Cue Biopharma Presents New Positive Data from Phase 1 Trials of CUE-101 in Head and Neck Cancer and CUE-102 in Wilms' Tumor 1 Positive Cancers at SITC 2023

November 3, 2023

- *Overall response rate (ORR) of 47% and disease control rate (DCR) of 65% in first line (1L) recurrent/metastatic HNSCC patients treated with CUE-101 and KEYTRUDA® (pembrolizumab)*
  - *ORR of 56% in patients with low expression of PD-L1 in the tumor*
- *Median overall survival (mOS) of 20.8 months in second line (2L) and beyond patients treated with CUE-101 monotherapy, compared to the historic reported survival of approximately eight months observed in patients treated in 2L in the KEYNOTE-040 trial of pembrolizumab*
- *No dose limiting toxicities (DLTs) observed or maximum tolerated dose (MTD) reached to date with CUE-102 at the dose escalation phase*
- *CUE-102 demonstrated a 75%-80% DCR at the 4mg/kg and 2mg/kg doses respectively with two patients demonstrating tumor reductions of -30% and -29%*

BOSTON, Nov. 03, 2023 (GLOBE NEWSWIRE) -- Cue Biopharma, Inc. (Nasdaq: CUE), a clinical-stage biopharmaceutical company developing a novel class of T cell engagers to selectively modulate tumor-specific T cells, announced today the presentation of new positive data from its ongoing fully enrolled Phase 1 trials evaluating its lead interleukin-2 (IL-2)-based T cell engager, CUE-101, as a monotherapy and in combination with KEYTRUDA® (pembrolizumab) for patients with recurrent/metastatic HPV+ head and neck squamous cell carcinoma (HNSCC). New clinical data will also be reported from the company's ongoing Phase 1 trial evaluating its second candidate, CUE-102, for the treatment of Wilms' Tumor 1 positive (WT1+) recurrent/metastatic cancers.

The data will be presented in two posters at the Society for Immunotherapy of Cancer's 38th Anniversary Annual Meeting (SITC 2023) being held in San Diego, California and virtually November 1-5.

"I am pleased to observe the clinical benefit patients are deriving and encouraged by the positive enhancement of data from the CUE-101 clinical trials," said Christine Chung, M.D., Chair, Department of Head and Neck-Endocrine Oncology, Moffitt Cancer Center, and a principal investigator participating in the clinical trial. "The notable prolongation in overall survival to over 20 months in monotherapy represents a significant advancement of clinical benefit compared to the current standard of care for this population with advanced and refractory disease. Similarly, the reported enhanced overall response rate to date in combination with pembrolizumab, compared to the historical response rate for pembrolizumab alone, is very promising for first line patients. I look forward to evaluating the trial results as they continue to mature and remain highly encouraged by the observations to date. There is a significant unmet medical need for more efficacious and less toxic treatment options for patients with recurrent/metastatic head and neck cancer, and these results from the CUE-101 trial demonstrate the potential to address this need."

Key data highlights from the fully enrolled CUE-101 combination expansion portion of the trial evaluating CUE-101 at the recommended Phase 2 dose (RP2D) of 4mg/kg plus pembrolizumab, as of data cutoff of September 27 with 17 evaluable patients, include:

- DCR of 65% and ORR of 47%, demonstrating evidence of clinical activity in comparison to the 19% ORR observed with pembrolizumab treatment alone in the KEYNOTE-040 trial [1,2]- This includes one complete response (CR) and seven partial responses (PR), in addition to three durable stable diseases (DSD) of ≥ 12 weeks.
- 56% ORR in patients with combined positive score (CPS) 1-19, in comparison to the 14% with pembrolizumab monotherapy in the KEYNOTE-040 trial [1,2], with five of the eight responses in tumors with low PD-L1 expression (CPS less than 20).
- 21 of the 22 patients treated with CUE-101 and pembrolizumab remain alive at time of data cutoff, including eight patients living beyond 12 months.
- No unanticipated, significant safety concerns have emerged, and adverse events have been readily managed with appropriate medical care.

Key data highlights from the CUE-101 expansion portion of the Phase 1b trial evaluating CUE-101 at the RP2D as monotherapy to date with 19 evaluable patients, include:

- mOS of 20.8 months in 2L+ patients (majority 3L+) treated with CUE-101 monotherapy, notably longer than the historical mOS of 7.5 and 8.4 months reported from third-party clinical trials with checkpoint inhibitors in 2L R/M HNSCC in

CheckMate 1411 and KEYNOTE-040, respectively.[3]
- DCR of 37% in late stage, refractory patients, including one confirmed PR of > 36 weeks duration and six DSD of ≥ 12 weeks. Of note, one patient has maintained stable disease (SD) for over 22 months with no detectable evidence of HPV cell-free DNA (cfDNA) in their blood after starting CUE-101 treatment and this patient recently demonstrated an unconfirmed partial response (uPR).

Key data highlights from the CUE-102 Phase 1 clinical trial to date include:

- No DLTs reported to date in patients treated during the dose escalation phase at doses ranging between 1–8mg/kg of CUE-102 intravenously every 3 weeks; a MTD has not been reached.
- Two patients at the 2mg/kg dose, one with gastric cancer and one with ovarian cancer have demonstrated reduction in tumor burden.

Matteo Levisetti, M.D., chief medical officer of Cue Biopharma added, “It is highly gratifying to share the positive results from the ongoing Phase 1 trial of CUE-101, highlighting its clinical activity in combination with pembrolizumab in 1L patients and the prolonged survival observed in 2L+ patients treated with CUE-101 monotherapy. The promising data further supports our confidence in defining registrational trials for CUE-101, capitalizing on the previously granted Fast Track Designation. Concurrently, the unveiling of positive findings from the ongoing CUE-102 trial have provided early evidence of tolerability and clinical activity, including reductions in tumor burden. These observations are highly encouraging, suggesting that we may have opened up a path for immunotherapy in treating multiple cancers historically resistant to check point inhibitors. The cancers overexpressing WT1 represent substantial patient populations that may benefit from CUE-102 treatment. To date, the CUE-102 trial has been enrolling patients at a rapid pace, reflecting the significant and pressing unmet medical need in these indications.”

Dan Passeri, chief executive officer of Cue Biopharma, added, “The clinical data generated to date, from both our CUE-101 monotherapy and combination trials in HPV+ R/M HNSCC, as well as the early data observed in our ongoing WT1-specific CUE-102 dose escalation trial, demonstrate what we believe to be a best-in-class approach to immune modulation, and a clear path forward to realizing the full potential of activating the patient’s own immune system against cancer. We are pleased with our accomplishments to date and look forward to ongoing progress across our platform as we continue developing promising therapies for cancer patients with high, unmet medical needs.”

Presentation Details
Title: A phase 1 dose-escalation and expansion study of CUE-101, given as monotherapy in 3L and in combination with pembrolizumab in 1L recurrent/metastatic HPV16+ head and neck cancer patients
Abstract Number: 674
Presenter: Christine Chung, M.D., H. Lee Moffitt Cancer Center, Tampa, Fla. USA
Date: Saturday, November 4, 2023, Exhibit Halls A and B1, 9 a.m.–8:30 p.m. PDT

Title: A phase 1 trial of CUE-102, a novel WT1-pHLA-IL2-Fc fusion protein in HLA-A*0201 positive patients with WT1-positive recurrent/metastatic cancers
Abstract Number: 750
Presenter: Jennifer Eva Selfridge, M.D., Ph.D., University Hospitals Cleveland Medical Center, Cleveland, OH, USA
Date: Saturday, November 4, 2023, Exhibit Halls A and B1, 9 a.m.–8:30 p.m. PDT

All posters will be available to conference attendees as virtual e-posters on the virtual meeting platform November 3, 2023 at 9 a.m. PDT/12 p.m. EDT through January 12, 2024. Cue Biopharma’s posters will also be available on November 3, 2023 in the Investors & Media section of the Company’s website at www.cuebiopharma.com, under Scientific Publications and Presentations.

References:
[1]*Harrington, K. J., et al. (Feb 2023). Pembrolizumab With or Without Chemotherapy in Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma: Updated Results of the Phase III KEYNOTE-048 Study. Journal of clinical oncology, DOI: https://doi.org/10.1200/JCO.21.02508*

[2]*Burtness, B., et al. (Mar 2022) Pembrolizumab Alone or With Chemotherapy for Recurrent/Metastatic Head and Neck Squamous Cell Carcinoma in KEYNOTE-048: Subgroup Analysis by Programmed Death Ligand-1 Combined Positive Score. Journal of clinical oncology, DOI: https://doi.org/10.1200/JCO.21.02198*

[3]*Cohen, EW E. (Nov 2018) Pembrolizumab versus methotrexate, docetaxel, or cetuximab for recurrent or metastatic head-and-neck squamous cell carcinoma (KEYNOTE-040): a randomized, open-label, phase 3 study. The Lancet, DOI: http://dx.doi.org/10.1016/S0140-6736(18)31999-8*

About the CUE-100 Series
The CUE-100 series consists of Fc-fusion biologics that incorporate peptide-MHC (pMHC) molecules along with rationally engineered IL-2 molecules. This singular biologic is anticipated to selectively target, activate and expand a robust repertoire of tumor-specific T cells. 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 the 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 CUE-101 and the Phase 1 trial

CUE-101 is Cue Biopharma's lead clinical drug candidate from the CUE-100 series of interleukin 2 (IL-2)-based biologics. It is designed to activate and expand HPV16 tumor-specific T cells by presenting two signals or "cues" to T cells. Signal #1 incorporates the HPV E7 protein, harbored by HPV-induced cancer cells, to provide selectivity through interaction with the HPV-specific T cell receptor. Signal #2 consists of an engineered IL-2 variant to stimulate the activity of T cells. CUE-101 is currently being evaluated in a fully enrolled Phase 1 open-label, dose escalation and expansion study, for the treatment of HPV16+ driven recurrent/metastatic head and neck squamous cell carcinoma in second line (2L) and beyond patients as a monotherapy, and as a first line (1L) therapy in combination with pembrolizumab (KEYTRUDA®).

About CUE-102 and the Phase 1 trial
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. WT1 is a well-recognized onco-fetal protein known to be over-expressed in a number of cancers, including solid tumors and hematologic malignancies. CUE-102 is being evaluated in a Phase 1 open label, two-part dose escalation and expansion study, for patients with late-stage colorectal, gastric/gastroesophageal junction, pancreatic and ovarian cancers that express WT1.

About Cue Biopharma
Cue Biopharma, a clinical-stage biopharmaceutical company, is developing a novel class of injectable biologics to selectively engage and modulate disease-specific T cells directly within the patient's body. The company's proprietary platform, Immuno-STAT ™ *(Selective Targeting and Alteration of T cells)* and biologics are designed to harness the body's intrinsic immune system as T cell engagers without the need for ex vivo manipulation or broad systemic immune modulation.

Headquartered in Boston, Massachusetts, we are 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 please visit 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 present data from its ongoing CUE-101 and CUE 102 clinical trials and define registrational trials for CUE-101; 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, including potential corporate development opportunities. 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 or the company's ability to replicate in later clinical trials positive results found in preclinical studies and early-stage clinical trials of its product candidates, 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 the recent COVID-19 pandemic, 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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