August 15, 2016

Results from Phase 1 Trials with Ligand's LGD-6972 in Type 2 Diabetes Mellitus Published in Diabetes, Obesity and Metabolism

Clinical data demonstrate favorable safety, tolerability and pharmacokinetics, and improved glycemic response in healthy volunteers and patients with type 2 diabetes

SAN DIEGO-- **Ligand Pharmaceuticals Incorporated (Nasdaq: LGND)** announces that results from two Phase 1 clinical trials with LGD-6972, the company's investigational glucagon receptor antagonist, were published online in the August issue of the journal *Diabetes, Obesity and Metabolism*. The article is available here.

The single- and multiple-dose Phase 1a and Phase 1b studies demonstrated 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.

"These clinical results are encouraging as they demonstrate a favorable safety profile for LGD-6972 and show a robust glycemic response in both healthy subjects and subjects with diabetes," said John Higgins, CEO of Ligand. "This is a promising field for diabetes research, and we look forward to initiating a phase 2 trial next month."

In the randomized, double-blind, placebo-controlled Phase 1 trials, LGD-6972 was administered in single or multiple oral doses to both healthy subjects and subjects with type 2 diabetes to evaluate safety, tolerability, pharmacokinetics and pharmacodynamics. LGD-6972 is Ligand's novel, small-molecule glucagon receptor antagonist. Glucagon receptor antagonists are a leading non-insulin mechanism in development for the treatment of type 2 diabetes. Based on the Phase 1 trial results, Ligand believes LGD-6972 could have best-in-class properties given its potency in lowering plasma glucose in patients with type 2 diabetes and its preliminary safety profile.

Highlights of the Phase 1 studies include:

- LGD-6972, tested at single doses from 2 mg to 480 mg, and multiple daily doses of 5 mg, 10 mg and 15 mg over 14 days, was generally safe and well-tolerated with no clinically significant or dose-dependent changes in hematology, clinical chemistry or urinalysis panels, electrocardiography or vital signs, and no subject experienced a hypoglycemic event. There were no serious adverse events and no study discontinuations. Most 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 healthy volunteers and type 2 diabetes subjects, supporting once-daily dosing.
- LGD-6972 lowered fasting plasma glucose in normal healthy volunteers and in subjects with type 2 diabetes after single and multiple doses. Baseline adjusted glucose values showed dose-dependent effects of LGD-6972 on subjects with type 2 diabetes with a maximal decrease of 57 mg/dL on day 14.
- LGD-6972 decreased glucose in both fasting and post-prandial states, and was accompanied by an increase in insulin and a decrease in glucagon in response to an oral glucose load.
- The robust glycemic responses in subjects with type 2 diabetes treated with LGD-6972 were not associated with dose-related or clinically meaningful changes in liver enzymes during the 14-day treatment or follow-up periods.
- The safety and pharmacological profile of LGD-6972 after 14 days of dosing supports continued clinical development as an adjunct to diet and exercise for the treatment of type 2 diabetes.

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.

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.

Ligand is preparing to initiate a Phase 2 trial with LGD-6972 in September 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. The randomized, double-blind, multicenter trial will enroll 148 subjects whose blood glucose levels are inadequately controlled with metformin, and should be completed in 2017.

About Diabetes

Diabetes is a growing global epidemic that currently affects more than 415 million people worldwide[1]. In the North America, approximately 39 million people have diabetes, or roughly 11% of the total population[1]. If current trends continue, by 2050 fully 33% of the U.S. population will be affected[2]. 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[3].

The market for diabetes drugs is expected to nearly double to $68 billion by 2022[4] 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[5].

About Ligand Pharmaceuticals

Ligand is a biopharmaceutical company focused on developing or acquiring technologies that help pharmaceutical companies discover and develop medicines. Our business model creates value for stockholders by providing a diversified portfolio of biotech and pharmaceutical product revenue streams that are supported by an efficient and low corporate cost structure. Our goal is to offer investors an opportunity to participate in the promise of the biotech industry in a profitable, diversified and lower-risk business than a typical biotech company. Our business model is based on doing what we do best: drug discovery, early-stage drug development, product reformulation and partnering. We partner with other pharmaceutical companies to leverage what they do best (late-stage development, regulatory management and commercialization) to ultimately generate our revenue. Ligand's Captisol® platform technology is a patent-protected, chemically modified cyclodextrin with a structure designed to optimize the solubility and stability of drugs. OmniAb® is a patent-protected transgenic animal platform used in the discovery of fully human mono- and bispecific therapeutic antibodies. Ligand has established multiple alliances, licenses and other business relationships with the world's leading pharmaceutical companies including Novartis, Amgen, Merck, Pfizer, Celgene, Gilead, Janssen, Baxter International and Eli Lilly.

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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 the timing, size and protocol for a Phase 2 trial with LGD-6972, the potential for LGD-6972 to treat patients with type 2 diabetes, the anticipated safety and pharmacological profile in future clinical trials, the number of patients affected by diabetes, the number of patients who may be affected by diabetes in the future, the annual total sales of non-insulin diabetes drugs and the expected future sales of such drugs. Actual events or results may differ from our expectations. For example, Ligand may choose not to initiate or complete a Phase 2 clinical trial in LGD-6972 for a number of reasons, including new corporate priorities or additional data regarding LGD-6972; there can be no assurance that success in a Phase 1 clinical trial will result in success in future clinical trials; the safety and tolerability data from a new clinical trial in LGD-6972 may conflict with the results of the Phase 1 clinical trials; the number of patients diagnoses with diabetes may be more or fewer than Ligand believes; and the total sales of non-insulin diabetes drugs is dependent on

market acceptance of such drugs. 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 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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