Celcuity Announces Clinically Meaningful Improvement in Both Progression-Free Survival (“PFS”) Primary Endpoints from PIK3CA Wild-Type Cohort of Phase 3 VIKTORIA-1 Trial

July 28, 2025

Hazard Ratios and Improvements in Median PFS are Unprecedented in HR+/HER2- Advanced Breast Cancer (“ABC”)

- *Gedatolisib + palbociclib + fulvestrant (“gedatolisib triplet”) reduced the risk of disease progression or death by 76% vs. fulvestrant (HR=0.24; 95% CI: 0.17–0.35; p<0.0001). Median PFS was 9.3 months with the gedatolisib triplet versus 2.0 months with fulvestrant*
- *Gedatolisib + fulvestrant (“gedatolisib doublet”) reduced the risk of progression or death by 67% vs. fulvestrant (HR=0.33; 95% CI: 0.24–0.48; p<0.0001). Median PFS was 7.4 months with the gedatolisib doublet versus 2.0 months with fulvestrant*
- *The efficacy results establish several new milestones in the history of drug development for HR+/HER2- advanced breast cancer*
- *Treatment discontinuation due to a treatment-related adverse event for the gedatolisib triplet and gedatolisib doublet was lower than was observed in Arm D of Celcuity’s Phase 1b trial in ABC patients and lower than observed in any Phase 3 trials for currently approved drug combinations in HR+/HER2- ABC*
- *The favorable safety profile with the gedatolisib triplet and gedatolisib doublet was better than observed in the Phase 1b trial in ABC, including lower rates of hyperglycemia and stomatitis*
- *Full data from the PIK3CA wild-type cohort of the VIKTORIA-1 clinical trial will be presented at an upcoming medical conference later this year. Celcuity expects to submit a New Drug Application for gedatolisib to the U.S. Food and Drug Administration in the fourth quarter of 2025. Topline data for the VIKTORIA-1 PIK3CA mutation cohort is expected by the end of 2025.*
- *Management to host webcast and conference call today, July 28, 2025, at 8:00 a.m. ET*

MINNEAPOLIS, July 28, 2025 (GLOBE NEWSWIRE) -- Celcuity Inc. (Nasdaq: CELC), a clinical-stage biotechnology company pursuing development of targeted therapies for oncology, today announced positive topline results from the *PIK3CA* wild-type cohort of the Phase 3 VIKTORIA-1 clinical trial evaluating gedatolisib plus fulvestrant with and without palbociclib versus fulvestrant in adults with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, *PIK3CA* wild-type, locally advanced or metastatic breast cancer, following progression on, or after, treatment with a CDK4/6 inhibitor and an aromatase inhibitor.

In the trial, the gedatolisib triplet demonstrated a statistically significant and clinically meaningful improvement in PFS among patients, reducing the risk of disease progression or death by 76% compared to fulvestrant (based on a hazard ratio [HR] of 0.24, 95% confidence interval [CI] 0.17-0.35; p<0.0001). The mPFS, as assessed by blinded independent central review (“BICR”), was 9.3 months with the gedatolisib triplet versus 2.0 months with fulvestrant, an incremental improvement of 7.3 months.

The gedatolisib doublet also demonstrated a statistically significant and clinically meaningful improvement in PFS among patients, reducing the risk of disease progression or death by 67% compared to fulvestrant (HR of 0.33, 95% CI 0.24-0.48; p<0.0001). The mPFS, as assessed by BICR, was 7.4 months with the gedatolisib doublet versus 2.0 months with fulvestrant, an incremental improvement of 5.4 months.

The topline efficacy data from the VIKTORIA-1 *PIK3CA* wild-type cohort established several new milestones in the history of drug development for HR+/HER2- advanced breast cancer:

- The hazard ratios for the gedatolisib triplet and doublet are more favorable than have ever been reported by any Phase 3 trial for patients with HR+/HER2- ABC.
- The 7.3- and 5.4-months incremental improvements in median PFS for the gedatolisib triplet and gedatolisib doublet over fulvestrant, respectively, are higher than have ever been reported by any Phase 3 trial for patients with HR+/HER2- ABC receiving at least their second line of therapy.
- Gedatolisib is the first inhibitor targeting the PI3K/AKT/mTOR pathway to demonstrate positive Phase 3 results in patients with HR+/HER2-/*PIK3CA* wild-type ABC whose disease progressed on or after treatment with a CDK4/6 inhibitor.

Sara Hurvitz, MD, Senior Vice President, Clinical Research Division, Fred Hutchinson Cancer Center, Professor and Head, Division of Hematology and Oncology, University of Washington, Department of Medicine and co-principal investigator for the trial

said: “Patients with HR-positive, HER2-negative, *PIK3CA* wild-type advanced breast cancer whose disease has progressed while on, or after, treatment with a CDK4/6 inhibitor typically derive limited benefit from subsequent endocrine-based therapy. The topline data for both gedatolisib regimens from VIKTORIA-1 are potentially practice-changing. To my knowledge, we have not seen Phase 3 results in patients with HR-positive, HER2-negative advanced breast cancer before where there was a quadrupling of the likelihood of survival without disease progression relative to the study control.”

Treatment discontinuation due to a treatment-related adverse event for the gedatolisib triplet and gedatolisib doublet was lower than was observed in Arm D of the Phase 1b trial in patients with ABC, and lower than observed in any Phase 3 trials for currently approved drug combinations in HR+/HER2- ABC. Additionally, the gedatolisib triplet and gedatolisib doublet were better tolerated than was observed in the Phase 1b trial in patients with ABC, including lower rates of hyperglycemia and stomatitis.

Igor Gorbatchevsky, MD, Chief Medical Officer of Celcuity said: “The topline data from VIKTORIA-1 demonstrate the potential for gedatolisib to become a transformative new medicine for the treatment of patients with HR-positive, HER2-negative, *PIK3CA* wild-type advanced breast cancer whose disease progressed on or after treatment with CDK4/6 inhibitors. The 7.3 and 5.4-months incremental improvement in median PFS relative to fulvestrant for the gedatolisib regimens are potentially paradigm shifting results. We are also very excited that treatment with gedatolisib combined with fulvestrant with or without palbociclib was well-tolerated by the VIKTORIA-1 patients and that only a few patients discontinued treatment due to an adverse event.”

Brian Sullivan, Chairman, Chief Executive Officer and co-founder of Celcuity said, “The efficacy improvement relative to the control that each of the gedatolisib regimens demonstrated was historic for this patient population. We are excited about the potential opportunity to provide a breakthrough therapeutic option for patients with HR-positive, HER2-negative, *PIK3CA* wild-type advanced breast cancer.”

Full data from the *PIK3CA* wild-type cohort of the VIKTORIA-1 clinical trial will be presented at an upcoming medical conference later this year. Celcuity expects to submit a New Drug Application for gedatolisib to the U.S. Food and Drug Administration in the fourth quarter of 2025. Topline data for the VIKTORIA-1 *PIK3CA* mutation cohort is expected by the end of 2025.

Webcast and Conference Call Information
The Celcuity management team will host a webcast/conference call on Monday, July 28, 2025, at 8:00 a.m. ET to discuss the topline results from the Phase 3 VIKTORIA-1 trial. Those who would like to participate may access the live webcast here, or register in advance for the teleconference here. A replay of the webcast will be available on the Celcuity website following the live event.

Notes

HR+/HER2- Breast cancer
Breast cancer is the second most common cancer and one of the leading causes of cancer-related deaths worldwide.[1] More than two million breast cancer cases were diagnosed globally in 2022.[1] While survival rates are high for those diagnosed with early breast cancer, only approximately 30% of patients who are diagnosed with or who progress to metastatic disease are expected to live five years after their diagnosis.[2] HR+/HER2- breast cancer is the most common subtype of breast cancer, accounting for approximately 70% of all breast cancers.[2]

Three interconnected signaling pathways, estrogen, cyclin D1-CDK4/6, and PI3K/AKT/mTOR (PAM), are primary oncogenic drivers of HR+, HER2- breast cancer.[3] Therapies inhibiting these pathways are approved and used in various combinations for advanced breast cancer. Currently approved inhibitors of the PAM pathway for breast cancer target a single PAM pathway component, such as PI3Kα, AKT, or mTORC1.[4,5,6,7] However, resistance to CDK4/6 inhibitors and current endocrine therapies develops in many patients with advanced disease.[8] Survival rates are low with 30% of patients anticipated to live beyond five years after diagnosis.[2] Optimizing the inhibition of the PAM pathway is an active area of focus for breast cancer research.

VIKTORIA-1
VIKTORIA-1 is a Phase 3 open-label, randomized clinical trial to evaluate the efficacy and safety of gedatolisib in combination with fulvestrant with or without palbociclib in adults with HR+/HER2- ABC whose disease progressed on or after prior CDK4/6 therapy in combination with an aromatase inhibitor. The clinical trial is enrolling subjects regardless of *PIK3CA* status while enabling separate evaluation of subjects according to their *PIK3CA* status. Subjects who meet eligibility criteria and do not have confirmed *PI3KCA* mutations (WT) were randomly assigned (1:1:1) to receive a regimen of either gedatolisib, palbociclib, and fulvestrant, gedatolisib and fulvestrant, or fulvestrant. Subjects who meet eligibility criteria and have confirmed *PI3KCA* mutations (MT) are randomly assigned (3:3:1) to receive a regimen of either the gedatolisib triplet, alpelisib and fulvestrant, or the gedatolisib doublet.

Gedatolisib
Gedatolisib is an investigational, multi-target PAM inhibitor that potently targets all four class I PI3K isoforms, mTORC1, and mTORC2 to induce comprehensive blockade of the PAM pathway.[9,10,11] As a multi-target PAM inhibitor, gedatolisib’s mechanism of action is highly differentiated from currently approved single-target inhibitors of the PAM pathway.[11] Inhibition of only a single PAM component gives tumors an escape mechanism through cross-activation of the uninhibited targets. Gedatolisib’s comprehensive PAM pathway inhibition ensures full suppression of PAM activity by eliminating adaptive resistance cross-activation

that occurs with single-target inhibitors. Unlike single-target inhibitors of the PAM pathway, gedatolisib has demonstrated equal potency and comparable cytotoxicity in *PIK3CA*-mutant and -wild-type breast tumor cells in nonclinical studies and early clinical data.[11,12]

About Celcuity
Celcuity is a clinical-stage biotechnology company pursuing development of targeted therapies for treatment of multiple solid tumor indications. The company's lead therapeutic candidate is gedatolisib, a potent, pan-PI3K and mTORC1/2 inhibitor that comprehensively blockades the PAM pathway. Its mechanism of action and pharmacokinetic properties are differentiated from other currently approved and investigational therapies that target PI3Kα, AKT, or mTORC1 alone or together. A Phase 3 clinical trial, VIKTORIA-1, evaluating gedatolisib in combination with fulvestrant with or without palbociclib in patients with HR+/HER2- advanced breast cancer is currently enrolling patients. A Phase 1/2 clinical trial, CELC-G-201, evaluating gedatolisib in combination with darolutamide in patients with metastatic castration resistant prostate cancer, is ongoing. A Phase 3 clinical trial, VIKTORIA-2, evaluating gedatolisib plus a CDK4/6 inhibitor and fulvestrant as first-line treatment for patients with HR+/HER2- advanced breast cancer is currently enrolling patients. More detailed information about Celcuity's active clinical trials can be found at ClinicalTrials.gov. Celcuity is headquartered in Minneapolis. Further information about Celcuity can be found at www.celcuity.com. Follow us on LinkedIn and X.

Forward-Looking Statements
This press release contains statements that constitute "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 including statements relating to the potential therapeutic benefits of gedatolisib; the size, design and timing of our clinical trials; our interpretation of topline clinical trial data; the ability of our data to support the filing of an NDA with the FDA; our expectations regarding the timing of and our ability to obtain FDA approval to commercialize gedatolisib; and other expectations with respect to gedatolisib. Words such as, but not limited to, "look forward to," "believe," "expect," "anticipate," "estimate," "intend," "confidence," "encouraged," "potential," "plan," "targets," "likely," "may," "will," "would," "should" and "could," and similar expressions or words identify forward-looking statements. The forward-looking statements included in this press release are based on management's current expectations and beliefs which are subject to a number of risks, uncertainties and factors, including that our topline results are based on a preliminary analysis of key efficacy and safety data, and such data may change following a more comprehensive review of the data related to the clinical trial; unforeseen delays in our planned NDA for gedatolisib; and our ability to obtain and maintain regulatory approvals to commercialize gedatolisib. In addition, all forward-looking statements are subject to other risks detailed in our Annual Report on Form 10-K for the year ended December 31, 2024, and our Quarterly Report on Form 10-Q for the quarter ended March 31, 2025, as such risks may be updated in our subsequent filings with the Securities and Exchange Commission. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. All forward-looking statements are qualified in their entirety by these cautionary statements, and we undertake no obligation to revise or update this press release to reflect events or circumstances after the date hereof.

References:

1. Sung H, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021;10.3322/caac.21660.
2. National Cancer Institute. Surveillance, Epidemiology and End Results Program (Accessed July 2025). https://seer.cancer.gov/statfacts/html/breast-subtypes.html
3. Alves, C. L., & Ditzel, H. J. Drugging the PI3K/AKT/mTOR Pathway in ER+ Breast Cancer. Int J Mol Sci, 2023;24(5),4522. https://doi.org/10.3390/ijms24054522
4. United States Package Insert, US FDA, ITOVEBI
5. United States Package Insert, US FDA, PIQRAY
6. United States Package Insert, US FDA, TRUCAP
7. United States Package Insert, US FDA, AFINITOR
8. Lloyd M R, et al. Mechanisms of Resistance to CDK4/6 Blockade in Advanced Hormone Receptor-positive, HER2-negative Breast Cancer and Emerging Therapeutic Opportunities. Clin Cancer Res. 2022;28(5):821-30
9. Venkatesan, A. M., et al. Bis(morpholino-1,3,5-triazine) derivatives: potent adenosine 5'-triphosphate competitive phosphatidylinositol-3-kinase/mammalian target of rapamycin inhibitors: discovery of compound 26 (PKI-587), a highly efficacious dual inhibitor. J Med Chem, 2010;53(6), 2636-2645. https://doi.org/10.1021/jm901830p
10. Mallon, R., et al. Antitumor efficacy of PKI-587, a highly potent dual PI3K/mTOR kinase inhibitor. Clin Cancer Res, 2011;17(10), 3193-3203. https://doi.org/10.1158/1078-0432.CCR-10-1694
11. Rossetti, S., et al. Gedatolisib shows superior potency and efficacy versus single-node PI3K/AKT/mTOR inhibitors in breast cancer models. NPJ Breast Cancer, 2024;10(1), 40. https://doi.org/10.1038/s41523-024-00648-0
12. Layman, R., et al. Gedatolisib in combination with palbociclib and endocrine therapy in women with hormone receptor-positive, HER2-negative advanced breast cancer: results from the dose expansion groups of an open-label, phase 1b study. Lancet Oncol, 2024;25(4), 474-487. https://doi.org/10.1016/S1470-2045(24)00034-2

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