. 22

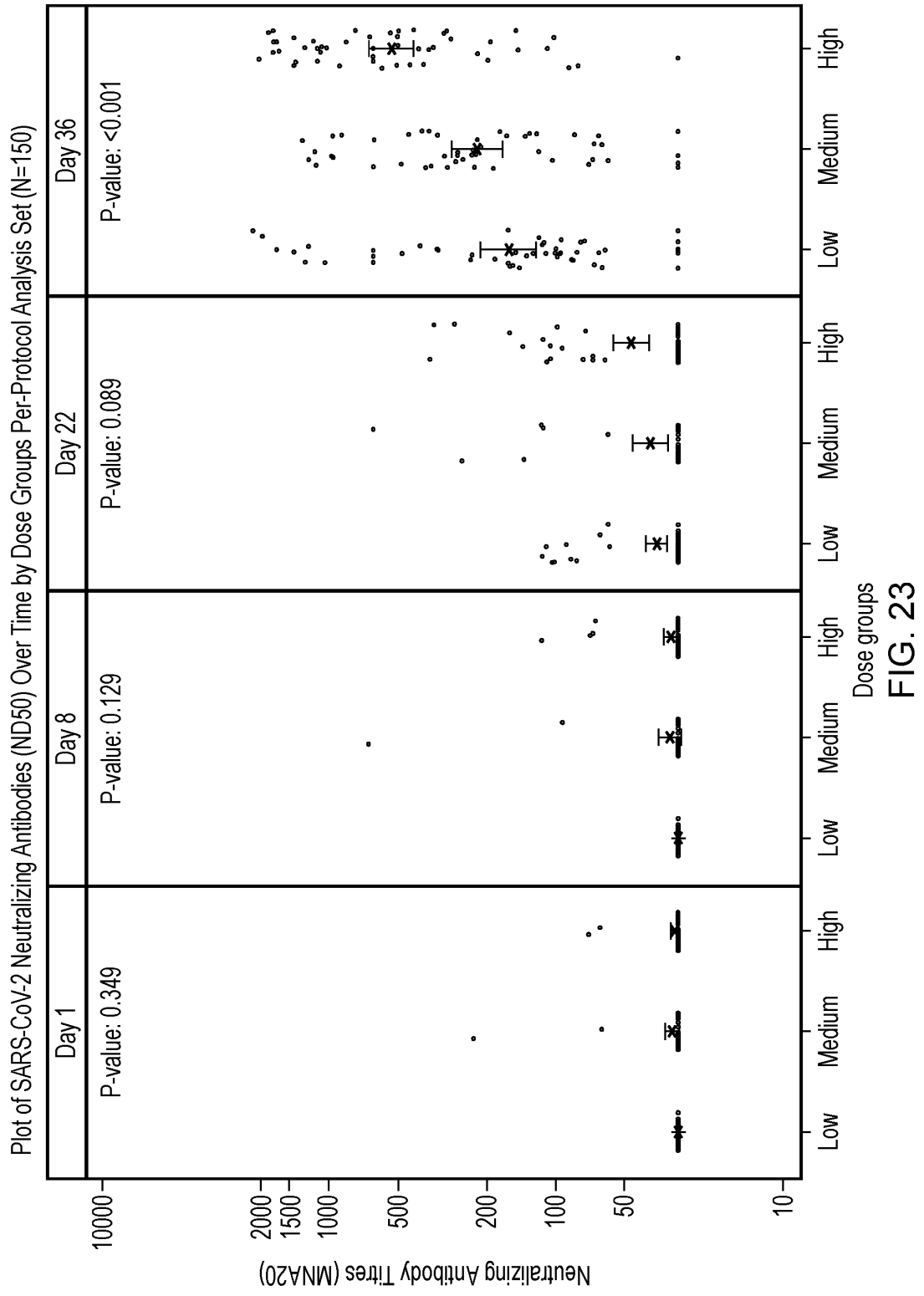

Plot of SARS-CoV-2 Neutralizing Antibodies (ND50) Over Time by Dose Groups Per-Protocol Analysis Set (N=150)
Day 1
Day 8
Day 22
Day 36
P-value: 0.349
P-value: 0.129
P-value: 0.089
P-value: <0.001
Neutralizing Antibody Titres (MNA20)
10000
2000
1500
1000
500
200
100
50
10
Low
Medium
High
Dose groups

FIG. 23

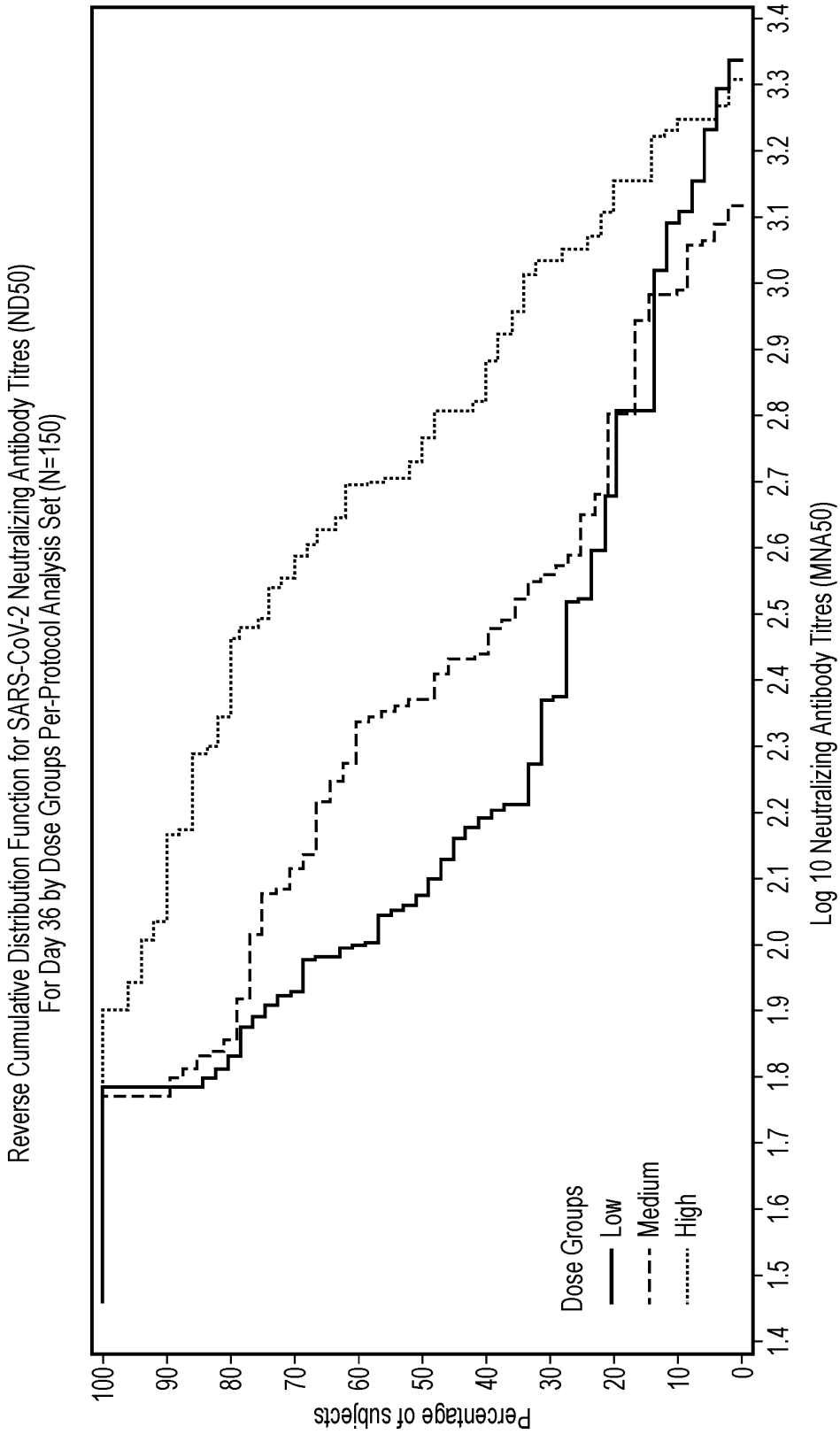

Reverse Cumulative Distribution Function for SARS-CoV-2 Neutralizing Antibody Titres (ND50)
For Day 36 by Dose Groups Per-Protocol Analysis Set (N=150)
Percentage of subjects
100
90
80
70
60
50
40
30
20
10
0
Dose Groups
Low
Medium
High
1.4
1.5
1.6
1.7
1.8
1.9
2.0
2.1
2.2
2.3
2.4
2.5
2.6
2.7
2.8
2.9
3.0
3.1
3.2
3.3
3.4
Log 10 Neutralizing Antibody Titres (MNA50)

FIG. 24

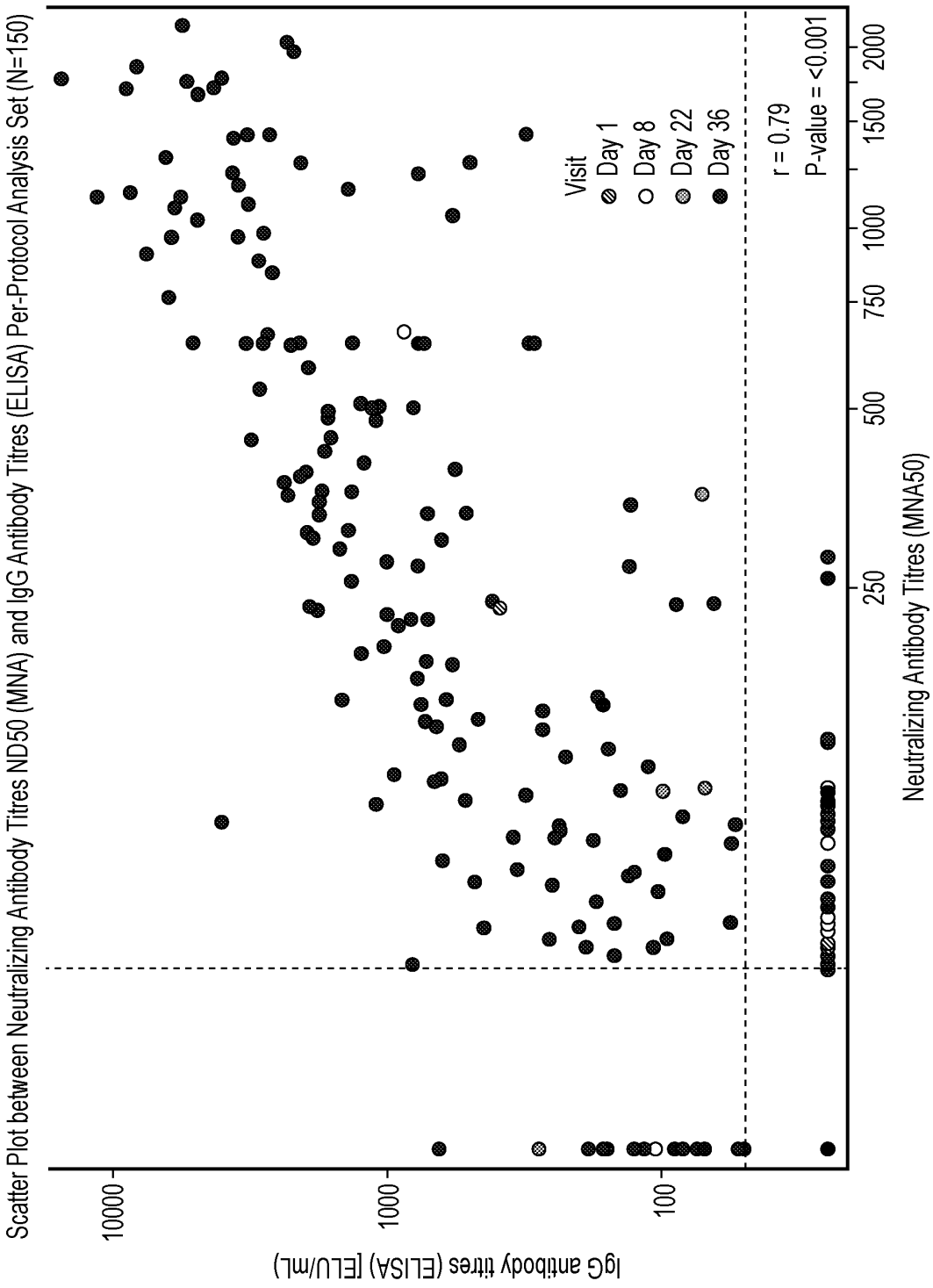

Scatter Plot between Neutralizing Antibody Titres ND50 (MNA) and IgG Antibody Titres (ELISA) Per-Protocol Analysis Set (N=150)
IgG antibody titres (ELISA) [ELU/mL]
10000
1000
100
Neutralizing Antibody Titres (MNA50)
250
500
750
1000
1500
2000
Visit
Day 1
Day 8
Day 22
Day 36
r = 0.79
P-value = <0.001

FIG. 25

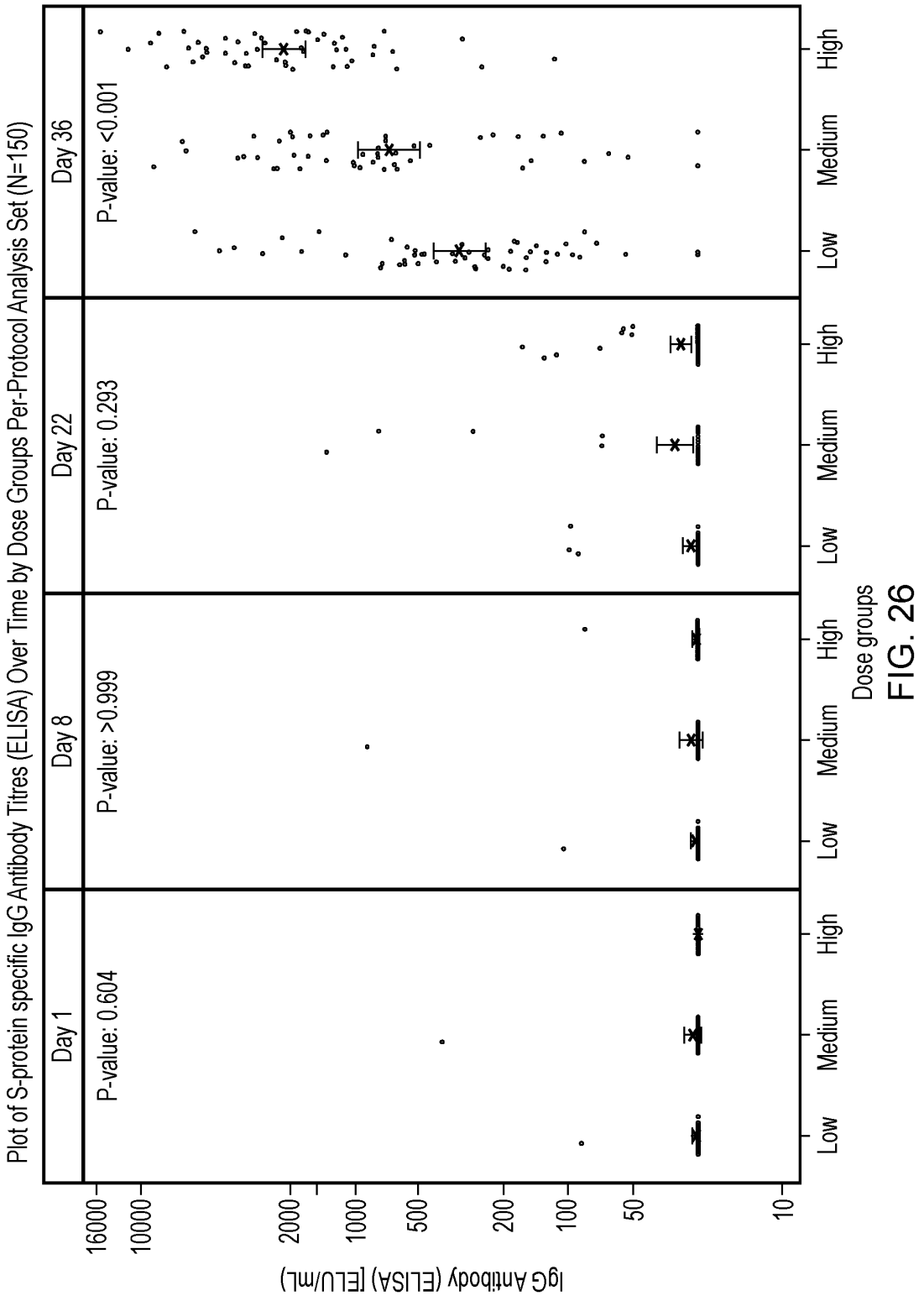

Plot of S-protein specific IgG Antibody Titres (ELISA) Over Time by Dose Groups Per-Protocol Analysis Set (N=150)
Day 1
Day 8
Day 22
Day 36
P-value: 0.604
P-value: >0.999
P-value: 0.293
P-value: <0.001
IgG Antibody (ELISA) [ELU/mL]
16000
10000
2000
1000
500
200
100
50
10
Low
Medium
High
Dose groups

FIG. 26

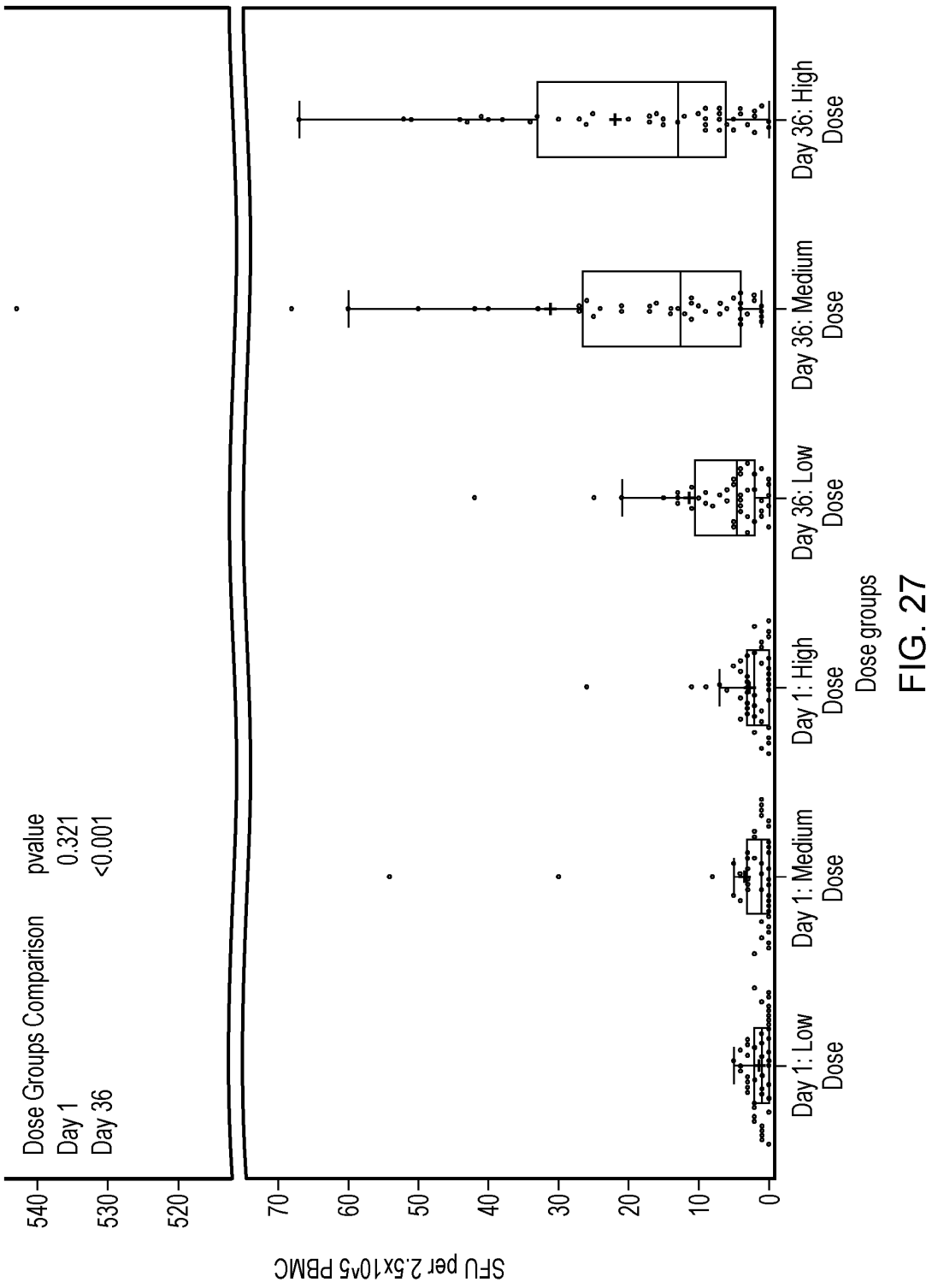

Dose Groups Comparison pvalue
Day 1 0.321
Day 36 <0.001
SFU per 2.5x10^5 PBMC
Dose groups
Day 1: Low Dose
Day 1: Medium Dose
Day 1: High Dose
Day 36: Low Dose
Day 36: Medium Dose
Day 36: High Dose

FIG. 27

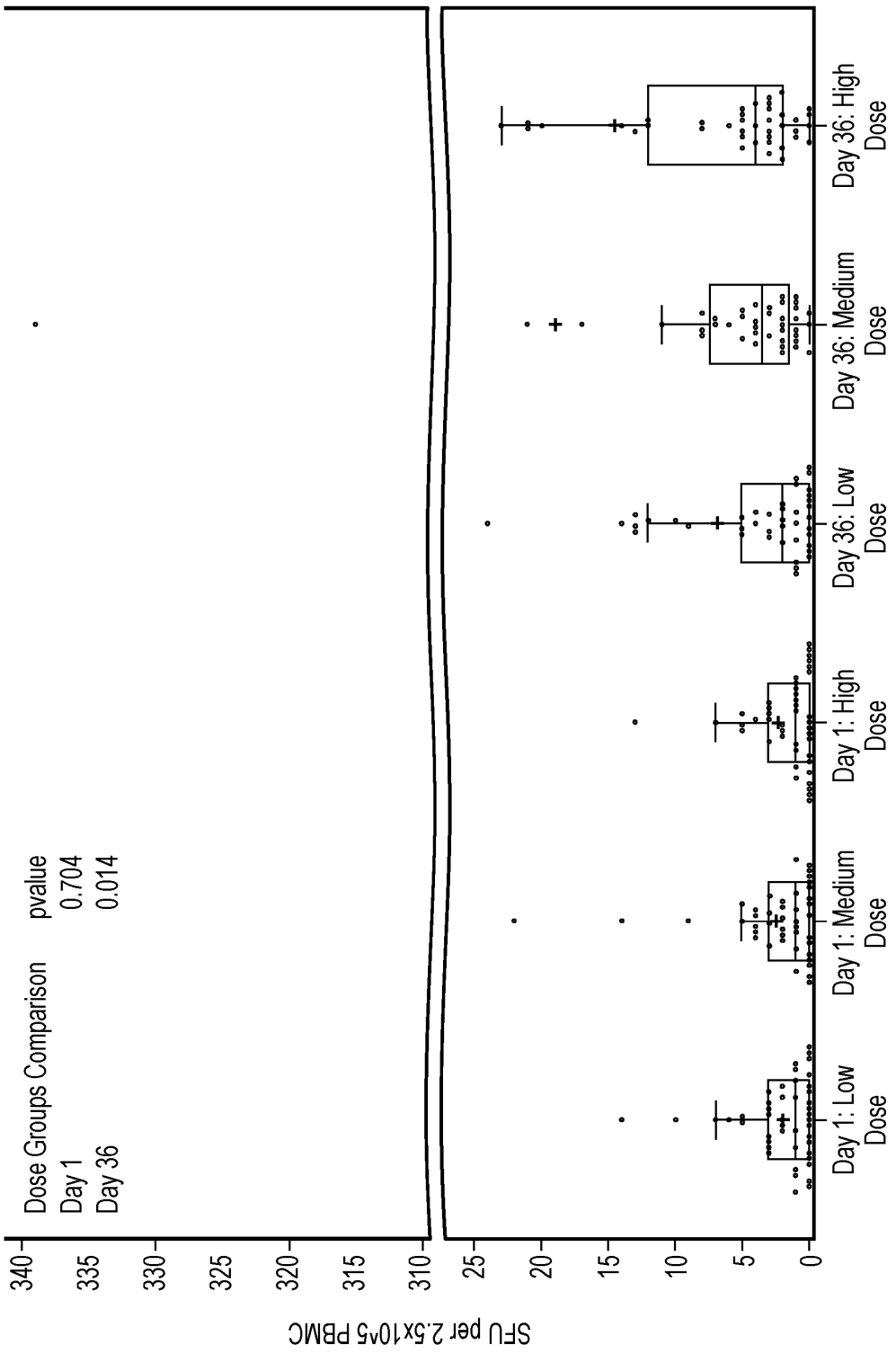

Dose Groups Comparison pvalue
Day 1 0.704
Day 36 0.014
SFU per 2.5x10^5 PBMC
340
335
330
325
320
315
310
25
20
15
10
5
0
Day 1: Low Dose
Day 1: Medium Dose
Day 1: High Dose
Day 36: Low Dose
Day 36: Medium Dose
Day 36: High Dose
Dose groups

FIG. 28

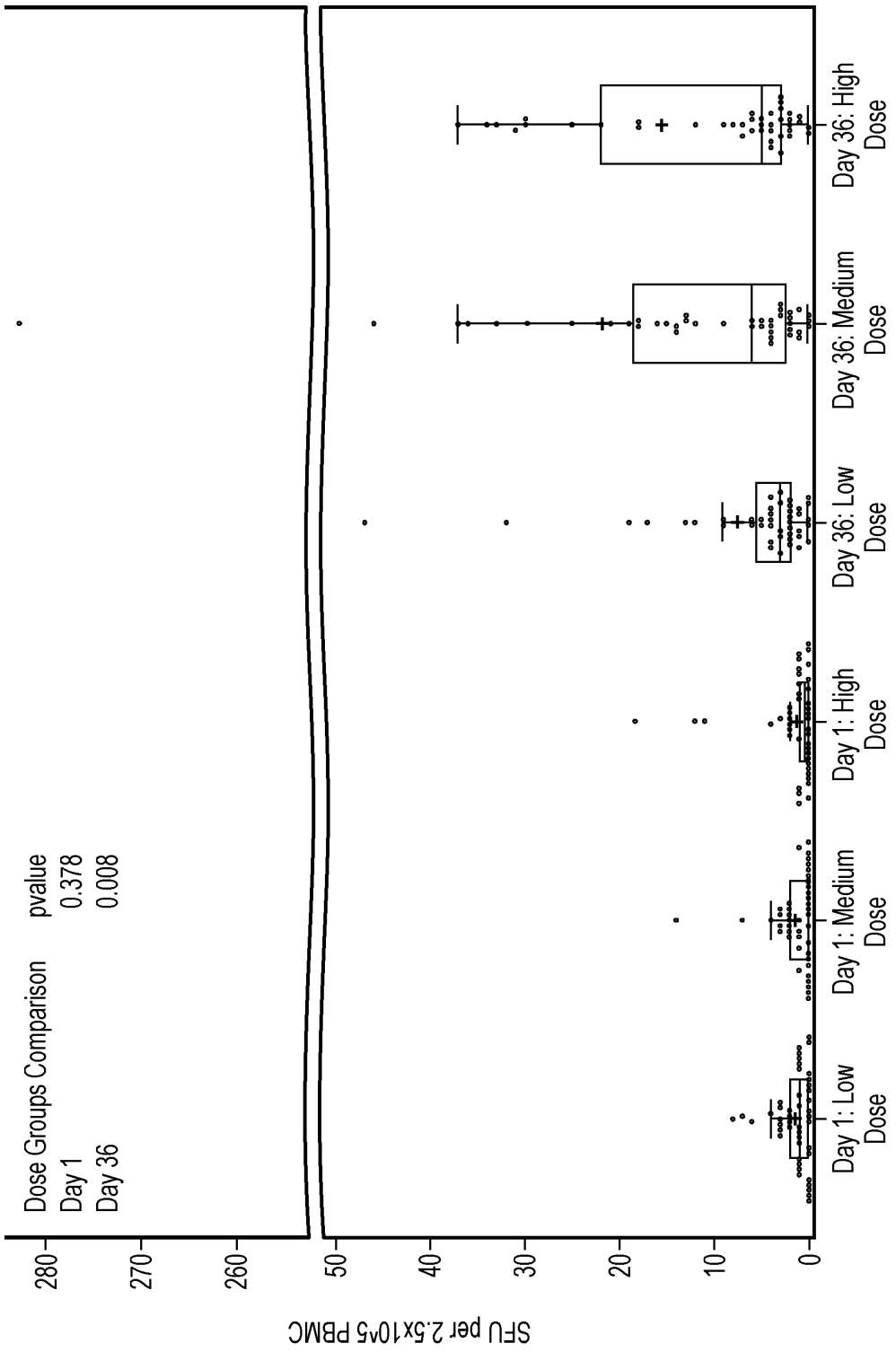

Dose Groups Comparison pvalue
Day 1 0.378
Day 36 0.008
SFU per 2.5x10^5 PBMC
280
270
260
50
40
30
20
10
0
Day 1: Low Dose
Day 1: Medium Dose
Day 1: High Dose
Day 36: Low Dose
Day 36: Medium Dose
Day 36: High Dose
Dose groups

FIG. 29