

## Ligand Announces Positive Preclinical Data on Small-Molecule GCSF Receptor Agonist at the 53rd 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 (GCSF) receptor program were featured in a poster presentation today at the 53rd Annual Meeting of the American Society of Hematology in San Diego. Ligand has discovered a novel series of small molecules, exemplified by the lead compound LG7455, that selectively activate human GCSFR function in a manner distinct from GCSF, but similar to the mechanism of small-molecule human thrombopoietin receptor (hTPOR) agonists, such as eltrombopag (Promacta®).

In preclinical studies, Ligand evaluated the effect of the GCSFR agonist LG7455 in well-established *in vitro* models of receptor function and on differentiation of CD34-positive human bone marrow cells into granulocytes.

The key findings include:

- LG7455 activates STAT5 and STAT3 signal transduction and increases the viability of cells containing human GCSFR
- LG7455 promotes the differentiation of human bone marrow cells into granulocytes, significantly increasing expression of the granulocyte-specific marker CD15
- The activity of LG7455 is dependent on the expression of human or monkey GCSFR
- A histidine in the human GCSFR transmembrane domain is needed for activity, similar to what has been found for small-molecule hTPOR agonists
- LG7455 increases GCSF receptor binding in a manner consistent with allosteric receptor modulation

Further optimization of the LG7455 structure series could lead to a new generation of orally-available small-molecule human GCSFR agonists for the treatment of neutropenia.

“We are pleased to feature exciting data from one of our novel programs in Ligand’s internal un-partnered pipeline,” said Matthew W. Foehr, Chief Operating Officer of Ligand Pharmaceuticals. “Our R&D team continues Ligand’s rich heritage of being at the forefront of new areas of drug discovery and development. This first-in-class program may provide the most significant innovation in the treatment of neutropenia since the approval of the first GCSF biologic in the early 1990’s.”

**About Ligand’s Small- Molecule GCSF Program**

GCSF is a glycoprotein growth factor and cytokine produced by different tissues to stimulate the bone marrow to produce granulocytes and stem cells. GCSF acts on its homodimeric receptor (GCSFR) to stimulate proliferation of granulocytic progenitor cells and induce their survival and differentiation into neutrophils. Several biologic versions of injectable recombinant human GCSF (e.g. Neupogen®, Neulasta® and Neutrogin®) are approved to treat chemotherapy-induced neutropenia, neutropenia associated with hematopoietic stem cell transplantation, and severe chronic neutropenia. Recently, additional roles for GCSFR have emerged outside the hematopoietic system, such as in neuroprotection and regeneration, potentially expanding the clinical applications of GCSF to include neurodegenerative disorders, stroke and ALS. The goal of Ligand's GCSF Program is to provide a non-peptide, small-molecule, oral GCSFR agonist that is a convenient, cost-sensitive alternative compared to recombinant human GCSF for the treatment of neutropenia and these possible expanded indications.

## **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 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 address the unmet medical needs of patients for a broad spectrum of diseases including hepatitis, muscle wasting, Alzheimer's disease, dyslipidemia, diabetes, anemia, COPD, asthma, rheumatoid arthritis 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, Merck, Pfizer, Baxter International, Bristol-Myers Squibb, Celgene, Onyx Pharmaceuticals, Lundbeck Inc. and The Medicines Company. Please visit [www.captisol.com](http://www.captisol.com) for more information on Captisol. For more information on Ligand, please visit [www.ligand.com](http://www.ligand.com).

Follow Ligand on Twitter @Ligand\_LGND.

## **Caution Regarding 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 GCSF, utility or potential benefits to patients, plans for continued development and further studies of GCSF. Actual events or results may differ from our expectations. For example, there can be no assurance that other trials or evaluations of GCSF 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 GCSF will provide utility or benefits to certain patients, that any presentations will be favorably received, that GCSF 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 GCSF 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](http://www.ligand.com). Ligand disclaims any intent or obligation to update these forward-looking statements beyond the date of this release.**

Ligand Pharmaceuticals Incorporated  
Rob McKay, Sr. Dir. Business Development and Investor Relations  
Erika Luib, Investor Relations  
(858) 550-7896  
or  
Lippert/Heilshorn & Associates, Inc.  
Don Markley  
[dmarkley@lhai.com](mailto:dmarkley@lhai.com)  
(310) 691-7100

Source: Ligand Pharmaceuticals Incorporated