Codiak Presents Preclinical Data on exoASO™-STAT6 and exoASO™-C/EBPβ Programs at the Society for Immunotherapy of Cancer (SITC) 2022 Annual Meeting

November 10, 2022

– exoASO-STAT6 demonstrated durable pharmacokinetic/pharmacodynamic profile in preclinical models; biomarkers with clinical translational potential identified, providing a rationale for selecting cancer subtypes for treatment with exoASO-STAT6 –

– Systemically administered exoASO-C/EBPβ demonstrated extra-hepatic delivery and potent systemic anti-tumor activity across multiple myeloid-derived suppressor cell (MDSC) rich tumor models –

– A Phase 1 clinical trial of exoASO-STAT6 in patients with advanced hepatocellular carcinoma (HCC), is ongoing; initial data expected in the first half of 2023 –

CAMBRIDGE, Mass., Nov. 10, 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 new preclinical data from its exoASO™-STAT6 and exoASO™-C/EBPβ programs. exoASO-STAT6, an engineered exosome precision medicine candidate designed to selectively deliver antisense oligonucleotides to disrupt STAT6 signaling in tumor-associated macrophages (TAMs) and induce an anti-tumor immune response, demonstrated a strong preclinical pharmacokinetic (PK) and pharmacodynamic (PD) profile in preclinical models. Codiak has also identified PD biomarkers with clinical translational potential and described a rationale for selecting cancer subtypes that could benefit from treatment with exoASO-STAT6.

exoASO-C/EBPβ further demonstrated it is a novel therapeutic that selectively targets and attenuates a critical transcription factor in immunosuppressive myeloid-derived suppressor cells (MDSCs), resulting in their immune modulation and potent systemic anti-tumor activity across multiple MDSC-rich tumor models. Anti-tumor activity is mediated by the broad delivery of exoASO-C/EBPβ-targeting antisense oligonucleotides (ASOs) to extra-hepatic myeloid cells in disseminated tumors throughout the body.

“Taken together, these data presented at SITC paint a compelling picture of the potential of our programs and our platform. Our work on exoASO-STAT6 highlights broad activity across multiple challenging, checkpoint therapy-resistant preclinical models, robust and consistent translation from these models to clinical readiness, and our PD-driven approach to patient selection. Targeted delivery to hepatic TAMs in HCC represents a novel strategy for the precise delivery of drug payloads to the right population of patients,” said Sriram Sathyanarayanan, Ph.D., Chief Scientific Officer, Codiak. “Our data with exoASO-C/EBPβ demonstrate the potential for broad anti-tumor activity in extra-hepatic tumors mediated by a differentiated mechanism of myeloid cell (monocyte and MDSC) delivery of ASOs to distant tumor sites, leading to modulation of MDSCs and resulting in a T-cell mediated anti-tumor activity.”

Key conclusions from the preclinical studies on exoASO-STAT6 at SITC 2022 include:

- Systemic administration of exoASO-STAT6 in mice and NHPs resulted in a durable, dose-dependent retention of the STAT6 ASO in the liver, detectable for up to 21 days at all dose levels.
- Systemic dosing of exoASO-STAT6 in preclinical models resulted in a durable, dose-dependent reduction of STAT6 mRNA in the liver, as well as a modulation of several downstream pathway genes.
- In line with its durable PK/PD attributes, exoASO-STAT6 demonstrated strong single agent antitumoral efficacy across multiple tumor models with local or systemic dosing.
- Histological analysis confirmed that STAT6 and IL-4 receptor (IL4R) are expressed by TAMs in human HCC tumors, supporting the rationale to use these two biomarkers in the clinic.
- A STAT6 macrophage transcriptional signature was identified, which is enriched at high levels in a subset of HCC patients and correlates with poor prognosis in HCC and other tumors such as bladder and stomach cancer.

Key conclusions from the preclinical studies on exoASO-C/EBPβ at SITC 2022 include:

- Exosome surface glycoproteins enabled the precise uptake of ASO payloads by MDSCs and monocytes, which facilitated the delivery of ASOs to distant extra-hepatic tumor sites. This novel mechanism opens the potential for targeting a broad range of tumors with Codiak’s exoASO™ platform.
- Systemic administration of exoASO-C/EBPβ resulted in immune modulation of MDSCs, resulting in a T-cell mediated systemic anti-tumor response, which was further elevated by combining with anti-PD1 therapy.
- Treatment with exoASO-C/EBPβ across multiple routes of administration demonstrated robust monotherapy efficacy in several challenging, checkpoint therapy-resistant preclinical models, exhibiting the potentially broad applicability of exoASO-C/EBPβ in the treatment of several cancer indications. Patient populations across The Cancer Genome Atlas (TCGA) database were also evaluated based on the expression of multiple C/EBPβ and MDSC-related gene signatures to assess potential cancer indications for exoASO-C/EBPβ.

“The data presented at SITC this year further demonstrate the potential of Codiak’s approach to targeting transcription factors in distinct macrophage and MDSC subpopulations with exoASO-STAT6 and exoASO- C/EBPβ,” said Douglas E. Williams, Ph.D., CEO, Codiak. “We are enthusiastic about the ongoing Phase 1 clinical study of exoASO-STAT6 and are on track to have preliminary monotherapy data in the first half of 2023.”

About exoASO™-STAT6
Codiak’s exoASO-STAT6 is an engineered exosome investigational therapeutic candidate designed to selectively deliver antisense oligonucleotides (ASOs) to disrupt STAT6 signaling in tumor-associated macrophages (TAMs) and induce an anti-tumor immune response. exoASO-STAT6 is Codiak’s first clinical candidate to evaluate a systemically administered exosome-based drug candidate. A Phase 1 clinical trial evaluating exoASO-STAT6 in patients with advanced hepatocellular carcinoma, liver metastases from primary gastric cancer, and colorectal cancer is underway.

In multiple *in vivo* preclinical studies, exoASO-STAT6 demonstrated potent single agent activity, including >90% tumor growth inhibition and 50-80% complete responses. In HCC models, exoASO-STAT6 induced significant knockdown of STAT6 mRNA, attenuated tumor growth and induced complete remission of tumor lesions in 50% of mice. This anti-tumor activity was enhanced (75% complete remissions) when exoASO-STAT6 was administered with anti-PD1 antibodies. The monotherapy activity was accompanied by remodeling of the tumor microenvironment, including significant expansion of M1-like macrophages and induction of an adaptive anti-tumor immune response, enabling tumor elimination.

About exoASO™-C/EBPβ
Codiak’s exoASO-C/EBPβ is designed to selectively deliver ASOs to down-modulate C/EBPβ, a transcription factor that regulates the immunosuppressive phenotype in TAMs and circulating myeloid-derived suppressor cells (MDSCs), two sub-populations of myeloid cells. High levels of C/EBPβ expression are associated with poor prognosis in multiple cancers, including non-small cell lung cancer (NSCLC).

In previous studies, *In vivo*, systemic administration of exoASO-C/EBPβ resulted in efficient delivery of ASOs to MDSCs, resulting in > 5-fold improvement in tumors and 11 to 12-fold improvement in the circulating blood compared to delivery of a non-exosome (or “free”) ASO. This precise cell targeting was coupled with effective silencing of C/EBPβ and a remodeling of the tumor microenvironment indicative of activation of an immune response. In a variety of *in vivo* tumor models, exoASO-C/EBPβ monotherapy generated up to 70% complete responses and, when combined with anti-PD1, significantly increased complete response rates to 90%. Notably, in a lung tumor model with widely dispersed tumors, systemic administration of exoASO-C/EBPβ resulted in resolution of tumor burden throughout the body. The profound monotherapy activity observed with exoASO-C/EBPβ in multiple tumor models refractory to anti-PD-1 therapy highlights the potential of this therapy to treat multiple anti-PD1 refractory patient populations.

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 diseases, spanning oncology, neuro-oncology, infectious disease, and rare 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 exoASO-STAT6 or exoASO-C/EBPβ, including timing of availability and release of data from development of those candidates, 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 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.

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