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Ligand Presents Positive LGD-4665 Phase I Clinical Trial Results at the American Society of Hematology Annual Meeting (ASH)

Provides Business Outlook

SAN DIEGO--

Ligand Pharmaceuticals Incorporated (NASDAQ:LGND) today announced positive results from a Phase I clinical trial with LGD-4665 in a poster titled "Single and Multiple Oral Doses of LGD-4665, a Small Molecule Thrombopoeitin Receptor Agonist, Increase Platelet Counts in Healthy Male Subjects," at the American Society of Hematology (ASH) 49th Annual Meeting, being held at the Georgia World Congress Center in Atlanta December 8-11, 2007.

The poster presentation highlighted LGD-4665 as an oral, small-molecule drug that mimics the activity of thrombopoietin (TPO), a growth factor that promotes growth and production of blood platelets. The poster presentation can be viewed by visiting the Investor Relations section of Ligand's website at www.ligand.com.

Ligand's Phase I clinical trial evaluated three dosing regimens of LGD-4665, including single doses, multiple daily doses for 14 days, and Day 1 loading doses followed by daily doses for 13 days. The drug was safe and well tolerated, and statistically significant platelet increases were observed in both single and multiple daily dose regimens.

"These efficacy results demonstrate potential use of this new molecule in thrombocytopenic patients that in the future could reduce the need for platelet transfusions, and ultimately improve patient outcomes," said James B. Bussel, M.D., Director of the Platelet Disorders Center, Children's Blood Foundation Division at the New York-Presbyterian Hospital/Weill Cornell Medical Center.

Summary Phase I Clinical Trial Results

- LGD-4665 showed impressive activity following single and multiple doses with an increase in mean maximum platelet counts of 58% with a single dose administration of 120 mg and 83% with 10 mg dosed daily for 14 days.

- Results demonstrated that with a Day 1 loading dose, the increase in mean maximum platelet counts was 27% with 2.5 mg, 43% with 5.0 mg and 79% with 7.5 mg daily for 13 days.

- A gradual decline in platelet levels was observed post-treatment.

-- The pharmacokinetic properties showed reliable absorption with a dose-proportional increase of systemic exposure in both single doses and multiple doses. The half-life of LGD-4665 was approximately 90 hours.

-- LGD-4665 was well-tolerated and demonstrated an encouraging safety profile at all dose levels and all dosing regimens. There were no serious adverse events. The majority of adverse events observed were mild-to-moderate with no apparent direct relationship to LGD-4665 exposure. There were no clinically significant or LGD-4665 related vital signs or laboratory abnormalities.

-- In clinical studies of 14-day dosing, LGD-4665 is 10 times more potent than eltrombopag, based on published data with 10-day dosing.

Pre-clinical Highlights

-- LGD-4665 is a highly selective full agonist mimetic of TPO.

-- LGD-4665 demonstrated an additive effect with TPO in the stimulation of thrombopoiesis by human bone-marrow hematopoietic stem cells.

"We are very encouraged by the promising activity and safety profile demonstrated with LGD-4665 in this Phase I study," said Zofia E. Dziewanowska, M.D., Ph.D., Ligand's Vice President of Clinical Research. "In addition, a pharmacokinetic profile of LGD-4665 allows not only for a once-a-day dosing but, due to its long half-life, potentially for a weekly dosing regimen, as well. Based on its strong potency, convenience and potential for dosing flexibility, we believe that LGD-4665 could be used as treatment for a wide variety of diseases associated with thrombocytopenia, including hepatitis C, chemotherapy-induced thrombocytopenia (CIT), myelodysplastic syndromes (MDS), idiopathic thrombocytopenic purpura (ITP) and several other cancers and liver diseases."

LGD-4665 Study Design

The placebo-controlled, double-blind, dose-escalating Phase I clinical trial was conducted at a single center in 106 healthy male subjects. In the single dose portion of the trial, six subjects were randomized in the several dose cohorts to receive either a single dose of LGD-4665 or placebo (in a 2:1 ratio). Dose levels ranged from 1 mg to 120 mg, and were escalated sequentially based on the review of safety and activity (increase in platelet levels) according to predefined criteria. In the multiple dose portion of the trial, at doses of 2.5 mg to 10 mg daily, 14 subjects at each dose level were randomized to placebo or LGD-4665 for 14 days, either with or without a one-time loading dose. Similar to the single dose study, dose escalation was determined following safety and activity evaluations conducted at the conclusion of each dose cohorts.

Eltrombopag and GlaxoSmithKline

In 1997, Ligand formed a research and development alliance with GlaxoSmithKline (GSK), which led to the discovery of eltrombopag (Promacta), a first generation TPO mimetic. Since then, GlaxoSmithKline has announced that it expects to submit an NDA for eltrombopag by year-end for the treatment of short-term ITP. In addition, two Phase III trials were initiated by

GSK in the fourth quarter of 2007 for hepatitis C, and GSK is studying the drug for CIT. GSK has made significant progress advancing its program, and eltrombopag may be the first oral TPO mimetic to be approved. Ligand will receive a royalty from eltrombopag sales.

Ligand's Next Generation TPO Program

The Ligand thrombopoietin program commenced after the conclusion of the GSK partnership and has focused on developing novel proprietary drug candidates that mimic the activity of thrombopoietin. LGD-4665 is the lead, small-molecule TPO mimetic under development at Ligand Pharmaceuticals. LGD-4665 binds to the thrombopoeitin receptor in a manner similar to TPO and activates the production of platelets by the bone marrow. In addition, several next generation molecules from a chemical series distinct from LGD-4665, are in the research phase with promising TPO mimetic activities.

Thrombocytopenia Market Opportunity

Thrombocytopenia is seen in 5-10% of all patients hospitalized for any cause. Several key indications for thrombocytopenia include ITP, hepatitis C and MDS/chemotherapy.

- ITP - According to the Platelet Disorder Support Association (PDSA), approximately 200,000 patients are affected by ITP in the U.S. In the current U.S. ITP population, half of the patients have thrombocytopenia and require drug interventions and/or platelet transfusions. A similar patient population exists in the European Union (EU).

- Hepatitis C - The Centers for Disease Control and Prevention (CDC) estimates that 2.7 million patients in the U.S. are chronically infected with HCV. Thrombocytopenia is a frequently reported complication of HCV and antiviral therapy. An estimated 10% of hepatitis C patients have clinically significant thrombocytopenia associated with cirrhosis.

- Chemotherapy - The American Cancer Society estimates 1.5 million new cases of non-skin cancers with the majority of patients expected to receive chemotherapy regimens. Thrombocytopenia is a frequently reported complication in approximately 10% of patients receiving chemotherapy

- Myelodysplastic Syndromes (MDS) - According to the Cleveland Clinic Foundation, 35,000 to 40,000 patients in the U.S. have MDS. In addition, 50% of patients with certain hematological malignancies such as MDS suffer from disease-induced thrombocytopenia.

LGD-4665 holds potential for additional medical applications including bone-marrow transplants, cirrhosis, lupus, intensive-care and peri-operative patients, HIV and for pre-treatment before a platelet donation. The worldwide market for innovative TPO drugs has the potential to generate billions of dollars of sales annually.

Business Outlook

Ligand expects to advance the development of LGD-4665 for multiple indications. In 2008, the Company currently expects to initiate clinical trials for ITP, MDS and hepatitis C. In addition, the Company plans to conduct further studies evaluating drug pharmacology

including the potential for weekly dosing with LGD-4665.

The Company anticipates that its total 2008 expenses for G&A and R&D costs to operate the Company, excluding stock-based compensation, to be approximately $35 million.

About Ligand Pharmaceuticals

Ligand discovers and develops new drugs that address critical unmet medical needs of patients in the areas of thrombocytopenia, hepatitis C, cancer, hormone-related diseases, osteoporosis and inflammatory diseases. Ligand's proprietary drug discovery and development programs are based on its leadership position in gene transcription technology, primarily related to intracellular receptors.

Caution Regarding Forward-Looking Statements

This press release contains forward-looking statements within the meaning of section 21E of the Securities Exchange Act of 1934, as amended, that involve risks and uncertainties and reflect Ligand's judgment as of the date of this press release. For example, we may spend more or less than the anticipated operational expense set forth herein, and operating expenses do not include any one-time charges. These statements also include those regarding data analysis and evaluation of LGD-4665, utility or potential benefits to patients, plans for continued development and further studies of LGD-4665 for the treatment of diseases associated with thrombocytopenia. Actual events or results may differ from our expectations. For example, there can be no assurance that other trials or evaluations of LGD-4665 or other TPO-related product candidates 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 LGD-4665 or other TPO-related product candidates will provide utility or benefits to certain patients, that any presentations will be favorably received, that LGD-4665 or other TPO-related product candidates will be useful as a single agent or in combination with other drugs, that marketing applications will be filed or, if filed, approved, or that clinical or commercial development of these product candidates will be initiated, completed or successful or that our rights to LGD-4665 and other TPO-related product candidates will not be successfully challenged. Our stock price may suffer as a result of the failure of any trials to be completed or meet their endpoints or if any actual events differ from our expectations. Additional information concerning these and other risk factors affecting Ligand can be found in prior press releases as well as in public periodic filings with the Securities and Exchange Commission, available via www.ligand.com. Ligand disclaims any intent or obligation to update these forward-looking statements beyond the date of this press release. This caution is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

Source: Ligand Pharmaceuticals Incorporated