Positive Clinical Data presented at the World Meeting on Sexual Medicine

18 December 2023

Highlights:

- **LTR Pharma's SPONTAN® (SDS-089) intranasal spray clinical data was presented at the World Meeting on Sexual Medicine (WMSM) in Dubai.**
- **The data was originally published in The Journal of Sexual Medicine and was presented by Professor Eric Chung.**
- **The study showed that the intranasal formulation achieved more rapid plasma concentration with one-third dose when compared with the oral administration.**

LTR Pharma Limited (**ASX:LTP**) ("**LTR Pharma**", "the **Company**"), shared positive results from a clinical trial in a presentation at The 24th World Meeting on Sexual Medicine (WMSM) in Dubai on 16 December 2023.

The abstract presentation is titled, *'Can Novel SDS-089 Nasal Vardenafil Spray Solution Achieve Satisfactory Drug Plasma Level Similar to Oral Vardenafil Formulation? A Bioanalysis Study Comparing Vardenafil Nasal vs Oral Formulations Using Liquid Chromatography Tandem Mass Spectrometry'.*

Associate Professor Eric Chung, a certified Fellow of the Royal Australasian College of Surgeons (RACS) and the Urological Society of Australia and New Zealand (USANZ), presented the data to a meeting of his peers in sexual health.

The core objective of the study was to assess the bioavailability of SPONTAN® (SDS-089 nasal Vardenafil solution) in human plasma levels (using liquid chromatography tandem mass spectrometry analysis). The study showed that SPONTAN delivered a high plasma concentration level of Vardenafil drug, based on pharmacokinetic LC/MS data analysis with robust accuracy and precision.

"This clinical study demonstrates the robust pharmacokinetics and methods applied in our analysis of the Vardenafil drug delivered as an oral tablet versus intranasal delivery with SPONTAN – and the conclusion is that the intranasal delivery formula achieved high plasma concentrations. The initial publication in leading industry journal, The Journal of Sexual Medicine, and follow up abstract at the World Meeting on Sexual Medicine has provided an invaluable platform to share this work internationally." Said **Professor Eric Chung, Urological surgeon and WMSM presenter.**

LTR Pharma is planning to expedite its FDA 505(b)(2) regulatory process for SPONTAN. The Company has received approval from the Bellberry Human Research Ethics Committee ("HREC") for a bioequivalence clinical trial comparing SPONTAN with the FDA approved ED drug Levitra®.

The trial will compare the pharmacokinetics, safety, and tolerability of Vardenafil following administration of SPONTAN and Levitra® tablets in healthy male adults. Patient recruitment is expected early next year, with trial sites to open in Sydney, Australia in Q1 CY24.

LTR Pharma Executive Chairman, Lee Rodne, said:

"We are pleased to share positive clinical results with industry peers at the World Meeting on Sexual Medicine. Having just listed the Company on the Australian Securities Exchange (ASX) under ticker code LTP, the LTR Pharma team is resolutely focused on progressing the next phase of our clinical trial program for SPONTAN and towards our FDA submission."

- ENDS -

This announcement has been approved by the Board of Directors.

For further information please contact:

Haley Chartres
Media Relations
haley@hck.digital

Jane Morgan
Investor Relations
jm@janemorganmanagement.com.au

About LTR Pharma

LTR Pharma is a public company, with operations based in Brisbane, Australia. Our focus is on holistically improving men's health, physically and mentally, through the commercialisation of an innovative intranasal spray treatment for Erectile Dysfunction (ED).

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.

Clinical Trial Absract

Can Novel SDS-089 Nasal Vardenafil Spray Solution Achieve Satisfactory Drug Plasma Level Similar to Oral Vardenafil Formulation? A Bioanalysis Study Comparing Vardenafil Nasal vs Oral Formulations Using Liquid Chromatography Tandem Mass Spectrometry.

Introduction:

The nasal drug delivery system offers many advantages when compared with oral administration, such as a faster onset of action, easily accessible, less drug degradation, and a high rate of absorption. The SDS-089 nasal Vardenafil (VDF) solution is a unique drug formulation designed to be delivered as a spray formulation.

Objective:

To assess the bioavailability of SDS-089 nasal Vardenafil solution in human plasma levels using Liquid Chromatography Tandem Mass Spectrometry analysis.

Methods:
The SDS-089 Vardenafil HCl formulation was prepared with the active pharmaceutical ingredient to the United States Pharmacopeia (USP) standard (batch 1704002361). The SDS-089 nasal spray solution was filtered (0.22 µm filter) and fitted with a nasal spray device to deliver 100 µL per spray which is equivalent to 2 mg Vardenafil HCl alcoholic solution per spray. This study received approval from the Institutional Review Board and Biosafety Committee (FB18/IRB/099). Blood samples from participants were collected at time 0 (pre-dose) and across different time intervals up to 10 hours and analyzed using Liquid Chromatography Tandem Mass Spectrometry (LC/MS) to quantify the level of Vardenafil and the internal standard. This protocol allows for the preparation and analysis of human samples, quality controls (QC), standard curve preparation, and instrumental analysis. During the validation experiments, each calibration standard and QC sample was prepared by spiking a specified amount of Vardenafil in human plasma with oral Vardenafil drug served as the internal standard for comparison. The concentration of analytes in each standard was quantified using LC/MS and detected using multiple reaction monitoring for each of the respective analytes. The lower limit of quantitation (LLOQ) was defined as the lowest concentration that could be quantified with accuracy and precision within 20%, as calculated from chromatograms for the independent samples. Intra- and inter-run accuracy and precision were calculated for the three QC samples, and independent triplicate measurements with best-fit lines were selected using a linear regression model with a 1/x2 weighting factor in the calibration curves.

Results:
The SDS-089 nasal Vardenafil solution showed excellent accuracy (mean 100, Standard Deviation, SD 4.1, % Relative Standard Deviation, RSD of 4%) and good precision (mean 50.1, SD 2.1, %RSD of 4%) on high (50ng/ml) QC assay tests. Similarly, the stability of QC on high (50ng/ml) plasma assay tests showed excellent accuracy (mean 100.8, SD 3.7, %RSD of 4%) and good precision (mean 50.4, SD 1.8, %RSD of 4%) on high (50ng/ml). Comparison between pharmacokinetic parameters of Vardenafil SDS-089 nasal spray (4mg) and oral tablet (10mg) showed T1/2 (2.52±0.99 vs 2.46±0.73 hour), Tmax (0.17±0.54 vs 0.97±0.35 hour), Cmax (time concentrations) (9.21±4.11 vs 11.24±7.83 ng/mL) and AUC0-inf (area under the curve from zero to infinity) (21.03±12.54 vs 37.25±41.51 ng/mL*h) (see Table 1: Pharmacokinetic parameters of Vardenafil HCl as SDS-089 nasal spray vs. oral tablet using non-compartmental analysis WinNonlin software).

Conclusions:
SDS-089 nasal formulation appeared to deliver a high plasma concentration level of Vardenafil drug based on pharmacokinetic LC/MS data analysis with robust accuracy and precision.

Figure 1:

Non-compartmental Model					
		Nasal spray (4 mg)		Oral tablet (10 mg)	
Parameters	Units	Average ± SD	Range	Average ± SD	Range
λ_z	1/h	0.305 ± 0.085	0.148-0.416	0.304 ± 0.084	0.183-0.423
$T_{1/2}$	h	2.517 ± 0.987	1.665-4.688	2.463 ± 0.737	1.640-3.778
T_{max}	h	0.167 ± 0.544	0.083-2.000	0.971 ± 0.349	0.750-2.000
C_{max}	ng/mL	9.216 ± 4.109	3.550-16.500	11.236 ± 7.830	2.040-27.900
AUC_{0-inf}	ng/mL*h	21.025 ± 15.538	10.010-67.069	37.252 ± 41.514	7.436-156.896

Note: The average values of above pharmacokinetic parameters are the mean value, except for T_{max} values are the median value to represent a more meaningful representation of T_{max}.

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