June 5, 2017

Celldex Presents Promising Overall Survival Data from Phase 2 Study of Single-agent Glembatumumab Vedotin in Patients with Checkpoint-Refractory Metastatic Melanoma

Combination study with checkpoint inhibitor currently enrolling; data from combination arm with varlilumab anticipated in fall of 2017

HAMPTON, N.J., June 05, 2017 (GLOBE NEWSWIRE) -- Celldex Therapeutics, Inc. (NASDAQ:CLDX) today presented positive, mature results from the Company's Phase 2 study of glembatumumab vedotin in patients with stage III/IV checkpoint inhibitor-refractory, and, if applicable, BRAF/MEK inhibitor-refractory metastatic melanoma (n=62). Glembatumumab vedotin is a fully human monoclonal antibody-drug conjugate (ADC) that targets glycoprotein NMB (gpNMB), a protein overexpressed by multiple tumor types, including metastatic melanoma, where more than 80% of patients overexpress the marker. High tumor expression of gpNMB is associated with shorter metastasis-free survival and reduced overall survival.[1] Study results were presented today in an oral presentation by Patrick A. Ott, M.D., Ph.D., Clinical Director of Dana-Farber Cancer Institute's Melanoma Center and its Center for Immuno-Oncology, Assistant Professor of Medicine at Harvard Medical School and an investigator in the study, at the 2017 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago.

Study Highlights

- Median overall survival (OS) for all patients was 9.0 months (95% CI: 6.1, 13.0).
- As previously reported in October 2016, 7 of 62 (11%) patients experienced a confirmed response, and an additional three patients also experienced single timepoint partial responses. Since data were reported in October, one patient converted from a confirmed partial response to a confirmed complete response.
- Patients who experienced rash in Cycle 1 experienced a more prolonged OS with a median of 15.8 months (p=0.026, HR=0.44) as compared to those who did not experience rash.

"It's exciting to see clinical activity in this study as very few treatment options exist for melanoma patients who progress after immune checkpoint inhibitors and BRAF targeted therapy," said Dr. Ott. "The single-agent response rate observed in this study, including a complete response, and the duration of the objective responses continue to suggest that glembatumumab vedotin is an active agent in this disease. I am hopeful that leveraging the immune system with checkpoint inhibition in combination with the cytotoxic and immunologic cell death induced by glembatumumab vedotin could bring benefit to an even larger number of patients with melanoma, and I look forward to the outcome of these additional cohorts."

Phase 2 Study Single-agent Cohort Overview and Previously Presented Results

Patients enrolled in this single-agent, open-label cohort of glembatumumab vedotin presented with unresectable stage IV (n=62) melanoma. The median number of prior therapies was three (range of 1 to 8). All patients had been heavily pre-treated and had progressed during or after checkpoint inhibitor therapy, and almost all patients had received both ipilimumab (n=58; 94%) and anti-PD-1/anti-PD-L1 (n=58; 94%) therapy. Twelve patients presented with BRAF mutation, and fifteen had prior treatment with BRAF or BRAF/MEK targeted agents. Patients received glembatumumab vedotin every three weeks until disease progression or intolerance. The safety profile was consistent with prior studies of glembatumumab vedotin with rash, neutropenia and neuropathy experienced as the most significant adverse events.

As previously reported, the primary endpoint of the cohort (6 or more objective responses in the first 52 patients enrolled) was exceeded. Seven of 62 (11%) patients experienced a confirmed response, and an additional three patients also experienced single timepoint responses. The median duration of response was 6.0 months. A 52% disease control rate (patients without progression for greater than three months) was demonstrated, and median PFS for all patients was 4.4 months. Consistent with previous studies in melanoma and breast cancer, rash was associated with greater clinical benefit. Patients who experienced rash in Cycle 1 experienced a 21% confirmed response rate, a more prolonged PFS with a median of 5.5 months (p=0.006; HR=0.39) and a more prolonged OS with a median of 15.8 months (p=0.026, HR=0.44).

Pre-treatment tumor tissue was available for 59 patients. All samples were gpNMB positive, and 78% of patients had tumors with 100% of their epithelial cells expressing gpNMB. Given both the high level of expression and the intensity of expression across this patient population, identifying a potential population for gpNMB enrichment is not feasible; therefore, all patients

with metastatic melanoma could be evaluated as potential candidates for treatment with glembatumumab vedotin in future studies.

Ongoing Cohorts Combining Glembatumumab Vedotin with Varlilumab or Checkpoint Inhibitor

In August 2016, the Company announced that the study protocol was amended to add a second cohort of patients to a glembatumumab vedotin and varlilumab combination. Varlilumab is Celldex's fully human monoclonal agonist antibody that binds and activates CD27, a critical co-stimulatory molecule in the immune activation cascade. This additional cohort has completed enrollment with data presentation expected in the fall of 2017. Celldex is now enrolling patients to a third arm in the study to assess a glembatumumab vedotin and checkpoint combination in patients who have previously progressed on checkpoint inhibitor. This rationale is strongly supported by preclinical data that suggest that the anti-tumor activity may be enhanced with the combination. In addition, due to their direct cytotoxic properties, microtubule-depolymerizing agents like MMAE also appear to convert tumor-resident tolerogenic dendritic cells into active antigen-presenting cells.[2]

The Company also intends to conduct exploratory analyses of pre-entry skin biopsies in future patients to investigate potential predictors of response to glembatumumab vedotin, given the association of rash and outcome.

About Glembatumumab Vedotin

Glembatumumab vedotin is a fully human monoclonal antibody-drug conjugate (ADC) that targets glycoprotein NMB (gpNMB). gpNMB is a protein overexpressed by multiple tumor types, including breast cancer, melanoma, lung cancer, uveal melanoma and osteosarcoma. gpNMB has been shown to be associated with the ability of the cancer cell to invade and metastasize and to correlate with reduced time to progression and survival in breast cancer. The gpNMB-targeting antibody, CR011, is linked to a potent cytotoxic, monomethyl auristatin E (MMAE), using Seattle Genetics' proprietary technology. Glembatumumab vedotin is designed to be stable in the bloodstream but to release MMAE upon internalization into gpNMB-expressing tumor cells, resulting in a targeted cell-killing effect. Glembatumumab vedotin is in development for the treatment of locally advanced or metastatic breast cancer with an initial focus in triple negative disease, stage III and IV melanoma, squamous cell lung cancer and uveal melanoma.

About Celldex Therapeutics, Inc.

Celldex is developing targeted therapeutics to address devastating diseases for which available treatments are inadequate. Our pipeline includes antibodies, antibody-drug conjugates and other protein-based therapeutics derived from a broad set of complementary technologies which have the ability to engage the human immune system and/or directly inhibit tumors to treat specific types of cancer or other diseases. Visit www.celldex.com.

Forward Looking Statement

This release contains "forward-looking statements" made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. These statements are typically preceded by words such as "believes," "expects," "anticipates," "intends," "will," "may," "should," or similar expressions. These forward-looking statements reflect management's current knowledge, assumptions, judgment and expectations regarding future performance or events. Although management believes that the expectations reflected in such statements are reasonable, they give no assurance that such expectations will prove to be correct or that those goals will be achieved, and you should be aware that actual results could differ materially from those contained in the forward-looking statements. Forward-looking statements are subject to a number of risks and uncertainties, including, but not limited to, our ability to successfully integrate the business and programs of Kolltan with our business and programs; our ability to successfully complete research and further development and commercialization of glembatumumab vedotin and other Company drug candidates; our ability to obtain additional capital to meet our long-term liquidity needs on acceptable terms, or at all, including the additional capital which will be necessary to complete the clinical trials that we have initiated or plan to initiate; the uncertainties inherent in clinical testing and accruing patients for clinical trials; our limited experience in bringing programs through Phase 3 clinical trials; our ability to manage and successfully complete multiple clinical trials and the research and development efforts for our multiple products at varying stages of development; the availability, cost, delivery and quality of clinical and commercial grade materials produced by our own manufacturing facility or supplied by contract manufacturers, who may be our sole source of supply; the timing, cost and uncertainty of obtaining regulatory approvals; our ability to maintain and derive benefit from the Fast Track designation for glembatumumab vedotin which does not change the standards for regulatory approval or guarantee regulatory approval on an expedited basis, or at all; the failure of the market for the Company's programs to continue to develop; our ability to protect the Company's intellectual property; the loss of any executive officers or key personnel or consultants; competition; changes in the regulatory landscape or the imposition of regulations that affect the Company's products; and other factors listed under "Risk Factors" in our annual report on Form 10-K and quarterly reports on Form 10-Q.

All forward-looking statements are expressly qualified in their entirety by this cautionary notice. You are cautioned not to

place undue reliance on any forward-looking statements, which speak only as of the date of this release. We have no obligation, and expressly disclaim any obligation, to update, revise or correct any of the forward-looking statements, whether as a result of new information, future events or otherwise.

References

1. Rose, *et al. Clin Cancer Res.* 2010; 16(7):2147-56.
2. Müller, *et al. Cancer Immunol. Res.* 2014; 2(8):741-55.

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