Cue Biopharma Presents New Positive Data from Ongoing Phase 1 Trial of CUE-101 in Combination with KEYTRUDA(R) for Recurrent/Metastatic HPV+ Head and Neck Cancer at the Society for Immunotherapy of Cancer's (SITC) 37th Annual Meeting

November 10, 2022

- *Overall response rate (ORR) of 40% and a clinical benefit rate (CBR) of 70% observed to date in first line (1L) recurrent/metastatic HNSCC patients treated with CUE-101 at the recommended Phase 2 dose and pembrolizumab.*
- *Median overall survival (mOS) approaching greater than 12 months in third line and beyond (3L+) patients treated to date with CUE-101 monotherapy, which is 50% greater than current standard of care (SOC) with anti-PD-1 therapy in second line (2L) patients.*
- *Company on track to define potential registrational CUE-101 monotherapy trial by mid-2023.*

BOSTON, Nov. 10, 2022 (GLOBE NEWSWIRE) -- Cue Biopharma, Inc. (Nasdaq: CUE), a clinical-stage biopharmaceutical company developing a novel class of injectable biologics to selectively engage and modulate tumor-specific T cells directly within the patient's body, announced today the presentation of new positive data from its ongoing Phase 1 trial evaluating its lead interleukin 2 (IL-2)-based biologic, CUE-101 in combination with pembrolizumab (KEYTRUDA), as a first line therapy for patients with recurrent/metastatic HPV+ head and neck squamous cell carcinoma (HNSCC). The data will be presented in a poster at the Society for Immunotherapy of Cancer's 37th Annual Meeting (SITC 2022), to be held in Boston, Massachusetts and virtually on November 8-12, 2022.

The poster will also provide an update from the Company's ongoing fully enrolled Phase 1b trial evaluating CUE-101 monotherapy as third line and beyond therapy in the same patient population. Additionally, the Company will present two posters discussing the design of its ongoing Phase 1 trial evaluating its second IL-2 based candidate, CUE-102, for the treatment of Wilms' Tumor 1 positive (WT1+) malignancies, and preclinical data regarding its mechanistic effect in vitro and in vivo.

"We are very encouraged with the overall response rate observed in the trial so far with CUE-101, and its potential to improve standard of care for HPV+ head and neck cancer patients," said Dr. Christine Chung, M.D., Chair, Department of Head and Neck-Endocrine Oncology, Moffitt Cancer Center, and a principal investigator participating in the clinical trial. "There is an urgent need for more effective and durable treatment options with less side effects as more than half of all patients with recurrent/metastatic HNSCC given the current standard of care will experience disease progression. I look forward to following this promising CUE-101 clinical data through."

Key data highlights from the CUE-101 dose escalation and patient expansion portion of the Phase 1 trial in combination with pembrolizumab with 16 evaluable patients to date, include:

- Overall response rate (ORR) of 40% and a clinical benefit rate (CBR) of 70% in the first 10 evaluable patients treated at the recommended Phase 2 dose (RP2D) of 4 mg/kg of CUE-101 and 200 mg of pembrolizumab administered every three weeks – This includes four confirmed partial responses (cPR) in addition to three durable stable disease (DSD) of ≥ 12 weeks. These responses include patients with low PD-L1 expression (combined positive score (CPS) less than 20).
- At the CUE-101 2 mg/kg dose plus pembrolizumab (n=3), one patient experienced a cPR and one DSD, for a CBR of 67%.
- At the CUE-101 1 mg/kg dose plus pembrolizumab (n=3), one patient experienced DSD, for a CBR of 33%.
- Notably, tumor reduction from baseline in the five patients with confirmed PRs was between 35% and 69%.

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

- 42% overall clinical benefit rate, including one PR of > 42 weeks duration and seven DSD.
- Median overall survival (mOS) approaching greater than 12 months in third line and beyond (3L+) patients treated with CUE-101 monotherapy, which is 50% greater than current standard of care (SOC) with anti-PD-1 therapies in second line (2L) patients.

CUE-101 continued to show a favorable tolerability profile both as monotherapy and in combination with pembrolizumab.

Ken Pienta, M.D., acting chief medical officer of Cue Biopharma, added, "This new data from our combination study demonstrates early evidence of complementary mechanistic activity of CUE-101 with pembrolizumab. In addition, the sustained clinical benefit rate with CUE-101 as monotherapy is very encouraging and has continued to demonstrate proof-of-concept of CUE-101 as a single agent. Overall, the data shows the potential of CUE-101 to provide patients with an improved clinical benefit rate and with lower toxicity than current standard of care. We look forward to continuing to evaluate data from the trial in addition to defining the potential registrational trial for CUE-101, which we anticipate in mid-2023."

Anish Suri, Ph.D., president and chief scientific officer of Cue Biopharma, said, "Initiation of the Phase 1 trial evaluating our second IL-2-based biologic, CUE-102, is also an important milestone for the company as we continue to demonstrate the versatility and modularity of our platform to potentially treat multiple cancers. CUE-102 shares the core molecular structure of CUE-101, with primary differences in the tumor-specific T cell epitope. This similarity together with our preclinical data that demonstrated CUE-102's ability to elicit selective expansion of WT1-specific T cells,

support our belief for a potential positive tolerability profile and clinical activity. We look forward to sharing updated data on this trial in the coming year."

Key data highlights from CUE-102 preclinical study to date include:

- CUE-102 selectively activated and expanded WT1-specific CD8+ T cells from peripheral blood mononuclear cells (PBMC) of healthy donors.
- 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 vitro and in vivo.

All three posters will be available in the Investor & Media section of the Company's website at www.cuebiopharma.com under Scientific Publications and Presentations.

SITC Presentation Details

Title: A phase 1 study of CUE-101, a novel HPV16 E7-pHLA-IL2-Fc fusion protein, as monotherapy and in combination with pembrolizumab in patients with recurrent/metastatic HPV16+ head and neck cancer
Abstract Number: 681
Presenter: Dr. Christine Chung, M.D., Chair, Department of Head and Neck-Endocrine Oncology, Moffitt Cancer Center, Tampa, Fla.
Date: Thursday, November 10, 2022, Poster Hall (Hall C) 9 a.m.–9 p.m. EST

Title: A phase 1, open-label, dose escalation and expansion study of CUE-102 monotherapy in HLA-A*0201 positive patients with WT1-positive recurrent/metastatic cancers
Abstract Number: 636
Presenter: Dr. Steven Margossian, M.D., Ph.D., Senior Medical Director at Cue Biopharma
Date: Friday, November 11, 2022, Poster Hall (Hall C) 9 a.m.–8:30 p.m. EST

Title: CUE-102 selectively activates and expands WT1-specific T cells for the treatment of patients with WT1+ malignancies
Abstract Number: 1323
Presenter: Dr. Natasha Girgis, Ph.D., Associate Director, Translational Pharmacology at Cue Biopharma
Date: Thursday, November 10, 2022, Poster Hall (Hall C) 9 a.m.–9 p.m. EST

About HPV+ Recurrent or Metastatic Head and Neck Cancer
Head and neck squamous cell carcinomas (HNSCC) are the 8th most common cancer in the world. A significant subset of the cases of HNSCC includes human papillomavirus (HPV) associated oropharyngeal tumors, with HPV16 detectable in 80%-90% of these cases. Despite the current standard of care treatments, more than 50% of patients with advanced HNSCC will experience recurrence, representing a significant unmet need.

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 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 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 SITC
Established in 1984, the Society for Immunotherapy of Cancer (SITC) is a nonprofit organization of medical professionals dedicated to improving cancer patient outcomes by advancing the development, science and application of cancer immunotherapy and tumor immunology. SITC is comprised of influential basic and translational scientists, practitioners, health care professionals, government leaders and industry professionals around the globe. Through educational initiatives that foster scientific exchange and collaboration among leaders in the field, SITC aims to one day make the word "cure" a reality for cancer patients everywhere. Learn more about SITC at sitcancer.org.

About Cue Biopharma
Cue Biopharma, a clinical-stage biopharmaceutical company, is developing a novel class of injectable biologics to selectively engage and modulate tumor-specific T cells directly within the patient's body to transform the treatment of cancer. 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.

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 beliefs about the potential benefits of CUE-101 and the CUE 100 series; the company's projections regarding the timing for clinical trial planning and availability of clinical trial data; 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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