Cullinan Therapeutics to Present First Data for CLN-619, a Novel Anti-MICA/B Antibody, in Combination with a Checkpoint Inhibitor and Updated Monotherapy Data at ASCO 2024

May 23, 2024

Preliminary data from CLN-619 in combination with checkpoint inhibitor pembrolizumab show objective responses in patients with tumor types that are typically unresponsive to pembrolizumab, such as non-small cell lung cancer (NSCLC) with oncogenic mutations

Longer term follow-up for patients treated with CLN-619 monotherapy demonstrates durable clinical benefit across multiple tumor types

CLN-619 continues to demonstrate a favorable safety profile and is well tolerated both as monotherapy and in combination with pembrolizumab

Based on observed clinical activity, Cullinan has initiated additional monotherapy and combination therapy expansion cohorts in NSCLC

CAMBRIDGE, Mass., May 23, 2024 (GLOBE NEWSWIRE) -- Cullinan Therapeutics, Inc. (Nasdaq: CGEM), a biopharmaceutical company focused on developing modality-agnostic targeted therapies, today announced first clinical data from its Phase 1 dose escalation cohort of CLN-619 in combination with checkpoint inhibitor (CPI) pembrolizumab and updated results from the monotherapy dose escalation cohort in patients with advanced solid tumors. Findings from the clinical trial will be shared at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting as a poster presentation during the “Developmental Therapeutics—Immunotherapy” session (Abstract #2588, Poster Bd 67) on June 1, 2024, 9:00 AM-12:00 PM Central Time.

Summary of Key Clinical Results from Combination Arm of Phase 1 Clinical Trial in Patients with Solid Tumors

- Of 22 patients treated with CLN-619 in combination with pembrolizumab, 18 were RECIST-evaluable for response.
- Confirmed partial responses (PR) were observed in 3 patients treated with CLN-619 at doses ≥3mg/kg in combination with pembrolizumab.
- Responses were observed in patients with tumor types not typically responsive to CPI treatment.

Characteristics of Responders

Tumor Type	Number of Prior Lines of Therapy	Prior CPI	CPI Responsive Tumor (Yes/No?)	Best Response	Duration of Response (Weeks)
NSCLC, *EGFR* exon 18/21	6	No	No	PR	24
NSCLC, *ALKr*	2	No	No	PR	12.7
Gastric, *HER2*+	3	No	Yes	PR	8.9+ (ongoing)

Summary of Efficacy in NSCLC (Monotherapy and Combination Cohorts)

- Objective responses and stable disease (SD) were observed in patients with NSCLC with oncogenic mutations in the CLN-619 monotherapy and combination cohorts.
  - 8 of the 11 patients with NSCLC were RECIST-evaluable; of these, 6 had oncogenic mutations.
  - 3 of the 6 patients with oncogenic mutations experienced clinical benefit – there were 2 PRs and 1 SD lasting >18 weeks.

Summary of Updated Key Clinical Results from Monotherapy Arm of Phase 1 Clinical Trial in Patients with Solid Tumors

- Among 42 patients treated with CLN-619 monotherapy, 29 received CLN-619 at a dose ≥1 mg/kg and were RECIST-evaluable.
- The clinical benefit rate (CBR) was 41.4% (1 complete response (CR), 2 PR, 9 SD ≥18 weeks).

Characteristics of Patients with Response or SD ≥18 Weeks

Tumor Type	Number of Prior Lines of Therapy	Best Response	Duration of Response (Weeks)
Responders (n=3)			
Mucoepidermoid parotid	2	CR	71
Endometrial (serous, MMRp)	5	PR	31
Endometrial (endometrioid, MMRp)	3	PR	55+ (ongoing)
SD ≥18 weeks (n=9) Cervical squamous (n=2); breast (ER/PR+, *HER2*−; n=1); ovarian (n=1); endometrial carcinosarcoma (n=1); mediastinal intimal sarcoma (n=1); adenoid cystic carcinoma (n=1); pancreatic adenocarcinoma (*KRAS* G12V; n=1); NSCLC (*STK11*m; n=1)	Mean: 3.6 Range: 1–7	SD ≥18 wks	Range: 18–56

Summary of Safety Data

CLN-619 was well tolerated in combination with pembrolizumab and as monotherapy. Most treatment-related adverse events (TRAEs) were grade 1/2.

TRAEs reported in ≥10% of safety-evaluable patients (combination: n=22; monotherapy: n=42) were infusion-related reactions (IRRs) (combination: 18.2%; monotherapy: 28.6%) and fatigue (combination: 18.2%; monotherapy: 9.5%). The only grade ≥3 TRAE reported in >5% of patients in any group was increased AST (combination: 0; monotherapy: 7.1%). One patient in each cohort discontinued study treatment due to TRAEs (4.5% combination and 2.4% monotherapy). There were no treatment-related deaths.

IRR was the most frequently reported TRAE with CLN-619. With administration of prophylactic pre-medications, most IRRs were grade 1 or 2, occurred on Day 1 of Cycle 1, and resolved quickly.

“Our initial clinical findings show that the combination of CLN-619, a novel antibody targeting MICA/B, with pembrolizumab may benefit patients whose cancer is not typically amenable to checkpoint inhibitor therapy. More specifically, we observed objective responses in patients with ALK- and EGFR-mutated NSCLC who had relapsed after tyrosine kinase inhibitors (TKIs), patients who do not typically respond to checkpoint inhibitors,” said Jeffrey Jones, MD, MBA, Chief Medical Officer, Cullinan Therapeutics. “Additionally, longer-term follow-up for patients treated with CLN-619 monotherapy shows favorable safety and durable clinical benefit with extended treatment, including objective responses and prolonged stable disease in multiple tumor types and in patients with disease progression after CPI therapy. We are encouraged by these data and have initiated monotherapy and combination expansion cohorts in NSCLC.”

“There remains significant unmet need for patients with NSCLC with oncogenic mutations relapsing after TKIs, so we see a potential benefit in novel therapies that can be easily combined with established CPIs,” said Alexander Spira, MD, PhD, FACP, FASCO, Director, Virginia Cancer Specialists Research Institute and Director, NEXT Oncology Virginia. “Combining CLN-619 with pembrolizumab engages multiple immune effector cells, including innate cells by CLN-619 and T cells by pembrolizumab. The safety profile of CLN-619 along with the biologic rationale for combination with CPI make this a potentially synergistic approach.”

CLN-619 Further Development Plan

CLN-619 is being studied in an ongoing Phase 1 clinical trial (NCT05117476) both as monotherapy and in combination with pembrolizumab. The study design allows dose level extensions as well as expansion in tumor-specific cohorts. Consistent with prespecified criteria and based on initial safety and efficacy observations, Cullinan has initiated monotherapy and combination expansion cohorts in NSCLC. Enrollment continues in previously declared expansion cohorts in cervical (monotherapy) and endometrial cancers (monotherapy and combination). CLN-619 will also be studied in a Phase 1 clinical trial (NCT06381141) in patients with relapsed/refractory multiple myeloma.

Virtual and Live Investor Event

Cullinan Therapeutics will host an Investor Event on Saturday, June 1, 2024, at 6:30 PM Central Time, during which Dr. Jeff Jones, Chief Medical Officer at Cullinan Therapeutics, will present the CLN-619 data shared at the 2024 ASCO Annual Meeting, and Dr. Alexander Spira, Director, Virginia Cancer Specialists Research Institute and Director, NEXT Oncology Virginia, will share an overview of the current treatment landscape for EGFR-mutated NSCLC. Investors and analysts are invited to register to attend in person by emailing Chad Messer, VP Investor Relations (cmesser@cullinantx.com). A live webcast will be available via the events page of the Company’s investor relations website at https://cullinantherapeutics.com/events-and-presentations/ and a replay will be available shortly after the conclusion of the live event.

About CLN-619

CLN-619 is a potential first-in-class humanized IgG1 monoclonal antibody that binds to the stress induced ligands MICA and MICB, which are expressed on a wide variety of solid tumors and hematologic malignancies. Engagement of MICA/B by the activating receptor NKG2D, present on both cytotoxic innate and adaptive immune cells, results in target cell lysis. However, tumor cells can shed MICA/B via proteases they release into the tumor microenvironment, resulting in evasion of immune-mediated destruction. CLN-619 functions by restoring MICA/B expression on the surface of tumor cells to reinvigorate NKG2D-mediated immune activation, and by inducing antibody-dependent cellular toxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP), together promoting anti-tumor activity via multiple immune-mediated mechanisms. CLN-619 is being studied in an ongoing Phase 1 clinical trial (NCT05117476) both as a monotherapy and in combination with pembrolizumab. The study design allows dose level extensions as well as expansion in tumor-specific cohorts. CLN-619 will also be studied in a Phase 1 clinical trial (NCT06381141) in patients with relapsed/refractory multiple myeloma.

About Cullinan Therapeutics

Cullinan Therapeutics, Inc. (Nasdaq: CGEM) is a biopharmaceutical company dedicated to creating new standards of care for patients. We have strategically built a diversified portfolio of clinical-stage assets that inhibit key drivers of disease or harness the immune system to eliminate diseased cells in both oncology and autoimmune diseases. Our portfolio encompasses a wide range of modalities, each with the potential to be best and/or first in class. Anchored in a deep understanding of oncology, immunology, and translational medicine, we create differentiated ideas, identify the most appropriate targets, and select the optimal modality to develop transformative therapeutics across a wide variety of cancer and autoimmune indications. We push conventional boundaries from candidate selection to differentiated therapeutic, applying rigorous go/no go criteria at each stage of development to fast-track only the most promising molecules to the clinic and, ultimately, commercialization. With deep scientific expertise, our teams exercise creativity and urgency to deliver on our promise to bring new therapeutic solutions to patients. Learn more about our Company at https://cullinantherapeutics.com/, and follow us on LinkedIn and X.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. These forward-looking statements include, but are not limited to, express or implied statements regarding Cullinan's beliefs and expectations regarding the potential benefits and therapeutic potential of CLN-619; our clinical development plans and timelines; our plans regarding future data presentations and other statements that are not historical facts. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "hope," "intend," "may," "plan," "potential," "predict," "project," "target," "should," "would," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

Any forward-looking statements in this press release are based on management's current expectations and beliefs of future events and are subject to known and unknown risks and uncertainties that may cause our actual results, performance or achievements to be materially different from any expressed or implied by the forward-looking statements. These risks include, but are not limited to, the following: uncertainty regarding the timing and results of regulatory submissions; success of our clinical trials and preclinical studies; risks related to our ability to protect and maintain our intellectual property position; risks related to manufacturing, supply, and distribution of our product candidates; the risk that any one or more of our product candidates, including those that are co-developed, will not be successfully developed and commercialized; the risk that the results of preclinical studies or clinical studies will not be predictive of future results in connection with future studies; and success of any collaboration, partnership, license or similar agreements. These and other important risks and uncertainties discussed in our filings with the Securities and Exchange Commission, including under the caption "Risk Factors" in our most recent Annual Report on Form 10-K and subsequent filings with the SEC, could cause actual results to differ materially from those indicated by the forward-looking statements made in this press release. While we may elect to update such forward-looking statements at some point in the future, we disclaim any obligation to do so, even if subsequent events cause our views to change, except to the extent required by law. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this press release. Moreover, except as required by law, neither the company nor any other person assumes responsibility for the accuracy and completeness of the forward-looking statements included in this press release. Any forward-looking statement included in this press release speaks only as of the date on which it was made.

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