Codiak Provides Platform-Validating Clinical Update and Data from Phase 1 Trials of exoSTING™ and exoIL-12™

June 30, 2022

– Codiak's engineered exosome candidates demonstrate potential for best-in-class profile, with tumor retention and delivery to the cells of interest allowing for increased therapeutic window –

– exoSTING and exoIL-12 demonstrated favorable safety and tolerability profile at repeat doses tested and antitumor activity was observed in both injected and uninjected/distal lesions –

– Codiak has identified recommended Phase 2 dose for each program and plans to initiate Phase 2 studies for both candidates in the first quarter of 2023 –

– Codiak to host conference call and webcast today at 8:00 am ET –

CAMBRIDGE, Mass., June 30, 2022 (GLOBE NEWSWIRE) -- Codiak BioSciences, Inc. (Nasdaq: CDAK), a clinical-stage biopharmaceutical company pioneering the development of exosome-based therapeutics as a new class of medicines, today announced platform-validating clinical data from Phase 1 trials of exoSTING™ and exoIL-12™ and plans to advance both candidates into Phase 2 trials. In an open-label Phase 1 trial, exoIL-12 demonstrated a differentiating favorable safety and tolerability profile, with no detectable systemic exposure of IL-12 and no treatment-related adverse events, which has not previously been reported by others with recombinant IL-12. The two patients with cutaneous T cell lymphoma (CTCL) who have been treated each received multiple (>20) injections of exoIL-12 and experienced tumor regressions in both injected and non-injected lesions, including a partial response in one patient. In the open-label Phase 1/2 clinical trial evaluating exoSTING as a single agent in patients with late-stage refractory solid tumors, data across all five dose cohorts showed repeat doses of exoSTING were well-tolerated, demonstrated tumor retention with no systemic exposure of the STING agonist, and in a subset of patients, tumor shrinkage was observed in injected and uninjected lesions.

"We believe these positive datasets from our two lead programs provide further clinical validation of our engEx® Platform and the target profile for our engineered exosome therapeutic candidates. In the studies, we were able to deliver exoSTING and exoIL-12, with repeat dosing, to the tumor with a high level of specificity, no observed systemic exposure or associated toxicity, and an enhanced therapeutic index–while demonstrating tumor shrinkage in both injected and uninjected lesions," said Douglas E. Williams, Ph.D., President and Chief Executive Officer of Codiak. "STING and IL-12 have been challenging targets that have historically been hampered by very toxic side effects, but we believe our approach may enable best-in-class therapies with favorable safety profiles. Based on these findings, we have identified a recommended Phase 2 dose for both programs. We plan to initiate a Phase 2 study of exoSTING in bladder cancer and a Phase 2 study of exoIL-12 in an expanded group of tumor types in the first quarter of 2023."

exoIL-12 Data and Development Plan

The Phase 1 clinical trial was designed in two parts, with the data from the healthy volunteer portion of the study reported last year. In the CTCL portion of the study, two patients with early stage CTCL whose disease progressed on prior therapy have been treated as of the June 10, 2022, data cut-off. Each patient has received more than 20 injections of exoIL-12 (6.0 µg) across multiple lesions. Duration of treatment has been greater than six months, and no treatment-related adverse events Grade 3 or higher or SAEs were observed, and no dose modifications were required.

exoIL-12 demonstrated improvement in overall tumor burden, as measured by mSWAT, and lesion severity, as measured by CAILS, in both patients treated. Patient 001 had a total of 5 skin lesions, 3 of which were injected and exhibited a partial response, as per mSWAT (a registrational endpoint) with a 61% decrease in disease burden. Improvement in CAILS scores for all skin lesions, both injected and uninjected, ranged from 20-80%. All skin lesions have resolved, and additional injections were deemed unnecessary by the treating physician. The patient remains on study. Patient 002 had 3 skin lesions, 2 of which were injected (20 injections to date) and has demonstrated a 43% decrease in disease burden. Improvement in CAILS scores have been seen ranging from 30-50% for all lesions, both injected and uninjected. This patient remains on study and continues to receive exoIL-12 injections.

Plasma pharmacokinetic (PK) measurements of both healthy volunteers and patients that received exoIL-12 showed no systemic exposure with levels of IL-12 below the limit of quantification. In contrast, previous rIL-12 clinical studies showed dose-dependent systemic exposure with dosages of 5 and 12 µg resulting in Cmax plasma levels of approximately 15 to 45 pg/ml within 6 to 12 hours after dosing.[1]

Data from the CTCL patients further validate 6 mcg as the intended dose for Phase 2 development. Codiak intends to conclude the current study in the UK and transition to a U.S. Investigational New Drug (IND) application. Codiak anticipates initiating a Phase 2 trial during the first quarter of 2023 in patients with cutaneous malignancies responsive to rIL-12 in studies historically, including CTCL, Kaposi's sarcoma, Merkel cell carcinoma, and squamous cell carcinoma – each orphan cutaneous diseases treated by the same physicians, where local treatment is common.

exoSTING Data and Development Plan

Data as of June 10, 2022, are being reported from all five escalation dose cohorts (0.3 mcg, 1.0 mcg, 3.0 mcg, 6.0 mcg and 12.0 mcg) enrolled in the Phase 1/2 study. Dosing is still underway in the 12.0 mcg cohort and all patients continue to be followed. Trial participants (n=23) were administered exoSTING intratumorally, and nearly all had received at least two prior therapies prior to study entry with most (65%) having progressed on checkpoint inhibitors.

Plasma pharmacokinetic (PK) measurements of patients that received exoSTING showed no systemic exposure to the agonist. Further, analyses of available plasma biomarkers indicated a lack of systemic inflammatory cytokines detectable in blood after exoSTING administration.

Within all dose cohorts, exoSTING was well-tolerated and no dose limiting toxicities or treatment-emergent adverse events of Grade 3 or higher were observed. Treatment-related serious adverse events (TRSAE) were observed in three patients (2 patients with Grade 2 cytokine release syndrome and 1 patient with Grade 1 pyrexia). All patients who experienced a TRSAE were retreated and remained on study without additional SAEs.

Blood biomarker assessments conducted post dosing demonstrated dose-dependent activation of the STING pathway at doses 100-fold lower in comparison to other free STING agonists. Paired tumor biopsies available from Cohorts 1-4 show evidence of an adaptive immune response, including consistent increases in CD-8 effector T-cells and PD-L1 in the tumor micro-environment.

Signs of antitumor activity were observed with tumor shrinkage in injected as well as distal, non-injected tumors.

The data support advancing exoSTING into Phase 2 development, particularly in early-stage disease where combination with immunotherapy may lead to enhanced activity. Codiak has identified 12.0 mcg as the intended dose for intratumoral administration and plans to file a protocol amendment with FDA later this year to enable initiation of a Phase 2 trial of exoSTING in patients with bladder cancer (Muscle Invasive Bladder Cancer or MIBC) during the first quarter of 2023.

“This is a critical milestone for Codiak because we met our objectives for the Phase 1 studies of exoSTING and exoIL-12 and the data support the differentiated target profile we had hoped to unlock with our engineered exosome platform. What is remarkable is that these exosomal formulations are demonstrating results that free STING agonists and systemic IL-12 were unable to achieve due to significant limitations in safety and therapeutic index, opening up the possibility that these two promising targets can benefit cancer patients,” said David Mauro, M.D., Ph.D., Chief Medical Officer of Codiak. “We are enthusiastic about moving these programs into Phase 2 early next year while continuing to monitor patients from ongoing studies and submitting data to upcoming medical meetings.”

Conference Call and Webcast
Codiak will host a conference call and webcast today at 8:00 a.m. ET. The webcast may be accessed through the “News & Events” page in the “Investors & Media” section of Codiak’s website at https://ir.codiakbio.com/news-events. A PDF of the accompanying slides will be available for download. Phone participants in the U.S and Canada may dial (800) 385-9715 and refer to conference ID 3799112 (international callers please use (409) 937-8965. To ensure timely access, participants are encouraged to connect to the call 10 minutes before the start time or to use the webcast link for listen-only access. The archived webcast will be available on Codiak’s website beginning approximately two hours after the event and will be available for replay for at least 90 days after the event.

About exoSTING™
exoSTING is Codiak’s exosome therapeutic candidate engineered to incorporate a proprietary STING (Stimulator of Interferon Genes) agonist inside the lumen of the exosome while expressing the exosomal protein, PTGFRN, on the exosome surface to facilitate specific uptake in tumor-resident antigen presenting cells. Codiak believes that exoSTING has the potential to overcome certain limitations of free STING agonists, and to enhance the therapeutic index and selectivity of delivery to desired cells in the tumor microenvironment.

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 IL-12 used as a monotherapy.

About the engEx® Platform
Codiak’s proprietary engEx Platform is designed to enable the development of engineered exosome therapeutics for a wide spectrum of diseases and to manufacture them reproducibly and at scale to pharmaceutical standards. By leveraging the inherent biology, function and tolerability profile of exosomes, Codiak is developing engEx exosomes designed to carry and protect potent drug molecules, provide selective delivery and elicit the desired pharmacology at the desired tissue and cellular sites. Through its engEx Platform, Codiak seeks to direct tropism and distribution by engineering exosomes to carry on their surface-specific targeting drug moieties, such as proteins, antibodies/fragments, and peptides, individually or in combination. Codiak scientists have identified two exosomal proteins that serve as surface and luminal scaffolds. By engineering the exosome surface or lumen and optimizing the route of administration, Codiak aims to deliver engEx exosomes to the desired cell and tissue to more selectively engage the drug target, potentially enhancing the therapeutic index by improving potency and reducing toxicity.

About Codiak BioSciences
Codiak is a clinical-stage biopharmaceutical company 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 disease areas, spanning oncology, neuro-oncology, infectious disease and rare disease. For more information, please visit www.codiakbio.com.

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 clinical development and therapeutic potential of exoSTING and exoIL-12. 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 Annual Report on Form 10-K for the year ended December 31, 2021, 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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