

Ligand Announces Positive Preclinical Data on Small Molecule Erythropoietin Receptor Agonists

SAN DIEGO-- Ligand Pharmaceuticals Incorporated (NASDAQ: LGND) announced data from a preclinical study on the erythropoietin (EPO) receptor agonist LG5640 at the upcoming 52nd American Society of Hematology (ASH) Annual Meeting being held in Orlando, Florida at the Orange County Convention Center, December 4 - 7, 2010. The poster presentation highlighted the unique mechanism of action and selective profile of LG5640, a novel oral EPO receptor agonist being developed as a more convenient and safer treatment alternative to current erythropoiesis-stimulating agent therapies (ESAs).

Ligand tested the effect of LG5640 on EPO-dependent cell lines and in cultures of CD34-positive human bone marrow cells, a well-established model for the effects of EPO on erythroid progenitor cells and their maturation into red blood cells (erythropoiesis). Ligand's findings suggest the potential for these small molecule EPOR agonists to provide additional benefit in the treatment of anemia with improved safety, tolerability, and patient acceptance due to the convenience of oral administration and the lack of excessive erythropoietic stimulation that may contribute to the adverse effects of the current injectable ESAs.

The study evaluated the activity of LG5640 versus rHuEPO in cell-based models of EPO-dependent proliferation and viability, on the various EPO-EPOR signaling pathways, and on the ability to induce erythroid differentiation in CD34-positive bone marrow cells, as measured by the expression of the erythroid marker CD235a and by formation of blast-forming erythroid colonies (BFUe). LG5640 displays an efficacy greater than the efficacy of the normal serum EPO concentration (~0.01 U/ml), but partial to the maximal effect induced by recombinant human EPO (rHuEPO) in models of EPO-stimulated erythropoiesis.

The poster presentation can be viewed by visiting the Investor Relations section of Ligand's Web site at www.ligand.com.

Pre-clinical Highlights

- LG5640 increased erythroid cell viability with partial efficacy to rHuEPO.
- LG5640 blocked erythroid cell apoptosis following EPO withdrawal with equivalent efficacy to rHuEPO.
- LG5640 increased differentiation of human CD34-positive bone marrow cells into erythrocytes. In addition, in combination experiments, LG5640 was seen to increase rHuEPO-stimulated erythropoiesis.
- LG5640 was found to display a unique mechanism of action, selectively activating the EPOR-GATA-1 signaling pathway, and induced the expression of GATA-1 regulated genes expressed during erythroid maturation.

Highly potent and selective EPOR agonists have been identified that display oral bioavailability in the mouse, rat and monkey, and have a desirable in vitro and in vivo safety profile for preclinical development.

About Small Molecule Programs Targeting Hematopoiesis

The proprietary research tools developed by Ligand have resulted in the discovery of small molecule agonists of Thrombopoietin (TPO), Erythropoietin (EPO) and Growth Colony Stimulating Growth Factor (G-CSF) receptors. Eltrombopag, a TPO receptor small molecule agonist approved in the U.S., Europe and Japan for the treatment of chronic idiopathic thrombocytopenic purpura (ITP), was discovered as a result of a research collaboration between Ligand and GlaxoSmithKline (GSK), and developed by GSK. In addition to the EPOR agonist program, Ligand is also conducting lead optimization studies with novel small molecule G-CSF receptor agonists for the treatment of neutropenia. Both EPOR and G-CSFR agonist programs are fully owned by Ligand.

About Ligand Pharmaceuticals

Ligand discovers and develops novel drugs that address critical 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 proprietary drug discovery and development programs are based on advanced cell-based assays, tissue-specific receptor ligand interactions and gene-expression tools. Among our peers, we believe Ligand has assembled one of the largest portfolio of assets including commercial therapies developed in partnership with pharmaceutical companies. Ligand has established multiple alliances with the world's leading pharmaceutical companies including GlaxoSmithKline, Merck, Pfizer, Bristol-Myers Squibb and AstraZeneca, and more than 30 programs in various stages of development.

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. These statements also include those regarding data analysis and evaluation of LG5640, utility or potential benefits to patients, plans for continued development and further studies of LG5640 for the treatment of diseases associated with anemia. Actual events or results may differ from our expectations. For example, there can be no assurance that trials or evaluations of LG5640 or other EPO-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 LG5640 or other EPO-related product candidates will provide utility or benefits to certain patients, that any presentations will be favorably received, that LG5640 or other EPO-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 LG5640 and other EPO-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