Exelixis and Cybrexa Therapeutics Establish Exclusive Collaboration Providing Exelixis the Right to Acquire CBX-12, a Potential First-in-Class Peptide-Drug Conjugate of Exatecan

November 1, 2022

– CBX-12 has potential to improve efficacy and reduce toxicity over systemic topoisomerase inhibitors –

– Deal reflects Exelixis' strategic focus on expanding its clinical pipeline and building upon its growing biotherapeutics expertise –

ALAMEDA, Calif. & NEW HAVEN, Conn.--(BUSINESS WIRE)--Nov. 1, 2022-- Exelixis, Inc. (Nasdaq: EXEL) and Cybrexa Therapeutics (Cybrexa) today announced that the companies have entered into an exclusive collaboration agreement providing Exelixis the right to acquire CBX-12 (alphalex™ exatecan), a clinical-stage, first-in-class peptide-drug conjugate (PDC) that utilizes Cybrexa's proprietary alphalex technology to enhance delivery of exatecan to tumor cells. CBX-12 is designed to increase the efficacy and reduce the toxicity of topoisomerase I inhibition by delivering exatecan, a highly potent, second-generation topoisomerase I inhibitor, directly to the tumor cells. This collaboration underscores Exelixis' commitment to expanding its clinical pipeline building upon its biotherapeutics and targeted drug therapy expertise.

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CBX-12 is composed of a pH-Low Insertion Peptide (pHLIP®), a linker and exatecan. As an antigen-independent therapy, CBX-12 may have broad utility in patients who are not eligible for antigen-targeted therapies, including monoclonal antibodies and antibody-drug conjugates (ADCs), and has potential for use in combination regimens with other anti-cancer agents and immunotherapies. Data from the ongoing phase 1 trial of CBX-12 in patients with metastatic solid tumors, reported in an oral presentation during a plenary session at the EORTC-NCI-AACR (ENA) 2022 Symposium on October 28, 2022, demonstrated preliminary anti-tumor activity in a heavily pretreated patient population. This included a complete response in a patient with ovarian cancer.

"This agreement aligns with Exelixis' goal of acquiring first- or best-in-class clinical-stage assets that may provide differentiated benefits to patients with cancer. Today's announcement further highlights our ongoing strategy to leverage our balance sheet to gain access to new assets with compelling potential upside in a risk-sharing model, where we can work with partners to further establish proof of concept before investing more heavily," said Michael Morrissey, Ph.D., President & CEO, Exelixis. "Robust preclinical data and initial clinical data from the ongoing phase 1 trial suggest that CBX-12 may provide differentiated clinical benefit in several solid tumors. Similar to our interest in antibody-drug conjugates, we believe this novel peptide-drug conjugate has transformative clinical potential, and this collaboration affords us the opportunity to expand our clinical pipeline with a best-in-class exatecan therapy if additional CBX-12 clinical data demonstrate enhanced safety and efficacy."

Cybrexa's proprietary alphalex technology is designed to increase the therapeutic index of potent anti-cancer compounds by targeting their delivery to tumor cells, thus reducing systemic exposure and thereby reducing toxicity. Importantly, this targeting is achieved through an antigen-independent mechanism, making the alphalex technology potentially applicable to diverse tumor types and providing a complementary approach to traditional ADCs. The alphalex technology platform utilizes pHLIPs combined with a linker to deliver anti-cancer compounds directly to tumor cells. In the acidic (low pH) tumor microenvironment, the pHLIP forms an alpha-helical structure that inserts itself into and across the tumor cell membrane. It is well established that many tumors have an altered metabolism that results in excretion of lactic acid into the tumor microenvironment, thereby reducing the local pH. The linker is cleaved within the cell, releasing the anti-cancer agent into the cell's cytoplasm. The alpha-helical structure of the peptide (pHLIP) does not form in the physiologic pH surrounding normal cells, preventing delivery to these cells and reducing toxicity.

"Cybrexa is focused on developing the next generation of cancer therapeutics that specifically target tumors and their underlying biology," said Per Hellsund, President & CEO, Cybrexa. "With its expanding portfolio of biotherapeutics, including ADCs, Exelixis and its partner network have significant and expanding expertise in PDC chemistries and development. Our alphalex PDC technology is an important complement to ADCs and other targeted therapies, and we are excited to bring Exelixis' insights and resources to the development of CBX-12."

Financial Considerations

Under the terms of the agreement, Exelixis will pay Cybrexa an upfront fee of $60 million in exchange for the right to acquire CBX-12 pending certain Phase 1 results and to fund certain development and manufacturing expenses incurred by Cybrexa to advance an agreed development plan. Cybrexa may also be eligible to receive up to an additional $642.5 million, including development, regulatory, and commercial milestone payments, as well as a fee for the acquisition of CBX-12 upon evaluation of a pre-specified clinical data package.

Please see Exelixis' disclosure in today's Form 10-Q filed with the Securities and Exchange Commission for additional details of the terms of the collaboration agreement.

About the alphalex™ Technology Platform

The Cybrexa alphalex™ technology is a novel antigen-independent peptide-drug conjugate (PDC) platform that enables targeted delivery of highly potent anticancer treatments and aims to revolutionize the standard of care in oncology. The platform consists of a pH-Low Insertion Peptides (pHLIPs®) peptide, linker, and small molecule anti-cancer agent. pHLIP peptides are a family of pH-Low Insertion Peptides that target acidic cell surfaces. pHLIP was developed at Yale University and the University of Rhode Island, and is exclusively licensed to pHLIP, Inc., and Cybrexa is a sublicensee of pHLIP, Inc.

About Cybrexa

Cybrexa is a privately held clinical-stage biotechnology company pioneering novel antigen-independent tumor-targeting peptide drug conjugate (PDC)

therapeutics. The company is led by a dynamic team of highly successful life science entrepreneurs and veteran drug development scientists. Cybrexa investors include Advantage Capital Connecticut, Connecticut Innovations, Elm Street Ventures and HighCape Capital. It is on a mission to create therapeutics that revolutionize the standard of care in oncology. Cybrexa's robust pipeline aims to combat breast, ovarian, non-small cell lung cancer and a range of other tumors. Its assets are built on Cybrexa's alphalex™ technology platform, which enables intracellular delivery of highly potent anticancer treatments. Cybrexa is based in New Haven, Conn. and was founded in 2017. For more information about Cybrexa, please visit www.cybrexa.com or follow us on LinkedIn and Twitter.

About Exelixis

Founded in 1994, Exelixis, Inc. (Nasdaq: EXEL) is a commercially successful, oncology-focused biotechnology company that strives to accelerate the discovery, development and commercialization of new medicines for difficult-to-treat cancers. Following early work in model system genetics, we established a broad drug discovery and development platform that has served as the foundation for our continued efforts to bring new cancer therapies to patients in need. Our discovery efforts have resulted in four commercially available products, CABOMETYX® (cabozantinib), COMETRIQ® (cabozantinib), COTELLIC® (cobimetinib) and MINNEBRO® (esaxerenone), and we have entered into partnerships with leading pharmaceutical companies to bring these important medicines to patients worldwide. Supported by revenues from our marketed products and collaborations, we are committed to prudently reinvesting in our business to maximize the potential of our pipeline. We are supplementing our existing therapeutic assets with targeted business development activities and internal drug discovery — all to deliver the next generation of Exelixis medicines and help patients recover stronger and live longer. Exelixis is a member of the Standard & Poor's (S&P) MidCap 400 index, which measures the performance of profitable mid-sized companies. For more information about Exelixis, please visit www.exelixis.com, follow @ExelixisInc on Twitter or like Exelixis, Inc. on Facebook.

Exelixis Forward-Looking Statements

This press release contains forward-looking statements, including, without limitation, statements related to: the therapeutic potential of CBX-12 to improve efficacy and reduce toxicity over systemic topoisomerase inhibitors; the potential for CBX-12 to be a first-in-class PDC of exatecan, with broad utility in patients with diverse tumor types who are not eligible for antigen-targeted therapies, including monoclonal antibodies and ADCs, and the potential for use in combination regimens with other anti-cancer agents and immunotherapies; Exelixis' ongoing strategy to leverage its balance sheet to gain access to new assets with compelling potential upside in a risk-sharing model, where Exelixis can work with partners to further establish proof of concept before investing more heavily; Exelixis' belief that CBX-12 has transformative clinical potential and may provide differentiated clinical benefit in several solid tumors, and that the collaboration with Cybrexa aligns with Exelixis' strategic goals by affording Exelixis an opportunity to expand its clinical pipeline with a best-in-class clinical-stage asset; Exelixis' immediate and future financial and other obligations under the exclusive collaboration agreement with Cybrexa; and Exelixis' plans to reinvest in its business to maximize the potential of the company's pipeline, including through targeted business development activities and internal drug discovery. Any statements that refer to expectations, projections or other characterizations of future events or circumstances are forward-looking statements and are based upon Exelixis' current plans, assumptions, beliefs, expectations, estimates and projections. Forward-looking statements involve risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in the forward-looking statements as a result of these risks and uncertainties, which include, without limitation: the level of costs associated with Exelixis' commercialization, research and development, in-licensing or acquisition of product candidates, and other activities; uncertainties inherent in the drug discovery and product development process; Exelixis' dependence on its relationship with Cybrexa, including Cybrexa's adherence to its obligations under the exclusive collaboration agreement; complexities and the unpredictability of the regulatory review and approval processes in the U.S. and elsewhere; Exelixis' and Cybrexa's continuing compliance with applicable legal and regulatory requirements; Exelixis' and Cybrexa's ability to protect their respective intellectual property rights; market competition; changes in economic and business conditions, including as a result of the COVID-19 pandemic and other global events; and other factors affecting Exelixis and its product pipeline discussed under the caption "Risk Factors" in Exelixis' Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on August 9, 2022, and in Exelixis' future filings with the SEC, including, without limitation, Exelixis' Quarterly Report on Form 10-Q expected to be filed with the SEC on November 1, 2022. All forward-looking statements in this press release are based on information available to Exelixis as of the date of this press release, and Exelixis undertakes no obligation to update or revise any forward-looking statements contained herein, except as required by law.

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