

Ligand Announces Presentation of Positive Data from a Phase 1 Study on the Effect of the SERM Lasofoxifene to Increase Testosterone Levels in Men

Presentation at ICE/ENDO 2014 shows that a single oral dose of lasofoxifene produced a robust increase in testosterone that was maintained for as long as 28 days

SAN DIEGO-- **Ligand Pharmaceuticals Incorporated (NASDAQ: LGND)** announced that data from a Phase 1 study of the selective estrogen receptor modulator (SERM) lasofoxifene were featured in a poster presentation today at ICE/ENDO 2014 in Chicago. The presentation provided data from a first-in-human clinical study of lasofoxifene that was performed by Pfizer and recently analyzed by Ligand demonstrating the potent and prolonged effect of a single dose to increase circulating testosterone and gonadotropin levels in healthy young men.

Highlights of the presentation include:

- In an investigator-blinded, randomized, placebo-controlled, single-ascending dose study involving 36 healthy male volunteers, lasofoxifene was well-absorbed after oral administration with peak plasma concentrations reached approximately 6 to 9 hours post-dose and a long elimination half-life of approximately 106 hours
- There were no serious adverse events and no clinically significant changes in safety laboratory, vital signs or ECG assessments
- Single oral doses of lasofoxifene of 1, 3, 10, 30 and 100 mg increased levels of testosterone (T); doses of 30 and 100 mg increased levels of T by more than 80%
- Levels of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) were also elevated with single oral doses of 30 and 100 mg
- Levels of T, LH and FSH peaked between 3 and 7 days post-dose and elevations induced by higher doses were maintained through at least 28 days
- T levels plateaued at the high normal range of 30-40 nmol/L between 7 and 28 days post-dose regardless of lasofoxifene dose or LH levels

“This is the first time clinical efficacy data for lasofoxifene in males has been presented,” commented Matthew W. Foehr, Executive Vice President and Chief Operating Officer of Ligand. “Significant market need exists for safe, effective and convenient oral treatments in this area, as approximately 5 million men in the US suffer from low testosterone. These data create yet another potential clinical-stage partnering opportunity for our lasofoxifene asset in a variety of growing and higher-profile men’s health applications, including secondary hypogonadism and other disorders that are associated with low testosterone levels.”

About SERM Treatment in Men

Certain SERMs, such as tamoxifen and raloxifene, have been shown to stimulate endogenous testosterone production in men after 4 weeks of treatment by influencing the gonadal axis. Furthermore, clomiphene and one of its stereoisomers, enclomiphene, have been shown to increase levels of T, LH, FSH and sperm count in men with secondary hypogonadism. The mechanism by which SERMs affect the gonadal axis has been shown to be through inhibition of estradiol feedback at the pituitary and hypothalamus. The effects of lasofoxifene on T, LH and FSH in normal healthy men have not been reported previously.

About Lasofoxifene

Lasofoxifene is a next-generation SERM that was the subject of a collaboration between Ligand and Pfizer. It has been tested by Pfizer in multiple clinical trials and was progressed by Pfizer through regulatory approval in the EU for the treatment of osteoporosis in postmenopausal women at increased risk of fracture under the trade name Fablyn[®]. In the Phase 3 Postmenopausal Evaluation And Risk-reduction with Lasofoxifene (PEARL) trial conducted by Pfizer, lasofoxifene was administered to approximately 6,000 postmenopausal women for 5 years. In postmenopausal women with osteoporosis a daily dose of 0.5 mg was shown to reduce the risk of nonvertebral and vertebral fractures, and also to reduce the risk of ER-positive breast cancer, symptoms associated with vaginal atrophy, major coronary events and stroke, but was associated with an increased risk of venous thromboembolic events. Full rights to and data for lasofoxifene were returned to Ligand from Pfizer in 2011. Pfizer retains all rights to the Fablyn trademark. The effects of lasofoxifene on the gonadal axis differentiates it from other SERMs and may warrant further study to determine the potential benefits of lasofoxifene treatment in hypogonadal men.

About Ligand Pharmaceuticals

Ligand is a biopharmaceutical company with a business model that is based upon the concept of developing or acquiring royalty revenue generating assets and coupling them to a lean corporate cost structure. Ligand's goal is to produce a bottom line that supports a sustainably profitable business. By diversifying our portfolio of assets across numerous technology types, therapeutic areas, drug targets and industry partners, we offer investors an opportunity to invest in the increasingly complicated and unpredictable pharmaceutical industry. In comparison to its peers, we believe Ligand has assembled one of the largest and most diversified asset portfolios in the industry with the potential to generate revenue in the future. These therapies address the unmet medical needs of patients for a broad spectrum of diseases including diabetes, hepatitis, muscle wasting, Alzheimer's disease, dyslipidemia, anemia, asthma and osteoporosis. Ligand's Captisol platform technology is a patent protected, chemically modified cyclodextrin with a structure designed to optimize the solubility and stability of drugs. Ligand has established multiple alliances with the world's leading pharmaceutical companies including GlaxoSmithKline, Onyx Pharmaceuticals (a subsidiary of Amgen Inc.), Merck, Pfizer, Baxter International, Eli Lilly & Co. and Spectrum Pharmaceuticals. Please visit www.captisol.com for more information on Captisol. For more information on Ligand, please visit www.ligand.com.

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Forward-Looking Statements

This news release contains forward-looking statements by Ligand that involve risks and uncertainties and reflect Ligand's judgment as of the date of this release. These include statements regarding data analysis and evaluation of lasofoxifene and other SERMs, utility or potential benefits to patients, plans for continued development and further studies of such compounds. Actual events or results may differ from our expectations. For example, there can be no assurance that other trials or evaluations lasofoxifene or other SERMs will be favorable or that they will confirm results of previous studies, that data evaluation will be completed or demonstrate any hypothesis or endpoint, that such compounds will provide utility or benefits to certain patients, that any presentations will be favorably received, that such compounds will be useful with other drugs, that marketing applications will be filed or, if filed, approved, or that clinical or commercial development of these drugs will be initiated, completed or successful or that our rights to lasofoxifene or other SERMs will not be successfully challenged. The failure to meet expectations with respect to any of the foregoing matters may reduce Ligand's stock price. Additional information concerning these and other risk factors affecting Ligand's business can be found in prior press releases available via www.ligand.com as well as in Ligand's public periodic filings with the Securities and Exchange Commission at www.sec.gov. Ligand disclaims any intent or obligation to update these forward-looking statements beyond the date of this release. This caution is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

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