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# Ligand Announces its Captisol Business is Positioned for Major Growth and Forecasts 2021 Captisol Material Sales of \$200 Million

*Recent partner contracts and manufacturing investments have Captisol business operating at record high levels*

*Continued clinical progress of Captisol-enabled drugs affirms the value of the proprietary technology*

SAN DIEGO--(BUSINESS WIRE)-- Ligand Pharmaceuticals Incorporated (NASDAQ: LGND) announces that recent new contracting with partners and investments in manufacturing capacity have contributed to its Captisol business operating at the highest levels in the history of the technology and position Captisol for major growth. Significant new clinical and regulatory developments with Evomela and Kyprolis, among other drugs, are reinforcing the role the proprietary technology serves in enabling important medicines. During 2020, Ligand has facilitated the successful installation of equipment to allow production at significantly higher levels to support anticipated demand. In addition to manufacturing at partner Hovione's facilities in Ireland and Portugal, Ligand has now added final step processing capacity for Captisol in both the United States and England. Ligand also introduces guidance for 2021 Captisol material sales of approximately \$200 million.

"The global medical need for Captisol-enabled drugs has never been higher," said John Higgins, Chief Executive Officer of Ligand. "Our recently expanded operating team has successfully positioned our Captisol technology for the substantial growth we now expect in 2021 and beyond. There is significant ongoing investment by our partners for over 30 Captisol-enabled medicines in clinical development. We have entered into more contracts this year than any other year and are proud to be working closely with Gilead under our recently extended 10-year supply contract. We continue to be pleased with the momentum relating to Captisol, as it is a critical component in multiple life-saving medicines."

Recent Captisol technology business highlights include the following:

- To date in 2020 Ligand has entered into more than 120 Captisol research use agreements and eight clinical and/or commercial license agreements. This is the highest number of use agreements to be signed in a single year since the invention of Captisol.
- Captisol is utilized in the formulation of Gilead Sciences' Veklury<sup>®</sup> (remdesivir), which has received emergency use authorizations or regulatory approvals for the treatment of moderate or severe COVID-19 in over 50 countries and is included in more than 30

ongoing clinical trials. Ligand is supplying Captisol to Gilead and the company's voluntary licensing partners who are supplying generic remdesivir to 127 low- and middle-income countries. Ligand expects Captisol orders into 2021 and beyond to Gilead and its partners to help countries around the world manage the pandemic.

- Ligand recently extended its Captisol supply agreement with Gilead until September 2030. The contract defines terms and conditions for forecasting, supply, order commitments and price.
- Ligand's manufacturing partner Hovione announced today that to meet Captisol demand associated with Veklury, Hovione will soon be producing more Captisol per month than it usually produces per year. "This spike in demand has required unique mobilization efforts across the Hovione network to secure additional raw material supply, execute major capital expenditure projects at our sites, maximize operational efficiency, hire additional talent and identify external partners to expand our overall capacity. The pharmaceutical supply chain is working together in an unprecedented fashion to treat patients and save lives. Hovione is privileged to be part of this truly global rapid response," said Jean-Luc Herbeaux, Chief Operating Officer of Hovione.
- Recent clinical data have been announced including publication of a study from the Medical College of Wisconsin that compared safety parameters for Captisol-enabled Evomela<sup>®</sup> versus Alkeran<sup>®</sup> in patients undergoing autologous stem cell transplantation for the treatment of multiple myeloma. The study of 294 patients demonstrated a statistically significant reduction in 30-day re-hospitalization rates for patients treated with Evomela (6.8% for Evomela vs. 17.9% for Alkeran,  $p=0.04$ )<sup>a</sup> with a similar safety profile to Alkeran. Evomela is marketed by Acrotech Biopharma in the U.S. and by CASI Pharmaceuticals in China.
- Partner Marinus was recently awarded a BARDA contract by the U.S. government to develop Captisol-enabled IV ganaxolone for the treatment of refractory status epilepticus caused by nerve agent exposure.
- Ligand's pivotal trial for Captisol-enabled Iohexol (CE-Iohexol) is planned to initiate in December 2020. CE-Iohexol is an iodine-based contrast agent for hospital-based imaging procedures. The market for iodinated contrast agents is substantial with approximately 20 million imaging procedures per year in the U.S., representing an estimated \$1.5 billion in sales. The objective of the clinical trial will be to demonstrate a reduction in the incidence of contrast-induced acute kidney injury and an equivalent image quality compared to GE's Omnipaque<sup>®</sup>. The trial is expected to enroll approximately 500 patients and results are expected within two years.

Ligand's forecast for 2021 Captisol material sales of approximately \$200 million is based on information it has on anticipated demand from its major partners given growth in existing and new markets, clinical requirements for Captisol-enabled development programs and binding orders from certain commercial or pre-commercial partners. The 2021 Captisol outlook compares with the Company's guidance for 2020 Captisol material sales of approximately \$90 million.

### **About Captisol<sup>®</sup>**

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 Gilead's VEKLURY<sup>®</sup>, Amgen's KYPROLIS<sup>®</sup>, Baxter International's NEXTERONE<sup>®</sup>, Acrotech Biopharma L.L.C.'s and CASI Pharmaceuticals' EVOMELA<sup>®</sup>, Melinta Therapeutics' BAXDELA<sup>™</sup> and Sage Therapeutics' ZULRESSO<sup>™</sup>. There are many Captisol-enabled products currently in various stages of development. Ligand maintains a broad global patent portfolio for Captisol with more than 400 issued patents worldwide relating to the technology (including 37 in the U.S.) and with the latest expiration date in 2033. Other patent applications covering methods of making Captisol, if issued, extend to 2040.

## **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<sup>®</sup> 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<sup>™</sup> technology and services for the design and preparation of customized antigens enable the successful discovery of therapeutic antibodies against difficult-to-access cellular targets. Icagen has established deep biological expertise focused on ion channels and transporters and has a strong track record in ion channel drug discovery from screening to lead optimization. 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](http://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: Ligand's expectation that Captisol demand will increase significantly in 2021 and beyond (particularly for sales to Gilead and to partners in Gilead's consortium) and Ligand's ability to supply Captisol to Gilead and other partners, including Ligand's ability to increase supply capacity; the timing of initiation, enrollment and expected

results with respect to the planned clinical trial of CE-lohexol; and guidance regarding Ligand's 2020 and 2021 Captisol material sales. Actual events or results may differ from Ligand's expectations due to risks and uncertainties inherent in Ligand's business, including, without limitation: Ligand may not receive expected revenue from 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 not achieve its Captisol material sales guidance for 2020 and/or 2021; remdesivir may be later shown to not be effective or safe for the treatment of COVID-19 and/or the FDA (and/or equivalent agencies in other countries) may revise or revoke its emergency use authorization for remdesivir for the treatment of COVID-19 in patients hospitalized with moderate or severe disease if the FDA (and/or another such agency) determines that authorization no longer meets the statutory criteria for issuance; alternative COVID-19 therapies or vaccines may be approved or the risk of coronavirus infection could significantly diminish, any of which could materially and adversely affect the commercial opportunity for remdesivir; Gilead may terminate the supply agreement without cause upon 30 days' prior written notice; Ligand may be unable to scale-up the supply of Captisol or at acceptable prices; Ligand is currently dependent on Hovione as a single source sole supplier for certain Captisol manufacturing functions and failures by such supplier may result in delays or inability to meet the Captisol demands of its partners; Amgen, Acrotech Biopharma or other Ligand partners may not execute on their sales and marketing plans for marketed products for which Ligand has an economic interest; Ligand or its Captisol partners may not be able to protect their intellectual property and patents covering certain products and technologies may be challenged or invalidated; Ligand's Captisol partners may terminate agreements or development or commercialization of products; Ligand may not generate expected revenues under its existing license agreements and may experience significant costs as the result of potential delays under its supply agreements; Ligand and its Captisol partners may experience delays in the commencement, enrollment, completion or analysis of clinical testing for product candidates, or significant issues regarding the adequacy of clinical trial designs or the execution of clinical trials, which could result in increased costs and delays, or limit the ability to obtain regulatory approval; unexpected adverse side effects or inadequate therapeutic efficacy of Ligand's or its Captisol partners' product(s) could delay or prevent regulatory approval or commercialization; and ongoing or future litigation could expose Ligand to significant liabilities and have a material adverse effect on the company. 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](http://www.ligand.com) as well as in Ligand's public periodic filings with the Securities and Exchange Commission available at [www.sec.gov](http://www.sec.gov). Ligand disclaims any intent or obligation to update these forward-looking statements beyond the date of this release. This caution is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

<sup>a</sup> Monahan, et al. Biology of Blood and Marrow Transplantation, September 2020

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