ASX Announcement

# VIRALEZE Protects Against Omicron in Viral Challenge Model

- **VIRALEZE™ broad-spectrum antiviral nasal spray has shown protection against infection with the highly transmissible SARS-CoV-2 Omicron variant in a stringent viral challenge model**
- **100% of animals treated with VIRALEZE™ before and after Omicron virus challenge had no detectable virus in lung, trachea or nasal cavity at up to four days after challenge**
- **VIRALEZE™ was also highly effective even if used *only after exposure* to virus – animals treated with VIRALEZE™ *only after dosing* with Omicron virus exhibited a >99.999% reduction in viral load in both lung and trachea, compared with saline-treated animals, at day seven**
- **All VIRALEZE™-treated animals also showed markedly reduced pro-inflammatory cytokines compared with saline-treated animals, indicating reduced severity of disease**
- **VIRALEZE™ is now registered in more than 30 countries, including Europe, and the UK where it is marketed by LloydsPharmacy UK**

**Melbourne, Australia; 20 July 2022: Starpharma** (ASX: SPL, OTCQX: SPHRY) today announced new results demonstrating the high level of protection afforded by VIRALEZE™ antiviral nasal spray against the highly infectious SARS-CoV-2 Omicron variant *in vivo* in a well-established humanised mouse challenge model[1] of coronavirus infection. Challenge models are often used in viral diseases to assess the ability of a product to treat or prevent an infection.

In this study, conducted at Scripps Research, 100% of animals treated with VIRALEZE™ before and after Omicron virus challenge had no detectable virus in lung, trachea or nasal cavity up to four days after exposure. Viral load in the lungs and trachea of these VIRALEZE™-treated animals was reduced by >99.999% compared with the virus levels in saline-treated animals when assessed seven days after viral challenge with SARS-CoV-2 Omicron. Notably, animals treated with VIRALEZE™ before and after infection had no detectable Omicron virus in the blood at any stage of the study.

These impressive results for VIRALEZE™ were in contrast to control saline-treated animals, where 100% had high levels of virus detected in blood, lung, trachea and nasal cavity from as early as two days post-challenge.

Animals treated with VIRALEZE™ *only after* intranasal viral SARS-CoV-2 Omicron challenge also exhibited >99.999% reduction of virus in the lungs and trachea seven days after infection compared with saline-treated animals. This finding is important because it suggests that even when VIRALEZE™ is used after exposure to virus (e.g., you forget to use the spray before exposure to a high-risk situation), it has potential to provide significant benefit. All VIRALEZE™-treated animals also exhibited a significant reduction in proinflammatory cytokines compared with saline-treated animals, indicating reduced severity of disease.

These new findings for VIRALEZE™ indicate that it is highly effective in inactivating and blocking Omicron virus *in vivo*, resulting in reduced viral load exposure, and thereby preventing or significantly reducing infection. Furthermore, despite significant mutation of the SARS-CoV-2 virus, VIRALEZE™ provided high levels of protection against the highly

[1] This widely used, WHO recommended model (K18-hACE2 mouse) utilises a specialized strain of mouse to mimic COVID transmission in humans. Each animal is administered a large dose of virus directly into the nose, so they represent a challenging assessment tool for preventative and therapeutic agents.

infectious Omicron variant. The results of this *in vivo* study are consistent with previous *in vitro* findings where VIRALEZE™ has demonstrated high levels of activity against all SARS-CoV-2 variants tested to date, including the highly infectious Omicron, Delta, Alpha, Beta, and Gamma variants.

Starpharma CEO, Dr Jackie Fairley, commented on the results:

*"Countries around the world are experiencing significant strain in their healthcare systems as a result of Omicron outbreaks. VIRALEZE™ represents an additional tool for use alongside vaccinations in these challenging times.*

*"These latest findings show VIRALEZE™ to be highly effective against SARS-CoV-2 Omicron infection in a well-established and stringent, WHO-recognised challenge model. These results build on previously reported and published data, demonstrating that our antiviral agent SPL7013, in VIRALEZE™, retains impressive antiviral effect, even against the most infectious variants of SARS-CoV-2. Further, they show that even when used only after exposure to virus VIRALEZE™ has the potential to provide significant benefit."*

In commenting on these findings, internationally recognised virologist and leader of Starpharma's ongoing scientific collaboration at Scripps Research, Professor Philippe Gallay, said:

*"This latest virus challenge study provides further evidence that VIRALEZE™ nasal spray can protect against SARS-CoV-2 Omicron infection in the nose, lungs, and trachea in a well-established model of coronavirus infection. When administered nasally, VIRALEZE™ significantly reduced the amount of virus in the respiratory tract and in blood, and the production of pro-inflammatory cytokines.*

*"Given the extraordinary infectivity of the SARS-CoV-2 Omicron variant, which is approximately 4 times as infectious as the highly infectious Delta variant, it is particularly impressive to see VIRALEZE™ retain such highly protective effects against infection when administered either before and after, or only after challenge. These findings highlight the potential for complementary measures such as VIRALEZE™ nasal spray to help fight the ongoing pandemic, given the ability of Omicron to evade immunity from vaccines."*

VIRALEZE™ is a broad-spectrum antiviral nasal spray that has been developed by Starpharma to be applied in the nasal cavity to help reduce exposure to virus. These new data provide further *in vivo* validation that VIRALEZE™ can block and inactivate virus in the nasal cavity, and suggest that VIRALEZE™ could be used to help to protect from infection with respiratory viruses, including SARS-CoV-2, and potentially as post-exposure prophylaxis to reduce severity of viral respiratory disease.

VIRALEZE™ also has a potential role in future pandemic preparedness given that SPL7013 in VIRALEZE™ has been shown to highly effectively block a broad spectrum of respiratory viruses, including pandemic-causing viruses, such as multiple variants of SARS-CoV-2, SARS-CoV, MERS-CoV, influenza A and B viruses, and respiratory syncytial virus (RSV) *in vitro*.

Data from around the world indicate that vaccines against COVID-19 are highly effective in preventing severe disease and death. However, with the Omicron variant, many vaccinated individuals still become infected, giving the opportunity for additional variants to develop, and some people will require hospitalisation. Complementary interventions, like VIRALEZE™, that can reduce viral load at the primary site of initial infection remain important to help reduce transmission of virus from infected individuals. This is particularly relevant in the current environment where the dominant variants of SARS-CoV-2, such as Omicron, have higher transmission rates and have demonstrated evidence of vaccine escape.

In this study, conducted at Scripps Research, a K18-hACE2 mouse model[2] was used to evaluate the anti-SARS-CoV-2-Omicron efficacy of VIRALEZE™ nasal spray. This model is an established challenge model, recognised by the World Health Organization (WHO) and other researchers, for investigation of coronavirus SARS-CoV-2 infection, where the animals express the human ACE2 receptor that is responsible for mediating virus and cell receptor interactions (i.e., allowing virus to enter the cell, which leads to infection).

## Experimental Details

In this experiment, three groups of animals (N=12 per group) were used. Two groups were administered VIRALEZE™ and the third group received phosphate-buffered saline (PBS) intranasally. On Day 0, one of the VIRALEZE™ groups and the PBS group received the allocated treatment intranasally 5 minutes prior to and 5 minutes after intranasal virus challenge with the SARS-CoV-2 Omicron variant (hCoV-19/USA/MD-HP20874/2021); the second VIRALEZE™ group was treated only 5 minutes after intranasal virus challenge.[3] Animals in all groups then received the allocated treatment intranasally once daily for 6 additional days. Four animals of each group were euthanized on Day 2, Day 4 and Day 7 for assessment of viral load and cytokines.

Status of infection was determined by measuring viral load by reverse transcription quantitative real-time polymerase chain reaction (RT-qPCR) in blood samples (Day 2, 4 and Day 7); and RT-qPCR from samples of nasal cavity swabs, and lung and trachea tissue homogenates (Days 2, 4 and 7). The inflammatory status was assessed by an enzyme-linked immunosorbent assay (ELISA) cytokine panel performed on plasma (Day 2, 4 and 7).

## Results

Virus was detected in PBS-treated animals from Day 2 post-infection and the amount of virus escalated significantly over the Day 4 and Day 7 timepoints in blood, lung trachea and nasal cavity. Treatment of animals with VIRALEZE™ pre- and post-infection markedly reduced SARS-CoV-2 Omicron viral load in the lungs, trachea, and nasal cavity compared with PBS.

Animals treated with VIRALEZE™ post-infection had only very low detectable virus on Day 2, which remained at a relatively low level on Days 4 and 7, indicating a potential role for VIRALEZE™ as a treatment for the reduction of virus replication in the body once it has been established. The level of pro-inflammatory cytokines in blood was correlated with the level of virus in the lung, trachea, nasal cavity and blood. Pro-inflammatory cytokines were, therefore, reduced in animals treated with VIRALEZE™ (both treatment strategies) compared to animals treated with PBS.

Data from the study, showing viral load in lung tissue, are provided in Figure 1, below. Full data are currently being prepared for scientific publication.

[2] The Jackson Laboratory (Bar Harbor, ME, USA; Stock No. 034860)

[3] In the current study, using the highly infectious Omicron variant, we used 1000 plaque forming units (PFU) virus particle equivalents, administered directly into the nose of mice.
For comparison, virus particles in the air in medical staff areas have been estimated to be approximately 40 viral RNA copies per cubic metre[1]. Considering less infectious early pandemic strains of SARS-CoV-2, a study suggested that the number of virus particles needed to infect an individual is the equivalent of approximately 10 to 100 PFU[2].


1. Liu, Y. et al. Aerodynamic analysis of SARS-CoV-2 in two Wuhan hospitals. *Nature* **2020**, 582, 557–560.
2. Smith, S.H. et al. Aerosol persistence in relation to possible transmission of SARS-CoV-2. *Phys. Fluids* **2020**, 32, 107108.

**SARS-CoV-2 Omicron Viral Load in Lung – VIRALEZE™ vs PBS/Saline Control**

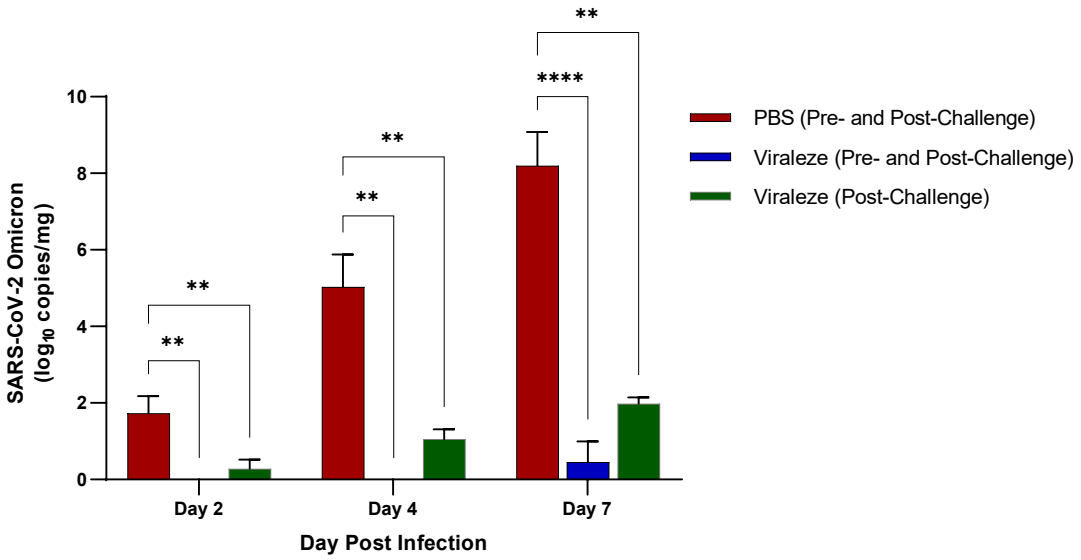


**Figure 1.** SARS-CoV-2 viral genome copies (RT-qPCR) per mg of lung in K18-hACE2 mice treated intranasally with PBS or VIRALEZE™ nasal spray pre- and post-challenge, and post-challenge only, with SARS-CoV-2 (Omicron hCoV-19/USA/MD-HP20874/2021). Columns and error bars represent mean ± SD. Statistical analyses were two-way analyses of variance (ANOVA) with Tukey multiple comparisons for PBS vs Viraleze groups. ** $p$ <0.01, **** $p$ <0.0001. Note: virus was undetectable in the Viraleze Pre- and Post-challenge group at both Day 2 and Day 4 post exposure.

## VIRALEZE™ Nasal Spray

VIRALEZE™ is a nasal spray that physically traps and blocks cold/respiratory viruses in the nasal cavity. VIRALEZE™ is applied in the nose where it forms a physical moisture barrier between viruses and the nasal mucous membrane that traps and blocks virus. VIRALEZE™ is highly stable and can be stored at room temperature.

VIRALEZE™ is registered as a medical device in more than 30 countries and is available in certain markets online. Product claims may differ by market. Starpharma markets VIRALEZE™ via commercial arrangements in countries in Europe, Asia, and the Middle East. VIRALEZE™ is not approved for sale or supply in Australia.

*VIRALEZE™ was developed with the support of $1 million in funding by the Australian Government's Medical Research Future Fund (MRFF) Biomedical Translation Bridge (BTB) Program, with support from UniQuest.*

*This study was conducted in strict accordance with protocols approved by The Scripps Research Institute Ethics Committee, the Institutional Animal Care and Use Committee, and with the recommendations in the Guide for the Care and Use of Laboratory Animals of the National Institute of Health (NIH). Starpharma is committed to upholding clear and strong bioethics principles and conducts its business in accordance with the highest standards of bioethics, throughout all areas of its business. These principles guide Starpharma in the conduct of clinical trials and the welfare of patients, the treatment of animals and the use of medical knowledge.*

**About Starpharma**

Starpharma Holdings Limited (ASX:SPL, OTCQX:SPHRY) is a global biopharmaceutical company and a world leader in the development of new pharmaceutical and medical products based on proprietary polymers called dendrimers, with programs for DEP® drug delivery, respiratory viruses and VivaGel®. Starpharma has developed VIRALEZE™, an antiviral nasal spray that is registered for sale in >30 countries, and available outside Australia in certain markets online. VIRALEZE™ is not approved for sale or supply in Australia. SPL7013 is utilised in approved products - the VivaGel® condom and VivaGel® BV. VivaGel® products have been licensed in >160 countries, are registered in >45 countries and available for sale in the UK, Europe, Japan, Southeast Asia, South Africa, Australia and New Zealand.

As a leading company in dendrimer-based drug delivery, Starpharma's proprietary drug delivery platform technology, DEP®, is being used to improve pharmaceuticals, to reduce toxicities and enhance their performance. There are numerous internal and partnered programs underway to develop DEP® versions of existing drugs, particularly in the area of anti-cancer therapies. DEP® partnerships include oncology programs with AstraZeneca, with Merck & Co., Inc., in the area of Antibody Drug Conjugates (ADCs), with Chase Sun in the area of anti-infectives and other world leading pharmaceutical companies. Starpharma's partnered DEP® programs have the potential to generate significant future milestones and royalties.

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**Disclosure**
This ASX Announcement was authorised for release by the Chairman, Mr Rob Thomas.

**Forward Looking Statements**

This document contains certain forward-looking statements, relating to Starpharma's business, which can be identified by the use of forward-looking terminology such as "promising", "plans", "anticipated", "will", "project", "believe", "forecast", "expected", "estimated", "targeting", "aiming", "set to", "potential", "seeking to", "goal", "could provide", "intends", "is being developed", "could be", "on track", or similar expressions, or by express or implied discussions regarding potential filings or marketing approvals, or potential future sales of product candidates. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no assurance that any existing or future regulatory filings will satisfy the FDA's and other authorities' requirements regarding any one or more product candidates nor can there be any assurance that such product candidates will be approved by any authorities for sale in any market or that they will reach any particular level of sales. In particular, management's expectations regarding the approval and commercialization of the product candidates could be affected by, among other things, unexpected trial results, including additional analysis of existing data, and new data; unexpected regulatory actions or delays, or government regulation generally; our ability to obtain or maintain patent or other proprietary intellectual property protection; competition in general; government, industry, and general public pricing pressures; and additional factors that involve significant risks and uncertainties about our products, product candidates, financial results and business prospects. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those described herein as anticipated, believed, estimated or expected. Starpharma is providing this information as of the date of this document and does not assume any obligation to update any forward-looking statements contained in this document as a result of new information, future events or developments or otherwise. Clinical case studies and other clinical information given in this document are given for illustrative purposes only and are not necessarily a guide to product performance and no representation or warranty is made by any person as to the likelihood of achievement or reasonableness of future results. Nothing contained in this document nor any information made available to you is, or shall be relied upon as, a promise, representation, warranty or guarantee as to the past, present or the future performance of any Starpharma product.