



New Study Shows Cialis® Significantly Improved Study Endpoints in Men with Both Erectile Dysfunction and Signs and Symptoms of Benign Prostatic Hyperplasia

Pivotal Phase III Study Met its Co-Primary Endpoints

INDIANAPOLIS, Oct. 12, 2011 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) announced today that a pivotal Phase III study of Cialis® (tadalafil) tablets 5 mg for once daily use met its co-primary endpoints, significantly improving measures of both erectile dysfunction (ED) and signs and symptoms of benign prostatic hyperplasia (BPH) in men with both conditions. The study is available online in *The Journal of Sexual Medicine*. It is one of three efficacy and safety studies included in the supplemental new drug application Lilly submitted to the U.S. Food and Drug Administration (FDA) last year seeking approval for Cialis in the treatment of the signs and symptoms of BPH and the treatment of both ED and the signs and symptoms of BPH (ED+BPH).

The FDA approved Cialis on Thursday for both new indications.

It is important to note that Cialis is not to be taken with medicines called "nitrates" (often prescribed for chest pain); or with recreational drugs called "poppers" like amyl or butyl nitrite, as the combination may cause an unsafe drop in blood pressure; or if allergic to Cialis or Adcirca® (tadalafil), or any of its ingredients. Anyone who experiences any symptoms of an allergic reaction, such as rash or hives, should call a healthcare provider or get help right away.

"We are pleased with the outcomes of this study," said Anthony Beardsworth, M.D., senior medical director for Eli Lilly and Company. "Lilly is committed to research that can help us offer new treatment options and advance our understanding of ED and BPH, conditions that affect millions of men worldwide."

About the Study

The study assessed the effects of Cialis 2.5 mg or 5 mg for once daily use on ED and the symptoms of BPH in men with both conditions. It is the first Lilly-sponsored study that evaluated the effect of Cialis exclusively in male patients with both ED and BPH symptoms.

The Phase III randomized, double-blind, placebo-controlled, parallel-design clinical study, conducted in 54 urology centers in nine countries, assessed the safety and efficacy of Cialis 2.5 or 5 mg for once daily use in 606 sexually active men aged 45 years and older who had experienced ED for at least 3 months and BPH symptoms for more than 6 months. The men were randomly assigned to receive placebo, Cialis 2.5 mg, or Cialis 5 mg in a 1:1:1 ratio for a period of 12 weeks.

The co-primary measures were the changes from baseline to week 12 of the International Index of Erectile Function-Erectile Function Domain (IIEF EF), a questionnaire evaluating sexual function where higher scores indicate better erectile function, and the International Prostate Symptom Score (IPSS), a questionnaire evaluating lower urinary tract symptoms occurring during the preceding month where lower scores indicate less severe symptoms. Key secondary measures were the change during treatment in the percentage of "yes" responses to question three of the Sexual Encounter Profile (SEP Q3) and BPH Impact Index (BII). The SEP Q3 asks "Did your erection last long enough for you to have successful intercourse?" The BII is a questionnaire evaluating the impact of urinary problems on overall health and activity, with lower scores indicating less impact.

Cialis 5 mg for once daily use significantly improved the mean differences from baseline on IIEF-EF Domain scores and IPSS scores through 12 weeks versus placebo (4.7 and -2.3, respectively, both $P < 0.001$). For the 2.5 mg once daily dose, significant improvements were seen versus placebo on IIEF EF Domain scores at 12 weeks (3.4, $P < 0.001$), but the difference from placebo in IPSS scores was not significant after 12 weeks (-0.8, $P = 0.18$).

On the key secondary measures, the mean differences from baseline with Cialis 5 mg compared to placebo after 12 weeks were 19.7% ($P < 0.001$) on the SEP Q3 and -0.9 ($P < 0.001$) on the BII. Cialis 2.5 mg for once daily use significantly improved the SEP Q3 (mean difference from baseline compared to placebo 12.5 %, $P < 0.001$), but the reduction in the BII was not significant (-0.4 versus placebo, $P = 0.16$).

The overall incidences of treatment-emergent adverse events (TEAEs) were: 19.5 % in patients treated with placebo, 25.3% in patients treated with Cialis 2.5 mg, and 27.4% in patients treated with Cialis 5 mg. The most common TEAEs in the Cialis 5 mg group were headache (5.8% versus 3% in placebo group), back pain (2.9% versus 1.5% in placebo group), and nasopharyngitis (2.4% versus 2.0% in placebo group). There were no reports of ejaculatory dysfunction or urinary retention in

any treatment group.

"It is encouraging that Cialis at 5 mg showed the potential to treat both ED and BPH symptoms," said lead author Blair Egerdie, M.D., Urologic Medical Research in Kitchener, Canada. "Given that the prevalence of coexisting ED and BPH is high, especially in older men, I believe that a single medical therapy approved to treat both conditions is a valuable therapeutic option."

About ED and BPH

ED is a condition where the penis does not fill with enough blood to harden and expand when a man is sexually excited, or when he cannot keep an erection. Approximately 50 percent of men between 40-70 years old have ED.(1)

BPH is a condition where the prostate enlarges, which can cause urinary symptoms.

ED and BPH are conditions that may occur in the same patient. Several studies have shown that many men with ED also experience the symptoms of BPH.(2-4)

About Cialis

Men with ED have two different dosing options with Cialis in the United States — Cialis for once daily use (2.5 mg and 5 mg) and Cialis for use as needed (5 mg, 10 mg and 20 mg).

Cialis for once daily use is approved to treat ED, the signs and symptoms of BPH, and ED and the signs and symptoms of BPH in men who have both conditions (ED+BPH). Only the 5 mg dose is approved to treat BPH and ED+BPH.

Cialis for once daily use can help men with ED be ready anytime between doses*, so they do not have to plan sexual activity around taking a pill. It can also treat the signs and symptoms of BPH. Cialis for once daily use is the only medication approved to treat both ED and the signs and symptoms of BPH.

Cialis for use as needed is approved to treat erectile dysfunction (ED). Cialis for use as needed should be taken before sexual activity. It may go to work quickly (in as little as 30 minutes in some men) and can work up to 36 hours.* #

The most common side effects with Cialis are headache, indigestion, back pain, muscle aches, flushing and stuffy or runny nose. These side effects usually go away after a few hours. Men who get back pain and muscle aches usually get it 12 to 24 hours after taking Cialis. Back pain and muscle aches usually go away within two days.

*Individual results may vary. Not studied for multiple attempts per dose.

#In clinical trials, Cialis for use as needed was shown to improve, up to 36 hours after dosing, the ability of men with ED to have a single successful intercourse attempt.

Important Safety Information for CIALIS® (tadalafil) tablets

What Is The Most Important Information I Should Know About CIALIS?

Do not take CIALIS if you:

- take medicines called "nitrates" which are often prescribed for chest pain as the combination may cause an unsafe drop in blood pressure
- use recreational drugs called "poppers" like amyl nitrite and butyl nitrite
- are allergic to CIALIS or ADCIRCA® (tadalafil), or any of its ingredients. Call your healthcare provider or get help right away if you experience any symptoms of an allergic reaction, such as rash or hives.

After taking a single tablet, some of the active ingredient of CIALIS remains in your body for more than 2 days. The active ingredient can remain longer if you have problems with your kidneys or liver, or you are taking certain other medications.

Stop sexual activity and get medical help right away if you get symptoms such as chest pain, dizziness, or nausea during sex. Sexual activity can put an extra strain on your heart, especially if your heart is already weak from a heart attack or heart disease.

What Should I Tell My Healthcare Provider Before Taking CIALIS?

CIALIS is not right for everyone. Only your healthcare provider and you can decide if CIALIS is right for you. Ask your healthcare provider if your heart is healthy enough for you to have sexual activity. You should not take CIALIS if your healthcare provider has told you not to have sexual activity because of your health problems. Before taking CIALIS, tell your healthcare provider about all your medical problems, particularly if you have or ever had:

- **heart problems** such as chest pain, heart failure, irregular heartbeats, or have had a heart attack
- **high or low blood pressure**
- **stroke**
- **liver or kidney problems**
- **severe vision loss, including a condition called NAION**
- **retinitis pigmentosa**, a rare genetic (runs in families) eye disease
- **a deformed penis shape** or Peyronie's disease
- **an erection that lasted more than 4 hours**
- **blood cell problems** such as sickle cell anemia, multiple myeloma, or leukemia

Can Other Medicines Affect CIALIS?

Tell your healthcare provider about all the medicines you take especially if you take:

- medicines called "nitrates" which are often prescribed for chest pain
- alpha-blockers often prescribed for prostate problems
- blood pressure medications
- medicines for HIV or some types of oral antifungal medications
- some types of antibiotics such as clarithromycin, erythromycin (several brand names exist, please contact your healthcare provider to determine if you are taking this medicine)
- other medicines or treatments for erectile dysfunction (ED)
- CIALIS is also marketed as ADCIRCA for the treatment of pulmonary arterial hypertension. Do not take both CIALIS and ADCIRCA. Do not take sildenafil citrate (Revatio®) with CIALIS.

What Should I Avoid While Taking CIALIS?

- Do not use other ED medicines or ED treatments while taking CIALIS.
- Do not drink too much alcohol when taking CIALIS (for example, 5 glasses of wine or 5 shots of whiskey). Drinking too much alcohol can increase your chances of getting a headache or getting dizzy, increasing your heart rate, or lowering your blood pressure.

What Are The Possible Side Effects Of CIALIS?

The most common side effects with CIALIS are: headache, indigestion, back pain, muscle aches, flushing, and stuffy or runny nose. These side effects usually go away after a few hours. Men who get back pain and muscle aches usually get it 12 to 24 hours after taking CIALIS. Back pain and muscle aches usually go away within 2 days. Call your healthcare provider if you get any side effect that bothers you or one that does not go away.

Uncommon but serious side effects include:

An erection that won't go away: If you get an erection lasting more than 4 hours, seek immediate medical help to avoid long-term injury.

In rare instances, men taking prescription ED tablets, including CIALIS, reported a sudden decrease or loss of vision or hearing (sometimes with ringing in the ears and dizziness). It's not possible to determine if these events are related directly to the ED tablets or to other factors. If you have a sudden decrease or loss of vision or hearing, stop taking any ED tablet, including CIALIS and call a healthcare provider right away.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

CIALIS does not:

- cure ED
- increase a man's sexual desire

- protect a man or his partner from sexually transmitted diseases, including HIV
- serve as a male form of birth control

CIALIS is not for women or children.

CIALIS must be used only under a healthcare provider's care.

CIALIS is available by prescription only. For additional information, talk to your doctor and see full Patient Information at <http://pi.lilly.com/us/cialis-ppi.pdf> and Prescribing Information at <http://pi.lilly.com/us/cialis-pi.pdf>, or visit www.cialis.com for more information.

TD Con-F ISI 06OCT2011

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. Additional information about Lilly is available at www.lilly.com.

Cialis® (tadalafil) is a registered trademark of Eli Lilly and Company.

P-LLY

(1) Feldman HA et al. Impotence and its medical and psychosocial correlates: results of the Massachusetts Male Aging Study. J Urol. 1994 Jan;151(1):54-61.

(2) Rosen R, Altwein J, Boyle P, Rogler SK, Lukacs B, Meuleman E, et al. Lower urinary tract symptoms and male sexual dysfunction: the multinational survey of the aging male (MSAM-7). Eur Urol. 2003;44(6):637-649.

(3) Brookes ST, Link CL, Donovan JL, and McKinlay JB. Relationship between lower urinary tract symptoms and erectile dysfunction: results from the Boston Area community Health Survey. J Urol 2008;179:250-255.

(4) Gacci M, et al. Critical analysis of the relationship between sexual dysfunctions and lower urinary tract symptoms due to benign prostatic hyperplasia. In press. Eur Urol 2011; doi:10.1016/j.eururo.2011.06.037.

(Logo: <http://photos.prnewswire.com/prnh/20031219/LLYLOGO>)

SOURCE Eli Lilly and Company

News Provided by Acquire Media