Codiak Reports Additional Positive Phase 1 Results for exoIL-12™ Confirming Local Pharmacology and Dose Selection for Safety and Efficacy Trial in Early-Stage Cutaneous T Cell Lymphoma (CTCL) Patients

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– Pharmacodynamic results confirm localized exoIL-12 pharmacologic activity

without systemic IL-12 exposure –

– Plan to initiate multi-dose study in CTCL patients, with data anticipated by year-end 2021–

CAMBRIDGE, Mass., Feb. 04, 2021 (GLOBE NEWSWIRE) -- Codiak BioSciences, Inc. (NASDAQ: CDAK), a clinical-stage biopharmaceutical company focused on pioneering the development of exosome-based therapeutics as a new class of medicines, today announced pharmacodynamic (PD) activity results from the healthy volunteer portion of its randomized, placebo-controlled, double-blind Phase 1 trial of the company's clinical candidate, exoIL-12. Analyses of skin punch biopsies bordering the subcutaneous injection site of exoIL-12 revealed local retention of immunologically detectable IL-12 at the injection site, and localized pharmacological activity as measured by levels of the T cell attractant chemokine, IP-10, in the skin. IL-12 was not detected in plasma at any dose of exoIL-12 tested and plasma IP-10 was only detectable at the highest, 12 µg dose. Results confirmed the desired localization and retention of IL-12 at the injection site for at least 24 hours, as well as prolonged IP-10 production for 8-15 days depending upon dose.

exoIL-12 is the first engineered exosome therapeutic candidate to be evaluated in humans and one of two Codiak programs currently in clinical development. exoIL-12 was engineered using the company's proprietary engEx™ Platform and designed to display functional IL-12 – a potent anti-tumor cytokine – on the exosome surface using the exosomal protein, PTGFRN, as a scaffold.

"We now have clinical evidence in healthy volunteers of local, IL-12-driven pharmacology without detectable systemic exposure to IL-12 or drug-related adverse events for exoIL-12," said Benny Sorensen, M.D., Ph.D., Senior Vice President and Head of Clinical Development, Codiak. "These results further support the target profile that we are hoping to achieve with this candidate and have enabled us to identify the optimal dose for the next phase of our clinical program in patients with active, early-stage CTCL. Moreover, this data further validates the capacity of our engEx Platform to engineer precise properties into our exosome-based therapeutic candidates that potentially expand their therapeutic index."

These results are consistent with Codiak's preclinical testing and confirm exoIL-12's target product profile of local drug retention at the injection site, prolonged local pharmacodynamic activity, and lack of systemic IL-12 exposure. Codiak plans to initiate the next portion of the Phase 1 clinical trial, evaluating the safety and efficacy of exoIL-12, in CTCL patients at the dose of 6 µg, which Codiak believes to be the optimal pharmacologically active dose based upon this healthy volunteer data and prior preclinical data with exoIL-12.

"We are pleased with the data we have obtained with exoIL-12 in healthy human volunteers and look forward to the initiation of trials in CTCL patients," said Douglas E. Williams, Ph.D., President and Chief Executive Officer, Codiak. "It is heartening to see one of the founding principles of Codiak validated in the current trial, namely that engineered exosomes can offer the opportunity to tailor therapeutic payloads to provide an active biological response while at the same time limiting unwanted side effects."

Pharmacodynamic Data from Healthy Volunteers
A total of five cohorts each with five subjects were enrolled, randomized 3:2 active drug to placebo, and dosed in the first part of the Phase 1 study. Each cohort received a subcutaneously administered single ascending dose of exoIL-12: 0.3 µg, 1.0 µg, 3.0 µg, 6.0 µg or 12.0 µg, respectively.

PD measurements including skin IL-12 levels post-injection and IL-12 receptor-mediated signaling assessed by induction of IP-10, were measured in skin punch biopsies at a 1.5 cm radius from the subcutaneous injection site. Samples were collected immediately prior to dosing (placebo or exoIL-12) and at 24 hours, Day 8 and Day 15 after administration. Results showed detectable IL-12 near the injection site as much as 24 hours post injection at the 6 µg dose. Samples collected at the 8-day and 15-day time points did not have detectable IL-12. In contrast, doses from 1.0 µg to 12µg (not 0.3 µg) showed significant induction of IP-10 production in the skin detectable for 8-15 days confirming robust and durable local pharmacology. At the highest 12 µg dose, IP-10 was also detectable in the plasma, but not at any of the lower doses. As previously described, no detectable IL-12 was present in plasma and no drug-related adverse events were observed across the entire dose range. These results confirm the prolonged, local activation of the IL-12 signaling cascade and give us confidence that 6 µg is the optimal dose to move forward in the next phase of clinical testing in CTCL patients.

During the planned part two of the Phase 1 trial, repeat doses of exoIL-12 at 6 µg will be administered into the lesions of stage IA-IIB CTCL patients. Patients will be monitored for safety, pharmacokinetic, and PD effects through analysis of blood and tumor biopsies, and for local and systemic anti-tumor efficacy using validated CTCL assessment criteria, including CAILS and mSWAT scores. The study is being conducted in the United Kingdom. Given COVID-19-related restrictions involving new study initiation, Codiak is working closely with study sites to open enrollment and commence dosing of patients when allowable and appropriate. Safety, biomarker and preliminary anti-tumor efficacy results are anticipated by the end of 2021.

In prior clinical trials conducted by others of recombinant IL-12 (rIL-12), CTCL patients have shown single-agent treatment responses (56-74% overall response rate and up to 22% complete responses[1]). However, the utility of rIL-12 has been greatly limited due to serious adverse events caused by systemic exposure. To overcome these limitations, exoIL-12 was designed to facilitate dose control of IL-12 and limit systemic exposure and associated toxicity by localizing IL-12 in the tumor microenvironment in order to potentially expand the therapeutic index.

There is currently no standard of care treatment for early-stage CTCL. Physicians often employ a variety of non-specific interventions, including repetitive radiation therapy, photo therapy, high-potency steroids and local chemotherapy to inhibit tumor growth and halt disease progression. There is a need for treatments that can induce local as well as systemic anti-tumor activity.

About exoIL-12™
exoIL-12 is Codiak's exosome therapeutic candidate engineered to display fully active IL-12 on the surface of the exosome, using the exosomal protein, PTGFRN, as a scaffold, and designed to facilitate potent local pharmacology at the injection site with precisely quantified doses. By limiting systemic exposure of IL-12 and associated toxicity, Codiak hopes to enhance the therapeutic index with exoIL-12, delivering a more robust tumor response, dose control and an improved safety profile.

Codiak intends to focus development of exoIL-12 on tumors that have, in previous clinical testing, shown clinical responses to rIL-12 used as a monotherapy. This list includes CTCL, melanoma, Merkel cell carcinoma, Kaposi sarcoma, glioblastoma multiforme, triple negative breast cancer, among others.

About Codiak BioSciences
Codiak is a clinical-stage biopharmaceutical company focused on pioneering the development of exosome-based therapeutics, a new class of medicines with the potential to transform the treatment of a wide spectrum of diseases with high unmet medical need. By leveraging the biology of exosomes as natural intercellular transfer mechanisms, Codiak has developed its proprietary engEx Platform to expand upon the innate properties of exosomes to design, engineer and manufacture novel exosome therapeutic candidates. Codiak has utilized its engEx Platform to generate a deep pipeline of engineered exosomes aimed at treating a broad range of diseases, spanning oncology, neuro-oncology, neurology, neuromuscular disease and infectious disease. For more information, visit http://www.codiakbio.com and follow @CodiakBio.

Forward-Looking Statements
This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, including, among other things, statements concerning the development and therapeutic potential of exoIL-12, including expected design of clinical trials and timing of commencement of part two of Codiak's Phase 1 clinical trial in CTCL patients, timing of release of data, and statements regarding the capabilities and potential of Codiak's engEx Platform and engineered exosomes generally. Any forward-looking statements in this press release are based on management's current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. For a discussion of these risks and uncertainties, and other important factors, any of which could cause our actual results to differ from those contained in the forward-looking statements, see the section entitled "Risk Factors" in Codiak's Quarterly Report on Form 10-Q for the quarter ended September 30, 2020, and in subsequent filings with the Securities and Exchange Commission, as well as discussions of potential risks, uncertainties and other important factors in Codiak's subsequent filings with the Securities and Exchange Commission. All information in this press release is current as of the date of this report, and Codiak undertakes no duty to update this information unless required by law.

[1] Gokhale MS, Vainstein V, Tom J, et al. Single low-dose rHuIL-12 safely triggers multilineage hematopoietic and immune-mediated effects. Exp Hematol Oncol. 2014;3(1):11. Published 2014 Apr 11. doi:10.1186/2162-3619-3-11

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