ABRAXANE® Plus Gemcitabine Improves Survival in Phase III Study of Patients with Advanced Pancreatic Cancer

MELBOURNE, Australia – January 23, 2013 – Australian biopharmaceutical company Specialised Therapeutics Australia announces that a phase III clinical trial of world leading breast cancer drug ABRAXANE® (nanoparticle albumin-bound paclitaxel) in combination with current standard of care gemcitabine in patients with advanced pancreatic cancer has demonstrated substantially improved survival times, with double the number of patients surviving two years.[1]

The MPACT (Metastatic Pancreatic Adenocarcinoma Clinical Trial) investigation involved 861 treatment naïve patients internationally.

Researchers found those patients treated with ABRAXANE plus gemcitabine had a statistically significant improvement in overall survival compared to patients receiving gemcitabine alone .[1]

Moreover, ABRAXANE plus gemcitabine demonstrated a 59% increase in one-year survival (35% vs. 22%, p=0.0002) and demonstrated double the rate of survival at two years (9% vs. 4%, p=0.02) as compared to gemcitabine alone.[1]

ABRAXANE plus gemcitabine also demonstrated statistically significant improvements in key secondary endpoints compared to gemcitabine alone, including a 31% reduction in the risk of progression or death with a median progression-free survival (PFS) of 5.5 vs. 3.7 months (HR 0.69, P=0.000024) and an overall response rate (ORR) of 23% compared to 7% (response rate ratio of 3.19, $p=1.1 \times 10^{-10}$). Another endpoint assessed included time to treatment failure, which was significantly improved with the ABRAXANE combination compared to gemcitabine alone .[1]

“The past few decades have brought us very few treatment advances for patients

with advanced pancreatic cancer, which is both deadly and incredibly difficult to treat with success," said Daniel D. Von Hoff, M.D., F.A.C.P., Lead Principal Investigator of the MPACT study and Chief Scientific Officer for Scottsdale Healthcare's Virginia G. Piper Cancer Centre Clinical Trials and Physician-In-Chief for TGen. "The fact that ABRAXANE plus gemcitabine demonstrated an overall survival benefit, and also did so at one and two years, is a significant step forward in offering potential new hope for our patients."

Professor John Zalcberg, Chief Medical Officer and Executive Director of Cancer Medicine at the Peter MacCallum Cancer Centre in Melbourne, said the evidence strongly supported using ABRAXANE in combination with gemcitabine as a new standard of care to treat appropriate patients, many of whom were not diagnosed until the disease was metastatic.

While acknowledging that this advance could not be seen as a cure for pancreatic cancer, Professor Zalcberg said the 59% increase in the number of patients who lived beyond 12 months was very encouraging.

"We are extremely encouraged by the results of this study involving ABRAXANE and regard this outcome as a significant breakthrough in terms of the future management of this disease," he said.
"In addition to treating women with metastatic breast cancer with ABRAXANE in the appropriate setting, we look forward to its approval in Australia for treating patients with advanced pancreatic cancer."

Specialised Therapeutics Australia (STA) Chief Executive Officer Mr Carlo Montagner said the positive data paved the way for Australian patients with advanced pancreatic cancer to access more effective treatment options.

He commented: "In Australia, pancreatic cancer is the fourth most common cause of death from cancer for both men and women2 and very few treatment options exist for this group of patients. We are extremely pleased to demonstrate that ABRAXANE is capable of prolonging survival for patients with advanced pancreatic cancer and we hope to have ABRAXANE approved by the Australian Therapeutic Goods Administration (TGA) in the latter half of 2014."

The most common grade ≥ 3 treatment-related adverse events in the study for ABRAXANE plus gemcitabine vs. gemcitabine alone were neutropenia (38% vs. 27%), fatigue (17% vs. 7%), and neuropathy (17% vs. 1%). In the ABRAXANE plus

gemcitabine arm, the median time to neuropathy improvement was 29 days. There was no difference in serious life threatening toxicity (4% in each arm).[1]

Further details of the study will be highlighted in a late-breaking oral presentation by Dr. Daniel D. Von Hoff:

Abstract: LBA #148: Final results of a randomized phase III study of weekly nab-paclitaxel plus gemcitabine versus gemcitabine alone in patients with metastatic adenocarcinoma of the pancreas. Friday, January 25th between 2:00 to 3:30 pm PST at the American Society of Clinical Oncology's (ASCO) 2013 Gastrointestinal Cancers Symposium in San Francisco, CA.

These results are from an investigational study. ABRAXANE is not approved for the treatment of advanced pancreatic cancer. Following TGA review and approval, STA will seek to have ABRAXANE included on the Pharmaceutical Benefits Scheme (PBS) for the reimbursement of ABRAXANE for advanced pancreatic cancer.

About the MPACT Study[1]

In the MPACT (**M**etastatic **P**ancreatic **A**denocarcinoma **C**linical **T**rial) study, a Celgene-sponsored, open-label, randomised, international study of 861 patients with metastatic pancreatic cancer were randomised to receive either ABRAXANE plus gemcitabine (125 mg/m^2 followed by 1000 mg/m^2 gemcitabine for 3 weeks followed by a week of rest) or gemcitabine alone (1000 mg/m^2 administered weekly for 7 weeks followed by a week of rest followed by cycles of weekly administration for 3 weeks followed by one week of rest).

The primary endpoint for the study is improvement in overall survival. Secondary endpoints were progression-free survival, and overall response rate determined by independent radiological review. Other endpoints included progression-free survival, overall response rate determined by investigator and the safety and tolerability of this combination in this patient population.

About Advanced Pancreatic Cancer

Advanced pancreatic cancer is a difficult-to-treat cancer with the lowest survival rates among all cancer types. Across all patients with pancreatic cancer, relative 5-year survival is 6% and is less than 2% for those with advanced disease. There are two main types of pancreatic cancer – adenocarcinomas, which accounts for approximately 90% of all pancreatic cancer, and neuroendocrine tumors. Pancreatic cancer is relatively uncommon with new cases accounting for only 2.1% of all newly diagnosed cancers. However, pancreatic cancer is the fourth most common cause of cancer death for men and women in the United States and Australia, and the ninth most commonly diagnosed cancer in Australia.[2]

About ABRAXANE®

ABRAXANE is a solvent-free, nanoparticle chemotherapy treatment option for metastatic breast cancer.[3] In Australia, ABRAXANE is currently listed on the PBS for the treatment of metastatic breast cancer and HER2 positive breast cancer in combination with trastuzumab.

ABRAXANE is approved for metastatic breast cancer in over 40 countries including the U.S., Canada, European Union, Japan and China, and more than 500,000 cancer patients have received ABRAXANE therapy in the past five years.

In Australia, ABRAXANE has been granted orphan drug designation by the Therapeutic Goods Administration for the treatment of pancreatic cancer. Orphan drug status is granted to drugs used to treat relatively rare diseases such as pancreatic cancer and may allow for priority evaluation by the TGA.

ABRAXANE is currently in various stages of investigation for the treatment of the following cancers: metastatic melanoma, bladder, ovarian, and expanded applications for breast cancer.

Developed using the proprietary *nab*™ technology platform, ABRAXANE is a nanoparticle protein-bound chemotherapy agent. ABRAXANE combines paclitaxel with albumin, a naturally-occurring human protein, to deliver the drug and

eliminates the need for solvents in the administration process. Nanoparticle technology allows ABRAXANE to deliver a 49% higher dose compared to regular solvent-based paclitaxel without compromising safety and tolerability.[3-4]

In a randomised phase III study of metastatic breast cancer patients, ABRAXANE demonstrated nearly double the overall tumour response rate compared to solvent-based paclitaxel. [3-4]

Anthracycline pre-treated patients in the study lived significantly longer.[5] The tolerability with ABRAXANE and solvent-based paclitaxel was comparable, despite the 49% greater dose of paclitaxel administered as ABRAXANE.[3-4] Neutropenia was lower with ABRAXANE compared to solvent-based paclitaxel, although there was an increase in incidence of grade 3 peripheral neuropathy with ABRAXANE. However the median time to improvement, from grade 3 peripheral neuropathy to grade 2 or lower, was 22 days. No adverse events were reported that were not already known for paclitaxel.[3-4]

Contraindications and side effects[3]:

Like all medications, ABRAXANE may cause side effects.
ABRAXANE should not be used in patients who have baseline neutrophil counts of $<1.5 \times 10^9$ /L.
In patients who have exhibited hypersensitivity reactions to paclitaxel or albumin, patients should not be treated with ABRAXANE.

ABRAXANE is contraindicated during pregnancy and lactation.

Most common side effects (≥1/10) caused by ABRAXANE include; neutropenia, anemia, leucopenia, thrombocytopenia, lymphophenia, anorexia, peripheral neuropathy, hypoaesthesia, paraethesia, nausea, diarrhoea, vomiting, constipation, stomatitis, alopecia, rash, arthralgia, myalgia, fatigue, asthenia, pyrexia.

For further information regarding ABRAXANE and potential side effects, physicians should review the ABRAXANE Product Information and patients should

consult their oncologist or the ABRAXANE Consumer Medicine Information available on www.specialisedtherapeutics.com.au.

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About Specialised Therapeutics Australia, Pty Ltd

Specialised Therapeutics Australia Pty Ltd (STA) is a biopharmaceutical company dedicated to working with leading pharmaceutical companies worldwide to provide acute care therapies for high unmet medical needs to people living in Australia and New Zealand.

Currently STA markets two world leading cancer and cancer supportive care therapies, ABRAXANE® (nab-paclitaxel) and ALOXI® (palonosetron HCl) respectively, and has recently licensed two new agents from the Helsinn Group. Firstly Anamorelin, which is a novel ghrelin receptor agonist for the treatment of anorexia-cachexia in NSCLC, and a fixed-dose combination product (in both oral and intravenous forms) containing netupitant, a neurokinin-1 (NK1) receptor antagonist, combined with Aloxi, a serotonin-3 (5-HT_3) receptor antagonist. STA also has interests in the therapeutic areas of anti-infectives with the rights to commercialise DIFICID® (fidaxomicin) for the treatment of Clostridium difficile infections, respiratory, dermatology, endocrinology and central nervous system (CNS). Additional information can be found at www.specialisedtherapeutics.com.au

- ABRAXANE plus gemcitabine demonstrated highly statistically significant and clinically meaningful results across primary and key secondary endpoints and patient subgroups
- ABRAXANE plus gemcitabine patients showed 59% higher chance of survival at one year; survival rates doubled at two years
- A new standard of care for patients with advanced pancreatic cancer
- Oral Presentation Scheduled for Friday, January 25th at ASCO’s Gastrointestinal Cancers Symposium Annual Meeting

References:

1. Von Hoff DD et al. Abstract: LBA #148: Final results of a randomized phase III study of weekly nab-paclitaxel plus gemcitabine versus gemcitabine alone in patients with metastatic adenocarcinoma of the pancreas. ASCO GI 2013

2. Cancer in Australia. An Overview 2012. Australian Institute of Health and Welfare (AIHW)

3. Abraxane Product Information

4. Gradishar WJ et al. J Clinical Oncology 2005;23:7794-7803

5. Vukelja SJ et al. ASCO 2008, Abstract 1082