# SPONTAN® achieves positive primary and secondary clinical study results

**7 June 2024**

## Highlights:

- **Initial results show SPONTAN® achieves rapid absorption and faster onset of action compared to oral PDE5 inhibitors (i.e., vardenafil, sildenafil, tadalafil)**
- **SPONTAN's nasal spray technology delivered a similar amount of drug (Cmax) at half the dose of the oral PDE5 and was significantly faster**
- **Better safety profile for SPONTAN compared to oral PDE5 dosing**
- **Positive data results will be used for regulatory filings in key markets**
- **Critical Company milestone showing that SPONTAN could disrupt the global PDE5 market**



**LTR Pharma Limited** (**ASX:LTP**) ("**LTR Pharma**", "the **Company**") is very pleased to announce extremely positive initial results from its pivotal bioequivalence clinical study of SPONTAN® Nasal Spray treatment of Erectile Dysfunction ("the **Study**").

Initial data from the Study shows that SPONTAN reached the same Cmax (maximum concentration) level as an oral administration, depite being administered at a lower dose. This was achieved in as little as 9 minutes with an average of 12 minutes across the Study compared to 56 minutes (Tmax) in patients receiving oral treatment. The statistical analysis of the data is yet to be completed and further information will be disclosed in a final results announcement.

Importantly, SPONTAN also demonstrated an improved safety and tolerance profile, providing reassurance and confidence in its use. The Study also showed better consistency in response for the nasal spray patient cohort, thus achieving both primary and secondary endpoints.

**LTR Pharma Chairman, Lee Rodne, said:** *"The initial results from our pivotal clinical study are encouraging. SPONTAN has the potential to make a significant impact on the global PDE5 inhibitor market, providing men with a more convenient and effective solution for erectile dysfunction (ED). This Study further underscores the rapid onset of action of SPONTAN and represents a significant advancement over existing gold-standard oral therapies, which can take over an hour to take effect. This milestone brings us closer to our mission of enhancing men's health and quality of life."*

## Primary and Secondary Endpoints

The study was a randomized, open-label, single-dose, two-period, two-treatment, cross-over study. The Study's primary objective was to evaluate the relative bioavailability of SPONTAN nasal spray (5 mg vardenafil) compared to vardenafil tablets (10 mg vardenafil) in 18 healthy adult male subjects aged 18-45 years of age under fasting conditions. This is a crucial measure of the drug's effectiveness and how much is absorbed into the bloodstream. The Study also assessed the safety and tolerability of SPONTAN, further confirming its potential as a safe and effective treatment option.

The results demonstrated that SPONTAN achieves rapid absorption and faster onset of action at a substantially lower dose compared to traditional PDE5 oral tablets, significantly improving bioavailability and drug dosing. By bypassing the digestive system, the intranasal delivery technology of SPONTAN results in a faster effect within an average of 12 minutes, with a Tmax range of 9 to 15 minutes. This is compared to the Tmax in oral administered patients of 56.4 minutes with the longest time in the oral dosed cohort of 150 minutes. The patients receiving SPONTAN also experienced greater consistency in their results compared to the oral-treated patients.

The Study also showed no significant difference between the Cmax in either the nasal or oral-treated patients. Given the Cmax and Tmax time, the Study illustrates that the same effect for a PDE5 inhibitor can be achieved using SPONTAN. HOWEVER, SPONTAN was able to achieve this in 9 minutes, which is significantly faster than oral administration.

Patients receiving the SPONTAN nasal spray ED treatment showed no serious adverse events, further emphasising the strong safety profile of SPONTAN. One patient withdrew from the study due to an adverse event with the oral tablet. No patients withdrew from the SPONTAN treatment arm.

Based on these promising results, LTR Pharma plans to use this data to support an expedited 505(b)(2) regulatory filing in the United States and subsequent filings in Australia and other key markets including in Europe, Asia, MENA and LATAM. This strategic move will enable the Company to bring SPONTAN to international markets, meeting the high demand for new and innovative ED treatments globally.

The successful Study aligns with LTR Pharma's mission to commercialise a first-in-class, rapid-onset ED treatment, reinforcing the Company's commitment to advancing men's health.

## Clinical study overview

**Title:** Randomized, Open-label, Single-dose, Two-period, Two-treatment, Cross-over Study Comparing the Pharmacokinetics of Vardenafil Following Administration of SDS-089 Nasal Spray and Vardenafil Tablet in Healthy Male Adult Subjects.

**Number of subjects:** Total of 18 healthy males.

**Study protocol**

The aim of the study was to enrol 18 healthy makes into two cohorts (oral and nasal administration) of vardenafil and compared the pharmacokinetics (Cmax) and time to Cmax (Tmax) as a direct comparison of the two administration routes. No placebo was used in the study. Each patient had a pre-dosing screening period of 28 days. Each patient was dosed under fasting conditions, that being fasting from food overnight for at least 10 hours until 4 post post-dosing. Post the initial dosing (either oral or nasal), each patient crossed over to the other cohort (cross-over study) and received the other form of dosing (nasal then oral OR oral then nasal). Each patient had a 3 day ‘wash-out period before their second, alternative delivery method dosing. Blood samples were taken from the patients one hour before dosing, then 17 samples were taken post dosing starting 2 minutes post dosing through to 24 hours post dosing. Adverse and serious adverse events were monitored. Blood samples were analysed for drug levels (Cmax) across all blood samples. See Figure 1 for study design.

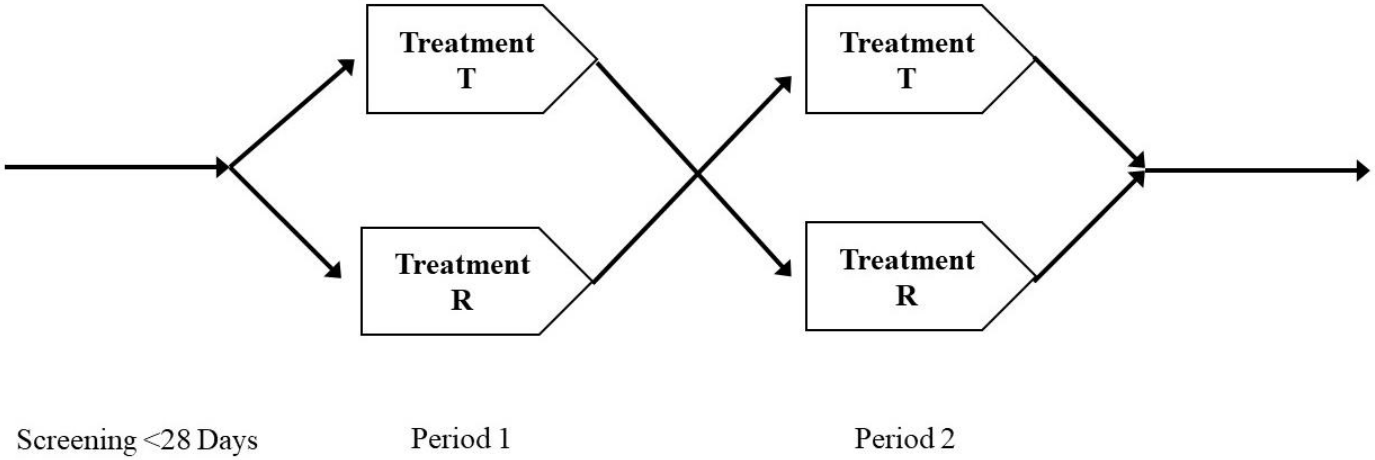


**Figure 1: Schematic Diagram of Study Design**
Treatment T (Test Product): SDS-089 nasal spray, 5 mg vardenafil
Treatment R (Reference Product): Vardenafil tablet, 10 mg vardenafil.

**Study Primary Objective**
To assess the relative bioavailability of vardenafil following administration of SDS-089 nasal sprays (single 2.5 mg vardenafil spray in each nostril for a 5 mg dose) compared to vardenafil tablet (10 mg vardenafil) in healthy adult male subjects under fasting conditions.

**Study Secondary Objectives**
To assess the single dose safety and tolerability of SDS-089 nasal sprays (5 mg) compared to vardenafil tablet (10 mg) in healthy adult subjects.

**Data**

**Table 1.** Complete data pre statistical analysis of for the nasal and oral delivery of vardenafil in 18 patients, examining the Cmax and Tmax responses in the study participants.

| Parameter | 5mg SPONTAN (Nasal) | 10mg vardenafil (oral) |
|---|---|---|
| Cmax | 12.885 ± 9.072 | 16.737 ± 14.504 |
| Tmax (min) | 12.12 ± 2.556 | 56.39 ± 30.684 |
| Tmax range (min) | 9 – 15 | 56.39 ± 30.684 |
| Serious Treatment Emergent Adverse Event | 0 | 0 |
| Treatment Emergent Adverse Event leading to discontinuation | 0 | 1 |
| Grade 3 or 4 SAEs | 0 | 0 |

LTR Pharma in collaboration with its CRO will complete statistical analysis over the coming month with a view to releasing the results in a future company announcement. This analysis will compare the statistical difference between the Cmax and Tmax results above.

The safety profile of the two doses were comparable, however the oral deliver did result in one participant withdrawing due to treatment adverse events. No serious adverse events were observed in either cohort.

**Conclusions**

In conclusion, both Vardenafil nasal spray and tablet formulations show variability in peak concentrations, with the tablet form exhibiting a wider range. This variability must be taken into account when considering these formulations for therapeutic use. The nasal administration was considerably faster to Cmax. Both administration routes showed good safety profiles, however the tablets did have one withdrawal. No Serious Adverse Events were observed with SPONTAN.

**Comparative Analysis**

- Variability: The nasal spray and tablet forms show variability in Cmax values, but the tablet form has a significant wider range.
- Clinical Implications: The variability in Cmax values could imply differing clinical responses among patients, necessitating careful monitoring and potential dose adjustments to achieve the desired therapeutic effect.

**-ENDS-**

This announcement has been approved by the Board of Directors.

**About LTR Pharma**

LTR Pharma is focused on improving men's health, physically and mentally, through the commercialisation of an innovative nasal spray treatment for Erectile Dysfunction. ED is a pressing health issue for millions of men that can negatively impact self-esteem and relationships across multiple age brackets. LTR Pharma's lead product, SPONTAN, is set apart from existing ED therapies by its mechanism of action – intranasal delivery technology of a PDE5 inhibitor. The nasal cavity is a highly vascular part of the body, supporting even and rapid absorption of the drug, empowering it to work within 10 minutes or less. LTR Pharma is proudly aiming to restore greater control over the timing, spontaneity, and enjoyment of sexual experiences.

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