Newly Published Study Showed Axiron® (testosterone) Topical Solution Restored Testosterone Levels to Normal Range in Hypogonadal Men

INDIANAPOLIS, June 28, 2011 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) announced that a pivotal Phase III Axiron study, published on the Clinical Endocrinology website, showed that Axiron® (testosterone) topical solution CIII, when applied to the underarm, met the primary study objective to restore testosterone levels to the normal range (300 — 1050 ng/dL) in men with low testosterone. In addition, secondary outcomes showed that the treatment of Axiron improved symptoms associated with low testosterone.

Testosterone deficiency, also known as hypogonadism or low testosterone, is a clinical condition in which the testicles, hypothalamus or pituitary gland is affected by disease or damage that results in inhibiting hormone secretion and testosterone production.(i)

About the Study

The Phase III open label, 120-day clinical study, conducted in 26 centers throughout the world, assessed the safety, pharmacokinetics and efficacy of a 2% formulation of testosterone topical solution (Axiron) applied daily to the underarm. All 155 men began the study on a 60 mg dose and had their dose adjusted on Days 45 and 90, if necessary, to maintain their testosterone levels within the physiological range based on an average serum testosterone levels tested on Days 15 and 60, respectively. On Day 120, of the 138 men for which there was evaluable data, 84% had an average testosterone concentration within the normal range (300-1050 ng/dL). On Day 120, the majority of the men, 97 subjects, remained on 60 mg starting dose; three men were on 30 mg; 25 men were on 90 mg; and 10 men were on 120 mg.

The study also assessed the effect of treatment on symptoms associated with low testosterone as measured by the Psychosexual Daily Questionnaire. Improvement in sexual desire and activity were apparent as early as 15 days (1.9 and 0.93 point improvement, respectively, both $P<0.0001$) and were sustained throughout the study (3.36 and 1.84 point, respectively, both $P<0.0001$). There were also statistically significant improvements from baseline in erection maintained for satisfactory duration, positive mood and negative mood (4.29, 4.86 and 1.44 point, respectively, all $P<0.0001$). Additionally, the study evaluated the effect of treatment on men's general well-being as measured by the SF-36 questionnaire. There were significant mean changes from baseline to Day 120 on both the SF-36 Physical Component and SF-36 Mental Component scores (1.55 point, $p=0.0254$ and 4.54 point, $p<0.0001$, respectively).

Since Axiron is applied to the underarm, the study also evaluated the potential impact of the use of deodorants or antiperspirant and of washing the application area. Among those who completed 120 days of treatment, the proportion of men with testosterone levels in the normal range was similar among those who used deodorant or antiperspirant since the last visit (83.3%); those who used deodorant or antiperspirant every day since the last visit (83.1%); those who did not use any deodorant or antiperspirant since the last visit (88.3%); and those who did not use deodorant or antiperspirant every day since the last visit (88.3%). At the end of the study, Day 120, among men (n=34) who reported showering/washing the application site at least two hours or more after Axiron application during the 24-hour sampling period, 82.4% had testosterone levels within the normal range compared to 86.9% of men (n=99) who reported not showering/washing the application site during the 24-hour sampling period.

The most common adverse reactions reported during the study were application site reaction (7.7%), application site redness (5.2%), headache (5.2%), increased red blood cell count (3.9%), nasopharyngitis (3.9%), diarrhea (2.6%), and vomiting (2.6%). Additionally, there was an increase in blood level of Prostate Specific Antigen (a test used to screen for prostate cancer) to > 4ng/ml in three patients.

The study authors concluded that Axiron, which uses an applicator to apply testosterone solution to the underarm, provides a treatment option that is efficacious and generally well-tolerated.

About Axiron

Axiron was approved by the FDA in November 2010 as a prescription medicine used to treat adult males that have low or no testosterone.

Axiron is not intended for use in women or anyone under 18 years of age. It is not known if Axiron is safe and effective in

children younger than 18 years old. Improper use may affect bone growth in children.

Axiron contains testosterone, a Schedule III controlled substance as defined by the Anabolic Steroid Control Act of 2004 and can be a target for people who abuse prescription medicines. Patients should keep Axiron in a safe place and it should never give it to anyone else, even if they have the same symptoms.

Important Safety Information for AXIRON

***What is the most important information I should know about AXIRON*?**

AXIRON can transfer from your body to others. This can happen if other people come into contact with the area where the AXIRON was applied. Signs of puberty that are not expected (for example, pubic hair) have happened in young children who were accidentally exposed to testosterone through skin to skin contact with men using topical testosterone products like AXIRON. Women and children should avoid contact with the unwashed or unclothed area where AXIRON has been applied. If a woman or child makes contact with the application area, the contact area on the woman or child should be washed well with soap and water right away.

To lower the risk of transfer of AXIRON from your body to others, follow these important instructions:

- Apply AXIRON **only** to your armpits.
- Wash your hands **right away** with soap and water after applying AXIRON.
- After the solution has dried, **cover the application area with clothing**. Keep area covered until you have washed the application area well or have showered.
- **If you expect another person to have direct skin-to-skin contact with your armpits, first wash the application area well with soap and water.**

Stop using AXIRON and call your healthcare provider right away if you see any signs and symptoms in a child or a woman that may have occurred through accidental exposure to AXIRON. Signs and symptoms in children may include enlarged penis or clitoris; early development of pubic hair; increased erections or sex drive; aggressive behavior. **Signs and symptoms in women** may include changes in body hair and a large increase in acne.

Who should not use AXIRON?

Do not use AXIRON if you:

- have or might have prostate cancer
- have breast cancer
- are pregnant or may become pregnant or are breast-feeding. AXIRON may harm your unborn or breast-feeding baby.

Women who are pregnant or who may become pregnant should avoid contact with the area of skin where AXIRON has been applied.

What should I tell my healthcare provider before using AXIRON?

Before you use AXIRON, tell your healthcare provider if you have:

- breast cancer
- or might have prostate cancer
- urinary problems due to an enlarged prostate
- heart problems
- kidney or liver problems
- problems breathing while you sleep (sleep apnea)
- any other medical conditions

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements. Using AXIRON with other medicines can affect each other. **Especially, tell your healthcare provider if you take:**

- insulin
- medicines that decrease blood clotting

- corticosteroids

What are the possible side effects of AXIRON?

AXIRON can cause serious side effects. Call your healthcare provider right away if you have any of the following:

- **If you already have enlargement of your prostate gland**, your signs and symptoms can get worse while using AXIRON. This can include: increased urination at night, trouble starting your urine stream, having to pass urine many times during the day, having an urge that you have to go to the bathroom right away, having a urine accident, being unable to pass urine or weak urine flow.
- **Possible increased risk of prostate cancer.** Your healthcare provider should check for prostate cancer or any other prostate problems before you start and while you use AXIRON.
- **In large doses AXIRON may lower your sperm count.**
- **Swelling of your ankles, feet, or body.**
- **Enlarged or painful breasts.**
- **Problems breathing while you sleep (sleep apnea**).
- **Blood clots in the legs. This can include pain, swelling or redness of your legs.**

The most common adverse events include: skin redness or irritation where AXIRON is applied, increased red blood cell count, headache, diarrhea, vomiting, and increase in blood level of Prostate Specific Antigen (a test used to screen for prostate cancer). **Other side effects include** more erections than are normal for you or erections that last a long time.

AXIRON is flammable until dry. Let AXIRON dry before smoking or going near an open flame.

For additional safety information, please see the medication guide at http://pi.lilly.com/us/axiron-medguide.pdf. For full Prescribing Information including the Boxed Warning regarding the risk of secondary exposure, please visit http://pi.lilly.com/us/axiron-pi.pdf, or visit www.axiron.com for additional information.

About Eli Lilly and Company

Lilly, a leading innovation-driven corporation, is developing a growing portfolio of pharmaceutical products by applying the latest research from its own worldwide laboratories and from collaborations with eminent scientific organizations. Headquartered in Indianapolis, Ind., Lilly provides answers — through medicines and information — for some of the world's most urgent medical needs.

Axiron® (testosterone) solution CIII

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(i) Winters, S. Current Status of Testosterone Replacement in Men. Archives of Family Medicine. 1999;8:257-263. Available at http://archfami.ama-assn.org/cgi/content/full/8/3/257. Last accessed June 21, 2011.

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