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Ligand Announces Amgen's KYPROLIS® Approved by FDA as Combination Regimen with DARZALEX® and Dexamethasone in Once- and Twice-Weekly Dosing Regimens for Patients with Relapsed/Refractory Multiple Myeloma

KYPROLIS is an Amgen product that utilizes Captisol® in its formulation

Approval based on the CANDOR and EQUULEUS Studies

SAN DIEGO--(BUSINESS WIRE)-- **Ligand Pharmaceuticals Incorporated (NASDAQ: LGND)** announces that a major Captisol customer Amgen (NASDAQ: AMGN) has received U.S. Food and Drug Administration (FDA) approval for the expansion of the KYPROLIS® (carfilzomib) U.S. prescribing information to include its use in combination with DARZALEX® (daratumumab) plus dexamethasone (DKd) in once- and twice-weekly dosing regimens for the treatment of patients with relapsed or refractory multiple myeloma (R/R MM) who have received one to three previous lines of therapy.

"We are proud of the ongoing work by Amgen to expand the use of KYPROLIS in combination with other therapies. This FDA approval came earlier than we had anticipated and allows for KYPROLIS to be used with DARZALEX and dexamethasone in patients in the U.S. with an incurable type of blood cancer," said John Higgins, Chief Executive Officer of Ligand. "We are very pleased with the impact that Captisol-enabled medicines are having to-date in 2020 for the treatment of multiple serious diseases, including relapsed/refractory multiple myeloma and COVID-19."

The CANDOR trial was the first Phase 3 randomized trial to compare DKd versus KYPROLIS and dexamethasone (Kd) alone in R/R MM patients. The study met its primary endpoint and resulted in a 37% reduction in the risk of disease progression or death in patients receiving DKd (HR=0.63; 95% CI: 0.464, 0.854; 1-sided p-value=0.0014) compared to Kd alone.

In CANDOR, the safety of DKd was generally consistent with the known safety profiles of the individual agents. The most frequently reported (≥ 20% of subjects in either the DKd or Kd treatment arm) treatment-emergent adverse events (AEs) included infusion-related reactions, anemia, diarrhea, fatigue, hypertension, pyrexia, upper respiratory tract infection, thrombocytopenia, neutropenia, lymphopenia, cough, dyspnea and insomnia, headache and back pain. The incidence of treatment-emergent Grade 3 or higher, serious and fatal AEs

was higher in the DKd arm compared to the Kd arm. The most common reason for fatal treatment-emergent AEs in both arms was infection. The rate of treatment discontinuation due to AEs was similar in both arms.

The expansion of KYPROLIS's prescribing information to include once-weekly dosing of KYPROLIS within the DKd regimen was supported by the open-label, multi-cohort Phase 1b EQUULEUS trial, in which the safety and efficacy of DKd was assessed among R/R MM patients using a once-weekly dosing regimen for KYPROLIS.

Amgen has submitted additional marketing applications globally.

DARZALEX® is a registered trademark of Janssen Pharmaceutica NV.

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®, Gilead's VEKLURY®, Acrotech Biopharma L.L.C.'s and CASI Pharmaceuticals' EVOMELA®, Melinta Therapeutics' BAXDELA™ and Sage Therapeutics' ZULRESSO™. There are many Captisol-enabled products currently in various stages of development.

About CANDOR

CANDOR, a randomized, open-label Phase 3 study of KYPROLIS, DARZALEX and dexamethasone (DKd) compared to KYPROLIS and dexamethasone (Kd), has evaluated 466 relapsed or refractory multiple myeloma patients who have received one to three prior therapies. Patients were treated until disease progression. The primary endpoint was progression-free survival (PFS), and the key secondary endpoints were overall response rate, minimal residual disease and overall survival. PFS was defined as time from randomization until disease progression or death from any cause.

In the first arm, patients received KYPROLIS twice weekly at 56 mg/m^2 and dexamethasone in combination with DARZALEX. In the second arm (control), patients received KYPROLIS twice weekly at 56 mg/m^2 and dexamethasone.

CANDOR was initiated as part of a collaboration with Janssen, and under the terms of the agreement, Janssen co-funded the study. For more information about this trial, please visit www.clinicaltrials.gov under trial identification number NCT03158688.

About EQUULEUS

EQUULEUS was an open-label, Phase 1b, multi-cohort trial that evaluated the combination of KYPROLIS with intravenous DARZALEX and dexamethasone in 85 patients with relapsed or refractory multiple myeloma who had received one to three prior lines of therapy.

KYPROLIS was evaluated at a starting dose of 20 mg/m^2, which was increased to 70 mg/m^2 on Cycle 1, Day 8 and onward.

The most frequently reported all-grade, treatment-emergent AEs (occurring in 20% or more of patients) were thrombocytopenia, respiratory tract infection, anemia, nausea, fatigue, vomiting, diarrhea, pyrexia, neutropenia, lymphopenia, infusion related reactions, dyspnea, cough, insomnia, hypertension, headache and back pain.

At a median follow-up of 16.6 months, the overall response rate was 81% in all treated patients: 21% achieved a stringent complete response, 14% a complete response, 33% a very good partial response and 13% a partial response.

About Multiple Myeloma

Multiple myeloma is an incurable blood cancer, characterized by a recurring pattern of remission and relapse.[1] It is a rare and life-threatening disease that accounts for approximately one percent of all cancers.[2,3] Worldwide, approximately 160,000 people are diagnosed with multiple myeloma each year, and 106,000 patient deaths are reported on an annual basis.[4]

About KYPROLIS® (carfilzomib)

Proteasomes play an important role in cell function and growth by breaking down proteins that are damaged or no longer needed.[4] KYPROLIS has been shown to block proteasomes, leading to an excessive build-up of proteins within cells.[5] In some cells, KYPROLIS can cause cell death, especially in myeloma cells because they are more likely to contain a higher amount of abnormal proteins.[4,5]

Since its first approval in 2012, approximately 150,000 patients worldwide have received KYPROLIS.[6] KYPROLIS is approved in the U.S. for the following:

- for the treatment of patients with relapsed or refractory multiple myeloma who have received one to three lines of therapy in combination with
    - Lenalidomide and dexamethasone; or
    - Dexamethasone; or
    - Daratumumab and dexamethasone.
- as a single agent for the treatment of patients with relapsed or refractory multiple myeloma who have received one or more lines of therapy.

KYPROLIS is also approved in Algeria, Argentina, Australia, Bahrain, Belarus, Brazil, Canada, Chile, Colombia, Ecuador, Egypt, European Union, Hong Kong, India, Israel, Japan, Jordan, Kazakhstan, Kuwait, Lebanon, Macao, Malaysia, Mexico, Morocco, New Zealand, Oman, Peru, Philippines, Qatar, Russia, Saudi Arabia, Serbia, Singapore, S. Africa, S. Korea, Switzerland, Taiwan, Thailand, Turkey and United Arab Emirates.

U.S. KYPROLIS® (carfilzomib) Important Safety Information

INDICATIONS

- KYPROLIS® (carfilzomib) is indicated in combination with dexamethasone or with lenalidomide plus dexamethasone or with daratumumab and dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma who have received one to three lines of therapy.
- KYPROLIS® is indicated as a single agent for the treatment of adult patients with relapsed or refractory multiple myeloma who have received one or more lines of therapy.

IMPORTANT SAFETY INFORMATION FOR KYPROLIS

Cardiac Toxicities

- New onset or worsening of pre-existing cardiac failure (e.g., congestive heart failure, pulmonary edema, decreased ejection fraction), restrictive cardiomyopathy, myocardial ischemia, and myocardial infarction including fatalities have occurred following administration of KYPROLIS. Some events occurred in patients with normal baseline ventricular function. Death due to cardiac arrest has occurred within one day of administration.
- Monitor patients for signs or symptoms of cardiac failure or ischemia. Evaluate promptly if cardiac toxicity is suspected. Withhold KYPROLIS for Grade 3 or 4 cardiac adverse events until recovery, and consider whether to restart at 1 dose level reduction based on a benefit/risk assessment.
- While adequate hydration is required prior to each dose in Cycle 1, monitor all patients for evidence of volume overload, especially patients at risk for cardiac failure. Adjust total fluid intake as clinically appropriate.
- For patients ≥75 years, the risk of cardiac failure is increased. Patients with New York Heart Association Class III and IV heart failure, recent myocardial infarction, conduction abnormalities, angina, or arrhythmias may be at greater risk for cardiac complications and should have a comprehensive medical assessment prior to starting treatment with KYPROLIS and remain under close follow-up with fluid management.

Acute Renal Failure

- Cases of acute renal failure, including some fatal renal failure events, and renal insufficiency adverse events (including renal failure) have occurred. Acute renal failure was reported more frequently in patients with advanced relapsed and refractory multiple myeloma who received KYPROLIS monotherapy. Monitor renal function with regular measurement of the serum creatinine and/or estimated creatinine clearance. Reduce or withhold dose as appropriate.

Tumor Lysis Syndrome

- Cases of Tumor Lysis Syndrome (TLS), including fatal outcomes, have occurred. Patients with a high tumor burden should be considered at greater risk for TLS. Adequate hydration is required prior to each dose in Cycle 1, and in subsequent cycles as needed. Consider uric acid lowering drugs in patients at risk for TLS. Monitor for evidence of TLS during treatment and manage promptly, and withhold until resolved.

Pulmonary Toxicity

- Acute Respiratory Distress Syndrome (ARDS), acute respiratory failure, and acute diffuse infiltrative pulmonary disease such as pneumonitis and interstitial lung disease have occurred. Some events have been fatal. In the event of drug–induced pulmonary toxicity, discontinue KYPROLIS.

Pulmonary Hypertension

- Pulmonary arterial hypertension (PAH) was reported. Evaluate with cardiac imaging and/or other tests as indicated. Withhold KYPROLIS for PAH until resolved or returned to baseline and consider whether to restart based on a benefit/risk assessment.

Dyspnea

- Dyspnea was reported in patients treated with KYPROLIS. Evaluate dyspnea to exclude cardiopulmonary conditions including cardiac failure and pulmonary syndromes. Stop KYPROLIS for Grade 3 or 4 dyspnea until resolved or returned to baseline. Consider whether to restart based on a benefit/risk assessment.

Hypertension

- Hypertension, including hypertensive crisis and hypertensive emergency, has been observed, some fatal. Control hypertension prior to starting KYPROLIS. Monitor blood pressure regularly in all patients. If hypertension cannot be adequately controlled, withhold KYPROLIS and evaluate. Consider whether to restart based on a benefit/risk assessment.

Venous Thrombosis

- Venous thromboembolic events (including deep venous thrombosis and pulmonary embolism) have been observed. Thromboprophylaxis is recommended for patients being treated with the combination of KYPROLIS with dexamethasone or with lenalidomide plus dexamethasone. The thromboprophylaxis regimen should be based on an assessment of the patient's underlying risks.
- Patients using hormonal contraception associated with a risk of thrombosis should consider an alternative method of effective contraception during treatment.

Infusion Reactions

- Infusion reactions, including life–threatening reactions, have occurred. Signs and symptoms include fever, chills, arthralgia, myalgia, facial flushing, facial edema, laryngeal edema, vomiting, weakness, shortness of breath, hypotension, syncope, chest tightness, or angina. These reactions can occur immediately following or up to 24 hours after administration. Premedicate with dexamethasone to reduce the incidence and severity of infusion reactions. Inform patients of the risk and of symptoms and seek immediate medical attention if they occur.

Hemorrhage

- Fatal or serious cases of hemorrhage have been reported. Hemorrhagic events have included gastrointestinal, pulmonary, and intracranial hemorrhage and epistaxis. Promptly evaluate signs and symptoms of blood loss. Reduce or withhold dose as

appropriate.

Thrombocytopenia

- KYPROLIS causes thrombocytopenia with recovery to baseline platelet count usually by the start of the next cycle. Monitor platelet counts frequently during treatment. Reduce or withhold dose as appropriate.

Hepatic Toxicity and Hepatic Failure

- Cases of hepatic failure, including fatal cases, have occurred. KYPROLIS can cause increased serum transaminases. Monitor liver enzymes regularly regardless of baseline values. Reduce or withhold dose as appropriate.

Thrombotic Microangiopathy

- Cases of thrombotic microangiopathy, including thrombotic thrombocytopenic purpura/hemolytic uremic syndrome (TTP/HUS), including fatal outcome, have occurred. Monitor for signs and symptoms of TTP/HUS. Discontinue if diagnosis is suspected. If the diagnosis of TTP/HUS is excluded, KYPROLIS may be restarted. The safety of reinitiating KYPROLIS is not known.

Posterior Reversible Encephalopathy Syndrome (PRES)

- Cases of PRES have occurred in patients receiving KYPROLIS. If PRES is suspected, discontinue and evaluate with appropriate imaging. The safety of reinitiating KYPROLIS is not known.

Increased Fatal and Serious Toxicities in Combination with Melphalan and Prednisone in Newly Diagnosed Transplant-ineligible Patients

- In a clinical trial of transplant-ineligible patients with newly diagnosed multiple myeloma comparing KYPROLIS, melphalan, and prednisone (KMP) vs bortezomib, melphalan, and prednisone (VMP), a higher incidence of serious and fatal adverse events was observed in patients in the KMP arm. KMP is not indicated for transplant-ineligible patients with newly diagnosed multiple myeloma.

Embryo-fetal Toxicity

- KYPROLIS can cause fetal harm when administered to a pregnant woman.
- Females of reproductive potential should be advised to avoid becoming pregnant while being treated with KYPROLIS and for 6 months following the final dose. Males of reproductive potential should be advised to avoid fathering a child while being treated with KYPROLIS and for 3 months following the final dose. If this drug is used during pregnancy, or if pregnancy occurs while taking this drug, the patient should be apprised of the potential hazard to the fetus.

Adverse Reactions

- The most common adverse reactions in the combination therapy trials: anemia, diarrhea, dyspnea, fatigue, thrombocytopenia, pyrexia, insomnia, cough, upper

respiratory tract infection, hypertension.
- The most common adverse reactions in monotherapy trials: anemia, fatigue, thrombocytopenia, nausea, pyrexia, dyspnea, diarrhea, headache, cough, edema peripheral.

Please see accompanying full Prescribing Information at www.kyprolis.com.

About Ligand Pharmaceuticals

Ligand is a revenue-generating 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 OmniAb® technology platform is a patent-protected transgenic animal platform used in the discovery of fully human mono- and bispecific therapeutic antibodies. The Captisol platform technology is a patent-protected, chemically modified cyclodextrin with a structure designed to optimize the solubility and stability of drugs. The Vernalis Design Platform (VDP) integrates protein structure determination and engineering, fragment screening and molecular modeling, with medicinal chemistry, to help enable success in novel drug discovery programs against highly-challenging targets. Ab Initio™ technology and services for the design and preparation of customized antigens enable the successful discovery of therapeutic antibodies against difficult-to-access cellular targets. Ligand has established multiple alliances, licenses and other business relationships with the world's leading pharmaceutical companies including Amgen, Merck, Pfizer, Sanofi, Janssen, Takeda, Servier, Gilead Sciences and Baxter International. For more information, please visit www.ligand.com.

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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. Words such as "plans," "believes," "expects," "anticipates," and "will," and similar expressions, are intended to identify forward-looking statements. These forward-looking statements include, without limitation, statements regarding: whether KYPROLIS will be used in combination with DARZALEX to treat patients with R/R MM; Ligand's expectation that Amgen will be a major Captisol customer; and estimates of the number of patients with multiple myeloma. Actual events or results may differ from Ligand's expectations due to risks and uncertainties inherent in Ligand's business, including, without limitation: patients and physicians may not prescribe KYPROLIS in combination with DARZALEX for the treatment of R/R MM; Ligand may not receive expected revenue from royalties from sales of KYPROLIS or related Captisol sales the COVID-19 pandemic has disrupted Ligand's and its partners' business, including delaying manufacturing, preclinical studies and clinical trials and product sales, and

impairing global economic activity, all of which could materially and adversely impact Ligand's results of operations and financial condition; Ligand may be unable to scale-up the supply of Captisol or at acceptable prices; Amgen may not execute on its sales and marketing plans for marketed products for which Ligand has an economic interest; Ligand or its partners may not be able to protect their intellectual property and patents covering certain products and technologies may be challenged or invalidated; and Ligand's partners may terminate any of its agreements or development or commercialization of any of its products. 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 risk factors affecting Ligand can be found in 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 release, including the possibility of additional contract revenue we may receive. This caution is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

Other Disclaimers and Trademarks

The information in this press release regarding certain third-party products and programs, including KYPROLIS, an Amgen product, comes from information publicly released by the owners of such products and programs. Ligand is not responsible for, and has no role in, the development of such products or programs.

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