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# CStone Announces That OmniAb-derived CS1001 (Anti-PD-L1) Phase 3 Trial Met the Primary Endpoint as First-Line Treatment in Stage IV Squamous and Non-squamous Non-Small Cell Lung Cancer and Announces Plans to Submit a New Drug Application

***CS1001 is the first anti-PD-L1 mAb to demonstrate overwhelming efficacy as First Line treatment of Stage IV squamous and non-squamous NSCLC in a randomized, double-blind Phase 3 trial***

***CS1001 combined with chemotherapy had a statistically significant prolongation of progression-free survival (PFS), the primary endpoint of the trial, compared with placebo combined with chemotherapy, reducing the risk of disease progression or death by 50%***

SAN DIEGO--(BUSINESS WIRE)-- **Ligand Pharmaceuticals Incorporated (NASDAQ: LGND)** announces CStone Pharmaceuticals ("CStone", HKEX: 2616) recently reported that its OmniAb-derived anti-PD-L1 mAb CS1001 combined with platinum-based chemotherapy met its pre-specified primary endpoint, as assessed by the independent Data Monitoring Committee at the planned interim analysis of CS1001-302, a randomized, double-blind Phase 3 clinical trial for the first-line treatment of stage IV squamous and non-squamous NSCLC patients.

Key data highlights include:

- In the overall population containing both squamous and non-squamous NSCLC patients, investigator-assessed progression free survival (PFS) HR (95% CI) was 0.50 (0.39, 0.64), p<0.0001. The median PFS was 7.8 months vs. 4.9 months in CS1001 combined with chemotherapy and placebo combined with chemotherapy, respectively.
- Subgroup analyses showed clinical benefit across histology subtypes and PD-L1 expression levels.
- Blinded independent central review (BICR)-assessed PFS as a secondary endpoint was consistent with the investigator-assessed PFS. Other secondary endpoints also supported the primary endpoint result.
- CS1001 in combination with chemotherapy was well tolerated, with no new safety signal detected.

“This is an outstanding clinical report by CStone and also the most substantial, pivotal-stage data to be reported to date for an OmniAb-derived antibody,” said John Higgins, Chief Executive Officer of Ligand. “These results, coupled with data recently announced by Genentech relating to their OmniAb-derived anti-TIGIT program, are ushering in what we believe will be a period of major data, breakthroughs and late-stage developments for new potential OmniAb-derived human therapeutics. Our OmniAb platform continues to be a valuable tool to efficiently discover high-quality fully human antibody therapeutics. We congratulate CStone on this remarkable achievement and contribution to improving potential treatment options for lung cancer.”

Dr. Frank Jiang, Chairman and CEO of CStone, said, “Currently, there is no anti-PD-L1 monoclonal antibody approved for NSCLC in China. CS1001 is the first anti-PD-L1 monoclonal antibody combined with chemotherapy to demonstrate significant improvement in PFS in Chinese NSCLC patients. It has the potential of becoming the world’s first anti-PD-L1 monoclonal antibody that can be combined with chemotherapy as the first-line treatment of both squamous and non-squamous NSCLC patients. This further strengthens our confidence in the development of CS1001 and greatly expediate CStone’s commercialization progress.”

Dr. Jason Yang, Chief Medical Officer of CStone, said, “Compared with published results of other anti-PD-1/PD-L1 monoclonal antibodies in combination with chemotherapy in first-line NSCLC trials, the CS1001-302 study, with an innovative design, is the first phase 3 clinical study in China for the first-line treatment of both squamous and non-squamous NSCLC subtypes. We will continue to make every effort to promote and more extensively evaluate the potential clinical benefit of this product in patients with hematological malignancies, stage III NSCLC, advanced gastric cancer, liver cancer and esophageal cancer.”

**About OmniAb®**

OmniAb is a three-species transgenic-animal platform consisting of five different technologies used for producing mono- and bispecific human therapeutic antibodies. OmniRat® animals comprise the industry’s first human monoclonal antibody technology based on rats. Because they have a complete immune system with a diverse antibody repertoire, OmniRat animals generate antibodies with human idiotypes as effectively as wild-type animals make rat antibodies. OmniMouse® is a transgenic mouse that complements OmniRat and expands epitope coverage. OmniFlic® is an engineered rat with a fixed light chain for development of bispecific, fully human antibodies. OmniChicken animals comprise the industry’s first human monoclonal antibody technology based on chickens. The OmniClic chicken is specifically developed to facilitate the generation of bispecific antibodies and retains the ability to generate diverse, high quality affinity matured antibodies. All five types of OmniAb therapeutic human antibody platform, OmniRat, OmniFlic, OmniMouse, OmniChicken® and OmniClic®, use patented technology, have broad freedom to operate, produce highly diversified, fully human antibody repertoires optimized in vivo for immunogenicity, manufacturability, and therapeutic efficacy, and deliver fully human antibodies with high affinity, specificity, expression, solubility and stability - Naturally Optimized Human Antibodies®.

**About Non-Small Cell Lung Cancer and China**

In contrast to most Western countries, where lung cancer death rates are decreasing, lung cancer incidence rates are still increasing in China. There were approximately 770,000 new cases of lung cancer in China in 2018, and it is the leading cause of cancer-related death in both men and women, with approximately 690,500 deaths in China in 2018. Non-small cell lung cancer comprises the most common form of lung cancer in China.

**CS1001-302 Study**

CS1001-302 is a multicenter, randomized, double-blind Phase 3 clinical trial (CS1001-302; clinicaltrials.gov registration number: NCT03789604; drug clinical trial registration number: CTR20181452), designed to evaluate the efficacy and safety of CS1001 in combination with platinum-containing chemotherapy versus placebo in combination with platinum-containing chemotherapy in first-line naïve patients with stage IV NSCLC. The primary endpoint of the trial was PFS as assessed by the investigators; the secondary endpoints include overall survival, PFS and the safety profile as assessed by BICR committee.

**About CS1001**

CS1001 is an investigational anti-PD-L1 monoclonal antibody discovered by CStone using Ligand Pharmaceuticals' OmniRat® transgenic animal platform, which can generate fully human antibodies. As a fully human, full-length anti-PD-L1 monoclonal antibody, CS1001 mirrors the natural G-type immunoglobulin 4 (IgG4) human antibody, which can reduce the risk of immunogenicity and potential toxicities in patients, representing a unique advantage over similar drugs. CS1001 has completed a Phase 1 dose-escalation study in China. During Phase 1a and Phase 1b of the study, CS1001 showed good antitumor activity and tolerability in multiple tumor types. Currently, CS1001 is being investigated in a number of ongoing clinical trials. In addition to a Phase 1 bridging study in the U.S., the clinical program in China includes one multi-arm Phase 1b study for several tumor types, two Phase 2 registrational studies for lymphoma, and four Phase 3 registrational studies, respectively, for stage III/IV NSCLC, gastric cancer, and esophageal cancer.

**About CStone**

CStone Pharmaceuticals (HKEX: 2616) is a biopharmaceutical company focused on developing and commercializing innovative immuno-oncology and precision medicines to address the unmet medical needs of cancer patients in China and worldwide. Established in 2015, CStone has assembled a world-class management team with extensive experience in innovative drug development, clinical research, and commercialization. The company has built an oncology-focused pipeline of 15 drug candidates with a strategic emphasis on immuno-oncology combination therapies. Currently, five late-stage candidates are at pivotal trials. With an experienced team, a rich pipeline, a robust clinical development-driven business model and substantial funding, CStone's vision is to become globally recognized as a leading Chinese biopharmaceutical company by bringing innovative oncology therapies to cancer patients worldwide.

**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. These forward-looking statements include, without limitation, statements regarding: the potential for major data, breakthroughs and developments for new potential OmniAb-derived therapeutics; Ligand's belief that the OmniAb platform can efficiently discover high-quality antibody therapeutic candidates; and the potential that CS1001 could be a treatment option for lung cancer patients. Actual events or results may differ from Ligand's expectations due to risks and uncertainties inherent in Ligand's business, including, without limitation: regulatory authorities such as FDA may not agree with CStone's interpretation of the results from the Phase 3 clinical trial; CS1001 may not be approved for lung cancer or any other indication and Ligand may not receive any milestone payments or royalties from the development of CS1001; the OmniAb platform faces specific risks, including the fact that no product using antibodies from the platform has been approved by the FDA or similar regulatory agency; unexpected adverse side effects or inadequate therapeutic efficacy of Ligand's or Ligand's partners' product(s) could delay or prevent regulatory approval or commercialization; and other risks described in Ligand's prior press releases and filings with the SEC. The failure to meet expectations with respect to any of the foregoing matters may reduce Ligand's stock price. Ligand disclaims any intent or obligation to update these forward-looking statements after the date hereof. This caution is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

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