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Efficacy and Safety of Oral Testosterone Replacement Therapy (LPCN 1021): Analysis of Two Fixed-Dose Regimens

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Exhibit 99.1

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Introduction

- The clinical presentation of hypogonadism includes low levels of testosterone (T) and associated symptoms
- Testosterone replacement therapy (TRT) has been shown to restore T levels and improve symptoms
- The most common routes of administration for TRT include intramuscular injections and topical application
- LPCN 1021 is an oral formulation using testosterone undecanoate combined with a novel delivery system to allow efficient absorption and to restore T levels in hypogonadal patients
- A previous 52-week, phase 3 clinical study established the safety and efficacy of LPCN 1021
  - LPCN 1021 restored T levels and improved hypogonadal symptoms with a safety profile comparable to the active comparator used in the study (T gel)

Aim

- To evaluate the efficacy and safety of a novel, oral TRT, LPCN 1021 (testosterone undecanoate), using two fixed-dose regimens

Methods

- Two multicenter, open-label, single-arm studies were conducted to assess different fixed-dose regimens (no titration) for LPCN 1021
- Both studies were of similar design and included hypogonadal males with low T (<300 ng/dL) who received 24 days of treatment with a 450-mg daily dose of LPCN 1021
- The daily dose was divided into either 2 equal doses (twice daily [BID] study) or 3 equal doses (3 times daily [TID] study) taken with food
- In total, 95 and 100 patients were enrolled into the BID and TID studies, with 94 and 97 patients completing the studies, respectively
- The primary endpoint was the percentage of patients with 24-hour average serum T levels (Cavg) within the normal range (defined as 300 to 1080 ng/dL) after 24 days of treatment
- Safety assessments included adverse events (AEs) and standard laboratory evaluations

Results: Patient Demographics

- Patient demographics were similar in the 2 studies (**Table 1**)
- In both studies, the majority of patients were aged ≤65 years and white, with a body mass index of ≥30 kg/m^2

Table 1. Patient demographics in BID and TID studies

Characteristic	BID study (N = 95)	TID study (N = 100)
Age, mean, years (SD)	56.0 (8.9)	54.1 (8.8)
≤65 years, n (%)	79 (83.2)	91 (91.0)
>65 years, n (%)	16 (16.8)	9 (9.0)
Sex, n (%)		
Male	95 (100)	100 (100)
Race, n (%)		
Asian	1 (1.1)	1 (1.0)
Black or African American	15 (15.8)	13 (13.0)
White	77 (81.1)	84 (84.0)
Multiple	2 (2.1)	2 (2.0)
Body mass index,[a] mean (SD)	32.8 (5.5)	32.8 (5.5)
<25 kg/m^2, n (%)	3 (3.2)	3 (3.0)
≥25 to <30 kg/m^2, n (%)	26 (27.4)	28 (28.0)
≥30 kg/m^2, n (%)	66 (69.5)	69 (69.0)
Weight, mean, kg (SD)	103.6 (18.7)	106.6 (19.3)

SD, standard deviation

[a]Calculated as weight (kg)/height (m^2)

Results: Safety Summary

- The AE profiles of LPCN 1021 in both BID and TID studies were comparable to previous TRT studies, including a 52-week safety study with LPCN 1021
- Treatment-related AEs were reported in 6.3% of patients **(Table 3)**
  - All were either mild or moderate in intensity; none were severe
- One patient discontinued the BID study due to an AE that was deemed by the investigator to be unrelated to the study **(Table 3)**
- One serious AE was reported in the BID study, but was deemed by the investigator to be unrelated to the study **(Table 3)**

Table 3. Safety summary

Preferred term	BID study (N = 95) Patients n (%)	BID study (N = 95) Events n	TID study (N = 100) Patients n (%)	TID study (N = 100) Events n
Any TEAE	20 (20.1)	33	9 (9.0)	10
Any treatment-related TEAE	6 (6.3)	9	1 (1.0)	1
Any treatment-related and severe TEAE	0	0	0	0
Any TEAE leading to discontinuation	1 (1.1)	1	0	0
Any treatment-emergent SAE	1 (1.1)	1	0	0
Any treatment-related, treatment-emergent SAE	0	0	0	0
Any TEAE resulting in death	0	0	0	0

AEs were classified into system organ class and preferred term by using Medical Dictionary for Regulatory Activities Version 17.1. AEs were considered as drug reactions if the relationship to study drug was related. Patients were counted only once per system organ class and per preferred term. Percentages are based on N. SAE, serious adverse event; TEAE, treatment-emergent adverse event

Results: Treatment-related AEs reported in ≥1% of patients

- The most common treatment-related AE in the BID study was increased blood prolactin, which was reported in 4 patients (4.2%) **(Table 4)**
- In the TID study, one patient (1.0%) experienced treatment-related peripheral edema **(Table 4)**
- No safety concerns with respect to cardiac or hepatic AEs were noted

Table 4. Treatment-related AEs reported in ≥1% of patients in BID and TID studies

Preferred term	Patients n (%)	Events n
BID study (N = 95)		
Blood prolactin increased	4 (4.2)	4
Blood FSH decreased	1 (1.1)	1
Blood LH decreased	1 (1.1)	1
PSA increased	1 (1.1)	1
Weight increased	1 (1.1)	1
Headache	1 (1.1)	1
TID study (N = 100)		
Edema peripheral	1 (1.0)	1

AEs were classified into system organ class and preferred term by using Medical Dictionary for Regulatory Activities Version 17.1. AEs were considered as drug reactions if the relationship to study drug was related. Patients were counted only once per system organ class and per preferred term. Percentages are based on N. FSA, follicle stimulating hormone; LH, luteinizing hormone; PSA, prostate-specific antigen

Results: Pharmacokinetics

- BID dosing of LPCN 1021 met the primary efficacy endpoint
- 81% of patients in the BID study achieved a Cavg within the normal range (lower bound CI = 72%) compared with 70% in the TID study (lower bound CI = 60%) (Table 2)
- The BID study met the primary endpoint for each analysis performed
- The average daily T level in the BID study was 476 ng/dL compared with 386 ng/dL in the TID study

Table 2. Primary efficacy endpoint in BID and TID studies

Parameter	BID study				TID study			
Patient population	**Safety set**		**Full set**	**PK set**	**Safety set**		**Full set**	**PK set**
Imputation model	**Model-based imputation**	**B/LOCF**	**None**	**None**	**Model-based imputation**	**B/LOCF**	**None**	**None**
N	95	95	94	90	100	100	98	88
Patients achieving 24-hour average serum T concentration within normal range, %[a]	81	80	81	81	70	69	70	72
95% CI, %[b]	72, 88	72, 88	73, 89	73, 89	60, 78	60, 78	61, 80	62, 81

[a]Normal range: 300 to 1080 ng/dL. [b]A 95%, 2-sided, binomial CI surrounding the point estimate was calculated.
B/LOCF; last observation carried forward; CI, confidence interval; T, total testosterone

Conclusions

- BID administration of a fixed dose of LPCN 1021 restored T levels in hypogonadal men
- AE and other safety parameters were consistent with previous studies
- LPCN 1021 does not require titration
- The efficacy and safety data from these studies indicate that a fixed BID dose is the appropriate regimen for LPCN 1021

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