Cue Biopharma Announces Publication in Nature Journal, Scientific Reports, of Immunotherapeutic Platforms Immuno-STAT and Neo-STAT

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- *Research demonstrates that platform technologies generate therapeutic molecules for selective delivery of immune activating signals, such as IL-2, to disease-relevant T cells, hence avoiding systemic activation of the broader immune compartment*

- *Publication details the peptide-HLA-based platform's versatility, modularity and vast potential to develop therapeutics for oncology, infectious disease and autoimmune disease*

CAMBRIDGE, Mass., Sept. 28, 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 publication of research titled "*Peptide-HLA-based immunotherapeutics platforms for direct modulation of antigen-specific T cells*" in the peer-reviewed Nature journal, *Scientific Reports*. The article describes Cue Biopharma's IL-2 based CUE-100 series technology platforms, Immuno-STAT™ (*Selective Targeting and Alteration of T cells)* and Neo-STAT™, being leveraged for the development of first-in-class biologics that enable selective activation of cancer-killing immune T cells within the patient's body.

"We believe our platforms address a significant challenge in immunotherapy of ensuring selective targeting of activation signals to anti-tumor T cells in the patient while sparing the indiscriminate systemic activation of the immune system," said Anish Suri, Ph.D., president and chief scientific officer of Cue Biopharma. "Adoptive cell therapy such as chimeric antigen receptor T-cell (CAR-T) therapies have demonstrated highly encouraging results for some patients but remain limited by the need of cellular ex-vivo manipulation and manufacturing challenges. Similarly, systemic approaches with immunostimulatory molecules, such as interleukin 2 (IL-2) or bispecific molecules, activate T cells indiscriminately and are associated with common severe adverse events, significantly limiting clinical benefit and applicability. Cue Biopharma's approach and resulting platform, represents a potential breakthrough in the ability to selectively and safely modulate the immune system in a highly controlled and targeted manner directly in the patient's body with the potential to create life-changing therapeutics with demonstrated improved efficacy and reduced toxicities."

Key aspects of Cue Biopharma's technologies discussed in the article include:

- The Immuno-STAT platform enables development of first-in-class off-the-shelf biologic molecules designed to selectively engage and activate disease-relevant T cells via the T cell receptors (TCR), mimicking the natural immune process, through the presentation of complimentary and synergistic signals, or "cues." An Immuno-STAT is engineered to include:
    - A first signal, or "cue" involving the presentation of a targeted and specific epitope, via a major histocompatibility (MHC)-peptide complex, to T cell receptors, or TCRs, of disease-specific T cells, to selectively engage a repertoire of T cells relevant to a particular disease such as cancer.
    - A corresponding second signal, or "cue" comprising the immunostimulant IL-2 molecule engineered with particular modifications for activation and expansion of CD8+ cytotoxic T cells, the relevant type of T cells with cancer-killing activity and minimize off-target binding and activation.
- The Immuno-STAT is constructed upon a portion of a human antibody (the "Fc portion") that serves as the molecule's backbone or scaffold and provides manufacturability and structural stability.
- Through this design, Immuno-STATs enable disease specificity, targeted selective activation of CD8+ T cells and a larger therapeutic window for IL-2 effectiveness.
- Neo-STAT is a plug-and-play variation of the Immuno-STAT™ platform designed with an empty "pocket" for the peptide presentation signal, enabling easy integration of disease-specific antigens a-posteriori to target a variety of cancers and infectious diseases.
- The modular Immuno-STAT framework is compatible with diverse co-modulators, including immuno-suppressive molecules, with potential to address a variety of autoimmune diseases.

Ken Pienta, M.D., acting chief medical officer of Cue Biopharma, added, "We have identified a potential solution to safety and scalability challenges based on natural signals governing T cell function: peptide-HLA and costimulatory ligands, embodied in the Immuno-STAT and Neo-STAT immunotherapy platforms. The versatility and modularity of the platform as described in the paper, in addition to the clinical data to date supports the premise that our approach could be the next-generation solution to utilizing IL-2 as a targeted and selective immune activator for treating multiple cancers."

Cue Biopharma's lead Immuno-STAT asset, CUE-101 has already shown encouraging results as a monotherapy in a Phase 1 dose escalation trial in late stage second line and beyond patients with HPV+ recurrent/metastatic head and neck cancer, which included a confirmed partial response with approximately 65% durable and ongoing tumor reduction and eight confirmed stable disease responses, controlling tumor growth for at least 12 weeks.

The Company is preparing for an Investigational New Drug filing for their next Immuno-STAT clinical candidate, CUE-102, which targets Wilms Tumor

1 (WT1), expressed in numerous solid tumors and hematological cancers.

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 estimate of the period in which it expects to have cash to fund its operations; 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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