ASX Announcement

SPL7013 in VIRALEZE™ virucidal against Omicron

- **The antiviral agent in VIRALEZE™ antiviral nasal spray, SPL7013, achieved >99.5% reduction of virus infectivity (the maximal possible reduction) against the highly contagious Omicron variant of SARS-CoV-2**
- **SPL7013 showed potent antiviral activity and was virucidal against the Omicron variant**
- **SPL7013 outperformed other antiviral agents used in marketed nasal sprays, including iota-carrageenan and nitric oxide, in the studies conducted at The Scripps Research Institute**
- **The potent activity of SPL7013 against the Omicron variant is consistent with previous data demonstrating virucidal activity against multiple variants of SARS-CoV-2, including Delta, Alpha, Beta, Gamma, and Kappa**
- **SPL7013 has also previously demonstrated potent antiviral activity against respiratory viruses, including influenza, RSV, and viruses that cause the common cold**
- **VIRALEZE™ is registered in more than 30 countries, including in Europe, and available online in these and certain other markets**

Melbourne, Australia; 1 March 2022: Starpharma (ASX: SPL, OTCQX: SPHRY) today announced that SPL7013, the antiviral agent in VIRALEZE™ antiviral nasal spray, achieved the maximal possible reduction of virus infectivity (>95% within 1 minute of exposure and >99% within 5 minutes, achieving a maximal reduction of >99.5%) against the Omicron variant of SARS-CoV-2, in laboratory-based antiviral and virucidal assays. Testing of SPL7013 against Omicron was conducted in the laboratory of internationally recognised virologist, Professor Philippe Gallay, at The Scripps Research Institute in the US.

In the antiviral assays conducted by Scripps, the activity of SPL7013 against the Omicron variant outperformed other agents used in antiviral nasal sprays, including iota-carrageenan and heparin. SPL7013 was approximately 30 times more potent than iota-carrageenan against the Omicron variant, which is currently in multiple marketed nasal sprays, and 70 times more potent than heparin, which is currently being contemplated as a nasal spray.

This activity of SPL7013 against the Omicron variant is consistent with the antiviral and virucidal activity demonstrated (>99%) against multiple other variants of SARS-CoV-2, including the Delta, Alpha, Beta and Gamma 'Variants of Concern'. These data on the effect of SPL7013 against these other SARS-CoV-2 variants was recently presented at the major international scientific meeting, Conference on Retroviruses and Opportunistic Infections (CROI) 2022, by Prof. Gallay.[1]

The consistency and retention of SPL7013 activity does not appear to be adversely impacted by multiple spike mutations, which is thought to be due to its mechanism of action that is not reliant on specific binding sites within the spike protein.

The broad-spectrum activity of SPL7013 against multiple respiratory viruses (e.g., influenza, RSV, and cold viruses), including all nine coronavirus variants tested, is a positive feature of

[1] Gallay P, Luscombe C, Stauffer W, et al. Effect of astodrimer sodium against SARS-CoV-2 variants (α, β, γ, δ, κ) in vitro. [CROI Abstract 478]. Abstracts From CROI 2022 Conference on Retroviruses and Opportunistic Infections. CROI 2022 Abstract eBook. 2022;478.

VIRALEZE™, particularly as the SARS-CoV-2 virus mutates and challenges global public health efforts.

In commenting on the significance of these new findings, Professor Philippe Gallay from The Scripps Research Institute, said:

> *"Our antiviral studies have found that SPL7013 can abolish infection with all nine SARS-CoV-2 variants tested. These include the most highly infectious Omicron, and the virulent Delta variant.*
>
> *"In fact, it appears that SPL7013 is even better able to block the more highly infectious variants than the early variants of SARS-CoV-2. This effect appears to be due to the mechanism of action of SPL7013 that involves interaction with multiple regions of the virus spike protein. Mutations in the highly infectious virus variants appear to have introduced even more potential binding sites for SPL7013 to interact with. Omicron has over 30 mutations in the spike protein that have made it extremely highly transmissible in the community.*
>
> *"To suppress this transmission, we need to have additional tools that can block SARS-CoV-2 infection of the nose, and SPL7013 could play an important role."*

Dr Jackie Fairley, CEO of Starpharma, commented:

> *"Starpharma is pleased to see that SPL7013 is virucidal and achieved >99.5% reduction of infectious virus in the Omicron variant.*
>
> *"SPL7013 has now demonstrated impressive performance against all five 'Variants of Concern' tested, including Delta, Alpha, Beta, Gamma, and now also Omicron. The high level of activity against Omicron is entirely consistent with previous data for SPL7013, which has shown antiviral and virucidal activity in multiple viruses. This new data further illustrates SPL7013's breadth of activity and the potential real-world benefits of VIRALEZE™."*

Experimental Details

In the virucidal assays, SPL7013 was incubated with the Omicron (B.1.1.529) strain, hCoV-19/USA/MD-HP20874/2021, for 30 seconds, 1, 5, 15 or 30 minutes. Following incubation, virus was pelleted to separate and neutralise SPL7013 in solution. The treated virus was then gently re-suspended and added to Vero-E6-hACE2-TMPRSS2 cells for quantitation of infectious virus by plaque assay (plaque forming units (pfu)/mL). Virus controls, which were not exposed to SPL7013, were run in parallel.

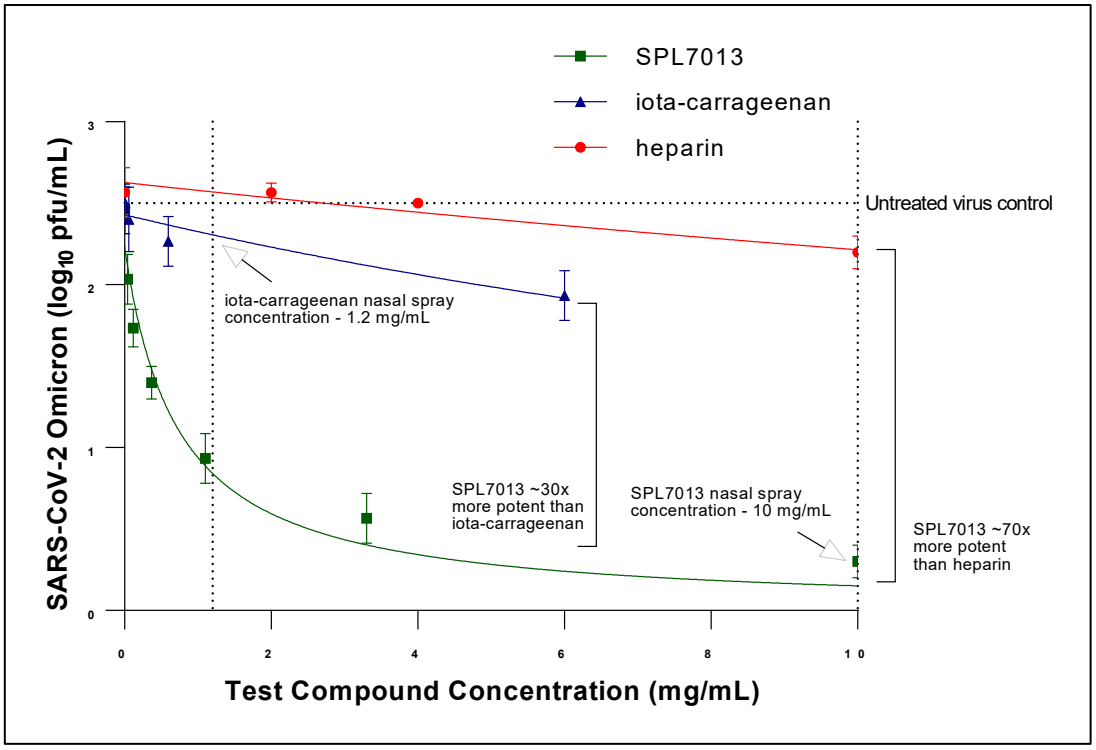
SPL7013 at 10 mg/mL (the concentration of SPL7013 in VIRALEZE™) achieved the maximum possible (>99.5%) reduction in infectious virus compared with virus control (maximal possible reduction from baseline viral titre of approximately 2.5 $\log_{10}$ pfu/mL reducing to 0 $\log_{10}$ pfu/mL) (see Table 2, below).

In the antiviral assays, SPL7013 (0.04 to 10 mg/mL), iota-carrageenan (0.006 to 6 mg/mL), the nitric oxide producing substance, S-nitroso-N-acetylpenicillamine (SNAP) (200 to 400 µM), or heparin (2 to 20 mg/mL; 1,000 to 10,000 IU/mL) were added to Vero-E6-hACE2-TMPRSS2 cells at the same time as SARS-CoV-2 Omicron virus infection. After multiple virus replication cycles, the amount of infectious virus was quantitated by plaque assay (pfu)/mL). Virus controls, which were not exposed to SPL7013 or other test compounds, were run in parallel.

SPL7013, including at the concentration used in VIRALEZE™ (10 mg/mL), achieved significantly greater reduction in virus infectivity compared with other agents tested at

concentrations reported to be used in nasal sprays (e.g., iota-carrageenan, 1.2 mg/mL) (see graph below). SPL7013 was approximately 30 and 70 times more potent than iota-carrageenan and heparin, respectively, against the Omicron variant (expressed as the concentration of compound effectively inhibiting 50% of virus infectivity, EC_{50}) (see Table 1, below).

Infectivity of SARS-CoV-2 Omicron variant (log_{10} pfu/mL) in the presence of increasing concentrations of SPL7013, iota-carrageenan, and heparin (mg/mL)



Curves calculated using GraphPad Prism 9.3.1; SNAP (nitric oxide) data not shown in graph due to different concentration units

Table 1: Potency (EC_{50}) of SPL7013, iota-carrageenan, heparin and SNAP (nitric oxide) against SARS-CoV-2 Omicron Variant

Test Compound	SARS-CoV-2 Omicron EC_{50} (mg/mL)
SPL7013	0.73
iota-carrageenan	22.5
heparin	53.6
SNAP (nitric oxide)	656 µM

EC_{50}, concentration of test compound achieving 50% effective reduction of virus infectivity; EC_{50} calculated using GraphPad Prism 9.3.1

Table 2: Percent reduction in infectious SARS-CoV-2 Omicron Variant after incubation with SPL7013 at 10 mg/mL (concentration in VIRALEZE™)

Virus:SPL7013 Incubation Time	Percent Reduction in Infectious Omicron vs Virus Control^
30 seconds	90%
1 minute	95%
5 minutes	99.2%
15 minutes	99.5%
30 minutes	>99.6%†

^ virus without exposure to SPL7013; † Maximal possible reduction from baseline viral titre of approximately 2.5 $\log_{10}$ pfu/mL reducing to 0 $\log_{10}$ pfu/mL

VIRALEZE™ Antiviral Nasal Spray

VIRALEZE™ is a broad-spectrum antiviral nasal spray. The antiviral agent in VIRALEZE™, referred to as SPL7013, has been shown to have potent antiviral and virucidal activity in multiple respiratory viruses (including influenza and RSV), including virucidal activity of more than 99% in multiple variants of SARS-CoV-2, in laboratory studies. VIRALEZE™ is applied in the nose to provide a physical barrier - between viruses and the nasal mucous membrane - that traps and irreversibly inactivates virus. Importantly, the mechanism of action of VIRALEZE™ means that mutations of the spike protein that make SARS-CoV-2 more infectious, as occurred for the Delta strain, appear to make the virus more susceptible to trapping and blocking by SPL7013.

VIRALEZE™ is registered in more than 30 countries, including Europe, Vietnam, India, New Zealand, and Saudi Arabia, and available in certain markets online. VIRALEZE™ is partnered with LloydsPharmacy in the UK, ADMENTA Italia Group in Italy, HealthCo/TBL in Vietnam, and E&N in countries in the Middle East. VIRALEZE™ is not approved for sale or supply in Australia.

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

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 respiratory viruses, DEP® drug delivery and VivaGel®. Starpharma has developed VIRALEZE™, an antiviral nasal spray that is registered for sale in the Europe, Vietnam, India, Saudi Arabia, and New Zealand, 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, South East 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 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.