Ligand Announces Positive Preclinical Data on Small-Molecule G-CSF Receptor Agonist at the 55th Annual Meeting of the American Society of Hematology

SAN DIEGO--Ligand Pharmaceuticals Incorporated (NASDAQ: LGND) announced that data from preclinical studies on its granulocyte colony stimulating factor (G-CSF) receptor agonist program were featured in a poster presentation today at the 55th Annual Meeting of the American Society of Hematology (ASH) in New Orleans.

In preclinical studies, Ligand evaluated the ability of LGD-7455 to stimulate neutrophil (white blood cell) counts in cynomolgus monkeys and investigated the role that metal ions play in the activity of LGD-7455 on the G-CSF receptor (G-CSFR). Additionally, the effects and mechanisms of LGD-7455 on tumor cell growth were examined.

The key findings include:

- LGD-7455 is a novel small-molecule, selective human G-CSFR agonist that activates the receptor in a manner distinct from native G-CSF, but similar to the mechanism of small-molecule oral thrombopoietin receptor (TPOR) agonists.
- LGD-7455 significantly increases peripheral blood neutrophils, demonstrating the first reported proof-of-concept for a small molecule G-CSFR agonist in a primate model.
- LGD-7455 inhibits tumor cell growth and increases apoptosis, mediated by intracellular metal chelation and an increase in reactive oxygen species formation.

“We are pleased to present this scientifically important work from one of Ligand’s internal un-partnered programs,” said Matthew W. Foehr, Chief Operating Officer of Ligand. “Ligand’s R&D team continues to make scientific advancements like this first reported proof-of-concept for a small molecule G-CSF in a primate model. Further optimization of the LGD-7455 series may lead to a novel oral anticancer therapy that also serves as a supportive care agent to treat neutropenia in patients receiving bone-marrow suppressive treatments. The worldwide market for injectable G-CSF is currently over $6 billion, and we believe there is a substantial unmet medical need and market opportunity for a G-CSF receptor agonist that offers a novel route of administration and differentiated profile with the potential to have anti-tumor efficacy in addition to increasing neutrophils.”

About Ligand’s Small-Molecule Oral G-CSF Program

G-CSF is a glycoprotein growth factor and cytokine produced by different tissues to
stimulate the bone marrow to produce granulocytes and stem cells. G-CSF acts on its homodimeric receptor, G-CSFR, to stimulate proliferation of granulocytic progenitor cells and induce their survival and differentiation into neutrophils. Several biologic versions of injectable recombinant human G-CSF (e.g., Neupogen®, Neulasta® and Neutrogin®) are approved to treat chemotherapy-induced neutropenia, neutropenia associated with hematopoietic stem cell transplantation and severe chronic neutropenia. The goal of Ligand’s G-CSF Program is to provide a non-peptide, small-molecule, oral G-CSFR agonist that is a convenient alternative to injectable G-CSF therapy for the treatment of neutropenia with potential advantages, including anti-tumor activity, that have not been observed with recombinant G-CSF.

Ligand has previously reported the discovery of a novel series of molecules, exemplified by LGD-7455, that selectively activate human G-CSFR function in a manner distinct from G-CSF, but similar to the mechanism of small-molecule TPOR agonists, such as eltrombopag (Promacta®). The new preclinical studies find that LGD-7455 is a metal chelator with anti-proliferative effects on tumor cells. Ligand believes that the use of metal chelators has potential in anti-cancer treatment, as neoplastic cells have a high requirement for metal ions, such as iron and copper, related to their rapid rate of replication. Limiting the availability of these metal ions to tumor cells or reducing their intracellular content may be an advantageous strategy to inhibit uncontrolled cancer cell proliferation.

About Ligand Pharmaceuticals

Ligand is a biopharmaceutical company focused on assembling a large portfolio of revenue-generating assets through licensing and acquisition with the goal to generate sustainable cash-flow and profitability. Ligand has a diverse asset portfolio addressing the unmet medical needs of patients for a broad spectrum of diseases including thrombocytopenia, multiple myeloma, diabetes, hepatitis, muscle wasting, dyslipidemia, anemia 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, Bristol-Myers Squibb, Lundbeck Inc., Eli Lilly & Co. and Spectrum Pharmaceuticals. Please visit www.captisol.com for more information on Captisol or www.ligand.com for more information on Ligand.

Forward-Looking Statements

This news release contains certain forward-looking statements by Ligand that involve risks and uncertainties and reflect Ligand's judgment as of the date of this release. These statements include those related to the use and market potential of LGD-7455 and other metal chelators in anti-cancer treatment and to treat neutropenia in patients receiving bone-marrow suppressive treatments. The failure to meet expectations with respect to any of the foregoing matters may reduce Ligand's stock price. Additional information concerning 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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