

**Press Release**

For immediate release

**Æterna Zentaris Partner Keryx Reports a Statistically Significant Benefit in Survival from Updated Results of a Randomized, Double-Blind, Placebo-Controlled Phase 2 Study of Perifosine (KRX-0401) in the Treatment of Advanced Metastatic Colon Cancer**

**Data Reported at the 2010 ASCO GI Cancers Symposium Demonstrate a Statistically Significant Improvement in Both Time to Tumor Progression and Overall Survival in the Perifosine + Capecitabine Arm Versus Placebo + Capecitabine Arm**

**Québec City, Canada, January 25, 2010** – Æterna Zentaris Inc. (Nasdaq: AEZS; TSX: AEZ) (the “Company”), a late-stage drug development company specialized in oncology and endocrinology, today announced that its partner, Keryx Biopharmaceuticals (Nasdaq: KERX), presented updated results yesterday on the clinical activity of perifosine (KRX-0401), the Company's PI3K/Akt pathway inhibitor for cancer, in combination with capecitabine (Xeloda<sup>®</sup>) as a treatment for advanced, metastatic colon cancer. Abstract #447, entitled, “*Randomized Phase II study of perifosine in combination with capecitabine (P-CAP) versus capecitabine plus placebo (CAP) in patients with second- or third-line metastatic colon cancer (mCRC): Updated results*”, was presented yesterday in a poster during the 2010 American Society of Clinical Oncology (ASCO) Gastrointestinal Cancers Symposium, held in Orlando, Florida. Keryx is Æterna Zentaris’ partner and licensee for perifosine in the United States, Canada and Mexico. Perifosine is also out-licensed to Handok in South Korea while Æterna Zentaris retains rights for the rest of the world.

**Study Design**

In this randomized, double-blind, placebo-controlled study conducted at 11 centers across the United States, heavily pre-treated patients with second- or third-line metastatic colon cancer were randomized to receive capecitabine (a chemotherapy used in advanced metastatic colon cancer which is marketed by Roche as Xeloda<sup>®</sup>) at 825 mg/m<sup>2</sup> BID (total daily dose of 1,650 mg/m<sup>2</sup>) on days 1 – 14 every 21 days plus either perifosine or placebo at 50 mg daily. The study enrolled a total of 38 patients, 34 of which were third-line or greater. Of the 38 patients enrolled, 35 were evaluable for response (20 patients on the perifosine + capecitabine arm and 15 patients on the placebo + capecitabine arm). Three patients on the

placebo + capecitabine arm were not evaluable for response (2 patients were unevaluable due to toxicity (days 14, 46) and 1 was unevaluable due to a new malignancy on day 6). All patients in the perifosine + capecitabine arm were evaluable for response.

The patients in the study were heavily pre-treated, with the arms well-balanced in terms of prior treatment regimens. The median number of prior treatment regimens for all 38 patients was two, with prior treatment regimens for the P-CAP arm versus CAP arm shown in the table below. Notably, all of the patients (with the exception of one CAP arm patient) had been treated with FOLFIRI and/or FOLFOX, almost 80% treated with Avastin<sup>®</sup>, and half treated with an EGFR antibody:

Prior RX	P-CAP (n=20)	CAP (n=18)	All Patients (n=38)
FOLFIRI	18 (90%)	16 (89%)	34 (89%)
FOLFOX	15 (75%)	13 (72%)	28 (74%)
FOLFIRI & FOLFOX	13 (65%)	12 (67%)	25 (66%)
Avastin <sup>®</sup>	15 (75%)	15 (83%)	30 (79%)
EGFR Antibody (1)	9 (45%)	10 (56%)	19 (50%)
5-FU Refractory Status	14 (70%)	13 (72%)	27 (71%)
Third Line or >	18 (90%)	16 (89%)	34 (89%)

(1) Prior treatment with Erbitux<sup>®</sup> and/or Vectibix<sup>®</sup>

The primary endpoint of this study was to measure Time to Progression (TTP). Overall Response Rate (ORR), defined as Complete Responses (CR) + Partial Responses (PR) by RECIST, and Overall Survival (OS) were measured as secondary endpoints.

## Study Results

The P-CAP arm demonstrated a statistically significant advantage for TTP and OS, as well as for the percentage of patients achieving Stable Disease lasting 12 or more weeks (SD) or better, as compared to the CAP arm. The P-CAP arm demonstrated a greater than 60% improvement in OS, a more than doubling of median TTP, and almost a doubling of the percentage of patients achieving SD or better. In addition, the ORR was 20% (including one CR, and durable responses) in the P-CAP arm vs 7% in the CAP arm. The updated efficacy results for all evaluable patients are as follows:

Group	n	ORR % CR / PR (Duration of Response)	≥ SD (min 12 wks) n (%) p=0.036	Median TTP Weeks p=0.0012	Median OS* Months p=0.0136
P-CAP	20	20% 1 CR (34 mos - ongoing) 3 PR (21, 19, 11 mos)	15 (75%)	28 [95% CI (12-48)]	18 [95% CI (10.8-25.7)]
CAP	15	7% 1 PR (7 mos)	6 (40%)	11 [95% CI (9-15.9)]	11 [95% CI (5.3-16.9)]

\* Survival is calculated from date of randomization until the date of death from any cause, whether or not additional therapies were received after removal from treatment.

NOTE: Kaplan-Meier method used to calculate both TTP and OS. In addition, TTP and Progression Free Survival (PFS) are identical for all patients in the study.

Of notable interest, and for the first time presented, were data showing a highly statistically significant benefit in median OS (more than doubling) and TTP for the subset of patients who were refractory to a 5-FU (Fluorouracil) chemotherapy-based treatment regimen. 5-FU is a core component of the standard of care FOLFIRI and FOLFOX regimens, and capecitabine is a 5-FU pro-drug. These results are shown below:

Group	5-FU Ref n (%)	≥ SD (min 12 wks) n (%) p=0.066	Median TTP Weeks p=0.0004	Median OS Months p=0.0088
P-CAP	14 (70%)	1 PR / 8 SD (64%)	18 [95% CI (12-36)]	15.3 [95% CI (8.4-26)]
CAP	11 (73%)	0 PR / 3 SD (27%)	10 [95% CI (6.6-11)]	6.8 [95% CI (4.8-11.7)]

All 38 patients were evaluable for safety. The P-CAP combination was well-tolerated with Grade 3 and Grade 4 adverse events of > 10% incidence for P-CAP arm versus CAP arm as follows: anemia (15% vs. 0%), fatigue (0% vs. 11%), abdominal pain (5% vs. 11%) and hand-foot syndrome (30% vs. 0%). Of note, incidence of Grade 1 and Grade 2 hand-foot syndrome was similar in both the P-CAP and CAP arms (25% vs. 22%, respectively). Hand-foot syndrome is a reported adverse event with capecitabine monotherapy. Patients who remained on treatment longer in the Phase 2 study had a greater chance to develop hand-foot syndrome as illustrated by a median time to onset of Grade 3 and Grade 4 hand-foot syndrome in the P-CAP arm of 19 weeks.

Commenting on the data, Dr. Cathy Eng, Associate Medical Director for Colorectal Cancer at MD Anderson Cancer Center in Houston, Texas, stated, "This randomized Phase 2 trial demonstrates the very promising activity of perifosine (an oral AKT pathway inhibitor) for response, PFS, and OS in the care of previously treated, advanced colorectal cancer. Akt is downstream from the EGFR receptor and may have a role also in KRAS mutant tumor types. Preclinical data suggest that the Akt pathway inhibitors may be of benefit not only with chemotherapy but also in combination with other biologic agents. Perifosine is definitely worthy of further analysis and should be pursued in a Phase 3 trial in this indication."

Dr. Paulo Hoff, Professor of Medicine and Chairman of Medical Oncology at the University of Sao Paulo, Brazil and the lead investigator for the capecitabine (Xeloda<sup>®</sup>) Phase 3 approval study stated, "The data we see in this study for the capecitabine alone group is very much in line with expectation and, therefore, the combination data of perifosine plus capecitabine appears very compelling. It seems that the inhibition of Akt and other pathways by perifosine modulates the activity of capecitabine. What is of particular interest to me is the TTP and OS data for the 5-FU refractory patients, which holds great promise and I urge the Company to move forward into Phase 3."

Juergen Engel, Ph.D., President and CEO at Æterna Zentaris stated, "This is a very positive development to begin the Year 2010. We now have a lot of options to create value for our shareholders with our late-stage compounds in oncology, perifosine and AEZS-108, as well as in endocrinology with AEZS-130, thanks to the successful collaboration with our partner Keryx and the continuous interest of dedicated investigators. We now look forward to the further development of perifosine."

A copy of the abstract is available upon request.

## **About Colorectal Cancer**

According to the American Cancer Society, colorectal cancer is the third most common form of cancer diagnosed in the United States. It is estimated that over 146,100 people will be diagnosed with some form of colorectal cancer with over 49,000 patients dying from colorectal cancer in 2009. Surgery is often the main treatment for early stage colorectal cancer. When colorectal cancer metastasizes (spreads to other parts of the body such as the liver) chemotherapy is commonly used. Treatment of patients with recurrent or advanced colorectal cancer depends on the location of the disease. Chemotherapy regimens (i.e. FOLFOX or FOLFIRI either with or without bevacizumab) have been shown to increase survival rates with some stages of colorectal cancer. Currently, there are seven approved drugs for patients with metastatic colorectal cancer: 5-fluorouracil (5-FU), capecitabine (Xeloda<sup>®</sup>), irinotecan (Camptosar<sup>®</sup>), oxaliplatin (Eloxatin<sup>®</sup>), bevacizumab (Avastin<sup>®</sup>), cetuximab (Erbix<sup>®</sup>), and panitumumab (Vectibix<sup>®</sup>). Depending on the stage of the cancer, two or more of these types of treatment may be combined at the same time or used after one another. For example, FOLFOX combines 5-FU, leucovorin and oxaliplatin and FOLFIRI combines 5-FU, leucovorin and irinotecan. Avastin<sup>®</sup>, a VEGF monoclonal antibody inhibitor, is commonly administered together with FOLFIRI and FOLFOX. Typically, patients who fail FOLFIRI and/or FOLFOX (+ Avastin<sup>®</sup>) and who are considered EGFR-positive (non-mutated, wild-type KRAS status), receive the EGFR monoclonal antibody inhibitors Erbix<sup>®</sup> or Vectibix<sup>®</sup>. However, patients who continue to progress beyond these treatments have a poor prognosis.

## **About Perifosine (KRX-0401)**

Perifosine is a novel oral anticancer agent that modulates several key signal transduction pathways, including Akt, MAPK, and JNK that have been shown to be critical for the survival of cancer cells. Perifosine has demonstrated both safety and clinical efficacy in several tumor types, both as a single agent and in combination with novel therapies. Perifosine is currently in a Phase 3 trial, under Special Protocol Assessment (SPA), in multiple myeloma for which it has received Orphan Drug and Fast Track designations from the FDA in this indication. Perifosine is also in Phase 2 clinical trials for several other tumor types.

## **About Æterna Zentaris Inc.**

Æterna Zentaris Inc. is a late-stage drug development company specialized in oncology and endocrinology. News releases and additional information are available at [www.aezsinc.com](http://www.aezsinc.com).

## **Forward-Looking Statements**

This press release contains forward-looking statements made pursuant to the safe harbor provisions of the U.S. Securities Litigation Reform Act of 1995. Forward-looking statements involve known and unknown risks and uncertainties, which could cause the Company's actual results to differ materially from those in the forward-looking statements. Such risks and uncertainties include, among others, the availability of funds and resources to pursue R&D projects, the successful and timely completion of clinical studies, the ability of the Company to take advantage of business opportunities in the pharmaceutical industry, uncertainties related to

the regulatory process and general changes in economic conditions. Investors should consult the Company's quarterly and annual filings with the Canadian and U.S. securities commissions for additional information on risks and uncertainties relating to the forward-looking statements. Investors are cautioned not to rely on these forward-looking statements. The Company does not undertake to update these forward-looking statements. We disclaim any obligation to update any such factors or to publicly announce the result of any revisions to any of the forward-looking statements contained herein to reflect future results, events or developments except if we are required by a governmental authority or applicable law.

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