

2.6.3 Pharmacology Tabulated Summary

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2.6.3.1 PHARMACOLOGY: OVERVIEW

Study Title	Test Articles	Species/Strain	Method of Administration	Testing Facility	Study Number (GLP Status)	Location in eCTD
Primary Pharmacodynamics						
Evaluation of immunogenicity of Omicron-matched mRNA vaccines as primary series in mice	PBS control mRNA-1273 mRNA-1273.529 mRNA-1273.214	Mouse/ BALB/c	IM	ModernaTX, Inc. Cambridge, MA	MOD-5156 (non-GLP)	4.2.1.1
Evaluation of immunogenicity and antigen-reactive B cell responses of Omicron-matched mRNA vaccine boosters in mice	PBS control mRNA-1273 mRNA-1273.529 mRNA-1273.214	Mouse/ BALB/c	IM	ModernaTX, Inc. Cambridge, MA	MOD-5019 (non-GLP)	4.2.1.1
Primary series and booster studies in mice of mRNA-1273 and mRNA-1273.529 immunogenicity and protection from Omicron challenge	mRNA control PBS control mRNA-1273 mRNA-1273.529	Mouse/ K18-hACE2 BALB/c 129S2	IM	ModernaTX, Inc. Cambridge, MA Washington University School of Medicine St. Louis, MO	WASHU-01- MOD-5020 (non-GLP)	4.2.1.1
mRNA-1273 primary series and mRNA-1273 versus mRNA-1273.529 booster regimen in a rhesus macaque SARS-CoV-2 Omicron challenge model	mRNA control mRNA-1273 mRNA-1273.529	Non-human primate/ Rhesus macaques	IM	BIOQUAL, Inc. Rockville, MD	VRC-20-857 (non-GLP)	4.2.1.1

Abbreviations: eCTD = electronic common technical document; GLP = Good Laboratory Practice; IM = intramuscular; mRNA = messenger RNA;

PBS = phosphate-buffered saline; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

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2.6.3.2 PRIMARY PHARMACODYNAMICS

Study Title	Test Articles	Species/ Strain	Method of Admin.	Doses (µg/dose)	No. per Group	Noteworthy Findings	Study Number (GLP Status)
Evaluation of immunogenicity of Omicron-matched mRNA vaccines as primary series in mice	PBS control, mRNA-1273, mRNA-1273.529, mRNA-1273.214	Mouse/ BALB/c	IM	0 (PBS control), 1	8	<ul style="list-style-type: none"> Mice vaccinated with mRNA-1273.214 or mRNA-1273.529 achieved numerically higher S-2P.529 IgG titers than those vaccinated with mRNA-1273. mRNA-1273.214 provided the broadest neutralization coverage across the variants tested (WA. 1D614G, BA.1, and BA.2). 	MOD-5156 (non-GLP)
Evaluation of immunogenicity and antigen-reactive B cell responses of Omicron-matched mRNA vaccine boosters in mice	PBS control, mRNA-1273, mRNA-1273.529, mRNA-1273.214	Mouse/ BALB/c	IM	0 (PBS control), 0.25	8	<ul style="list-style-type: none"> Boosting with Omicron-matched vaccines showed equivalent or better BA.1 and BA.2 variant-specific neutralization response than mRNA-1273 but had lower neutralization activity against the WT WA1 strain. A single Omicron booster drove expansion of Omicron antigen-reactive B cells that were available to respond rapidly to subsequent vaccination with mRNA-1273.529. A dramatic increase of BA.1 and BA.2 neutralization was noted after Dose 4. 	MOD-5019 (non-GLP)

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Study Title	Test Articles	Species/ Strain	Method of Admin.	Doses (µg/dose)	No. per Group	Noteworthy Findings	Study Number (GLP Status)
Primary series and booster studies in mice of mRNA-1273 and mRNA-1273.529 immunogenicity and protection from Omicron challenge	mRNA control, mRNA-1273	Mouse/ K18-hACE2	IM	0.1, 5	3 to 12	<ul style="list-style-type: none"> Boosting with mRNA-1273 or mRNA-1273.529 enhanced protection against BA.1 infection. The difference in protective efficacy between the 2 boosters was limited. Either booster offered protection against the historical WA1 D614G variants and increased neutralization titers and protection against BA.1 and BA.2. 	WASHU-01-MOD-5020 (non-GLP)
	mRNA control, mRNA-1273	Mouse/ K18-hACE2		0.25, 5 (primary series) 1 (booster)			
	PBS control, mRNA-1273, mRNA-1273.529	Mouse/ BALB/c		0 (PBS control), 0.1, 1			
	mRNA control, mRNA-1273 (primary series) mRNA control, mRNA-1273, mRNA-1273.529 (booster)	Mouse/ 129S2		5, 0.25 (primary series) 1 (booster)			
mRNA-1273 primary series and mRNA-1273 versus mRNA-1273.529 booster regimen in a rhesus macaque SARS-CoV-2 Omicron challenge model	mRNA-1273, (primary series) mRNA control, mRNA-1273, mRNA-1273.529 (booster)	Non-human primate/ Rhesus macaques	IM	100 (primary series) 50 (booster)	4	<ul style="list-style-type: none"> Boosting with mRNA-1273 or mRNA-1273.529 led to comparable and significant increases in neutralizing antibody responses against all VOCs. Boosting was important for enhancing mucosal antibody binding and neutralization responses. Cross-reactive B cells were expanded following a boost with either mRNA-1273 or mRNA-1273.529, while only mRNA-1273 was capable of boosting memory B cells specific for WA1 alone. Protection against Omicron was robust in the lungs, regardless of booster selection. 	VRC-20-857 (non-GLP)

ModernaTX, Inc.

mRNA-1273.214

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Abbreviations: GLP = Good Laboratory Practice; IM = intramuscular; mRNA = messenger RNA; PBS = phosphate-buffered saline; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VOC = variant of concern; WT = wild-type.

2.6.3.3 SECONDARY PHARMACODYNAMICS

No secondary pharmacodynamic studies have been performed with mRNA-1273.214.

2.6.3.4 SAFETY PHARMACOLOGY

No safety pharmacology studies have been performed with mRNA-1273.214.

2.6.3.5 PHARMACODYNAMIC DRUG INTERACTIONS

No pharmacodynamic drug interaction studies have been performed with mRNA-1273.214.