Cue Biopharma Reports Confirmed Partial Response (PR) in Ongoing Phase 1 Monotherapy Study of CUE-101 in Late Stage Second Line and Beyond Patients with HPV+ Recurrent/Metastatic Head and Neck Cancer

May 10, 2021

And Provides Interim Clinical Data Update

- *Partial response data demonstrates activity of CUE-101 as monotherapy in patient with human papilloma virus positive recurrent/metastatic head and neck squamous cell carcinoma (HPV+ R/M HNSCC)*
- *The objective tumor response observed in this patient establishes initial clinical proof of concept for therapeutic modulation of the endogenous anti-tumor T-cell repertoire by the Immuno-STAT™ (Selective Targeting and Alteration of T cells) platform*
- *Company will discuss results during its upcoming quarterly business update call on May 17, 2021 at 4:30 p.m. EDT*

CAMBRIDGE, Mass., May 10, 2021 (GLOBE NEWSWIRE) -- Cue Biopharma, Inc. (Nasdaq: CUE), a clinical-stage biopharmaceutical company engineering a novel class of injectable biologics designed to selectively engage and modulate targeted T cells within the patient's body, announced today interim clinical data, including a confirmed partial response (PR), from its ongoing Phase 1a/1b monotherapy study of CUE-101 as second-line treatment for patients with HPV+ R/M HNSCC. To date, CUE-101 has demonstrated a favorable tolerability profile in a monotherapy dose escalation trial and continues to generate encouraging emerging data pertaining to its pharmacokinetic (PK) and pharmacodynamic (PD) profiles, as well as clinical anti-tumor activity.

"We are very excited by the partial response observed in this patient, since it demonstrates single-agent activity of CUE-101, so rarely seen in mono-immunotherapy treatments," said Ken Pienta, M.D., acting chief medical officer of Cue Biopharma. "Based on recent clinical observations, we have delivered CUE-101 to patients at tolerated doses, achieving a confirmed PR as well as stable disease (SD) in several patients while still in the dose escalation portion of the trial. This provides evidence that CUE-101 is an active agent with promising potential for HPV+ HNSCC patients. This is bolstered by the supporting pharmacodynamic data in which we have observed activation of disease-specific T cells and NK cells in the blood of our treated patients. We look forward to initiating the expansion phase of the Phase 1 trial which may provide a potential path forward for a registration-directed clinical trial for CUE-101 as a monotherapy for HPV+ R/M HNSCC."

Key interim analysis of patient data from the ongoing open-label Phase 1a/1b study include:

- Confirmed PR in one patient and SD in five patients, all confirmed by RECIST criteria, in the dose escalation phase of the study to date, providing early signs of potential single-agent activity of CUE-101.
- Demonstrated evidence of both tumor-specific CD8+ T cell expansion as well as dose-dependent increases in NK cells in patients.
- Observed immune cell infiltration and tumor cell necrosis in patient tumor biopsies after CUE-101 treatment, supporting CUE-101's mechanism of action at engaging and modulating targeted T cells within the patient's body.
- Dose-proportional PK profile and comparable drug exposure levels in patients receiving repeated dosing cycles, consistent with a lack of drug-clearing anti-drug antibodies.
- No maximum tolerated dose (MTD) observed in patients dosed with up to 8 mg/kg of CUE-101.

Dan Passeri, chief executive officer of Cue Biopharma added, "Receiving early confirmation of clinical activity of CUE-101 as a monotherapy in this challenging patient population is an important validation of the potential of the CUE-101 program for oncology, as well as for our follow-on programs such as CUE-102, from the IL2-based CUE-100 series. This confirmed PR provides valuable proof of concept of the Immuno-STAT™ platform to activate and expand disease specific T cells and NK cells as a method to treat other cancers. We anticipate a number of important milestones throughout this year with the potential of further data to inform CUE-101's clinical application. These milestones include, the potential selection of a recommended Phase 2 dose of CUE-101 by mid-2021 for further development as a single-agent treatment for HPV+ 2L+ head and neck squamous cell carcinoma; our plans to report initial Phase 1 results from the combination study of CUE-101 with pembrolizumab in the second half of 2021; and our plans to initiate a Phase 2 neoadjuvant study to evaluate the effects of CUE-101 on the tumor microenvironment, which is also expected to start in the second half of 2021."

Conference Call
Cue Biopharma will discuss these new data points during its first quarter business update call and webcast on May 17 at 4:30 p.m. ET. Please check the Events page of the Investor and Media section of the Company's website at www.cuebiopharma.com for details. A live and archived version of the webcast will be available for 30 days after the call.

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 HPV16-driven recurrent/metastatic HNSCC and

HLA-A*02:01 serotype. Based on translational data from the trial, a maximum tolerated dose (MTD) or recommended Phase 2 dose will be determined. The company has expanded the study to evaluate CUE-101 in combination with KEYTRUDA® (pembrolizumab) as first-line treatment in patients with HPV16-driven recurrent/metastatic HNSCC.

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. 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 Immuno-STAT
The company's Immuno-STAT ™ *(Selective Targeting and Alteration of T cells)* biologics are designed for targeted modulation of disease-associated T cells in the areas of immuno-oncology and autoimmune disease. Each of our biologic drugs is designed using our proprietary scaffold comprising: 1) a pMHC to provide selectivity through interaction with the T cell receptor (TCR), and 2) a unique co-stimulatory signaling molecule to modulate the activity of the target T cells.

The simultaneous engagement of co-regulatory molecules and pMHC binding mimics the signals delivered by antigen presenting cells (APCs) to T cells during a natural immune response. This design enables Immuno-STAT biologics to engage with the T cell population of interest, resulting in selective T cell modulation. Because our drug candidates are delivered directly in the patient's body (in vivo), they are fundamentally different from other T cell therapeutic approaches that require the patients' T cells to be extracted, modified outside the body (ex vivo), and reinfused.

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 within the patient's body to transform the treatment of cancer, infectious disease and autoimmune disease. The company's proprietary platform, Immuno-STAT ™*(Selective Targeting and Alteration of T cells)* is designed to harness the body's intrinsic immune system without the need for ex vivo manipulation.

Headquartered in Cambridge, 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, visit www.cuebiopharma.com and follow us on Twitter at https://twitter.com/CueBiopharma.

Cautionary Note Regarding 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 potential for CUE-101 to treat HPV+ R/M HNSCC; the company's plans to select the CUE-101 monotherapy Phase 2 clinical trial dose in mid-2021; the company's plans to report initial Phase 1 results of the CUE-101 +pembrolizumab combination trial in the second half of 2021; anticipated initiation of the CUE-101 Phase 2 clinical trial to evaluate effects of CUE-101 on tumor microenvironment and expand patient access and market potential for CUE-101 in the second half of 2021; the potential of the CUE 100 series for anti-tumor activity; the potential benefits of the company's Immuno-STAT™ platform biologics; the anticipated results of the company's drug development efforts, including study results; the company's expectations regarding regulatory developments and expected future operating results; and statements regarding the company's strategies, prospects, financial condition, operations, costs, plans and objectives. 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. 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 history of losses; the company's ability to achieve profitability; potential setbacks in the company's research and development efforts 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 operations and clinical 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; 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 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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