May 31, 2015

Randomized Phase 2 ReACT Study of RINTEGA(R) in Recurrent Bevacizumab-naive Glioblastoma Demonstrates Statistically Significant Overall Survival and Emergence of Long-term Survival Benefit; Primary Endpoint of PFS6 Met

--Clinical benefit observed across multiple endpoints, including PFS, OS, ORR and steroid requirement--
--All subgroup analyses favor RINTEGA treatment--

HAMPTON, N.J., May 31, 2015 (GLOBE NEWSWIRE) -- Celldex Therapeutics, Inc. (Nasdaq:CLDX) today presented positive results from the Company's randomized, double-blind Phase 2 study of RINTEGA® (rindopepimut) in patients with EGFRvIII-positive, recurrent glioblastoma at the 2015 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago. The primary endpoint of the study, progression-free survival at six months (PFS6) was met, and a clear advantage was demonstrated across multiple, clinically important endpoints including overall survival (OS), long-term progression-free survival, objective response rate (ORR) and need for steroids. The data were presented in an oral 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. A webcast/conference call will be held Monday, June 1, 2015 at 8:00 a.m. ET to discuss the results; details are provided below.

RINTEGA is an investigational EGFRvIII specific therapeutic vaccine. Patients with glioblastoma that express the EGFRvIII mutation typically have a worse prognosis than the overall glioblastoma population, including poor long-term survival.

"The results of the ReACT study are striking because we are observing an extremely rare overall survival advantage that is now translating into long-term survival for a number of patients—something not seen in highly aggressive, EGFRvIII-positive glioblastoma," said David A. Reardon, M.D. "Importantly, patients on the RINTEGA arm are not only surviving longer, they are experiencing a notable decrease in the need for steroids and the numerous side effects associated with their use. We are in dire need of better treatment options, and I believe RINTEGA could become a critical therapy for patients with EGFRvIII-positive glioblastoma. Above all, I think these results offer much needed hope to patients, their families and the physicians who treat them that progress is being made in treating this devastating disease."

"The ReACT study tells a compelling story across multiple, clinically relevant endpoints where the data consistently favor RINTEGA," said Thomas Davis, M.D., Executive Vice President and Chief Medical Officer of Celldex. "This is one of the most challenging disease settings, and we were extremely pleased to see that even in patients with bulky, growing tumors, RINTEGA generated remarkably frequent and robust anti-EGFRvIII immune responses, which strongly correlated with meaningful clinical activity. These results mirror 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."

As previously guided, if updated data remained consistent with previously reported results, the Company intended to discuss the potential significance of the ReACT study with regulatory bodies. Given the consistency of the results, this process is ongoing, and the Company will communicate the outcome of these discussions when they are completed.

Presentation Highlights

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); n=67 per protocol (PP)] were bevacizumab-naïve at study entry. Investigator-reported interim data including study results through October 2014 were presented in late 2014. Data presented at ASCO were adjudicated by an independent review committee (IRC) blinded to treatment group assignment and included study results through March 2015 for both ITT and PP populations; tumor responses were evaluated in accordance with RANO criteria. The IRC analyses are statistically equivalent with and confirm the previously reported results.

- **PFS6:** The primary endpoint of PFS6 was met. 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.

	PFS6 (Crude Rate)	
	ITT Population	**Per Protocol**
RINTEGA + BV	10/36 (28%)	10/33 (30%)
Control + BV	6/37 (16%)	4/34 (12%)
	p=0.1163	p=0.0310

- **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 an emerging "tail" on the RINTEGA survival curve with multiple patients exceeding what is customary survival for EGFRvIII-positive glioblastoma. Nine patients (ITT) on the RINTEGA arm continue to be followed for survival, including six without disease progression receiving ongoing treatment. Six patients on the control arm continue to be followed for survival, including two without disease progression receiving ongoing treatment. At 12 months, 45% of RINTEGA patients (ITT) were alive versus 31% of control patients. While these data are early and continue to mature, at 18 months, 30% of RINTEGA patients (ITT) were alive versus 15% of control patients. The Company will continue to follow patients for long-term survival and will update these numbers at an appropriate scientific conference.

	Overall Survival					
	ITT Population			**Per Protocol Population**		
Hazard Ratio (HR)	HR = 0.57 (0.33, 0.98); p=0.0386			HR = 0.53 (0.30, 0.93); p=0.0244		
	Median (95% CI)	**OS 12**	**OS 18**	**Median (95% CI)**	**OS 12**	**OS 18**
RINTEGA + BV	11.6 (10.0, 16.2)	45%	30%	10.9 (9.7, 16.2)	41%	30%
Control + BV	9.3 (7.1, 11.3)	31%	15%	8.5 (6.8, 11.1)	28%	10%

- **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. Nine out of 29 evaluable PP patients (31%) on the RINTEGA arm experienced a confirmed objective response versus five out of 32 evaluable patients (16%) 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 one year (range of 14.8+ to 18.4+ months). In contrast only one patient on the control arm experienced a durable response greater than six months, and none experienced a response greater than one year.
- **STEROID USE:** Further emphasizing the level of disease control, 56% of patients on the RINTEGA arm who were on steroids at the start of treatment were able to stop steroids during treatment versus 42% on the control arm, and 44% of patients on the RINTEGA arm were able to stop steroids for at least two months during treatment versus only 21% on the control arm. Six 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, though 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:** Subgroup analyses, including performance status, steroid use and recent resection, favor RINTEGA treatment.
- **SAFETY:** RINTEGA was very well tolerated without additive toxicity to bevacizumab.

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

Conference Call Details

Celldex will host a conference call at 8:00 a.m. ET on Monday, June 1, 2015 to discuss the ReACT data. The conference call and presentation will be webcast live over the Internet and can be accessed by going to the "Events & Presentations" page under the "Investors & Media" section of the Celldex Therapeutics website at www.celldex.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 conference ID number is 55717378.

A replay of the call will be available through June 7, 2015. To access the replay, dial (855) 859-2056 (within the United States) or (404) 537-3406 (outside the United States). The conference ID number is 55717378. The webcast will also be archived on the Company's website.

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 2015, the U.S. Food and Drug Administration (FDA) granted RINTEGA Breakthrough Therapy Designation for the treatment of adult patients with EGFRvIII-positive glioblastoma (GBM).

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.

CONTACT: Company Contact

Sarah Cavanaugh,

Vice President of Investor Relations

& Corp Communications

Celldex Therapeutics, Inc.

(781) 433-3161

scavanaugh@celldex.com

Media Inquiries

Dan Budwick, Pure Communications, Inc.

(973) 271-6085

dan@purecommunicationsinc.com

Celldex Therapeutics logo

Source: Celldex Therapeutics, Inc.