



Advancing Novel SARS-CoV-2 Therapeutic Antibodies

September 2020

@TwistBioscience #WeMakeDNA



Novel Therapeutic Antibody Leads

IgG (TB181-8, 28, 36)
and
VHH (TB201-202)

Well Characterized

High affinity and unbiased,
leveraging Twist's
synthetic DNA platform

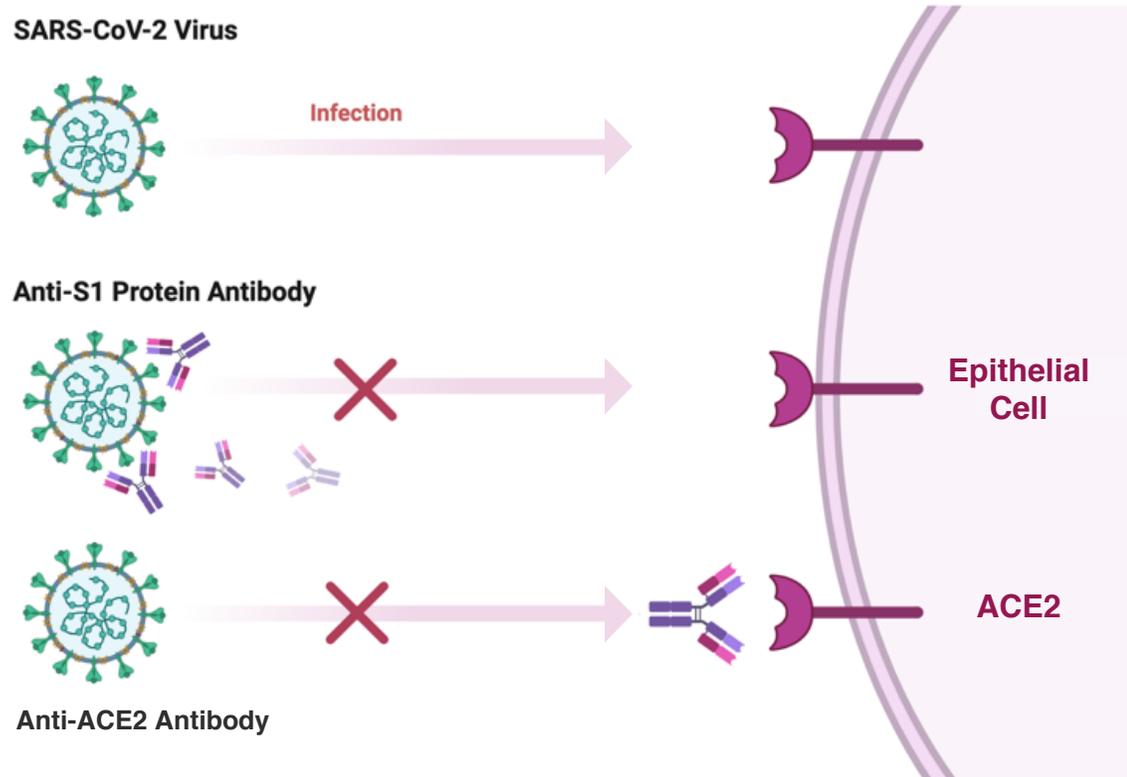
Well Validated

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

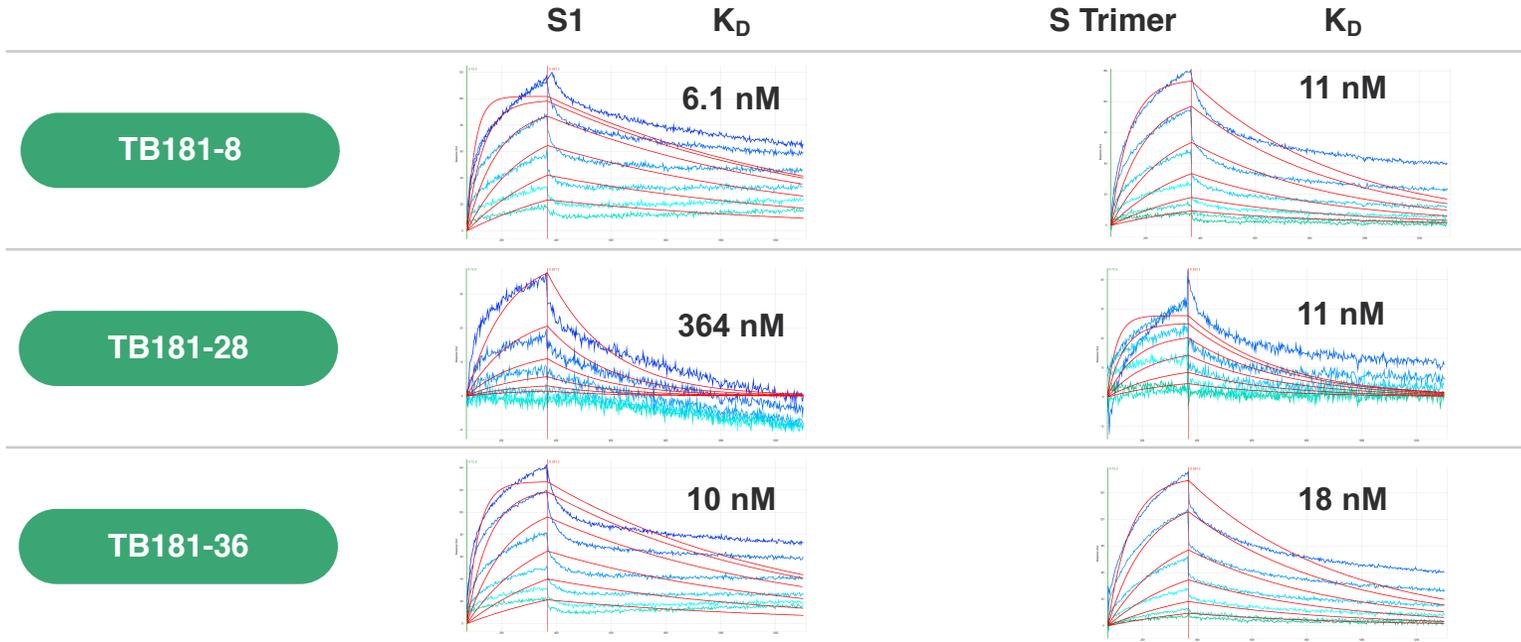


Fast Results
200+ antibody leads
in 6 weeks

TB181 – High Affinity Anti-S1 IgG Antibodies



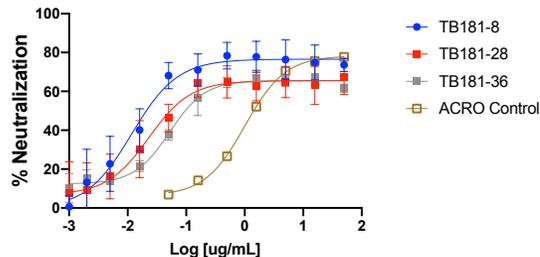
Affinity & Pseudovirus



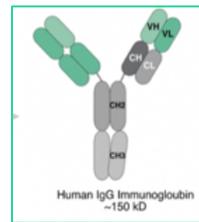
TB181-8

TB181-28

TB181-36

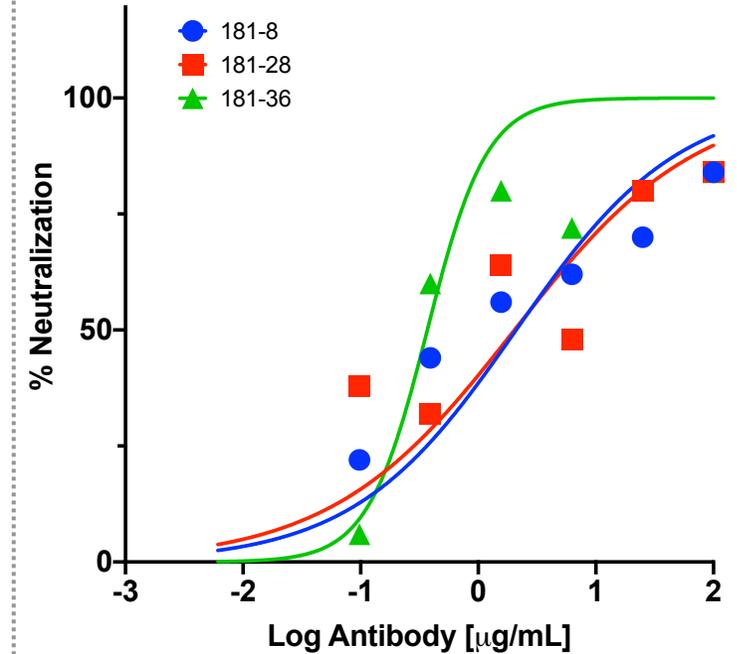


Antibody	EC50 (ug/mL)
TB181-8	0.01170
TB181-28	0.02293
TB181-36	0.05196
ACRO Control	1.011



Live Virus FRNT

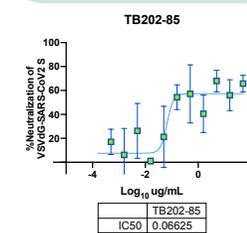
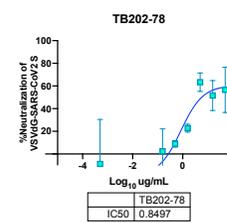
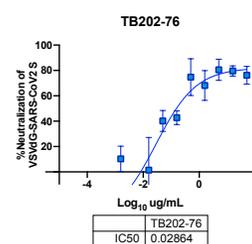
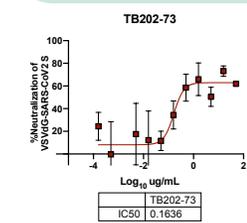
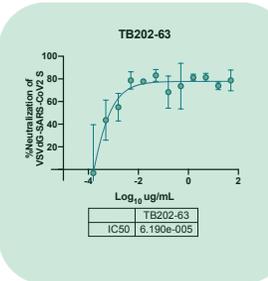
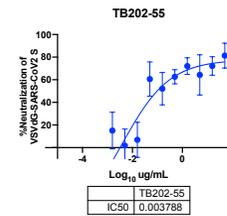
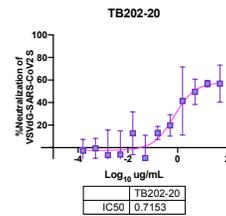
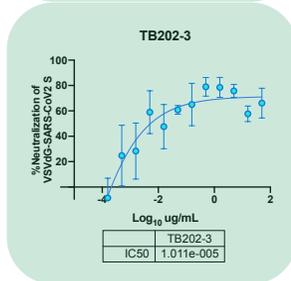
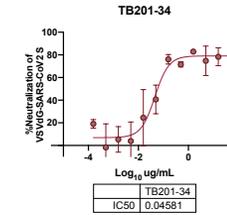
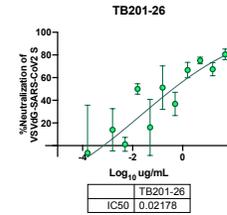
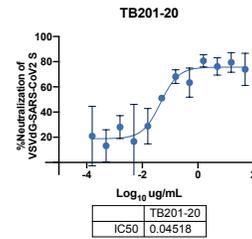
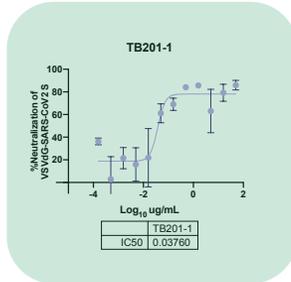
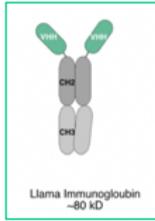
Conducted by Dr. James Brien,
Saint Louis University



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



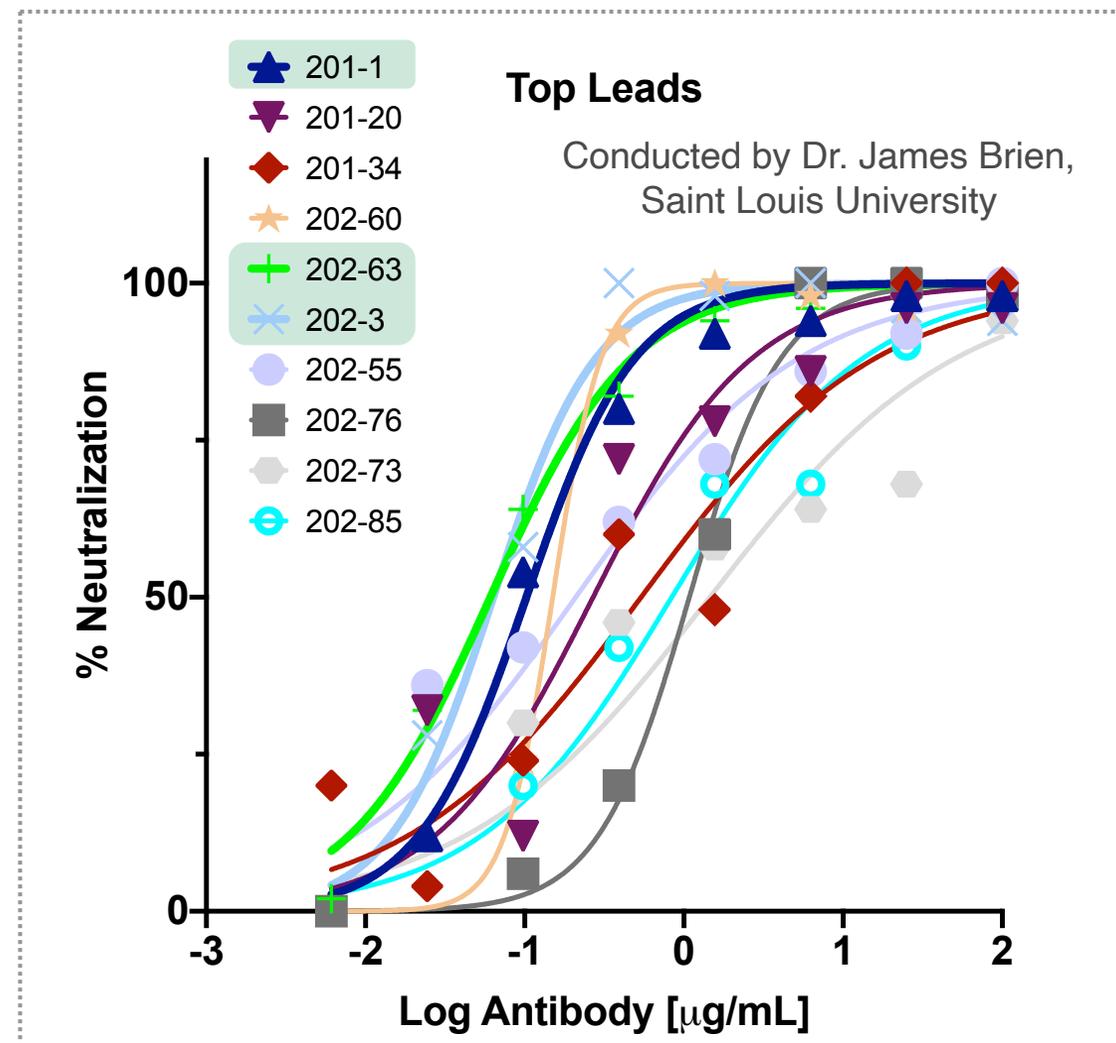
TB201-1, TB202-3
and TB202-63
are top candidates
from pseudovirus
testing

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

	Antibody	NC50 (ug/mL)
IgG		
VHH	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



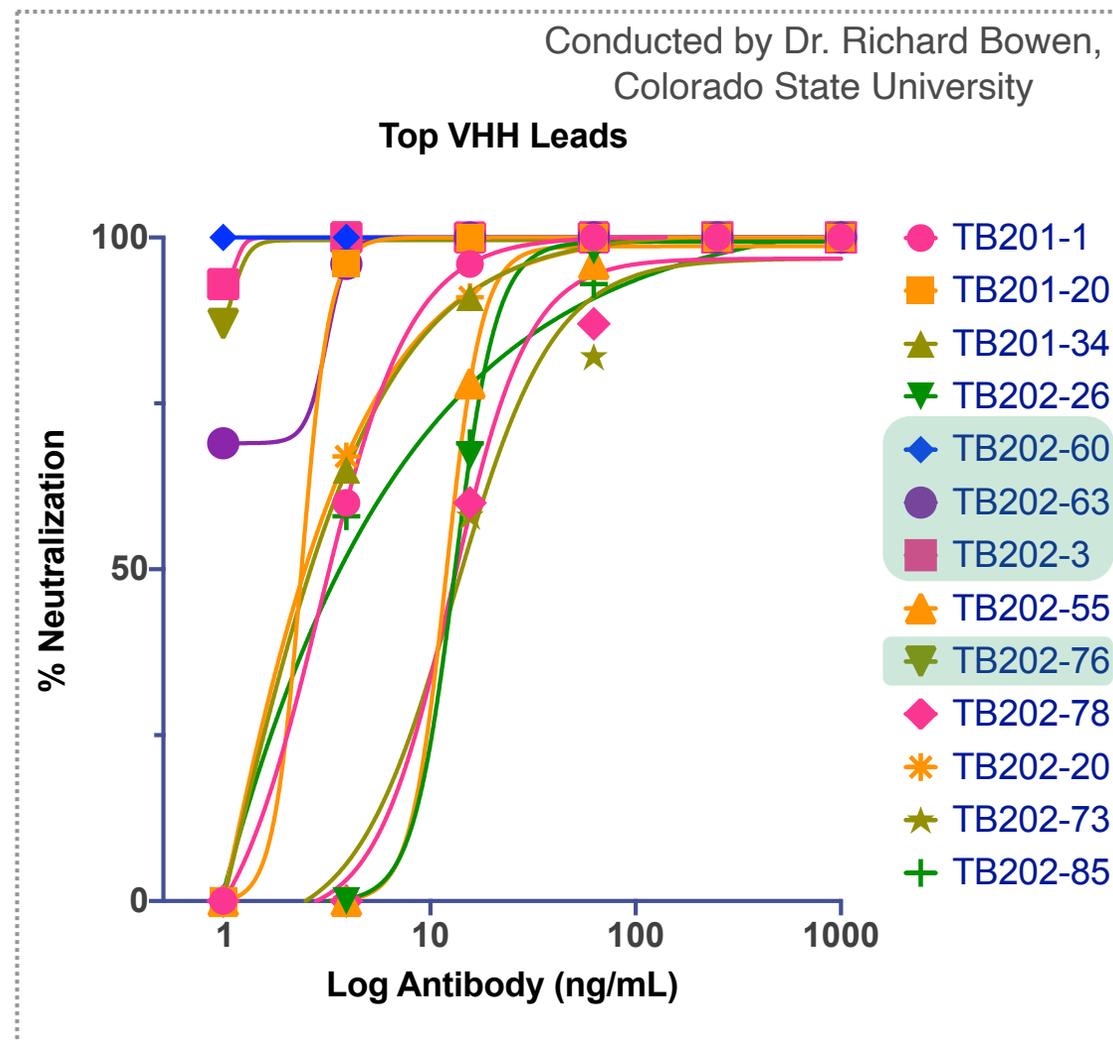
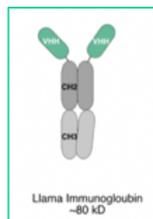
VHH Single Domain Leads (TB201-202) Show Potent Neutralization in Live SARS-CoV-2 Virus PRNT



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





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

