November 14, 2014

Interim Update from Randomized Phase 2 ReACT Study of Rindopepimut in Recurrent Bevacizumab-naive Glioblastoma Demonstrates Statistically Significant Survival Benefit

-Benefit observed across multiple endpoints in bevacizumab-naïve patients-

-Clear signs of clinical activity in difficult to treat bevacizumab-refractory patients-

HAMPTON, N.J., Nov. 14, 2014 (GLOBE NEWSWIRE) -- Celldex Therapeutics, Inc. (Nasdaq:CLDX) today announced an interim update from the Phase 2 ReACT study of rindopepimut in EGFR*vIII*-positive glioblastoma (GBM). The ReACT results demonstrate clear signs of clinical activity in patients with recurrent glioblastoma, including groups both naïve and refractory to bevacizumab (Avastin®). The data were presented in a platform presentation by David A. Reardon, M.D., Clinical Director, Center for Neuro-Oncology, Dana-Farber Cancer Center and Associate Professor of Medicine, Harvard Medical School, and the lead investigator of the ReACT study, at the 4th Quadrennial Meeting of the World Federation of Neuro-Oncology held in conjunction with the 19th Annual Meeting of the Society for Neuro-Oncology (SNO). A webcast/conference call will be held at 5:00 pm ET today to discuss the results (details provided below).

Rindopepimut (RINTEGA®) is an investigational immunotherapy that targets the tumor specific oncogene EGFR*vIII*. Patients with EGFR*vIII*-positive glioblastoma typically have a worse prognosis than the overall glioblastoma population, including poor long term survival.

Presentation Highlights—Interim Data Update

Group 1 - Recurrent GBM; bevacizumab (bev) naïve (randomized: rindo + bev vs. control + bev)

- Primary endpoint of PFS-6 (% alive without progression at 6 months)—rindopepimut 27% vs. control 11%; p=0.048
- Statistically significant overall survival benefit—hazard ratio of 0.47; p=0.0208; rindopepimut median 12.0 months vs. control median 8.8 months
- An increase in clinically meaningful tumor shrinkage
- Rindopepimut plus bevacizumab was well tolerated; no serious adverse events attributed to rindopepimut
- Early anti-EGFR*vIII* immune response correlates with survival benefit

Group 2/2C - Recurrent GBM; bev refractory (single arm: rindo + bev)

- Rare, but prominent anti-tumor activity did not meet high hurdle for expanded accrual of Group 2C
- Noteworthy overall survival compared to historical comparisons
- Rindopepimut plus bevacizumab was well tolerated; no serious adverse events attributed to rindopepimut
- Early anti-EGFR*vIII* immune response correlates with survival benefit

"The patients in this study have advanced and difficult to treat disease," said David Reardon, M.D. "While these are interim data, the ability to demonstrate a survival benefit in this patient population has been extremely rare. If final data are consistent with these results, it would be practice-changing for physicians treating glioblastoma and offer new hope to patients and their families."

"The interim data presented today are extremely encouraging and continue to add to an impressive and consistent data set for rindopepimut across multiple studies and stages of disease," said Thomas Davis, M.D., Executive Vice President and Chief Medical Officer of Celldex. "We believe these interim data are clinically important to patients with recurrent glioblastoma and, if the final data remain consistent, we intend to discuss the significance of these findings with regulatory authorities."

ReACT Study Design and Safety

ReACT is a Phase 2 exploratory study designed to determine if adding rindopepimut to standard of care bevacizumab improves the outcomes for patients with EGFR*vIII*-positive recurrent glioblastoma across multiple measures. The study

includes 3 groups:

- Group 1 - bevacizumab naive, n=72, patients randomized to receive either rindopepimut or Keyhole Limpet Hemocyanin (KLH) (administered as a control), each along with bevacizumab
- Group 2 - bevacizumab refractory (defined as having progressed/grown through bevacizumab by RANO criteria within two months of prior bev treatment), n=25, patients receive rindopepimut plus bevacizumab in a single treatment arm
- Group 2C (C = Confirmatory) - bevacizumab refractory expansion, n=up to 75 (Simon two-stage design; 1st cohort n=28), patients receive rindopepimut plus bevacizumab in a single treatment arm

Across Group 1, Group 2 and Group 2C, rindopepimut plus bevacizumab was very well tolerated (dosing up to 30+ months). There were no unexpected toxicities associated with concomitant bevacizumab administration and there were no serious adverse events attributed to study vaccination. One potentially treatment-related event of Grade 1 intratumoral hemorrhage resulted in discontinuation of rindopepimut treatment. Adverse events were consistent with prior studies of rindopepimut.

Detailed Clinical Activity Overview—Interim Data Update

Group 1

72 patients were randomized to receive either rindo + bev (n=35) or control + bev (n=37). 30 patients continue to be followed for survival, including 12 patients who continue to receive treatment.

- **PFS-6:** While the data continue to mature, the primary endpoint of the study, progression-free survival at 6 months, is currently positive with 27% of patients treated with rindopepimut still progression free compared to 11% of control patients (p=0.048).
- **Survival:** The Overall Survival Kaplan Meyer analysis currently demonstrates a statistically significant benefit (p=0.0208) with a hazard ratio of 0.47 (0.25, 0.91) in favor of the rindopepimut treated patients with early and consistent separation of the curves providing a median difference of 12.0 versus 8.8 months.
- **Response Rate:** 7 out of 29 patients (24%) evaluable for response on the rindopepimut arm experienced a confirmed objective response versus 5 out of 30 patients (17%) evaluable for response on the control arm. Assessments of response were conducted by study investigators according to RANO criteria.
- **Stable Disease:** 74% of patients in the rindopepimut arm had stable disease or better for greater than 2 months versus 57% in the control arm.
- **Steroid Use:** Further emphasizing the level of disease control, 55% of patients on the rindopepimut arm, who were on steroids at the start of treatment, were able to stop steroids during treatment versus 26% on the control arm and 50% of patients on the rindopepimut arm were able to stop steroids for greater than 2 months during treatment versus only 11% on the control arm.
- **Immune Response:** Improved survival was greatest among patients with rapid generation of anti-EGFR*vIII* humoral response, though even those with slower development of immune responses appear to benefit.
- **Other:** All subgroup analyses, including performance status, steroid use and recent resection, show a hazard ratio in favor of rindopepimut treatment.

Group 2/2C

Results are available for 53 (n=25 patients in Group 2; n=28 in Group 2C) patients enrolled in this arm. Thirteen patients continue to be followed for survival.

- **Survival:** The median OS of 5.1 months (95% CI 3.2, 6.5) is noteworthy in these heavily pretreated, refractory EGFR*vIII*-positive patients. A review of the literature assessing survival in recurrent patients who are bevacizumab-experienced across eight independent studies suggests a weighted-average survival of 3.6 months (range of 2.6 to 5.8 months) in all-comers. 46% of patients in Group 2/2C were alive at 6 months.
- **Response Rate:** As previously reported, two patients experienced complete response (one unconfirmed) and two patients experienced partial response (one unconfirmed). Two of these four patients did not meet the protocol defined definition of refractory in Group 2, the only two such patients enrolled. No additional objective responses were observed in Group 2C and the study did not meet the criteria (defined as two responses per RANO criteria in the first 23 patients enrolled in Group 2C) for continued enrollment. Ten patients with measurable disease experienced objective tumor shrinkage across Group 2/2C.
- **Stable Disease:** 19% of patients had stable disease or better for greater than 2 months (range 2.8 to 16.5 months).
- **Immune Response:** As observed in the bev-naïve patients, early development of high anti-EGFR*vIII* titer was associated with longer survival and may be predictive for improved outcome in this refractory patient population.

Additional Presentation at SNO: Rindopepimut Compassionate Use Experience

Data from the rindopepimut compassionate use program were also presented in a platform presentation at SNO by

Evangelia Razis, MD, PhD, Head, 3rd Oncology Unit Hygeia Hospital, Athens, Greece. Data were available for 64 patients with glioblastoma across six countries that did not qualify for enrollment into an open trial of rindopepimut (n=24 newly diagnosed and n=40 recurrent). As is typical of compassionate use programs, the patients who received compassionate use were a diverse group at different stages of disease with varied treatment regimens. Rindopepimut in combination with various anticancer therapies resulted in robust anti-EGFR*vIII* humoral response with minimal toxicity. In patients with newly diagnosed and recurrent glioblastoma, respectively, median OS was 20.5 and 6.9 months and median PFS was 11.1 and 2.5 months from first dose of rindopepimut. Tumor response (> 50% shrinkage in measurable disease) was observed in nine patients receiving rindopepimut with other potentially active agents including three patients with newly diagnosed GBM and six patients with recurrent GBM. Eight of these patients received concurrent temozolomide and four received bevacizumab. Six patients have had progression-free survival greater than one year on treatment with a range of 12.8 to 72.6+ months (n=3 newly diagnosed; n=3 recurrent). Fourteen additional patients continue to receive rindopepimut with a range of 2.4+ to 10.1+ months. While it is inappropriate to compare these results with specific historical data because of the heterogeneity of the patients and treatment, selective patient anecdotes provide unexpectedly positive outcomes. Rindopepimut appears to be well tolerated in combination, supporting additional studies with EGFR inhibitors, bevacizumab, additional tumor antigens, selected chemotherapy and radiation.

Conference Call and Webcast Information

Celldex will host a conference call and live webcast today, Friday, November 14, 2014 at 5:00 pm ET to review the data presented at SNO. The conference call and presentation will be webcast live over the Internet and can be accessed by logging on to the Events Calendar under the "News & Events" section of the Celldex Therapeutics website at www.celldextherapeutics.com. The call can also be accessed by dialing (866) 743-9666 (within the United States) or (760) 298-5103 (outside the United States). The passcode is 28183516. A replay of the call will be available approximately two hours after the live call concludes through November 21, 2014. To access the replay, dial (855) 859-2056 (within the United States) or (404) 537-3406 (outside the United States). The passcode is 28183516. The webcast will also be archived on the Company's website.

About Rindopepimut

Rindopepimut (RINTEGA®) is an investigational immunotherapy that targets the tumor specific oncogene EGFR*vIII* (v3), a functional and permanently activated variant of the epidermal growth factor receptor (EGFR), a protein that has been well validated as a target for cancer therapy. Expression of EGFR*vIII* correlates with increased tumorigenicity in mouse models and poor long term survival in clinical studies of patients with glioblastoma (GBM). In addition, EGFRvIII-positive cells are believed to stimulate proliferation of non-EGFR*vIII* cells through IL-6 cell-to-cell signaling and to release microvesicles containing EGFR*vIII*, which can merge with neighboring cells, transferring tumor-promoting activity. EGFR*vIII* expression may also be associated with tumor stem cells that have been identified in GBM. These stem cells contribute to resistance to cytotoxic therapy and tumor recurrence. EGFR*vIII* is expressed in tumors in about 30% of patients with GBM. It has not been detected at a significant level in normal tissues; therefore, targeting of this tumor-specific molecule is not likely to impact healthy tissues.

Three Phase 2 trials of rindopepimut—ACTIVATE, ACT II, and ACT III—have been completed in newly diagnosed EGFR*vIII*-positive GBM and have shown consistent improvements in both overall survival and median progression-free survival. The most common adverse events for rindopepimut include injection site reactions, fatigue, rash, nausea and pruritus. Rindopepimut is currently being studied in two clinical trials in EGFR*vIII*-positive GBM—an international Phase 3 study called ACT IV in newly diagnosed GBM that will complete enrollment in late 2014 and a Phase 2 study called ReACT in recurrent GBM that has completed enrollment.

About Celldex Therapeutics, Inc.

Celldex is developing targeted therapeutics to address devastating diseases for which available treatments are inadequate. Our pipeline is built from a proprietary portfolio of antibodies and immunomodulators used alone and in strategic combinations to create novel, disease-specific therapies that induce, enhance or suppress the body's immune response. 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, including those related to the Company's strategic focus and the future development and commercialization (by Celldex and others) of rindopepimut ("rindo"; CDX-110), glembatumumab vedotin ("glemba"; CDX-011), varlilumab ("varli"; CDX-1127), CDX-1401, CDX-301 and other products and our goals for 2014. 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 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 complete research and further development and commercialization of rindopepimut, glembatumumab vedotin and other 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; 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.

CONTACT: Company Contact

Sarah Cavanaugh

Vice President of Investor Relations & Corp Communications

Celldex Therapeutics, Inc.

(508) 864-8337

scavanaugh@celldex.com

Media Inquiries

Dan Budwick

Pure Communications, Inc.

(973) 271-6085

dan@purecommunicationsinc.com

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