Cue Biopharma Receives FDA Feedback on Pre-IND Briefing Document Reinforcing Company's Intention to Advance IND Submission for CUE-401 to Address Unmet Need in the Treatment of Autoimmune Disease

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CUE-401, a first-in-class bispecific molecule designed to induce and expand Tregs in vivo through the co-activity of transforming TGF-β and a modified variant of IL-2

BOSTON, June 24, 2025 (GLOBE NEWSWIRE) -- Cue Biopharma, Inc. (Nasdaq: CUE), a clinical-stage biopharmaceutical company developing a novel class of therapeutic biologics to selectively engage and modulate disease-specific T cells for the treatment of autoimmune disease, today announced it has received Pre-Investigational New Drug (Pre-IND) feedback from the U.S. Food and Drug Administration (FDA). The FDA reviewed the first-in-human trial design, including the Company's plan for dose escalation, proposed populations and safety monitoring plan. On the basis of the FDA feedback, the Company, intends to file an IND pending completion of final IND enabling studies. CUE-401 is the Company's lead autoimmune asset, a first-in-class bispecific fusion protein/molecule designed to induce and expand regulatory T cells (Tregs) in vivo through the co-activity of transforming growth factor beta (TGF-β) and a modified variant of interleukin 2 (IL-2).

"We are highly encouraged by the FDA's positive feedback on our proposed development plan for this important program. We believe CUE-401, with its first-in-class mechanism exploiting the combined activities of TGF-β and IL-2 is a potentially disruptive approach differentiated from other Treg-directed therapies, and has the potential to provide durable, long-lasting immune rebalance and tolerance addressing multiple, significant disease indications," said Daniel Passeri, chief executive officer of Cue Biopharma.

Dr. Dan Baker, chief development officer of Cue Biopharma commented, "CUE-401's mechanistic design extends beyond nTreg proliferation by transforming effector/autoreactive responses to an anti-inflammatory and/or suppressive response, with the prospects of establishing tolerance. The combination of interleukin 2 (IL-2) and transforming growth factor beta (TGF-ß) is considered the 'master switch' for conversion of activated T effector cells into T cells with a regulatory phenotype."

About CUE-401
CUE-401 is a preclinical, bispecific fusion protein designed to induce and expand regulatory T cells (Tregs) through the co-activity of modified variants of transforming growth factor beta (TGF-β) and interleukin 2 (IL-2) with therapeutic potential across a range of T-cell mediated autoimmune and inflammatory diseases.

CUE-401 has been engineered to harness the Treg induction capacity of TGF-β combined with IL-2 signaling to provide what Cue Biopharma believes to be superior quality and stability of Tregs. The design and specifications of CUE-401 have been guided by leading scientific publications demonstrating that both IL-2 and TGF-β are required for stable and efficient production of active and durable Tregs.

CUE-401 is designed to overcome multiple hurdles required to exploit the therapeutic potential of a master switch with a first-in-class, bispecific molecule integrating a masked TGF-ß, with our clinically validated, attenuated IL-2 with an antibody Fc fragment. This novel design provides for "conditional binding" and avoids off target activity, simplifies manufacturing and has highly differentiated findings in multiple pre-clinical models.

In these models, CUE-401 behaves as a master switch to convert autoreactive effector T cells (inflammatory cells) into stable, induced T-regulatory cells (iTregs). These findings suggest that CUE-401 acts by establishing a 'tolerance positive feedback loop' that not only increases nonspecific Treg populations, but critically, reduces and converts specific autoreactive T cells into transdifferentiated iTregs that are specific for the disease-causing autoantigens.

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 curative potential of the body's intrinsic immune system without the adverse effects of broad systemic immune modulation.

Headquartered in Boston, Massachusetts, we are led by an experienced management team 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 X and LinkedIn.

Forward-Looking Statements
This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Such forward-looking statements include, but are not limited to, those regarding: the company's expectations regarding the planned IND filing for CUE-401; the Company' expectations regarding the potential characteristics and benefit of CUE-401; the company's belief that the Immuno-STAT platform stimulates targeted immune modulation through the selective modulation of disease-relevant T cell and the applicability of the company's platform across many cancers and autoimmune diseases; 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 pipeline of product candidates and platforms, and its strategies, prospects, 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 ability to successfully advance is development plan for CUE-401; potential setbacks in the company’s research and development efforts including negative or inconclusive results from its preclinical studies or clinical trials 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; serious and unexpected drug-related side effects or other safety issues experienced by participants in clinical trials; its ability to secure required U.S. Food and Drug Administration (“FDA”) or other governmental approvals for its product candidates, including FDA clearance of any future IND submission for CUE-401, and the breadth of any approved indication; adverse effects caused by public health pandemics, including possible effects on the company’s 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 near term; 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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