November 20, 2015

Long-term Survival Benefit Demonstrated in Phase 2 ReACT Study of RINTEGA(R) in Recurrent Bevacizumab-naive Glioblastoma

-- At 2 years, 25% RINTEGA survival rate versus 0% for control --
-- Hazard ratio of 0.53 (p=0.0137) indicates a significant overall survival advantage for recurrent GBM patients --
-- Clinical benefit continues to be observed across multiple endpoints, including PFS, OS, ORR and steroid requirement with all OS subgroup analyses favoring RINTEGA treatment --

HAMPTON, N.J., Nov. 20, 2015 (GLOBE NEWSWIRE) -- Celldex Therapeutics, Inc. (NASDAQ:CLDX) today presented mature survival data from the Company's randomized, double-blind Phase 2 study of RINTEGA® (rindopepimut) in patients with EGFRvIII-positive, recurrent glioblastoma (GBM) at the 20th Annual Scientific Meeting of the Society for Neuro-Oncology (SNO). The data were presented in a podium presentation by David A. Reardon, M.D., Clinical Director, Center for Neuro-Oncology, Dana-Farber Cancer Institute; Associate Professor of Medicine, Harvard Medical School; and President of the Society for Neuro-Oncology, as well as the lead investigator of the ReACT study. RINTEGA is an investigational EGFRvIII specific therapeutic vaccine and was granted Breakthrough Therapy Designation in February 2014. Patients with recurrent glioblastoma that express the EGFRvIII mutation typically have a worse prognosis than the overall glioblastoma population, including poor long-term survival (median time from recurrence to death for EGFRvIII-positive patients is 8.7 months[1]). As previously reported, the primary endpoint of the study, progression-free survival at six months (PFS6) has been met.

- Mature overall survival (OS) data continue to show a marked benefit [hazard ratio = 0.53 (0.32, 0.88); p=0.0137] with a long-term survival benefit clearly seen in the RINTEGA arm. In May, the Company reported a hazard ratio of 0.57 (0.33, 0.98) (p=0.0386) for OS in the study.
- Nine of 10 patients (one patient lost to follow up) on the RINTEGA arm remain alive since the Company last presented data in May compared to only two out of five patients on the control arm.
- At two years, the survival rate for RINTEGA patients is 25% versus 0% for control patients in the intent to treat (ITT) population, with five patients extending beyond two years.
- Five patients in the RINTEGA arm continue survival follow-up without progression per central review, compared to only one patient on the control arm.
- A clear advantage continues to be demonstrated across multiple, clinically important endpoints including overall survival (OS), long-term progression-free survival (PFS), objective response rate (ORR) and need for steroids.
- 33% of patients on the RINTEGA arm who were receiving steroids at baseline were able to stop steroids for six months or longer compared to none on the control arm.

"The results of the ReACT study change the way we think about glioblastoma—offering patients and their families new hope in the face of one of the most difficult to treat cancers and upending the notion that the brain, masked behind the blood brain barrier, is beyond the reach of the promise of immunotherapy," said David A. Reardon, M.D. "The long-term survival benefit observed in this study is unprecedented as it is exceedingly rare for patients with highly aggressive, EGFRvIII-positive glioblastoma—even in the newly diagnosed setting—to live beyond two years. Most striking perhaps is that not only are patients living considerably longer, they are also living better, with minimal side effects and a reduced need for steroids. The ReACT data also build considerable anticipation for the ACT IV study in newly-diagnosed glioblastoma as these patients typically present with much stronger immune systems and stand to derive an even greater benefit."

"Patients with glioblastoma—especially those who are EGFRvIII-positive—face a staggering diagnosis, and in the face of this news, making the decision to participate in a clinical trial—especially a randomized study—is never an easy decision," said Thomas Davis, M.D., Executive Vice President and Chief Medical Officer of Celldex. "To this end, we are extremely gratified on behalf of our ReACT patients, their families and physicians that RINTEGA continues to tell a very consistent, impressive story across multiple, clinically relevant endpoints including, most importantly, long-term survival. These results replicate what we have seen in earlier RINTEGA studies conducted in newly-diagnosed patients, supporting our belief that RINTEGA will be an important treatment option for all patients with EGFRvIII-positive glioblastoma."

Presentation Details

ReACT is a randomized, controlled Phase 2 exploratory study designed to determine if adding RINTEGA to standard of care bevacizumab (BV; Avastin®) improves outcomes for patients with EGFRvIII-positive, recurrent glioblastoma across multiple

measures. Patients [n=73, intent to treat (ITT)] were bevacizumab-naïve at study entry. Tumor responses were evaluated in accordance with RANO criteria by an independent expert review committee blinded to treatment group assignment. Data for this long-term update included study results through September 1, 2015.

- **PFS6:** As previously reported, the primary endpoint of PFS6 was met. 10 out of 36 (28%) patients were alive at six months without progression on the RINTEGA arm compared to 6 out of 37 (16%) on the control arm (p=0.1163). Given the exploratory nature and size of the trial, the ReACT study required a PFS6 1-sided p-value of 0.2 (powered at 80%) for positivity.
- **SURVIVAL:** RINTEGA+BV demonstrated a statistically significant, clinically meaningful overall survival benefit compared to BV alone. Consistent with previous studies of RINTEGA and the published data observed for immune-mediated therapeutics, this survival benefit includes a "tail" on the RINTEGA survival curve with multiple patients exceeding what is customary survival for EGFRvIII-positive glioblastoma. Nine patients on the RINTEGA arm continue to be followed for survival, including five without disease progression per central review. Two patients on the control arm continue to be followed for survival, including one without disease progression per central review. At two years, the survival rate for RINTEGA patients in the ITT population is 25% versus 0% for control patients.

	Overall Survival (OS), Intent to Treat (ITT) Population			
Hazard Ratio (HR)	HR = 0.53 (0.32, 0.88); p=0.0137			
	Median (95% CI)	**OS 12 months**	**OS 18 months**	**OS 24 months**
RINTEGA + BV	11.3 (9.9, 16.2)	44%	32%	25%
Control + BV	9.3 (7.1, 11.4)	32%	13%	0%

- **OBJECTIVE RESPONSE RATE (ORR):** Nine out of 30 evaluable ITT patients (30%) on the RINTEGA arm experienced a confirmed objective response versus six out of 34 evaluable patients (18%) on the control arm. Five patients on the RINTEGA arm experienced durable responses greater than six months, and three of these patients experienced durable responses greater than 18 months (range of 18.6+ to 22.2 months). In contrast, only two patients on the control arm experienced a durable response greater than six months, and none experienced a response greater than 7.4 months.
- **STEROID USE:** Further emphasizing the level of disease control, 50% of the 18 patients on the RINTEGA arm who were on steroids at the start of treatment were able to stop steroids for at least two months during treatment versus only 26% of the 19 patients on the control arm who were on steroids at the start of treatment. 33% of patients on the RINTEGA arm were able to stop steroids for more than six months, and, of these, three were able to stop for more than one year versus none on the control arm for either time point.
- **IMMUNE RESPONSE:** Prolonged survival was associated with high anti-EGFRvIII humoral responses that were predominantly of the cell killing IgG1 isotype, and recent *in vivo* experiments have shown those immune responses had tumor killing function through antibody dependent cellular cytotoxicity (ADCC) of EGFRvIII-expressing tumor cells. This biologic effector function is rarely proven for immune therapies. Importantly, rapid generation of anti-EGFRvIII humoral response correlated with longer survival; however, even those with slower development of immune responses benefitted. No patient in the control arm had detectable EGFRvIII specific antibody response. This effect is consistent with RINTEGA's proposed mechanism of action as a targeted immunotherapeutic vaccine.
- **OTHER:** Multiple subgroup and adjusted analyses have concluded that the consistent survival benefit observed in the study was not influenced by potential imbalances in patient demographics.
- **SAFETY:** RINTEGA was very well tolerated without unexpected additive toxicity to bevacizumab.

RINTEGA® is a registered trademark of Celldex Therapeutics. Avastin® is a registered trademark of Genentech, Inc.

[1]Data provided the Radiation Therapy Oncology Group (RTOG).

About RINTEGA®

RINTEGA® is an investigational therapeutic vaccine that targets the tumor specific oncogene EGFRvIII, 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 EGFRvIII 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-EGFRvIII cells through IL-6 cell-to-cell signaling and to release microvesicles containing EGFRvIII, which can merge with neighboring cells, transferring tumor-promoting activity. EGFRvIII 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. EGFRvIII 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 RINTEGA—ACTIVATE, ACT II, and ACT III—have been conducted in newly diagnosed EGFRvIII-positive GBM and have shown consistent improvements in both overall survival and progression-free survival compared to matched historical controls. The most common adverse events for RINTEGA include injection site reactions, fatigue, rash, nausea and pruritus. RINTEGA is currently being studied in two clinical trials in EGFRvIII-positive GBM—an international Phase 3 study called ACT IV in newly diagnosed GBM and a Phase 2 study called ReACT in recurrent GBM. In February 2014, the U.S. Food and Drug Administration (FDA) granted RINTEGA Breakthrough Therapy Designation for the treatment of adult patients with EGFRvIII-positive glioblastoma. The first interim analysis for ACT IV occurred in June 2015, and the study's Data Safety and Monitoring Board recommended continuation of the study as planned. The Company anticipates that ACT IV will reach the required 75% of events (deaths) to perform the second interim analysis in late 2015 and that the analysis will occur in early 2016.

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 RINTEGA® ("rindopepimut"; "rindo"; CDX-110), glembatumumab vedotin ("glemba"; CDX-011), varlilumab ("varli"; CDX-1127), CDX-1401, CDX-301 and other products and our goals for 2015. 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 RINTEGA, 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; our ability to maintain and derive benefit from the Breakthrough Therapy Designation for RINTEGA, 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.

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