May 2, 2019

Ligand Completes Enrollment of Phase 1 Clinical Trial of Captisol-enabled Iohexol

Top-line data expected Q3 of 2019

Also reports recent results from clinician survey on radiocontrast agent selection and use

SAN DIEGO--(BUSINESS WIRE)-- **Ligand Pharmaceuticals Incorporated (NASDAQ: LGND)** announces completion of enrollment of the Company's Phase 1 clinical trial of its internal Captisol-enabled (CE) Iohexol program. The CE-Iohexol program is designed to develop a Captisol-enabled, next-generation contrast agent for diagnostic imaging with a reduced risk of renal toxicity. Ligand also provides below a summary of the findings of a survey of clinicians on radiocontrast agent selection and use.

"We are pleased to announce the progress of CE-Iohexol and look forward to reporting Phase 1 data later this year. This program holds the potential to increase the safety of widely-used commercial contrast agents, and, if successful, provide Ligand later-stage out-licensing opportunities," said John Higgins, Chief Executive Officer of Ligand. "A key priority of Ligand's business model is to conduct targeted R&D with the goal of advancing programs to secure significant financial terms upon out-license. Recent market research validates our view that there is a substantial unmet need for safer radiocontrast agents."

Overview:

- Contrast agents are used to enhance diagnostic imaging. Despite their benefits and widespread use, contrast agents may place patients at an increased risk for acute kidney injury (AKI), especially those with certain risk factors undergoing cardiac interventional procedures utilizing intravascular iodinated contrast.[1]
- CE-Iohexol is designed to reduce the risk of AKI during imaging procedures where iodinated contrast agents are administered.
- In animal models CE-Iohexol has been shown to prevent nephrotoxicity by more than 50%.[2]

Trial:

- The goal of the Phase 1 clinical trial is to establish pharmacokinetic bioequivalence to support subsequent clinical trials and to provide the basis for submitting a 505(b)(2) new drug application to the U.S. Food and Drug Administration.
- The trial design consists of a single-center, randomized, double-blind, two-period crossover study to determine relative bioavailability of CE-Iohexol and a reference Iohexol injection (OMNIPAQUE™) after IV administration in a population of 24 healthy adults (ClinicalTrials.gov identifier: NCT03869983).

Third Party Survey Results:

- The primary objective of this study sponsored by Ligand was to obtain directional guidance from hospital specialists involved in contrast-enhanced angiography, and to learn of perceptions, practices and unmet needs regarding radiocontrast agents used for angiography.
- More than 60 specialists from U.S. hospitals surveyed, including interventional cardiologists, radiologists, nephrologists and radiopharmacists.
- Safety was a clear, predominant priority identified for product improvement by all groups surveyed.
- Cardiologists also reported safety as the most important factor in selecting a contrast agent and identified safety as the greatest area for improvement.
- 98% of specialists surveyed reported pre-screening prospective patients for elevated kidney risk.
- Overall 23% of prescreened patients were identified as having elevated kidney risk. Nephrologists indicated the high-risk pool of patients to be twice as large as radiologists (32% vs. 16%, respectively).

- Among all groups the risk of contrast-induced AKI was highest among high renal risk patients and among patients undergoing emergency procedures.

About Captisol-enabled Iohexol

More than 30 million imaging procedures are performed each year in the U.S. Iodinated contrast agents represent more than 60% of all X-ray imaging agents sold with an annual U.S. market of approximately $1.5 billion.[3] Iohexol, the most widely-used injectable diagnostic contrast agent for imaging procedures, has global sales exceeding $500 million[3].

Contrast-induced acute kidney injury (CI-AKI) is the acute impairment of renal function following intravascular administration of an iodinated contrast agent, and occurs most frequently following coronary angiography, percutaneous coronary intervention and contrast-enhanced computed tomography, especially among patients at risk of renal injury such as those with advanced age, diabetes or heart failure. CI-AKI is an issue with broad medical visibility as more than 50% of cardiovascular imaging procedures are performed in patients age 65 or older.[4]

Currently no products are approved to prevent or treat CI-AKI in this setting, and therefore a significant opportunity exists for a safer formulation. The goal is for CE-Iohexol to establish a new safety standard that enables a future partner to gain meaningful market share.

About Captisol®

Captisol is a patent-protected, chemically modified cyclodextrin with a structure designed to optimize the solubility and stability of drugs. Captisol was invented and initially developed by scientists in the laboratories of Dr. Valentino Stella, University Distinguished Professor at the University of Kansas' Higuchi Biosciences Center for specific use in drug development and formulation. This unique technology has enabled several FDA-approved products, including Amgen's Kyprolis®, Baxter International's Nexterone®, Acrotech Biopharma's EVOMELA®, Melinta Therapeutics' Baxdela™ and Sage Therapeutics' ZULRESSO™. There are many Captisol-enabled products currently in various stages of development.

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 Amgen, Merck, Pfizer, 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 of results from our Phase 1 clinical trial of CE-Iohexol; the potential that Ligand's CE-iohexol program to increase the safety of widely-used commercial contrast agents and deliver significant out-licensing opportunities; the market size of contrast agent procedures and the addressable market of CE-Iohexol; the potential that CE-Iohexol could reduce renal toxicity and deliver a safer radiocontrast agent; Ligand's expectations that it will partner the program or obtain a higher royalty rate or milestone payments due to Ligand's development activities; Ligand's view of that there is a significant unmet need for safer radiocontrast agents; and the opinion of clinicians, including cardiologist, on the need to address safety for radiocontrast agents;. Actual events or results may differ from our expectations. For example, there can be no assurances that the Phase 1 clinical trial will be completed on the expected timeline or all; the Phase 1 clinical trial may not produce positive results; Ligand may choose to abandon the program for any reason or no reason; the anticipated benefits of CE-Iohexol, including the possible improvements in kidney safety, may not materialize; and

Ligand may be unable to secure licensing partners or buyers for products developed from the contrast agent program. 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.

References

1. McCullough, J Am College of Cardiology 2016;68:1465-73
2. Rowe ES, et al. Journal of Neuroimaging 2016; 26(5):511-8
3. The Global Imaging Agents Market (Report MCP-3336) Global Industry Analysts, Inc., September 2016
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