

Ligand Announces Favorable Results From Phase 1b Trial With LGD-6972 in Type 2 Diabetes and Plans to Initiate a Phase 2 Trial

Presentation at the American Diabetes Association 75th Scientific Sessions

SAN DIEGO-- **Ligand Pharmaceuticals Incorporated (NASDAQ: LGND)** announces results from a Phase 1b clinical trial with LGD-6972 that demonstrate favorable safety, tolerability and pharmacokinetics in normal healthy volunteers and in subjects with type 2 diabetes mellitus. The trial results also demonstrate a robust, dose-dependent reduction of fasting plasma glucose. LGD-6972 is Ligand's novel glucagon receptor antagonist, and these results were presented at the American Diabetes Association's 75th Scientific Sessions meeting underway in Boston.

Glucagon receptor antagonists are the leading non-insulin mechanism in development for the treatment of type 2 diabetes. Based on earlier data and these latest results, Ligand believes LGD-6972 has best-in-class properties given its potency, preliminary effectiveness in lowering plasma glucose in patients with type 2 diabetes and its safety profile demonstrated in two Ligand-sponsored clinical trials.

In this randomized, double-blind, placebo-controlled trial, LGD-6972 was administered in sequential increasing oral doses daily over two weeks to both healthy subjects and subjects with type 2 diabetes. A total of 48 subjects were enrolled in the trial.

Highlights of the study include:

- LGD-6972 tested at 5mg, 10mg and 15mg was safe and well-tolerated with no clinically significant or dose-dependent changes in hematology, clinical chemistry or urinalysis panels, ECG or vital signs. There were no serious adverse events and no study discontinuations. All treatment-emergent adverse events were of mild or moderate severity (grade 1 or 2).
- Plasma levels increased linearly with LGD-6972 dosage, and the pharmacokinetic profiles were comparable between normal and type 2 diabetes subjects, supporting once-daily dosing.
- LGD-6972 lowered fasting plasma glucose in normal subjects and in subjects with type 2 diabetes. Glucose was reduced throughout the 14-day dosing period. Baseline adjusted glucose values showed dose-dependent effects of LGD-6972 in type 2 diabetic subjects with a maximal decrease of 60 mg/dL.
- 7 point glucose measurements were performed at baseline and Day 14 and illustrated that LGD-6972 decreased glucose throughout a 24-hour period in both fasting and

post-prandial states.

- LGD-6972 is a highly potent and selective glucagon receptor antagonist and is a promising agent for the treatment of type 2 diabetes.

Ligand is preparing to initiate a Phase 2 trial with LGD-6972 in 2016 with the goal to establish additional safety and efficacy for the program in 12 consecutive weeks of dosing in subjects with type 2 diabetes. Approximately 100 subjects will be enrolled in this randomized, double-blind, multicenter trial. The trial is estimated to cost approximately \$10 million and should be completed in 2017. Any incremental increase to Ligand's annual R&D spending as a result of this program is expected to be covered within Ligand's financial operations, and there is no change to the company's long-term earnings guidance.

"We are very pleased with these most recent findings with LGD-6972 which build upon the Phase 1 single-ascending dose trial results we reported at last year's ADA meeting. We believe we are at the right place at the right time as given what we know about LGD-6972 and the programs underway at Eli Lilly and Pfizer, we may have the best-in-class molecule. Moreover, glucagon antagonism has emerged over the past few years as the leading non-insulin mechanism for type 2 diabetes in development," said John L. Higgins, Chief Executive Officer.

"We have the team, the capital and the financial strength to advance this program, and believe continued internal development of LGD-6972 is in the best interests of Ligand's shareholders," he added. "Against the backdrop of the largest product portfolio ever, promising late-stage partnered assets and an increasingly profitable business, we are excited to be advancing a potentially major novel molecule for a very large therapeutic opportunity."

About Ligand's Glucagon Receptor Antagonist Program

Glucagon is a hormone produced by the pancreas that stimulates the liver to produce glucose (sugar). Overproduction of glucose by the liver is an important cause of high glucose levels in patients with type 2 diabetes and is believed to be due in part to inappropriately elevated levels of glucagon. Glucagon receptor antagonists are designed to lower glucose levels by reducing the production of glucose by the liver. Glucagon receptor antagonists are novel molecules that have demonstrated a reduction of glucose and hemoglobin A1c (HbA1c) in mid-stage clinical trials.

LGD-6972 has been studied in previously-published preclinical and clinical studies. Presentations from preclinical studies have shown that LGD-6972 is highly potent and selective and inhibits glucagon-induced hyperglycemia in both rats and monkeys, and that it also significantly lowers glucose in a mouse model of type 2 diabetes. Additionally, LGD-6972 significantly lowered fasting and non-fasting glucose levels in a mouse model of type 1 diabetes and also reduced HbA1c, ketone bodies and free fatty acids. LGD-6972 also has been shown to have additive effects when used in combination with insulin therapy and may also be useful in an insulin-sparing regimen. In a previous Phase 1a single-ascending dose clinical study, LGD-6972 was well-tolerated, with no clinically significant or dose-dependent changes in hematology, clinical chemistry or urinalysis panels, ECG or vital signs, and no serious adverse events. After a single dose, LGD-6972 reduced fasting plasma glucose in normal healthy volunteers and in subjects with type 2 diabetes; fasting plasma glucose was reduced by 57 mg/dL (placebo-adjusted) in subjects with type 2 diabetes.

About Diabetes

Diabetes is a growing global epidemic that currently affects more than 387 million people worldwide. In the United States, approximately 29 million people have diabetes, or roughly 9% of the total population. If current trends continue, by 2050 fully 33% of the U.S. population will be affected. People with type 2 diabetes either are resistant to the effects of insulin or do not produce enough insulin to maintain a normal glucose level. Sustained high glucose levels can cause diabetic complications such as heart disease, stroke, kidney failure, neuropathy, lower-limb amputations and blindness. Although type 2 diabetes is more common in adults, it increasingly affects children as childhood obesity increases. An estimated 90% to 95% of Americans with diabetes have type 2 diabetes.

The market for diabetes drugs is expected to nearly double to \$68 billion by 2022 as treatment paradigms shift toward combination therapies and novel non-insulin drugs. The top 10 non-insulin diabetes drugs had total sales of \$12 billion in 2014, and sales are expected to increase to \$20 billion by 2020.

About Ligand Pharmaceuticals

Ligand is a biopharmaceutical company with a business model focused on developing or acquiring royalty generating assets and coupling them with a lean corporate cost structure. Ligand's goal is to produce a bottom line that supports a sustainably profitable business. By diversifying the 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 seek to 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; Novartis, Amgen, Merck, Pfizer, Baxter International and Eli Lilly.

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 forward-looking statements include comments regarding the costs and timing of future clinical trials, the ability of Ligand to enroll patients in a new clinical trial, the expectation that the results from completed clinical trials predict the results of future clinical trials, the ability of Ligand's cash flow from operations to cover the costs of a Phase 2 clinical trial, the impact of clinical trials on Ligand's financial guidance, the expected positive return to investors, as well as the growth of the population with diabetes and the trends in the market to treat diabetes. 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 important risk factors affecting Ligand (including Ligand's current reliance on revenues based on sales of Promacta[®] and Kyprolis[®], and various risks to which Ligand's Captisol[®] cyclodextrin operations are subject) can be found in Ligand's prior press releases available at

www.ligand.com as well as in Ligand's public periodic filings with the Securities and Exchange Commission, available at www.sec.gov. Ligand disclaims any intent or obligation to update these forward-looking statements beyond the date of this press release, except as required by law. This caution is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

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