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ASX Announcement

Viraleze shows antiviral efficacy in COVID-19 patients

Summary:

- Results from the Viraleze™ post-market, placebo-controlled study in participants with COVID-19 (94% vaccinated, median 3 vaccine doses) have demonstrated antiviral efficacy, with effects more pronounced in patient groups who may be at higher risk.
- Viraleze™ achieved a statistically significant reduction in SARS-CoV-2 viral load, the primary endpoint of the study, in the cohort of participants aged 45 and over (N=118, p=0.017).
- Less than 24 hours after starting dosing, Viraleze™ reduced SARS-CoV-2 viral load in the nose by 80% from baseline in participants aged 65 and over (N=50, p=0.008). In contrast, viral load in the placebo arm for this age group remained unchanged from baseline to day 2.
- Viraleze™ reduced viral load in the full study population including all patient age groups (N=197), although the difference vs placebo was not statistically significant.
- Viraleze™ demonstrated consistent antiviral effects resulting in clinical benefits across multiple other endpoints, including increased SARS-CoV-2 viral clearance rate, reduced time to negative PCR[1] test and improvement in COVID-19 symptoms, including recovery from loss of smell.
- Viraleze™ demonstrated a favourable safety profile and was well-tolerated.
- The benefits of Viraleze™ were more pronounced in older participants and have potential relevance to older individuals who are typically more susceptible to respiratory infection and disease.
- These findings are consistent with Starpharma's nonclinical *in vivo* and *in vitro* studies of Viraleze™ in SARS-CoV-2 and other cold/respiratory viruses, including influenza, and provide further support for Viraleze™ in helping to protect against respiratory infection and disease. Reduced viral load and increased viral clearance have the potential to protect against infection, improve symptoms, and reduce onward transmission.

Melbourne, Australia; 29 January 2024: Starpharma (ASX: SPL, OTCQX: SPHRY) today announces the results of the post-market[2] clinical study of Viraleze™ nasal spray in participants with COVID-19, demonstrating that Viraleze™ reduced SARS-CoV-2 viral load in the nose, increased the rate of virus clearance from the nose, improved key symptoms of COVID-19, including loss of smell (anosmia), and was well-tolerated.

The post-market, double-blind, placebo-controlled clinical study enrolled a total of 222 participants eligible for safety analyses, with 197 of these participants having laboratory-confirmed SARS-CoV-2 infection and eligible for efficacy analyses. Participants were randomised in a 1:1 ratio and self-administered Viraleze™ or a placebo nasal spray four times daily for seven days.

The results from this study provide significant clinical evidence of the performance of Viraleze™ in humans that will support regulatory processes for the transition to the new European Medical Device Regulations (MDR), which will come into full effect in 2029. The positive data will also support ongoing marketing and commercial activities for the product.

SARS-CoV-2 Viral Load

Viraleze™ achieved a statistically significantly lower level of SARS-CoV-2 viral load[3] in the nose over the 7-day treatment period, which was the primary endpoint of the study, than a placebo nasal spray in the cohort of participants aged 45 years and over (N=118, p=0.017).

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[1] Polymerase chain reaction.
[2] A post-market study is a study carried out after a product has been authorised to obtain further information, such as safety, efficacy, or risk profile. In this case, the study was required to provide data on the efficacy of Viraleze™ to support the transition to the new EU Medical Device Regulations (MDR), which will come into full effect in 2029.
[3] Viral load expressed as area under the curve (AUC) of nasal swab SARS-CoV-2 viral load (reverse transcription quantitative real-time polymerase chain reaction [RT-qPCR]) from Day 1 through Day 8 (log_{10} RNA copies/mL*Day).

The reduction in viral load for Viraleze™ was also statistically significant compared with placebo for the cohorts of participants aged 50 and over (N=101, p=0.018), 55 and over (N=84, p=0.024), 60 and over (N=66, p=0.003), and 65 and over (N=50, p=0.005). Notably, the magnitude of the reduction in viral load by Viraleze™ compared with placebo increased with age.

Viraleze™ reduced SARS-CoV-2 viral load in the nose by 80% from baseline in less than 24 hours after starting dosing in the group of patients aged 65 and over, whereas viral load in the placebo group remained unchanged from baseline to day 2 (p=0.008).

Viraleze™ reduced viral load compared with placebo in the full study population including all patient age groups (N=197), although this difference was not statistically significant. Of note, treatment compliance and vaccination rates were lowest in participants aged under 40.

Dr Stephen Winchester, Consultant Medical Virologist at Frimley Health NHS Foundation Trust and Principal Investigator of the Viraleze™ clinical study at Ashford and St Peter's Hospitals NHS Foundation Trust in the UK, commented:

"I am very impressed by these clinical data demonstrating the ability of Viraleze nasal spray to accelerate SARS-CoV-2 RNA clearance and recovery from clinically important symptoms such as anosmia in these fully vaccinated participants with COVID-19.

"The positive SARS-CoV-2 RNA clearance outcomes and evidence of clinical benefit in cohorts of older participants indicate that Viraleze could potentially be of significant benefit in people over 45 years of age to support their vaccine responses.

"Viraleze was very well tolerated and demonstrated no increase in side effects compared with the placebo.

"Based on these data, Viraleze, which is a broad-spectrum nasal spray, could have clinical benefit for protection against infection and treatment of individuals, as well as infection control of populations."

The significant reduction in viral load achieved with Viraleze™ in older age groups in this clinical study has particular relevance for older age groups in the wider population and potentially for immunocompromised groups, such as patients receiving chemotherapy or other immunosuppressive treatments and transplant recipients. Older age groups can be more susceptible to respiratory infections and disease due to the gradual weakening of the immune system with age and underlying health conditions[4,5]. In the Viraleze™ study, 60% of participants were aged 45+, representing a significant proportion of the study population.

The study also demonstrated a more rapid rate of viral clearance for Viraleze™, leading to an approximately 66% greater reduction in viral load compared with placebo between days 2 and 6 of treatment in participants of all ages, and the difference was statistically significant (-0.66 vs -0.54 logs per day, respectively, p=0.035, N=197).

Viral load and viral clearance rate are clinically important determinants of the severity and prognosis of respiratory viral infections, including SARS-CoV-2, and have been shown to be key drivers of transmission[6,7].

The time to recording a negative SARS-CoV-2 PCR test was faster for Viraleze™ compared with placebo in all cohorts of 45, 50, 55, 60 and 65 years of age and older, and these differences were statistically significant (p values [log rank] ranging from 0.014 to 0.048).

COVID-19 Symptoms

Although most participants in the study had a mild form of COVID-19, likely as a result of being vaccinated, the proportion of participants with resolution of COVID-19 symptoms was higher for

[4] Keilich SR, et al. Diminished immune responses with aging predispose older adults to common and uncommon influenza complications. *Cell Immunol*. 2019;345:103992. doi: 10.1016/j.cellimm.2019.103992.
[5] Watson A, Wilkinson TMA. Respiratory viral infections in the elderly. *Ther Adv Respir Dis*. 2021;15:1753466621995050. doi:10.1177/1753466621995050.
[6] Marks M, et al. Transmission of COVID-19 in 282 clusters in Catalonia, Spain: a cohort study. *Lancet Infect Dis*. 2021;21(5):629-636. doi:10.1016/S1473-3099(20)30985-3.
[7] Puhach O, et al. Infectious viral load in unvaccinated and vaccinated individuals infected with ancestral, Delta or Omicron SARS-CoV-2. *Nat Med* 2022;28:1491–1500. doi:10.1038/s41591-022-01816-0.

Viraleze™ compared to placebo across all categories of symptoms assessed (*i.e.,* nose, throat, eyes, chest/respiratory, gastrointestinal and systemic)[8], but not statistically significant.

Loss of smell (anosmia), a common side effect of COVID-19 that also occurs in some other respiratory infections, such as influenza, is related to damage to the olfactory sensory neurons following viral infection[9]. Loss of smell resolved more rapidly in participants using Viraleze™ compared with placebo. The percentage of participants reporting a loss of smell at any time after starting study treatment was also markedly lower in the Viraleze™ group compared with placebo. These differences were statistically significant in participants aged 55 and over (28.9% vs 51.1%, p=0.047) and 65 and over (18.2% vs 51.9%, p=0.019). Differences were borderline significant in the age groups 45+, 50+ and 60+.

After 7 days of using Viraleze™, the percentage of participants reporting continued loss of smell at Day 8 was markedly lower in the Viraleze™ group compared with the placebo group (see Figure 1).

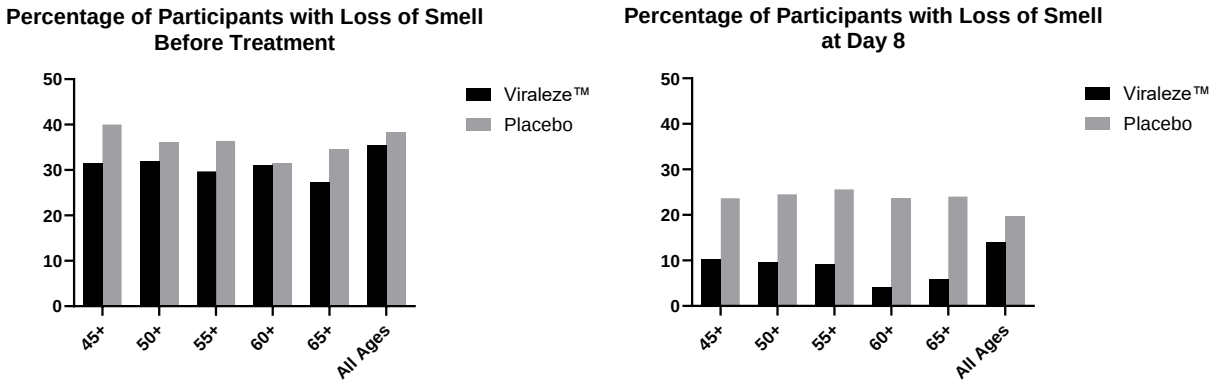

Figure 1. Percentage of participants with loss of smell (anosmia) before treatment and at Day 8 by age group

In participants aged 55 and over and 60 and over who had throat-related symptoms (scratchy or itchy throat, sore or painful throat and difficulty swallowing) at baseline, the proportion of Viraleze™ participants with resolution of these symptoms at day 8 was significantly higher compared to placebo (55+: 83.9% vs 56.4%, p=0.020; 60+: 86.4% vs 54.8%, p=0.019).

Professor George Kinghorn OBE MD FRCP, retired Consultant Physician and Clinical Research Director in Communicable Diseases, and Starpharma's independent medical representative for the Viraleze™ study, commented:

"These clinical data for Viraleze are very promising and indicate a consistent antiviral effect most significant in people aged 45 years and over. The antiviral effects of Viraleze, including reduced viral load and more rapid viral clearance, are of potential importance in reducing the transmission of infections. The study results also provide evidence of clinical benefit of Viraleze in terms of reduced duration of symptoms, particularly in the older age groups. The safety results indicate that Viraleze is very well tolerated and without significant adverse events.

"While Viraleze has the potential to help protect people from becoming infected with SARS-CoV-2 and other respiratory infections, the demonstration of a significant treatment benefit in participants already infected with COVID-19 is encouraging.

"Collectively, the efficacy and safety results indicate a favourable risk-benefit profile for Viraleze."

[8] Symptoms were assessed using the fully validated inFLUenza Patient-Reported Outcome Plus (FLU-PRO© Plus) symptoms questionnaire (Richard SA, Epsi NJ, Pollett S, et al. Performance of the inFLUenza Patient-Reported Outcome Plus (FLU-PRO Plus) Instrument in Patients with Coronavirus Disease 2019. *Open Forum Infect Dis*. 2021;8(12):ofab517. doi:10.1093/ofid/ofab517)
Symptoms in each category: i) Nose: runny or dripping nose, congested or stuffy nose, sneezing and sinus pressure; ii) Throat: scratchy or itchy throat, sore or painful throat and difficulty swallowing; iii) Eyes: teary or watery eyes, sore or painful eyes and eyes sensitive to light; iv) Chest/Respiratory: trouble breathing, chest congestion, chest tightness, dry or hacking cough, wet or loose cough, coughing and coughed up mucus or phlegm; v) Gastro-intestinal: nausea, stomach-ache, vomit and diarrhoea; vi) Systemic: felt dizzy, head congestion, headache, lack of appetite, sleeping more than usual, body aches or pains, weak or tired, chills or shivering, felt cold, felt hot and sweating.

[9] Meinhardt J, et al. Olfactory transmucosal SARS-CoV-2 invasion as a port of central nervous system entry in individuals with COVID-19. *Nat Neurosci*. 2021;24(2):168-175. doi:10.1038/s41593-020-00758-5.

Safety Results

The study also confirmed the favourable safety profile of Viraleze™. Adverse events (AEs) were reported in 16/109 (14.7%) of Viraleze™ participants and 15/113 (13.3%) of placebo participants. The vast majority of AEs in each group were of mild severity, and very few participants (4/222, 1.8%) had AEs that were considered possibly related to study treatment with either Viraleze™ or placebo.

Starpharma's Chief Executive Officer, Cheryl Maley, commented:

"The clinical study on Viraleze™ has shown positive antiviral efficacy in participants with COVID-19. These results are consistent with Starpharma's nonclinical studies, which also demonstrated that Viraleze™ protected against infection in a humanised mouse challenge model of COVID-19.

"SPL7013 in Viraleze™ has also been shown to have virucidal effects against all tested strains of SARS-CoV-2, including recently identified variants, with reductions of over 99.9% of infectious virus in laboratory studies. Viraleze™ has also demonstrated significant antiviral effects in vitro against a wide range of other respiratory viruses, including influenza viruses, respiratory syncytial virus (RSV), and common cold viruses, including human coronaviruses. Starpharma is grateful to the Principal Investigator of the study, Dr Stephen Winchester, and the Research and Development team at St Peter's Hospital in the UK for their efforts in conducting the study, as well as all the participants who took part in the study, for their time and effort in contributing to valuable scientific research."

Viraleze™ Nasal Spray

Developed by Starpharma, Viraleze™ is a topical nasal spray that physically traps and blocks a broad spectrum of cold/respiratory viruses in the nasal cavity. Viraleze™ is applied in the nose, where it forms a physical barrier between viruses and the nasal mucous membrane that traps and blocks virus.

Starpharma and its commercial partners have registered Viraleze™ in over 35 countries, including the UK and Europe. Product claims may differ by market. Starpharma markets Viraleze™ via commercial partner arrangements and online in certain markets. Viraleze™ is not approved for use or supply in Australia.

About Starpharma

Starpharma Holdings Limited (ASX: SPL, OTCQX: SPHRY) is a world leader in dendrimer technology for medical applications. As an innovative Australian biopharmaceutical company, Starpharma is focused on developing and commercialising novel therapeutic products that address significant global healthcare needs. Starpharma boasts a strong portfolio of products, partnerships, and intellectual property.

Starpharma's innovative technology is based on proprietary polymers called dendrimers, which are precise, synthetically manufactured, nanoscale molecules. The unique properties of dendrimers – including their size, structure, high degree of branching, polyvalency, and water solubility – are advantageous in medical and pharmaceutical applications.

Starpharma uses its dendrimer technology to develop novel therapeutics and to improve the performance of existing pharmaceuticals. Starpharma's portfolio includes multiple clinical-stage oncology products, which utilise its Dendrimer Enhanced Product ('DEP®') drug delivery technology, and marketed products, including VIRALEZE™ and VivaGel® BV, which utilise SPL7013, a proprietary dendrimer with antimicrobial properties.

Starpharma's DEP® drug delivery platform is being used to enhance the effectiveness of existing and novel therapies and to reduce drug-related toxicities through controlled and specified drug delivery.

In addition to Starpharma's internal DEP® programs, Starpharma has multiple DEP® partnerships with international biopharmaceutical companies, including AstraZeneca (oncology), MSD (Antibody-Drug Conjugates), Chase Sun (anti-infectives), and other world-leading pharmaceutical companies. Due to the broad applicability and optionality of Starpharma's DEP® platform, partnered DEP® programs have the potential to generate significant future milestones and royalties.

Starpharma's topical nasal spray, Viraleze™, is registered in over 35 countries, including Europe, the UK, and Asia. Starpharma's novel non-antibiotic vaginal gel, VivaGel® BV, for the treatment of bacterial vaginosis (BV) and prevention of recurrent BV, is registered in more than 50 countries, including in the UK, Europe, Southeast Asia, South Africa, Australia and New Zealand.

For more information about Starpharma, visit www.starpharma.com or connect with Starpharma on LinkedIn.

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Disclosure
This ASX Announcement was authorised for release by the Chair, 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", "outlook", 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 commercialisation 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 materialise, 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 future performance of any Starpharma product.