2 SYNOPSIS

Name of Sponsor/Company: Acrux Pharma Pty Ltd	Individual Study Table Referring to Part of the Dossier Volume: Page:	*(For National Authority Use Only)*
Name of Finished Product: Testosterone MD-Lotion® (cutaneous solution) 2%		
Name of Active Ingredient: Testosterone		

Title of Study:
A Phase III open-label titration trial to evaluate the effectiveness and safety of different doses of a dermal application of Testosterone MD-Lotion® (cutaneous solution) in hypogonadal men
&
A Phase III open-label extension of the MTE08 trial (A Phase III open-label titration trial to evaluate the effectiveness and safety of different doses of a dermal application of Testosterone MD-Lotion® (cutaneous solution) in hypogonadal men) to evaluate skin-safety

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[redacted]

UNITED STATES OF AMERICA

[redacted]

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[redacted]

[redacted]

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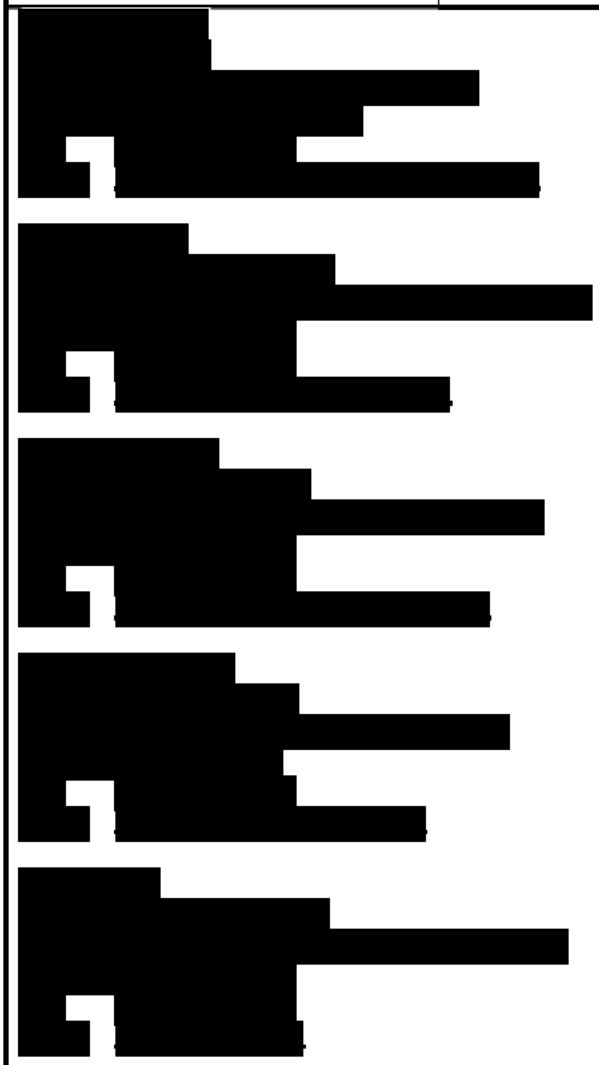

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UNITED KINGDOM

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[redacted]

Study Period:	**Phase of Development:**
There was a screening period of up to 40 days. MTE08 – 120 day treatment period MTE09 – 60 day treatment period dosing from Day 121 of the MTE08 trial There was a follow up period that occurred 7-10 days after the last study drug dose.	Phase III Pivotal & Extension to Pivotal Phase III MTE08 continuous use trial The MTE08 study was undertaken in 26 sites in the EU (Germany, Sweden, UK and France), US and Australia. The MTE09 study was conducted at the 12 US sites only.
First Subject Enrolled: 30th June 2008	**Last Subject Visit Complete:** 31st August 2009

Objectives:

MTE08

To confirm the efficacy and safety of four doses of Testosterone MD-Lotion® (cutaneous solution) for use by hypogonadal men via the axilla that may be taken to market. In addition, the trial will aim to achieve a C_{avg} for total testosterone in the defined normal range (300-1050 ng/dL).[2]

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MTE09
The aim and primary objective of MTE09 was to assess the occurrence of skin safety events for an additional two months of continuous use of Testosterone MD-Lotion® (i.e. up to a total of 6 months).

Primary endpoints:
MTE08
The primary endpoint for MTE08 was the proportion of subjects with C_{avg} (0-24 h) total testosterone within the normal range (300–1050 ng/dL) at Day 120.

MTE09
The primary endpoint for MTE09 was to observe the change in subject Draize Score (Day 1 to Day 180) after six months of continuous use of Testosterone MD-Lotion® (cutaneous solution).

Secondary endpoints:
MTE08
- Proportion of subjects with C_{max} >1500 ng/dL (at least 85% of subjects should have had a C_{max} less than 1500 ng/dL).
- Proportion of subjects with C_{max} between 1800 ng/dL and 2500 ng/dL (<5% of subjects).
- Proportion of subjects with C_{max} >2500 ng/dL (no subjects).
- Proportion of subjects with C_{min} <300 ng/dL.
- Changes from baseline in the following clinical endpoints:
  - Psychosexual Daily Questionnaire
  - SF-36 questionnaire
  - Fasting Insulin and Glucose levels
  - Prostate Specific Antigen (PSA) levels
  - LH, FSH and Estradiol levels
  - Haemoglobin and Haematocrit levels
- Confirm the safety of different doses of Testosterone MD-Lotion® (cutaneous solution).

MTE09
To collect adverse event and concomitant medication information over the two month trial period.
In addition, to compare the following data collected at the MTE09 Follow Up visit with the Screening data collected in the MTE08 trial:
- Fasting Insulin and Fasting Glucose levels
- Prostate Specific Antigen levels
- LH, Estradiol and FSH levels
- Haemoglobin and Haematocrit levels
- Total Testosterone, DHT and DHT:T ratio levels at Day 187-190

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Study Design and Methodology:

MTE08
Study Design: Open label, multi-centre, titration trial

Methodology:
Screening Phase
Potential subjects were consented to the trial. They underwent an evaluation for trial eligibility (including confirming International Prostate Symptoms Score was not≥ 19) and a physical examination including a digital rectal exam and evaluation of baseline biochemistry and haematology, hormonal analysis, urinalysis, vital signs and an electrocardiogram (ECG). They had their medical history, demographic, concomitant medication and any adverse event details recorded.

Eligible subjects taking testosterone therapy at the time of screening were required to cease their current therapy. Assessment of their baseline levels of testosterone occurred after a washout period of up to 7 days after ceasing their current buccal, oral or transdermal therapies and after a washout period of up to 30 days for subjects on intramuscular therapies (only testosterone enanthate or short acting testosterone). Potential subjects with testosterone levels equal to or below 300 ng/dL (after washout), were eligible to take part in the trial. Subjects were to complete the Psychosexual Daily Questionnaire for the seven (7) days preceding the Day 1 visit.

Treatment and Pharmacokinetic Periods:
At Day 1, subjects were started on the daily treatment dose of 3mL/60 mg of the investigational product. At Day 15, subjects underwent intensive pharmacokinetic sampling. Total testosterone and dihydrotestosterone (DHT) were measured and free testosterone calculated at pre-dose (0), and 2, 4, 8, 12, 16, 20 and 24 hours post-dose. Sex hormone binding globulin (SHBG) was measured in samples collected at pre-dose (0) and 24 hours. At Day 45, subjects returned to the trial centre. Subjects were titrated to the lower dose level, the next dose level, or remained on the 60 mg dose level, depending on their Day 15 total testosterone PK profile (C_{avg}). At Day 60, subjects underwent intensive pharmacokinetic sampling. Total testosterone and DHT was measured and free testosterone calculated at pre-dose (0), and 2, 4, 8, 12, 16, 20 and 24 hours post-dose. SHBG was measured in samples collected at pre-dose (0) and 24 hours. At Day 90 subjects remained on current dose, were titrated to the next dose level, went back to the previous dose level or were withdrawn from the trial depending on their Day 60 total testosterone PK profile. At Day 120, subjects underwent intensive pharmacokinetic sampling. Total testosterone and DHT were measured and free testosterone calculated at pre-dose (0), and 2, 4, 8, 12, 16, 20 and 24 hours post-dose. SHBG was measured in samples collected at pre-dose (0) and 24 hours. The ratio of DHT:T was also assessed at each time point during the intensive sampling periods.

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Vital signs, concomitant medications, adverse events and Draize score (skin safety assessment) were to be collected at each visit to the trial centre. Subjects also completed the Psychosexual Daily Questionnaire for the seven (7) days preceding visits at Day 1, 15, 60 and 120. The SF-36 questionnaire was completed pre-dose at the visits on Days 1 (pre-dose), 60 and 120. Subjects also underwent a physical examination at Day 90 which included a digital rectal examination.

Titration of trial dose:
Subjects may have had their dose of testosterone adjusted on Days 45 and 90 based on the total testosterone 24 hour PK profile (C_{avg}) collected at Days 15 and 60 respectively.

- Subjects with a total testosterone C_{avg} of 300 to 1050 ng/dL inclusive were to be maintained on their current dose.
- For subjects on the 30 mg dose who had C_{avg} total testosterone levels of <300 ng/dL the dose could be increased to 60 mg.
- Subjects on the 30 mg dose who had C_{avg} total testosterone levels of >1050 ng/dL were discontinued from the trial.
- For subjects on the 60 mg dose who had C_{avg} total testosterone levels of <300 ng/dL the dose could be increased to 90 mg.
- For subjects on the 60 mg dose who had C_{avg} total testosterone levels of >1050 ng/dL, the dose could be decreased to 30 mg.
- For subjects on the 90 mg dose who had C_{avg} total testosterone levels of <300 ng/dL, the dose could be increased to 120 mg.
- For subjects on the 90 mg dose who had C_{avg} total testosterone levels >1050 ng/dL, the dose could be decreased to 60 mg.

Follow up Visit/Early Withdrawal Visit:
All subjects were followed up at 7-10 days after their final dose of investigational product or at the time of study withdrawal. During this visit all subjects underwent an update of their medical history, physical examination including evaluation of vital signs, Draize score and an ECG. Blood samples were collected for total testosterone, DHT and free testosterone as well as for haematology and biochemistry. A urinalysis was performed during this visit. The ratio of DHT:T was also assessed. All adverse events and concomitant medications were recorded.

For subjects who withdrew prematurely from the trial, every effort was made to obtain an intensive PK profile for total testosterone, DHT and free testosterone at the time of trial withdrawal.

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MTE09

Study Design: Open label, multi-centre, extension, continuous use trial.

Methodology: For continuity, subjects visit days were counted from their Day 1 in the MTE08 trial.

Subjects were enrolled and rolled over into the MTE09 study in good faith on Day 120 of the MTE08 study. As such, if it was subsequently found that subjects did not meet all of the entry criteria for the MTE09 study, they were withdrawn.

Roll Over Phase:
Informed consent was obtained from subjects on or prior to Day 120 (of the MTE08 trial).

Treatment Period:
In accordance with MTE08 Trial Procedures subjects were confined on the evening of Day 120.

On Day 120/121 subjects were assessed for compliance with the inclusion and exclusion criteria (including confirming the IPSS was not $\geq$ 19) and were rolled over to MTE09.

Subjects continued to apply Testosterone MD-Lotion® (cutaneous solution) daily for 2 months (until Day 180) as per their Day 120 dosing regime. The dose of Investigational Product was applied on the morning (nominally 0800) of Day 121 under the supervision of trial staff prior to discharge from the site.

Subjects reported to the trial site prior to dosing on Day 150 and Day 180. During these visits the subjects had their vital signs assessed, concomitant medications and adverse events recorded and a Draize score assessment undertaken.

Follow up Visit/Early Withdrawal Visit:
All subjects were to return to the clinic 7 to 10 days after the final dose of Investigational Product (Day 187-190) for the Follow-up Visit or at the time of early withdrawal from the study. During this visit all subjects underwent an update of their medical history, physical examination including evaluation of vital signs, Draize score and an ECG. Blood samples were collected for total testosterone, DHT and free testosterone as well as for haematology and biochemistry. A urinalysis was performed during this visit. The ratio of DHT:T was also assessed. All adverse events and concomitant medications were recorded.

Number of Subjects (planned and analysed):
MTE08

- Planned: up to 150 subjects (to enable at least 107 completers)
- Analysed : 155

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MTE09

- Planned: At least 50 subjects were required to complete 180 days of treatment (available to all USA MTE08 subjects)
- Analysed : 71

Diagnosis and Main Criteria for Inclusion and Exclusion:

MTE08

Inclusion Criteria

1. Male subjects greater than 18 years of age with a prior documented definitive diagnosis of hypogonadism as evidenced by previously documented:
   - Hypothalamic, pituitary or testicular disorder or age related idiopathic hypogonadism,
   - Screening serum testosterone of≤ 300 ng/dL (based on the average of two morning samples taken at least 30 minutes apart),
2. Were currently receiving treatment (buccal, oral, transdermal or intramuscular androgen replacement) for hypogonadism in accordance with approved labelling, or in the Investigator's opinion were eligible to receive such treatment,
3. Body Mass Index (BMI) < 35.0kg/m^2,
4. Haemoglobin levels at screening ≥ 11.5g/dL,
5. Adequate venous access on left or right arm to allow collection of a number of samples by venipuncture,
6. Ability to communicate with the trial staff, understand the Trial Information Sheet and sign the Written Informed Consent Forms; willing to follow the Protocol requirements and comply with Protocol restrictions and procedures.

Exclusion Criteria

1. Current use of long acting testosterone injectables such as Nebido®,
2. Any significant history of allergy and/or sensitivity to the drug products or their excipients, including any history of sensitivity to testosterone and/or sunscreens,
3. Any clinically significant chronic illness or finding on screening physical exam and/or laboratory testing that makes it undesirable for the Investigator to enrol the trial subject in the trial and/or that in the Investigator's opinion, would interfere with the trial objectives or safety of the subject,
4. Chronic skin disorder (e.g. eczema, psoriasis) likely to interfere with transdermal drug absorption,
5. Men with suspected reversible hypogonadism (i.e. due to medications, stress),

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6. Any man in whom testosterone therapy is contraindicated, which includes those with:
   - Known or suspected carcinoma (or history of carcinoma) of the prostate, or clinically significant symptoms of benign prostatic hyperplasia and/or clinically significant symptoms of lower urinary obstruction and IPSS scores of ≥ 19,
   - Known or suspected carcinoma (or history of carcinoma) of the breast,
   - Severe liver disease (i.e. cirrhosis, hepatitis or liver tumours or liver function tests > 2 times the upper limit of the normal range values),
   - Active deep vein thrombosis, thromboembolic disorders or a documented history of these conditions,
   - Current significant cerebrovascular or coronary artery disease,
   - Untreated sleep apnoea,
   - Haematocrit of > 51%,
   - Untreated moderate to severe depression,
7. Men with clinically significant prostate exam (such as irregularities or nodules palpated) or clinically significant elevated serum Prostate Specific Antigen (PSA) levels (> 4 ng/mL), or age adjusted reference range of PSA values,
8. Current or history of drug or alcohol abuse (more than four standard drinks per day and/or abnormal liver function tests > two times the upper limit of the normal range values),
9. Men taking concomitant medications (prescribed, over-the-counter or complementary) that would affect SHBG or testosterone concentrations or metabolism, warfarin, insulin, opiates, GnRH, 5 alpha reductase inhibitors, propanolol, oxyphenbutazone, corticosteroids (except for physiological replacement doses), estradiol,
10. Men involved in sport in which there is screening for anabolic steroids,
11. Men with uncontrolled diabetes (HbA1c ≥ 10%),
12. Men currently taking any investigational product, or who have received an investigational product within 28 days prior to screening, or 5 half-lives (whichever is the longer),
13. Any contraindication to blood sampling,
14. Subjects intending to have any surgical procedure during the course of the trial,
15. Subjects with a partner of child bearing potential who are not willing to use adequate contraception for the duration of the trial,
16. Subjects whose partners are pregnant.

MTE09

Inclusion Criteria

1. Completed the MTE08 trial up to and including Day 120/121 in a compliant manner
2. Ability to communicate with the trial staff, understand the Trial Information Sheet and sign the Written Informed Consent Forms; willing to follow the Protocol requirements and comply with Protocol restrictions and procedures.

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Exclusion Criteria

1. Any clinically significant chronic illness or finding and/or laboratory testing that would interfere with the trial objectives or safety of the subject,
2. Any man in whom testosterone therapy is contraindicated, which included those with:
   - Known or suspected carcinoma (or history of carcinoma) of the prostate or clinically significant symptoms of benign prostatic hyperplasia and/or clinically significant symptoms of lower urinary obstruction and with a IPSS score of≥ 19,
   - Known or suspected carcinoma (or history of carcinoma) of the breast,
   - Severe liver disease (i.e. cirrhosis, hepatitis or liver tumours or liver function tests >2 times the upper limit of the normal range values),
   - Active deep vein thrombosis, thromboembolic disorders or a documented history of these conditions,
   - Current significant cerebrovascular or coronary artery disease,
   - Untreated sleep apnoea,
   - Haematocrit of > 54%,
   - Untreated moderate to severe depression,
3. Men with clinically significant prostate exam or clinically significant elevated serum Prostate Specific Antigen (PSA) level (> 4 ng/mL) or age adjusted reference range of PSA values,
4. Current or history of drug or alcohol abuse (more than four standard drinks per day and/or abnormal liver function tests two times the upper limit of the normal range values),
5. Men taking concomitant medications (prescribed, over-the-counter or complementary) that would affect SHBG or testosterone concentrations (excluding Testosterone MD-Lotion® (cutaneous solution)) or metabolism such as warfarin, insulin, opiates, gonadotropin-releasing hormone analogues (GnRH), 5 alpha reductase inhibitors, propanolol, oxyphenbutazone, corticosteroids (except for physiological replacement doses), estradiol
6. Men with uncontrolled diabetes (HbA1c ≥ 10%)
7. Subjects intending to have any surgical procedure during the course of the trial
8. Subjects with a partner of child bearing potential who are not willing to use adequate contraception for the duration of the trial
9. Subjects whose partners are pregnant.

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Test and Reference Products, Dose and Mode of Administration, Lot or Batch Numbers for MTE08/MTE09:

Testosterone Metered Dose (MD)-Lotion® (cutaneous solution):

- **Treatment A**: 1.5 mL (30 mg) of 2% Testosterone MD-Lotion® (cutaneous solution) applied daily by 1 dose to the axilla (1.5 mL to one axilla).
- **Treatment B**: 3.0 mL (60 mg) of 2% Testosterone MD-Lotion® (cutaneous solution) applied daily by 2 doses to the axilla (1.5 mL to each axilla).
- **Treatment C**: 4.5 mL (90 mg) of 2% Testosterone MD-Lotion® (cutaneous solution) applied daily by 3 doses to the axilla (2x1.5 mL to one axilla and 1x1.5 mL to the other axilla).
- **Treatment D**: 6.0 mL (120 mg) of 2% Testosterone MD-Lotion® (cutaneous solution) applied daily by 4 doses to the axilla (2x1.5 mL to each axilla).

Lot or Batch Numbers:

[redacted]

Duration of Treatment:

MTE08

The Trial consisted of a 120 day treatment period with a follow up visit 7 to 10 days after the final dose.
There was also a screening period of approximately 40 days.

MTE09

The Trial consisted of a 60 day treatment period (dosing from Day 121 of the MTE08 trial to Day 180) and a follow up trial visit on Day 187 – 190 (7-10 days after the last dose of study drug).

Criteria for Evaluation

Safety Assessments:

The following procedures were used to evaluate safety in both the MTE08 and MTE09 studies:

- Adverse events/reactions
- Serious adverse events (SAEs)
- ECG
- Vital signs
- Physical examination, including a digital rectal examination
- Draize score
- Clinical laboratory parameters, including prostate specific antigen (PSA), biochemistry (lipids, glucose, insulin), haematology (including haematocrit, haemoglobin A1c), hormonal assessments (testosterone, DHT, free testosterone, LH, FSH, Estradiol), urinalysis.

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Efficacy Assessments:
MTE08
The primary efficacy analysis for this trial will assess whether at Day 120:

- The proportion of subjects with C_{avg} total testosterone levels in the defined normal range was greater than or equal to 75%.

Other efficacy analyses:

- That C_{max} was less than 1500 ng/dL in at least 85% of subjects.
- That there were no subjects with C_{max} greater than 2500 ng/dL
- That the proportion of subjects with a C_{max} between 1800 ng/dL and 2500 ng/dL was low (less than 5% of subjects).

MTE09
There were no efficacy endpoints for this open label extension trial.

Pharmacokinetic and Pharmacodynamic Assessments:
MTE08

- Proportion of subjects with average serum total testosterone concentration (C_{avg} (0-24h)) in the defined normal range for each dose of Testosterone MD-Lotion® (cutaneous solution) on Days 15/16, 60/61 and 120/121.
- Steady state total testosterone pharmacokinetic parameters measured on Days 15/16, 60/61 and 120/121.
- Proportion of subjects with minimum serum concentration (C_{min}) in the defined normal range for each dose of Testosterone MD-Lotion® (cutaneous solution) on Days 15/16, 60/61 and 120/121.
- Proportion of subjects with maximum serum concentration (C_{max}) >1050 ng/dL and <1500 dL, >1500 ng/dL, >1500 ng/dL and <1800 ng/dL, >1800 ng/dL and <2500 ng/dL, >2500 ng/dL.
- Duration that subjects spent below <300 ng/dL
- Proportion of subjects that required dose titration
- DHT pharmacokinetic parameters at Days 15/16, Days 60/61 and Days 120/121.
- DHT:T ratio (C_{avg}) at Days 15/16, Days 60/61 and Days 120/121.
- Free testosterone pharmacokinetic parameters (calculated using SHGB collected at 0 and 24 hours) at Days 15/16, Days 60/61 and Days 120/121.

Assessments and validation of steady state was measured using samples collected during the intensive PK periods on Days 15/16, 60/61 and 120/121.

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MTE09
No PK assessments were made for the MTE09 study as this was a safety study.

Statistical Methods:

MTE08
The following non-baseline and baseline corrected pharmacokinetic parameters were to be determined from serum concentrations of total testosterone and calculated free testosterone, DHT and DHT:T ratio: AUC_{0-24}, C_{min}, C_{max}, C_{avg}, t_{max} and Degree of Fluctuation (DF).

Mean, standard deviation (SD) and coefficient of variation (CV) were to be calculated for pharmacokinetic parameters.

Analysis of linearity of dosing (eg ANOVA of log transformed dose normalised AUC data) would also be assessed.

All adverse events were coded and tabulated by severity and relationship to Investigational Product. Vital signs and clinical laboratory parameters were also tabulated for each trial subject.

The proportion of subjects who discontinued treatment due to any (serious) adverse event that had a suspected causal relationship to the Investigational Product was tabulated.

MTE09
The observed change in subject Draize Score (from Day 1 to Day 180) for the duration of the six month application of the Investigational Product was tabulated.

All adverse events were coded and tabulated by severity and relationship to Investigational Product. Vital signs and clinical laboratory parameters were also tabulated for each trial subject.

The proportion of subjects who discontinued treatment due to any (serious) adverse event that had a suspected causal relationship to the Investigational Product was tabulated.

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Results:

Disposition, Demographics, and Baseline Characteristics

The median age of subjects in the Safety Set in MTE08 was 53 years old, with a range of 19-78 years old. Of the subjects in the Safety Set whose race was recorded, 84.7% were Caucasian, 9.0% were Hispanic, 4.2% were African Americans, 0.7% was Asian and 1.4% had race recorded as "Other". The mean weight of subjects was 94.36 kg, and the mean height was 1.79 m. The mean baseline total testosterone level in the Safety Set was 196.7 ± 91 ng/dL.

The median age of subjects in the Safety Set in MTE09 was 53 years old, with a range of 21-78 years old. Of the subjects in the Safety Set, 76.1% were Caucasian, 14.1% were Hispanic, 8.5% were African Americans, and 1.4% had race recorded as "Other". The mean weight of subjects was 95.02 kg, and the mean height was 1.78 m.

Efficacy

A total of 105/138 subjects (76.1%), 117/138 subjects (84.8%) and 116/138 subjects (84.1%) were in the normal range for C_{avg} (0-24h) total testosterone on Days 15/16, 60/61 and 120/121, respectively. As the response rate was 84.1% (116/138) at Day 120, the primary objective of the study was met. Secondary efficacy objectives that C_{max} would be less than 1500 ng/dL in at least 85% of subjects, and that less than 5% of subjects would have a C_{max} between 1800ng/dL and 2500 ng/dL, were also met.

Sexual desire amongst all subjects who completed the trial increased by 79% from baseline, and overall sexual activity, increased from baseline by 68%, 86% and 104% after 15, 60 and 120 days of treatment respectively.

Safety

Studies MTE08 and MTE09 demonstrated a favourable safety and tolerability profile for the administration of Testosterone MD-Lotion® (cutaneous solution) for up to 180 days in hypogonadal men.

A total of three SAEs were reported, one in MTE08 and two in MTE09. Of the three subjects who experienced SAEs, one was on a 120 mg maintenance dose and the remaining two were on a 60 mg maintenance dose. None of the SAEs were considered to be treatment related.

There was no significant difference in the incidence of TEAEs in all subjects that were treated for four months (in the MTE08 study) as compared with the incidence in the smaller population of those subjects who undertook continuous use of the product for six months in total (MTE09 subjects). There were no deaths reported in the MTE08 or MTE09 studies.

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Pharmacokinetic and Pharmacodynamic

The primary efficacy objective of the trial – that the proportion of subjects with C_{avg} (0-24h) total testosterone levels in the defined normal range (300-1050 ng/dL) at Day 120 would be greater than or equal to 75% – was met. In addition, the secondary efficacy objectives that C_{max} would be less than 1500 ng/dL in at least 85% of subjects, and that less than 5% of subjects would have a C_{max} between 1800 ng/dL and 2500 ng/dL, were also met.

Data from MTE08 have also shown that there is no impact on efficacy of the concomitant use of deodorants or antiperspirants nor is there any impact on efficacy if the application site is washed two hours or more after application of the product.

Based on an in-depth analysis that compared serum testosterone concentrations at individual time points with actual C_{avg} values, it is recommended that the blood draw on which titration decision are made in clinical practice be taken between 2 and 8 hours after application of the product and most preferably 4 hours after application.

Non-PK related endpoints provided notable insight into the positive effects of testosterone replacement therapy on psychosexual health. Overall, the responses of the psychosexual daily questionnaire showed that there were statistically significant improvement on all sexual desire and enjoyment, sexual activity and sexual performance variables tested at all time points assessed. In addition, the overall mean summary scores showed significant increases in positive mood and significant decreases in negative mood.

In conclusion, the investigational product, Testosterone MD-Lotion® (cutaneous solution) successfully raises the testosterone and the overall hormonal levels (total testosterone, free testosterone and DHT) in hypogonadal men. The product also results in significant increases in measures of psychosexual health. Thus, once daily application of the investigational product, Testosterone MD-Lotion® (cutaneous solution), is an effective treatment for androgen replacement in hypogonadal men.

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Name of Active Ingredient: Testosterone		

Summary – Conclusions

Testosterone MD-Lotion® (cutaneous solution) was well tolerated by the hypogonadal men evaluated in this clinical development program. Common adverse events were consistent with the known effects of transdermal testosterone therapy, and very few subjects discontinued treatment due to drug-related adverse events. There was no change in the overall Draize score over time (from baseline to 180 days of treatment) or in relation to the dose given.

Within the range of doses studied in this program, there were no dose-related safety concerns. Testosterone MD-Lotion® (cutaneous solution) was easily titrated between the 30 mg, 60 mg, 90 mg and 120 mg doses, with the 60 mg starting dose providing an appropriate maintenance dose for the majority of subjects. Testosterone MD-Lotion® (cutaneous solution) provides a simplified process to achieve the effective testosterone dose for individual subjects in order to obtain testosterone levels in the normal range (300-1050 ng/dL), with an accompanying significant improvement in quality of life.

Testosterone MD-Lotion®'s (cutaneous solution) no-touch application method and the unique application to the axilla may provide a lower risk of inadvertent contact between the drug and other persons compared to the currently marketed transdermal testosterone products.

There was no impact upon efficacy from concomitant use of deodorants or antiperspirants, or when the application site was washed two hours or more after application.

The data also demonstrated that the blood draw on which titration decisions are made in clinical practice be taken between two and eight hours after application of the product and most preferably four hours after application.

At Day 120 the proportion of subjects with a C_{avg} value in the normal range on Day 120 in the Completer Set was 116/138 or 84.1%. The lower bound of the 95% confidence interval associated with the proportion is 78.0% i.e. above the 66.8% limit set by FDA. The primary endpoint of the study was therefore comfortably met in all data sets analysed

In summary, Testosterone MD-Lotion® (cutaneous solution) may provide a more effective means of establishing the dose required to maintain therapeutic goals and may provide relative safety benefits compared with current transdermal testosterone therapies for the treatment of hypogonadism. Testosterone MD-Lotion® (cutaneous solution) will also provide patients and physicians with another treatment option. Testosterone MD-Lotion® (cutaneous solution) delivers a measured dose of testosterone to the axilla as a solution in a discrete, convenient and potentially safer application than currently available transdermal testosterone products.

Date of Report: 18 December 2009