Cue Biopharma Presents Updated Data from Lead Program CUE-101 for the Treatment of Recurrent/Metastatic HPV+ Head and Neck Cancer and Additional Pipeline Progress at the Society for Immunotherapy of Cancer's (SITC) 36th Annual Meeting

November 12, 2021

- *Monotherapy data further enhances confidence in CUE-101 potential as single agent therapeutic in the refractory/metastatic human papillomavirus positive head and neck squamous cell carcinoma (HPV+ HNSCC) setting*
- *Early CUE-101 combination data with KEYTRUDA® (pembrolizumab) supports potential mechanistic activity*
- *CUE-102 in vivo data demonstrated ability to selectively activate and expand Wilms' Tumor 1 (WT1)-specific T cells for the treatment of WT1-expressing cancers, supporting clinical advancement of CUE-102*

CAMBRIDGE, Mass., Nov. 12, 2021 (GLOBE NEWSWIRE) -- Cue Biopharma, Inc. (Nasdaq: CUE), a clinical-stage biopharmaceutical company engineering a novel class of injectable biologics to selectively engage and modulate targeted T cells directly within the patient's body, announced today the presentation of interim data further demonstrating the tolerability and antitumor activity potential of CUE-101 as a monotherapy as part of the Company's ongoing clinical trial for the treatment of recurrent/metastatic HPV+ head and neck cancer in a poster at the Society for Immunotherapy of Cancer's 36th Annual Meeting (SITC 2021). Early data from the CUE-101 combination study with pembrolizumab will also be discussed, supporting the potential for mechanistic activity in frontline HPV+ HNSCC patients. SITC 2021 will be held in Washington, D.C. and virtually November 10-14.

Additionally, the Company will present two posters highlighting the broad potential of the interleukin 2 (IL-2)-based CUE-100 series for treating multiple cancers. This includes representative preclinical data from CUE-102, Cue Biopharma's next clinical candidate developed to selectively target Wilms' Tumor 1 (WT1) cancers, and preclinical progress on the Company's Neo-STAT™ and RDI-STAT ™*(Re-Directed Immuno-STAT)* platforms, which provide modularity, flexibility and scalability and address tumor heterogeneity and tumor resistance or escape mechanisms.

SITC 2021 Presentation Highlights:

Title: A phase 1 trial of CUE-101, a novel HPV16 E7-pHLA-IL2-Fc fusion protein, alone and in combination with pembrolizumab in patients with recurrent/metastatic HPV16+ head and neck cancer
Poster #: 438
Presenter: Dr. Sara I. Pai, M.D., Ph.D., associate professor, Department of Surgery; Director, Translational Research in Head and Neck Cancer Massachusetts General Hospital, Harvard Medical School, Boston MA
Date: Saturday, November 13, 2021, Poster Hall (**Hall E**) 7 a.m.–8:30 p.m. EST

Data as of November 2, 2021, include:

- A durable partial response (PR) with an ongoing duration of 30 weeks and five durable stable disease responses (SD), as determined by RECIST 1.1. criteria, out of the 13 evaluable patients dosed at the recommended Phase 2 dose of 4mg/kg as part of the monotherapy trial.
- Pharmacodynamic (PD) signals of expansion of HPV16+ cytotoxic T cells were observed in the monotherapy trial, which confirm CUE-101 mechanism of action by activation of tumor-specific T cells.
- Demonstrated favorable tolerability to date, with more than 190 cumulative doses administered. Reported mild adverse events resolved while patients continued therapy.
- Early signs of clinical activity of CUE-101 in combination with pembrolizumab with 3 out of 3 patients from cohort 2 at 2mg/kg, demonstrating tumor reductions in target lesions on their first scan after having received two cycles of therapy. Cohort 3 is currently enrolling.

"I am encouraged by the preliminary anti-tumor activity of CUE-101 and the positive tolerability profile, which are necessary to improve the survival and quality of care for this relatively young patient population," said Sara Pai M.D., Ph.D., associate professor of surgery and director of Translational Research in Head and Neck Cancer at the Massachusetts General Hospital, and principal investigator of the CUE-101 Phase 1 clinical trial. "Until this trial we haven't seen an 'off-the-shelf' HPV-targeted biologic administered in an outpatient setting with such durable responses in the second- and third-line treatment for recurrent/metastatic HPV16+ head and neck cancer patients and it is a significant advancement, presenting a potential path forward for a new therapeutic standard."

Ken Pienta, acting chief medical officer of Cue Biopharma, added, "We are very pleased by the emerging clinical data and growing body of evidence demonstrating the clinical potential of CUE-101 as a monotherapy in a highly pretreated, refractory, metastatic HPV+ HNSCC setting. In addition, we are encouraged by the promising, albeit early, emerging data from our combination study with pembrolizumab demonstrating potential mechanistic activity with the prospects of expanding patient reach and enhancing therapeutic responses. It is also encouraging to observe histology data demonstrating enhanced penetration of cytotoxic CD8+ T cells or "killer" T cells within the tumor and anti-tumor activity in patients failing 2-3+ previous lines of treatment."

Title: CUE-102 selectively activates and expands WT1-specific T cells for the treatment of patients with WT1+ malignancies
Poster #: 720

Presenter: Dr. Christie Zhang, Ph.D., senior scientist, discovery and translational immunology, Cue Biopharma
Date: Friday, November 12, 2021, Poster Hall (**Hall E**) 7 a.m.–8:30 p.m. EST

- Multiple in vitro assessments demonstrated that CUE-102 selectively activated and expanded WT1-specific CD8+ T cells from peripheral blood mononuclear cells (PBMC) of healthy donors.
- These CUE-102-expanded CD8+ T cells exhibited polyfunctional and cytotoxic responses upon challenge with WT1-presenting target cells.
- Data showed that the attenuation of the interleukin 2 (IL-2) domains of CUE-102 led to a reduction of indiscriminate IL-2 activity, similar to results obtained with CUE-101.
- *In vivo* studies in human leukocyte antigen (HLA)-A2 transgenic mice confirmed that CUE-102 elicited and expanded WT1-specific CD8+ T cells from naïve mice without significantly altering the frequencies of other immune lineages.
- The WT1-specific CD8+ T cells expanded *in vivo* exhibited polyfunctionality and selectively killed WT1-presenting target cells in vivo.

Title: Targeting engineered interleukin-2 (IL-2) to antigen specific T cells via novel biologic platforms
Poster #: 793
Presenter: Raymond J. Moniz, associate director, discovery and translational immunology, Cue Biopharma
Date: Friday, November 12, 2021, Poster Hall (**Hall E**) 7 a.m.– 8:30 p.m. EST

- Data demonstrated that the Company's Neo-STAT (NST) biologics can be engineered with a diversity of T cell epitopes by efficient conjugation into an empty HLA-binding pocket, and that these molecules activated and expanded antigen specific T cells *in vitro.*
- Data additionally demonstrated that the Company's RDI-STAT biologics, were able to expand anti-viral T cell repertoires and drive anti-viral T cell redirected killing of tumor-associated antigen (TAA)-expressing cells.
- In contrast to pan anti-CD3 bispecific molecules, RDI-STATs demonstrated significantly lower induction of pro-inflammatory cytokines, thus avoiding systemic activation of all T cells and offering a superior safety profile.

Anish Suri, Ph.D., president and chief scientific officer of Cue Biopharma, said, "The demonstration of CUE-102 to activate and expand WT1-specific cytotoxic CD8+ T cells *in vivo* further supports the modularity of our platform and enhances the potential of our CUE-100 series to address a diversity of cancers, supporting the advancement of CUE-102 into the clinic. An Investigational New Drug filing for CUE-102 is scheduled for the first quarter of 2022. In addition, the data presented on our Neo-STAT and RDI-STAT platforms continue to demonstrate the versatility and modularity of our biologics to potentially address multiple cancers with flexibility and scalability. We are highly encouraged as we continue to explore the breadth of opportunities with our Immuno-STAT™, Neo-STAT and RDI-STAT biologics platforms, to develop novel therapies that address diverse patient populations, tumor heterogeneity and tumor escape mechanisms."

For more information on all three posters please visit: https://www.cuebiopharma.com/investors-media/publications-presentations/.

About the CUE-100 Series
The CUE-100 series consists of Fc-fusion biologics that incorporate peptide-major histocompatibility complex (pMHC) molecules along with rationally engineered interleukin 2 (IL-2) molecules. These singular biologics are anticipated to selectively target, activate and expand a robust repertoire of tumor-specific T cells directly in the patient's body. The binding affinity of IL-2 for its receptor has been deliberately attenuated to achieve preferential selective activation of tumor-specific effector T cells while reducing potential for effects on regulatory T cells (Tregs) or broad systemic activation, potentially mitigating the dose-limiting toxicities associated with current IL-2-based therapies.

About the CUE-101 Clinical Trial
The trial (NCT03978689) is a multi-center, first-in-human, open-label Phase 1 dose escalation and expansion study evaluating the safety, anti-tumor effect and immunogenicity of CUE-101 as a monotherapy in second-line patients with confirmed human papilloma virus positive recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HPV+ HNSCC) and HLA-A*02:01 serotype. Patients receive CUE-101 as a monotherapy ranging from 0.06 mg/kg to 8 mg/kg. The maximum tolerated dose (MTD) has not been identified and a Phase 2 4 mg/kg dose has been selected. The company has expanded the study to evaluate CUE-101 in combination with 200 mg of KEYTRUDA® (pembrolizumab) as first-line treatment in patients with HPV16-driven recurrent/metastatic HNSCC. Enrollment continues in both monotherapy and combination cohorts.

About CUE-102
Leveraging the Immuno-STAT ™*(Selective Targeting and Alteration of T cells)* platform of targeted interleukin 2 (IL-2) therapies and the ongoing development of CUE-101, CUE-102 is being developed as a novel therapeutic fusion protein to selectively activate tumor antigen-specific T cells to treat Wilms' Tumor 1 (WT1)-expressing cancers. CUE-102 consists of two human leukocyte antigen (HLA) molecules presenting a WT1 peptide, four affinity-attenuated IL-2 molecules, and an effector attenuated human immunoglobulin G (IgG1) Fc domain.

About the Neo-STAT and RDI-STAT *(Re-Directed Immuno-STAT)* Platforms
Immuno-STAT biologics are rationally engineered Fc fusion proteins comprised of bivalent tumor-peptide-human leukocyte antigen (pHLA) complexes and four affinity-attenuated interleukin 2 (IL-2) molecules to preferentially engage and activate tumor-specific T cells directly in the patient. Building on the CUE-100 series framework, our Neo-STAT (NST) platform contains HLA molecules manufactured with an "empty" peptide-binding pocket, into which diverse tumor-peptides can be chemically conjugated, hence addressing tumor heterogeneity in a cost- and time-efficient manner. Our RDI-STAT *(Re-Directed Immuno-STAT)* platform further expands on the Immuno-STAT biologics by redirecting the pre-existing protective viral-specific T cell repertoire to target tumor cells via scFv moieties. RDI-STATs are designed to circumvent potential tumor escape mechanisms linked to HLA loss or defects in antigen-presenting pathways.

About SITC
The **Society for Immunotherapy of Cancer (SITC)** is the world's leading member-driven organization specifically dedicated to improving cancer patient outcomes by advancing the science and application of cancer immunotherapy.

SITC is a 501(c)(3) not-for-profit medical professional society of influential research scientists, physician scientists, clinicians, patients, patient advocates, government representatives and industry leaders dedicated to improving cancer patient outcomes by advancing the science and application of cancer immunotherapy. Through educational programs that foster scientific exchange and collaboration, SITC aims to one day make the word “cure” a reality for cancer patients everywhere.

Currently, SITC has more than 4,650 members who represent over 35 medical specialties in 63 countries around the world.

Through emphasis on high-caliber scientific meetings; dedication to education and outreach activities; focus on initiatives of major importance in the field; and commitment to collaborations with like-minded domestic and international organizations, government and regulatory agencies, associations and patient advocacy groups, SITC brings together all aspects of the cancer immunology and immunotherapy community.

About Cue Biopharma
Cue Biopharma, a clinical-stage biopharmaceutical company, is engineering a novel class of injectable biologics to selectively engage and modulate targeted T cells directly within the patient’s body to transform the treatment of cancer, infectious disease and autoimmune disease. The company’s proprietary Immuno-STAT ™*(Selective Targeting and Alteration of T cells)* platform, is designed to harness the body’s intrinsic immune system without the need for ex vivo manipulation.

Headquartered in Cambridge, Massachusetts, the company is led by an experienced management team and independent Board of Directors with deep expertise in immunology and immuno-oncology as well as the design and clinical development of protein biologics.

For more information, visit https://www.cuebiopharma.com and follow us on Twitter at https://twitter.com/CueBiopharma.

Forward-Looking Statements
This press release contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, that are intended to be covered by the safe harbor created by those sections. Such forward-looking statements include, but are not limited to, those regarding: the company’s plans to submit an IND for CUE-102; the company’s belief that the Immuno-STAT platform stimulates targeted immune modulation through the selective engagement of disease-relevant T cells; and the company’s business strategies, plans and prospects. Forward-looking statements, which are based on certain assumptions and describe the company’s future plans, strategies and expectations, can generally be identified by the use of forward-looking terms such as “believe,” “expect,” “may,” “will,” “should,” “would,” “could,” “seek,” “intend,” “plan,” “goal,” “project,” “estimate,” “anticipate,” “strategy,” “future,” “likely” or other comparable terms, although not all forward-looking statements contain these identifying words. All statements other than statements of historical facts included in this press release regarding the company’s strategies, prospects, financial condition, operations, costs, plans and objectives are forward-looking statements. Important factors that could cause the company’s actual results and financial condition to differ materially from those indicated in the forward-looking statements include, among others, the company’s limited operating history, limited cash and a history of losses; the company’s ability to achieve profitability; potential setbacks in the company’s research and development efforts including negative or inconclusive results from its preclinical studies, its ability to secure required U.S. Food and Drug Administration (“FDA”) or other governmental approvals for its product candidates and the breadth of any approved indication; adverse effects caused by public health pandemics, including COVID-19, including possible effects on the company’s trials; negative or inconclusive results from the company’s clinical trials or preclinical studies or serious and unexpected drug-related side effects or other safety issues experienced by participants in clinical trials; delays and changes in regulatory requirements, policy and guidelines including potential delays in submitting required regulatory applications to the FDA; the company’s reliance on licensors, collaborators, contract research organizations, suppliers and other business partners; the company’s ability to obtain adequate financing to fund its business operations in the future; operations and clinical the company’s ability to maintain and enforce necessary patent and other intellectual property protection; competitive factors; general economic and market conditions and the other risks and uncertainties described in the Risk Factors and in Management's Discussion and Analysis of Financial Condition and Results of Operations sections of the company’s most recently filed Annual Report on Form 10-K and any subsequently filed Quarterly Report(s) on Form 10-Q. Any forward-looking statement made by the company in this press release is based only on information currently available to the company and speaks only as of the date on which it is made. The company undertakes no obligation to publicly update any forward-looking statement, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise.

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