TWIST BIOPHARMA

Advancing Novel SARS-CoV-2 Therapeutic Antibodies

September 2020

@TwistBioscience #WeMakeDNA

Making Progress on a Global Need

Novel Therapeutic Antibody Leads	Well Characterized	Well Validated
IgG (TB181-8, 28, 36) and VHH (TB201-202)	High affinity and unbiased, leveraging Twist's synthetic DNA platform	Extensive pseudovirus and live virus data

Our DNA Platform Has Enabled a Rapid Discovery Process

Dual Focus

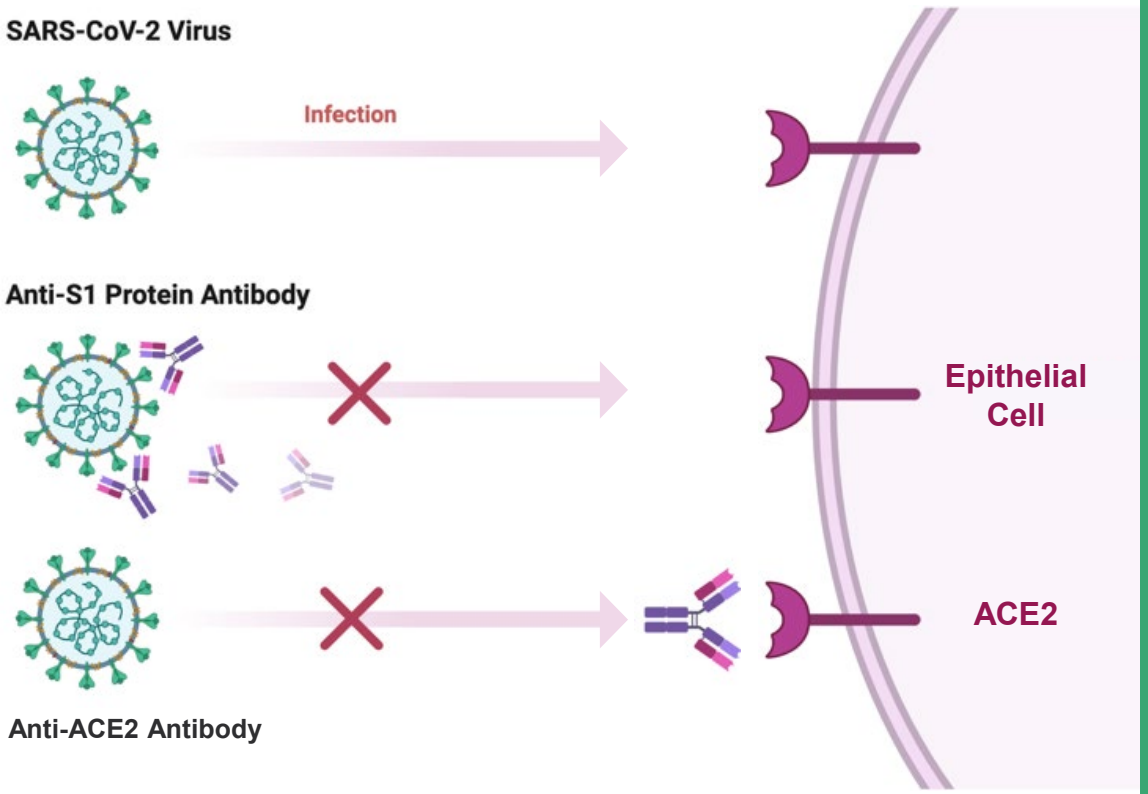
TWIST

#1

Spike Protein Neutralizing Ab

#2

Anti-ACE2 Blocking Ab



Synthetic Libraries

VANDERBILT UNIVERSITY MEDICAL CENTER

Based on Sequence of COVID-19 Survivor

Human Fab and VHH Libraries

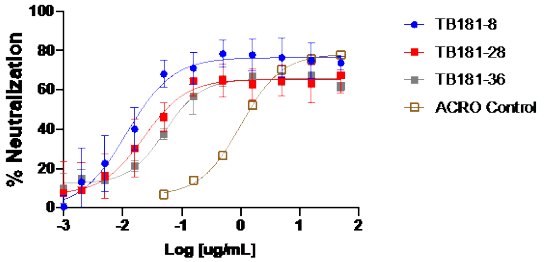
Fast Results

200+ antibody leads in 6 weeks

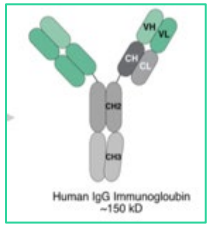
TB181 – High Affinity Anti-S1 IgG Antibodies

Affinity & Pseudovirus

	S1 K_D	S Trimer K_D
TB181-8	6.1 nM	11 nM
TB181-28	364 nM	11 nM
TB181-36	10 nM	18 nM

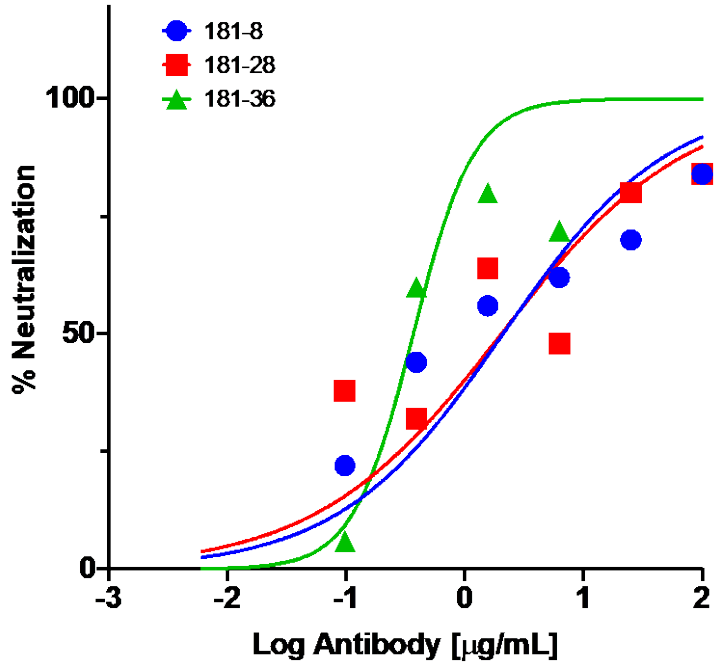


TB181-8	TB181-28	TB181-36	ACRO Control
0.01170	0.02293	0.05196	1.011



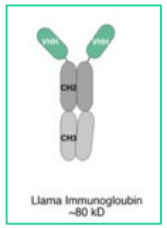
Live Virus FRNT

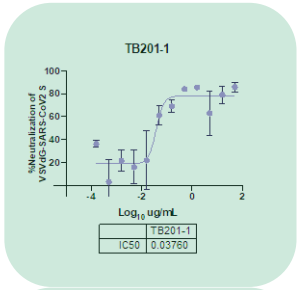
Conducted by Dr. James Brien, Saint Louis University

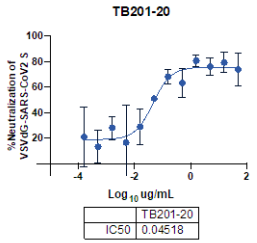


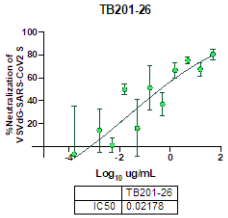
Antibody	EC50 (ug/mL)
181-36	0.37
181-28	2.03
181-8	2.10

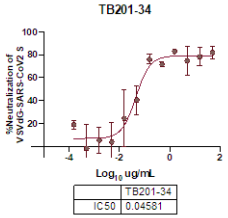
TB201-202 – High Affinity Anti-S1 VHH Single Domain Antibodies
VSV-pseudotype SARS-CoV2 Neutralization Analysis

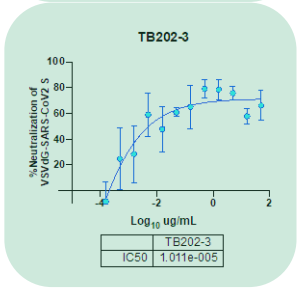


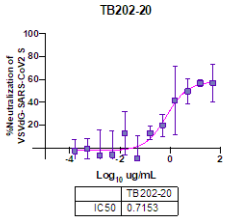


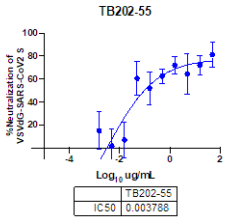


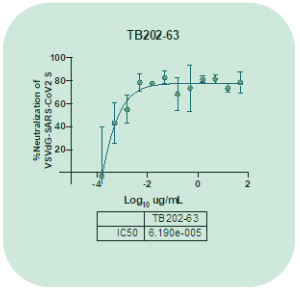


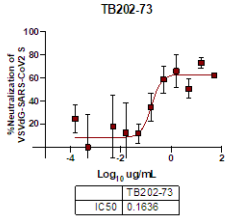


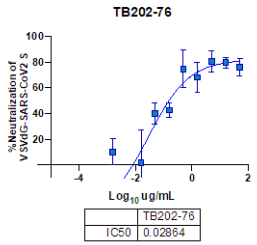


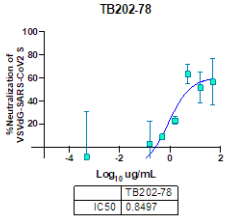


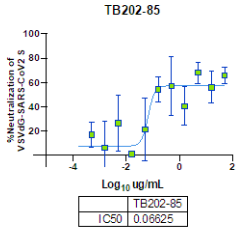












TB201-1, TB202-3 and TB202-63 are top candidates from pseudovirus testing

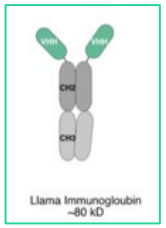
VHH Single Domain Leads (TB201-202) Show Higher Neutralization vs. IgG in Live SARS-CoV-2 Virus FRNT

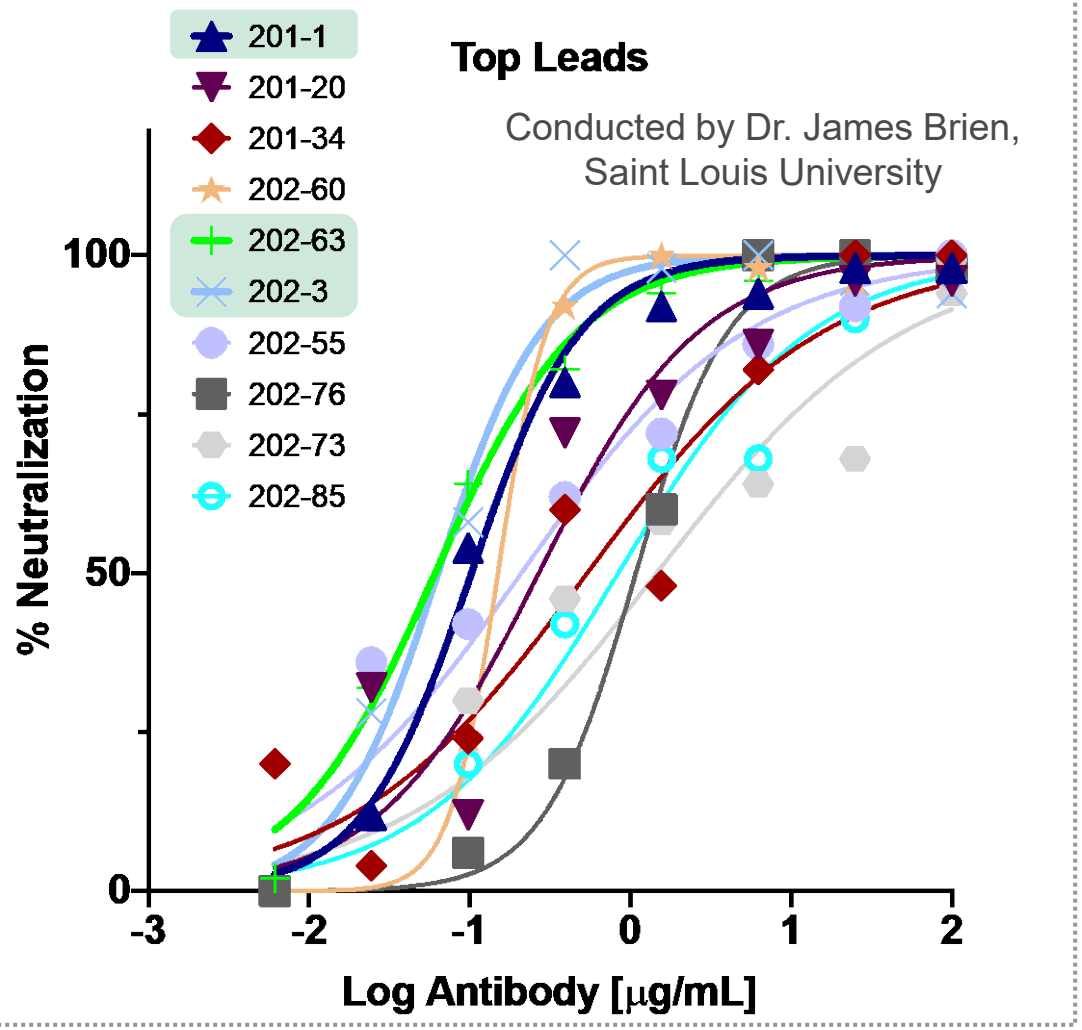
TB202-63, TB202-3, & TB201-1 show potent neutralization in live virus FRNT

IgG

VHH

Antibody	NC50 (ug/mL)
202-63	0.06
202-3	0.06
201-1	0.10
202-60	0.15
202-55	0.21
201-20	0.27
181-36	0.37
201-34	0.54
202-85	0.84
202-76	1.08
202-73	1.46
181-28	2.03
181-8	2.10
202-26	2.97
202-20	5.03
202-78	8.26
182-7	11.77
182-3	18.31
182-4	67.57
181-63	106.90



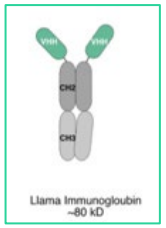


VHH Single Domain Leads (TB201-202) Show Potent Neutralization in Live SARS-CoV-2 Virus PRNT

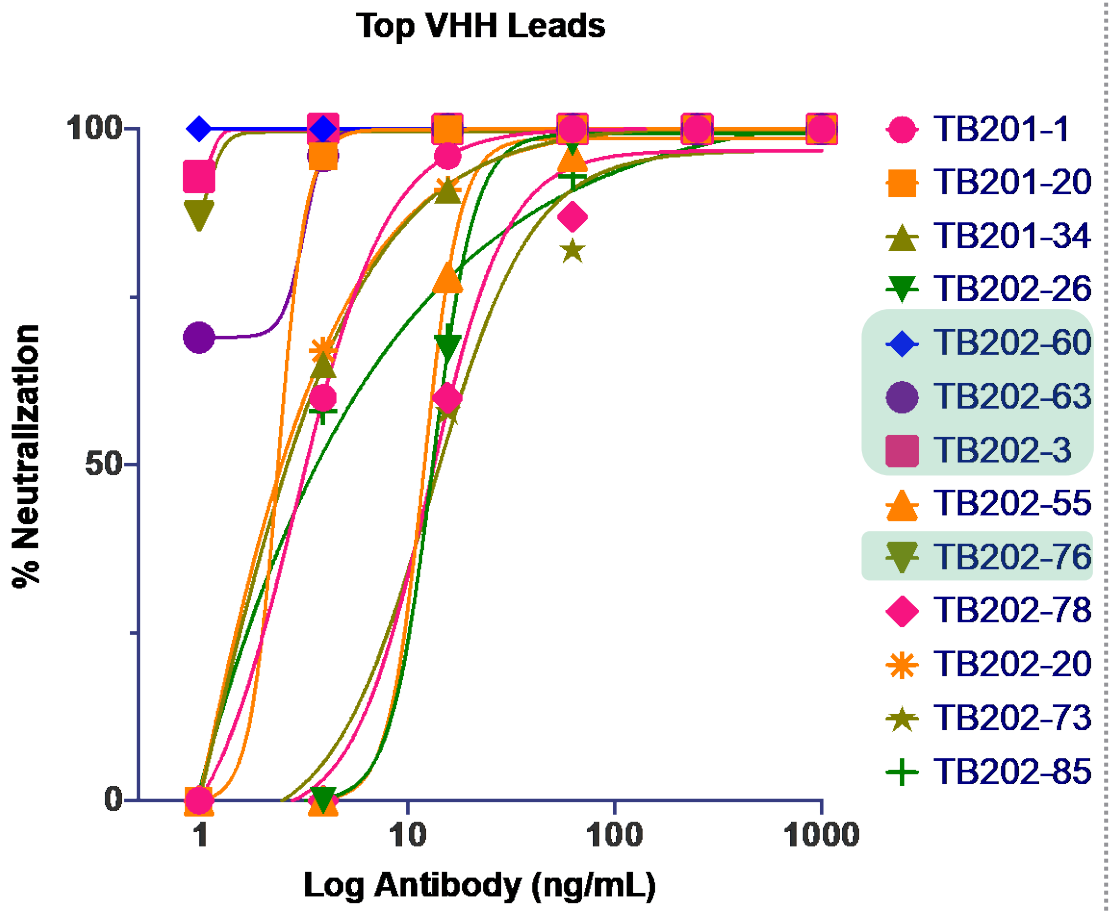
TB202-3, TB202-60, TB202-63, & TB202-76 show potent neutralization in live virus PRNT

Antibody	PRNT90 (ng/mL)*
TB201-1	15.6
TB201-20	3.9
TB201-34	15.6
TB202-26	62.5
TB202-60	<0.98
TB202-63	3.9
TB202-3	<0.98
TB202-55	62.5
TB202-76	3.9
TB202-78	250
TB202-20	15.6
TB202-73	250
TB202-85	62.5

* The antibody concentration required to reduce the number of plaques by 90% compared to free virus



Conducted by Dr. Richard Bowen, Colorado State University



Promising Development Potential

Path to Development

- Hamster *in vivo* Protection Studies
- Multivalent homo- and heterotrimeric VHH Fc Designs to increase potency
- Identify partner for rapid antibody scale-up of clinical supply

Next Steps