Cue Biopharma Announces Clinical Trial Collaboration Agreement with Merck to Evaluate CUE-101 in Combination with KEYTRUDA® (pembrolizumab) as First-line Treatment For HPV+ Recurrent/Metastatic Head and Neck Cancer

April 20, 2020

- Ongoing Phase 1 dose escalation and expansion study with CUE-101 as a monotherapy in post first-line recurrent/metastatic HNSCC patients to be amended to include combination of CUE-101 with standard of care KEYTRUDA as first-line therapy
- Preliminary data from early patient cohorts in the current ongoing CUE-101 monotherapy Phase 1 trial in post first-line recurrent/metastatic HNSCC patients demonstrates tolerability and drug exposure, and provides confidence for drug activity consistent with projections based on preclinical data
- Recent publication in Clinical Cancer Research includes supporting preclinical data for CUE-101 demonstrating anti-tumor efficacy as monotherapy and in combination with anti-PD-1 treatment

CAMBRIDGE, Mass., April 20, 2020 (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 within the body, announced today it has entered into a clinical collaboration agreement with Merck (known as MSD outside the United States and Canada), through a subsidiary, to evaluate the combination of Cue Biopharma's investigational product candidate CUE-101, a first-in-class biologic, with Merck's anti-PD-1 therapy, KEYTRUDA® (pembrolizumab) in patients with advanced head and neck cancer.

Collaboration with Merck
Under the terms of the agreement, Cue Biopharma will conduct a Phase 1 study, KEYNOTE-A78, evaluating CUE-101 in combination with KEYTRUDA in first-line HPV+ advanced head and neck cancer. KEYNOTE-A78 will be conducted in parallel with the ongoing Phase 1 monotherapy study of CUE-101 post first-line treatment. The early monotherapy PK data from the first two dosing cohorts demonstrates dose-related drug exposure consistent with preclinical modeling. Subsequent to the respective dose escalations, expansion cohorts evaluating CUE-101 as a monotherapy and in combination with KEYTRUDA will be conducted at optimized dosing regimens.

"We are very pleased to collaborate in this important study with Merck, an established leader in cancer immunotherapy, with our first clinical asset, CUE-101, which represents our IL-2 variant CUE-100 Series," said Daniel Passeri, chief executive officer of Cue Biopharma. "Through the monotherapy and combination studies, we believe we will be able to demonstrate the mechanistic advantages of our approach and platform for modulating disease-relevant T cells directly in the patient's body to safely enhance efficacy over current standards of care."

"Immunotherapies have revolutionized the treatment of patients with certain types of cancers. However significant unmet need remains – particularly in those individuals who do not respond or develop resistance to checkpoint therapy," said Ken Pienta, M.D, acting chief medical officer of Cue Biopharma. "Based on a novel mechanism of action designed to induce and expand tumor-specific T cells in the patient's body, we believe CUE-101 may lead to enhanced anti-tumor activity in combination with KEYTRUDA."

CUE-101 is a fusion protein comprised of a human leukocyte antigen (HLA) complex, an HPV16 E7 peptide epitope, reduced affinity human interleukin-2 (IL-2) molecules, and an effector attenuated human immunoglobulin G (IgG1) Fc domain. In preclinical studies, CUE-101 has demonstrated selective induction and expansion of HPV16 E7-specific cytotoxic T cells with both in vitro and in vivo evidence supporting its potential for clinical efficacy both as a monotherapy and in combination with anti-PD1 checkpoint blockade.

KEYTRUDA® is a registered trademark of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

Phase 1 Trial Update
The Phase 1 CUE-101 monotherapy study is ongoing, with enrollment of patients at 13 leading centers in the United States for the treatment of post first-line metastatic and recurrent HPV+ advanced head and neck cancer. We have initiated the dosing of 3 patients in Cohort 3 and pending safety evaluation, we anticipate initiating the dosing of patients in Cohort 4 later this quarter. By design, CUE-101 includes 4 molecules of attenuated IL-2 and Cohort 2 patients were exposed to drug concentrations equivalent to those achieved with systemic IL-2 administration of aldesleukin (Proleukin) with no evidence of cytokine release syndrome. The Phase 1 monotherapy portion of the study is a standard dose escalation of CUE-101. After demonstration of safety at several dose levels, a parallel Phase 1 dose escalation of CUE-101 in combination with KEYTRUDA will be initiated in first-line patients. The primary endpoints of the dose escalation phase of the trials are to evaluate the safety, tolerability, and the pharmacokinetics/pharmacodynamics of the two regimens. Monitoring of disease-relevant T cells and additional biomarkers of anti-tumor immune response and exploration of response prediction markers employing multiple methodologies are included in the study design.

Preliminary data from early patient cohorts demonstrates tolerability and drug exposure, and provides confidence for drug activity consistent with projections based on preclinical data. Cue Biopharma expects to report initial pharmacodynamic data from the Phase 1 monotherapy portion of the study in the first half of 2020. Additional information about the trial can be found at clinicaltrials.gov (NCT03978689).

***Clinical Cancer Research* Publication**
CUE-101 preclinical data were recently published in *Clinical Cancer Research,* a journal of the American Association for Cancer Research. (https://clincancerres.aacrjournals.org/content/26/8/1953)

The article titled, *CUE-101, a Novel HPV16 E7-pHLA-IL2-Fc Fusion Protein, Enhances Tumor Antigen Specific T Cell Activation for the Treatment of HPV16-Driven Malignancies*, includes CUE-101 data that demonstrate selective binding, activation and expansion of HPV16-specific, disease-relevant, T cells. A murine surrogate molecule (mCUE-101) administered to HPV16 E7 tumor bearing mice resulted in selective expansion of disease-

relevant T cells, anti-cancer efficacy and immunologic memory. In addition, mCUE-101 administered as a combination therapy with anti-PD-1 checkpoint inhibition further enhanced anti-tumor efficacy.

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 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
Immuno-STAT™ 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 peptide-MHC complex (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 highly targeted T cell modulation. Because our drugs 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 body to transform the treatment of cancer and autoimmune diseases. 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 the design and clinical development of protein biologics, immunology and immuno-oncology.

For more information, visit www.cuebiopharma.com and follow us on Twitter 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. Forward-looking statements, which are based on certain assumptions and describe our 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. All statements other than statements of historical facts included in this press release regarding our strategies, prospects, financial condition, operations, costs, plans and objectives are forward-looking statements. Examples of forward-looking statements include, among others, statements we make regarding anticipated results of our drug development efforts, including the study results from the Phase 1 monotherapy portion of our CUE-101 Phase 1 trial in the first half of 2020, and our expectations regarding regulatory developments and expected future operating results. As noted above, Cue Biopharma expects to report initial pharmacodynamic data from the Phase 1 monotherapy portion of the study in the first half of 2020, and for multiple reasons, including the current COVID-19 situation, there can be no assurance that such data will be reported in the first half of 2020 or demonstrate drug activity consistent with projections based on preclinical data. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based only on our current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, projections, anticipated events and trends, the economy and other future conditions. Because forward-looking statements relate to the future, they are subject to inherent uncertainties, risks and changes in circumstances that are difficult to predict and many of which are outside of our control. Our actual results and financial condition may differ materially from those indicated in the forward-looking statements. Therefore, you should not rely on any of these forward-looking statements. Important factors that could cause our actual results and financial condition to differ materially from those indicated in the forward-looking statements include, among others, our limited operating history, limited cash and a history of losses; our ability to achieve profitability; our ability to secure required U.S. Food and Drug Administration ("FDA") or other governmental approvals for our product candidates and the breadth of any approved indication; negative or inconclusive results from our clinical studies or serious and unexpected drug-related side effects or other safety issues experienced by participants in our clinical trials; delays and changes in regulatory requirements, policy and guidelines including potential delays in submitting required regulatory applications to the FDA; our reliance on third parties to conduct our clinical trials as well as licensors, collaborations and strategic alliances; our ability to obtain adequate financing to fund our business operations in the future; uncertainties associated with COVID-19 or coronavirus, including its possible effects on our operations and clinical trial; 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 our 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 us in this press release is based only on information currently available to us and speaks only as of the date on which it is made. We undertake 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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