ASX Announcement

VIRALEZE SPL7013 virucidal (>99.99%) against Delta variant

- **New antiviral testing demonstrates SPL7013, the antiviral agent in VIRALEZE™ nasal spray, has potent virucidal activity against the globally significant Delta variant of SARS-CoV-2, reducing infectivity of the virus by >99.99% after 30 seconds of exposure**
- **The Delta variant of SARS-CoV-2 is believed to be the most transmissible variant yet, and has spread to at least 102 countries worldwide[1] resulting in multiple outbreaks in Europe/UK, Australia, India, Indonesia, US, and Japan**
- **The Delta variant is classified by the World Health Organisation (WHO) as a 'Variant of Concern' because there is evidence of increased transmissibility, immune escape, and therapeutic escape compared with the original SARS-CoV-2 strain[2]**
- **SPL7013, the antiviral agent in VIRALEZE™, has now been shown in laboratory studies to be virucidal against all four coronavirus SARS-CoV-2 Variants of Concern: Alpha, Beta, Gamma and Delta**
- **Testing also confirmed potent virucidal activity of SPL7013 against the closely related Kappa SARS-CoV-2 variant**
- **These latest data further illustrate the broad-spectrum antiviral activity of SPL7013, which has been demonstrated against multiple respiratory viruses, including influenza and RSV, as well as its consistent and potent activity against multiple SARS-CoV-2 variants**
- **VIRALEZE™ antiviral nasal spray is registered for sale in Europe and India, and available in certain markets online. VIRALEZE™ is partnered with LloydsPharmacy in the UK, and Starpharma is in advanced discussions with potential commercial partners in India, Europe, and multiple other regions. VIRALEZE™ is not registered for sale or supply in Australia**
- **Starpharma was awarded $1 million in funding in September 2020 for the development of VIRALEZE™ by the Australian Government's Medical Research Future Fund (MRFF) under the Biomedical Translation Bridge (BTB) Program**

Melbourne, Australia; 27 July 2021: Starpharma (ASX: SPL, OTCQX: SPHRY) today announced new data demonstrating that SPL7013, the antiviral agent in VIRALEZE™ nasal spray, is active against the highly transmissible **Delta** variant of SARS-CoV-2, achieving more than 99.99% reduction of infectious virus in laboratory-based virucidal assays.

The antiviral testing of SPL7013 was conducted in the laboratory of internationally recognised virologist, Professor Philippe Gallay, at The Scripps Research Institute in the US, where previous studies have also demonstrated potent antiviral and virucidal activity of SPL7013 against multiple variants of SARS-CoV-2, including the globally important **Alpha**, **Beta** and **Gamma** 'Variants of Concern'. The Scripps Research Institute has previously been recognised as the most influential research institution in the world.[3]

[1] https://cov-lineages.org/lineage.html?lineage=B.1.617.2
[2] https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/
[3] Nature Index 2017 Innovation, Vol. 548 No. 7666 ppS3-40

The most recent testing also demonstrated potent virucidal activity of SPL7013 against the Kappa variant of SARS-CoV-2. For the Delta and Kappa variants, SPL7013 achieved >99.99% and >99.9% reduction of infectious virus, respectively, within 30 seconds of exposure.

The virucidal activity of SPL7013 against the Delta and Kappa variants in the current assays is consistent with the activity demonstrated in the original US strain of SARS-CoV-2 (2019-nCoV/USA-WA1/2020) (i.e., >99.9% reduction of infectious virus vs virus control)[4]. These new findings indicate that there is no loss of potency for SPL7013 against the Delta and Kappa variants compared with earlier strains of the virus. The consistency and retention of SPL7013's activity is thought to be due to its mechanism of action, which is not reliant on specific binding sites within the spike protein.

The broad-spectrum activity of SPL7013 against multiple viruses and retention of activity in multiple coronavirus variants are important features for VIRALEZE™, particularly as new variants continue to emerge and challenge global public health efforts.

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

"SARS-CoV-2 variants continue to emerge and dominate new infections worldwide. These variants have changes in several viral proteins, including in the spike protein that is essential for the virus to infect its host cell.

"It is remarkable that SPL7013 has demonstrated potent anti-SARS-CoV-2 activity against the broad-spectrum of Variants of Concern, Alpha, Beta, Gamma, and now importantly Delta, and Variant of Interest, Kappa, in vitro. SPL7013 acts as a barrier to viral infection and its broad-spectrum activity demonstrates its resilience against a rapidly changing target.

"SPL7013 in a nasal spray allows for direct delivery to the nose and creates an additional barrier at the gateway of respiratory viral infections, providing reinforcement to the immune system and potentially protecting against pathogen invasion and illness."

The Delta variant has been identified in at least 102 countries[5] and has been linked to a recent resurgence of COVID-19 cases in multiple regions, including India, Indonesia, Australia, Japan, US, Europe, and the UK.'[6]

The Delta variant has been reported to be about 60% more transmissible than the already highly infectious Alpha variant[7], and is now the most common variant in India and the UK, where it accounts for more than 90% of new cases.[8] The Delta variant also appears to be more problematic in children and younger adults, and in the UK is the most dominant strain and spreading through schools.[9]

Dr Jackie Fairley, CEO of Starpharma, commented: *"We are very pleased to confirm the rapid virucidal activity of SPL7013, with greater than 99.99% reduction of infectious virus in just 30 seconds against the Delta variant.*

"The Delta variant continues to challenge public health responses worldwide – most recently triggering lockdowns and emergency restrictions in Australia, Japan, and Indonesia.

[4] Paull, J.R.A. et al. Virucidal and antiviral activity of astodrimer sodium against SARS-CoV-2 *in vitro* (2021). Antiviral Research.
[5] https://cov-lineages.org/lineage.html?lineage=B.1.617.2
[6] https://covariants.org/variants/21A.Delta
[7] https://www.nature.com/articles/d41586-021-01696-3
[8] https://covariants.org/variants/21A.Delta
[9] https://www.bmj.com/content/373/bmj.n1445

"SPL7013, the active in VIRALEZE™, has a deep pedigree as an antiviral compound, with consistent and compelling broad-spectrum activity against multiple respiratory viruses and now multiple variants of SARS-CoV-2."

The importance of the Delta variant in the fight against COVID-19 was illustrated recently during an interview where Dr Anthony Fauci, Director of the National Institute of Allergy and Infectious Diseases, at the US National Institutes of Health said:

"Similar to the situation in the UK, the Delta variant is currently the greatest threat in the US to our attempt to eliminate COVID-19."[10]

Experimental Details

In this experiment, SPL7013 at concentrations ranging from 1.1 to 30 mg/mL was incubated with SARS-CoV-2 viruses for 30 seconds, 1 minute, 5 minutes, 15 minutes or 30 minutes:

- Delta (B.1.617.2) strain, hCoV-19/USA/PHC658/2021
- Kappa (B.1.617.1) strain, hCoV-19/USA/CA-Stanford-15_S02/2021
- US strain, 2019-nCoV/USA-WA1/2020

Following incubation, virus was pelleted to separate and neutralise SPL7013 in solution. Virus was then gently re-suspended and added to Vero-E6 cells for infection. After 6 hours, virus and compound were removed, and cells were left for multiple virus replication cycles. Supernatant was removed and assayed for the amount of infectious virus by plaque assay (plaque forming units/mL). Virus controls, which were not exposed to SPL7013, were run in parallel.

SPL7013 at 10 mg/mL (the concentration of SPL7013 in VIRALEZE™) resulted in >99.99% and >99.9% reduction in infectious virus compared with virus control within 30 seconds for the Delta and Kappa variants, respectively. Percent reductions of infectious virus achieved with 10 mg/mL SPL7013 are shown in the table below.

Virus: SPL7013† Incubation Time	Percent Reduction of Infectious Virus vs Virus Control^					
	US	Alpha	Beta	Gamma	Delta	Kappa
30 seconds	>99.9%	>99.9%	>99%	>99%	>99.99%	>99.9%
1 minute	>99.9%	>99.9%	>99%	>99%	>99.99%	>99.9%
5 minutes	>99.9%	>99.99%	>99.9%	>99.9%	>99.99%	>99.9%
15 minutes	>99.99%	>99.99%	>99.99%	>99.99%	>99.999%	>99.99%
30 minutes	>99.99%	>99.99%	>99.99%	>99.99%	>99.999%	>99.99%

† 10 mg/mL SPL7013; ^ virus without exposure to SPL7013

VIRALEZE™ Antiviral Nasal Spray

VIRALEZE™ contains SPL7013, which has been shown in laboratory studies to inactivate a broad spectrum of respiratory/cold viruses, including influenza, RSV, SARS, and MERS. VIRALEZE™ is registered for sale in Europe and India. VIRALEZE™ is not registered for sale or supply in Australia.

SPL7013 is also included in products registered in >45 countries and available for sale in the UK, Europe, Japan, South East Asia, Australia and New Zealand.

[10] https://www.cnbc.com/2021/06/28/how-the-uk-with-the-delta-variant-is-a-blueprint-for-the-us.html

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. Delivered by MTPConnect, the Australian Government's BTB program is a $22.3 million MRFF initiative that provides up to $1 million in matched funding to nurture the translation of new therapies, technologies and medical devices through to proof of concept to turn innovative medical ideas into reality.

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 UK/Europe and India, and available 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® BV has been licensed in >160 countries, is 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.