TEXAS BIOMEDICAL
RESEARCH INSTITUTE

STATEMENT OF WORK 2 (SOW)

To determine the anti-SARS-CoV-2 effect of 3VM-1000 suspension in K18 hACE-2 mice.

OBJECTIVE

This study is designed to test *in-vivo* toxicity and efficacy of 3VM-1000 suspension in a mouse model of SARS-CoV-2 infection by measuring the viral load and survival. There are two aims as listed below:

Aim 1: To determine *in-vivo* toxicity of 3VM-1000 suspension in K18-hACE-2 mice

Aim 2: *In-vivo* assessment of 3VM-1000 suspension on SARS-CoV-2 infectivity

Experimental design:

Aim1: To determine *in-vivo* toxicity of 3VM-1000 suspension in K18-hACE-2 mice

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Animals:	K18 hACE2 mice.
Age:	4-6 week old.
Sex:	Female
Treatment:	3VM1000 suspension for 7 days
Route drug administration:	Intranasal for 7 days
Concentration:	3VM-1000 (100%; 50%; 25%; 5%)
Experimental Groups:	Group 1: Mock- Vehicle-treated (n=10)
	Group 2: 3VM-1000 (100%) (n=10)
	Group 3: 3VM-1000 (50%) (n=10)
	Group 4: 3VM-1000 (25%) (n=10)
	Group 5: 3VM-1000 (5%) (n=10)
Total number of animals:	50 hACE2 transgenic mice.

Time points: Day 1 post final drug treatment: 5 animals from each group will be   euthanized.

Day 14 post treatment: 5 animals from each group will monitored for survival up to 14 days, at which survivors will be euthanized.

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Clinical Read-outs: Daily clinical observations, Daily body weight (morbidity – weight loss) and phenotypic visual observation and mortality (survival) will be recorded.

Experimental read-outs: Lungs and Liver will be collected for histopathology (H&E) analysis to determine organ damage
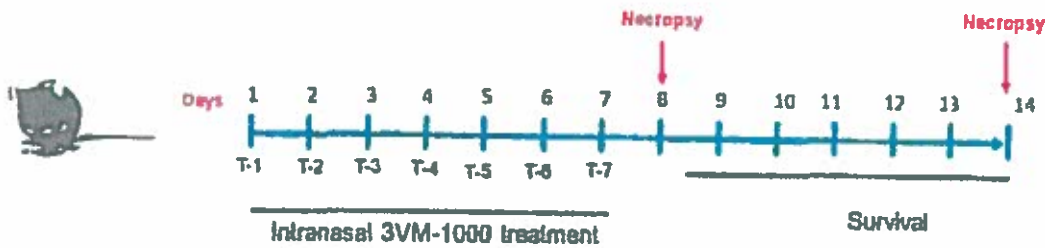
Note: we are recommending to perform an *in-vivo* cytotoxicity study as drug will be administered via intranasal route multiple days directly into the lungs, and we don't have information about the size of particles in suspension and if it causes damage to lungs. Therefore, it would be critical to evaluate the impact of drug on lungs primarily without SARS-CoV-2 infection. This study is not a comprehensive standard toxicity study, however it will help to interpret the data when used against SARS-CoV-2 infection.

The duly authorized party representatives execute this Statement of Work, including all its terms and conditions.

3V Medical Research Group, Inc.

By: _____

Name: **Dominic C Abbott**

Position: **Executive Vice President & COO**

Date: *11-16-2020*

Texas Biomedical Research Institute

By: _____

Name: **Bruce Edwards**

Position: **Vice President Finance & Administration, CFO**

Date: 11/17/2020

I acknowledge that I have read this Statement of Work in its entirety and will use reasonable efforts to uphold my obligations and responsibilities under this Statement of Work.

PRINCIPAL INVESTIGATOR

Signature: _____

Name: Varun Dwivedi, Ph.D.

Title: Staff Scientist I

Date: *11-16-2020*