



## ASX AND MEDIA RELEASE

### **Enrolment complete in US phase II AK trial; Results of pilot skin cancer trial**

**BRISBANE, Australia, 9 March 2007**

#### **Completion of enrolment in US phase II AK clinical trial: PEP005-006**

**Peplin Limited** (ASX:PEP) today announced the completion of enrolment of its 200 patient US based phase IIb clinical trial (PEP005-006), in actinic (solar) keratosis (AK). This study is being conducted under Peplin's open IND with FDA.

The study is designed to further evaluate the safety and efficacy of PEP005 Topical, Peplin's proprietary product candidate, when self-applied by patients to AK lesions within an area of sun damaged skin, in line with the expected use of the product following approval. Peplin expects to announce the preliminary results of this trial in July 2007.

Peplin Chief Executive Officer Michael Aldridge said he was very pleased with the progress of Peplin's lead product development program which was on track for its target milestones, in particular the start of phase III clinical trials in the US and Australia later this year.

"We announced in early February that we had enrolled 103 of the target 200 patients in this study," Mr Aldridge said. "With all investigator centres fully on stream, we have enrolled the balance in just five weeks. The US infrastructure we have established to conduct this trial positions us well for the rapid recruitment and completion of our phase III clinical program for this product in AK which we expect to initiate by the end of 2007."

#### **Results of Australian pilot skin cancer clinical trial: PEP005-008**

**Peplin Limited** (ASX:PEP) today also announced results from its Australian pilot clinical trial (PEP005-008) of its proprietary drug PEP005 Topical in squamous cell carcinoma *in situ* (SCCIS), a non-invasive form of squamous cell carcinoma, a form of skin cancer.

The goals of this clinical trial were to evaluate the safety and efficacy of PEP005 Topical (at a concentration of 0.05%) when applied once a day on two consecutive days in the treatment of SCCIS.

In this trial, PEP005 Topical demonstrated a favourable safety profile and was well tolerated. There were no drug related serious adverse events. The majority of local skin responses were graded mild and resolved spontaneously, typically within one month of treatment. These results are consistent with the safety profile previously reported in clinical trials of PEP005 Topical to treat superficial and nodular forms of basal cell carcinoma (BCC).

Efficacy was measured by tumour clearance rates. Application of PEP005 Topical on two consecutive days resulted in an overall histological clearance of 36% of SCCIS tumours and clinical clearance of 64% of SCCIS tumours.

The observed favourable safety profile of two days treatment at 0.05%, the concentration used in this study and the highest concentration used in earlier studies, gives Peplin confidence that it could explore the activity of PEP005 Topical in the treatment of non-melanoma skin cancer at a higher concentration.

Peplin has developed a dose escalation strategy to optimize the dosing of PEP005 Topical to potentially deliver higher tumour clearance rates. Peplin has recently initiated a US clinical trial (PEP005-009) which will assess several dose levels of PEP005, using a dose escalation format. This trial has the goal of optimising the dose of PEP005 Topical for the treatment of superficial basal cell carcinoma (sBCC). The 009 trial is expected to define the maximum tolerated dose (MTD) of PEP005 Topical gel when applied to a sBCC either with one application or two applications of drug, one week apart. It is being conducted under Peplin's open IND application with FDA.

Mr Aldridge said he was pleased to have again clearly demonstrated that PEP005 Topical can clear skin cancers quickly and effectively, using a short course of treatment and with an attractive side effect profile.

“The safety profile we have again demonstrated in this study supports our recently initiated dose escalation strategy for treating superficial basal cell carcinoma in which we anticipate taking the concentration of PEP005 Topical higher with a goal of achieving higher clearance rates.”

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**Details of the PEP005-006 clinical trial are set out below**

The clinical trial (PEP005-006) is a multi-centre, randomised, double-blind, double-dummy, vehicle-controlled study to determine the safety and efficacy of PEP005 Topical gel in patients with actinic keratosis lesions.

Treatment with PEP005 Topical gel at 0.025%, 0.05% or vehicle gel is on either two or three consecutive days. The first day's treatment is applied by the patient in the physicians office with subsequent treatments being applied by the patient at home. Drug is applied to a 25 cm<sup>2</sup> contiguous area containing 4 to 8 typical AK lesions on the arm, shoulder, chest, back or scalp.

The study is being conducted under Peplin's open IND with the US Food and Drug Administration (FDA). The trial objectives are to:

1. evaluate the safety and tolerability of PEP005 Topical gel; and
2. to evaluate the efficacy of PEP005 Topical gel.

The three measures of efficacy comprise:

- *Complete AK lesion clearance rate* defined as the proportion of patients at the day 57 post treatment visit with no clinically visible AK lesions in the treatment area
- *Baseline AK lesion clearance rate* defined as the proportion of patients at the day 57 post treatment visit with 100% reduction in the number of AK lesions identified at baseline in the treatment area
- *Partial clearance rate* defined as the proportion of patients at the day 57 post treatment visit with a 75% or greater reduction in the number of AK lesions identified at baseline in the treatment area

The study has completed enrolment.

**Details of the PEP005-008 clinical trial are set out below**

The clinical trial (PEP005-008) is a multi-centre, open-label, study to determine the safety and efficacy of PEP005 Topical gel at a single concentration of 0.05%, applied once daily for two consecutive days to patients with cutaneous squamous cell carcinoma *in situ* (SCCIS, Bowen's Disease) with either a 2 month (Day 57) or 3 month (Day 85) follow-up.

The study was initiated in May 2006.

**Description of trial subjects**

There were 25 subjects enrolled and treated with PEP005 Topical gel.

Study subjects were of either gender and at least 18 years old (excluding women of child bearing potential) with a biopsy confirmed SCCIS tumour located on the body, excluding the scalp, digits, lips, hands, feet or ano-genital region. Mean tumour diameter was 12.8 millimetres. All subjects were Caucasian and the majority of subjects had Fitzpatrick skin types that burn easily and tan rarely or minimally.

**Treatment method**

Study drug in the amount of 12, 25 or 40 micro litres (depending on tumour size) was applied to the SCCIS tumour once daily on the two treatment days and subjects were then followed for 57 or 85 days.

**Results**

The preliminary results relating to the objectives of the study are presented below.

**Safety:** 0.05% PEP005 Topical gel was safe and well tolerated. There were no drug related serious adverse events reported. All local skin responses had resolved by end of study.

Local skin responses over and above a pre-treatment base line were assessed by the investigator and graded as mild, moderate or severe. The most frequently reported local skin

responses were erythema, desquamation and swelling and the majority were mild. All local skin responses were expected and had been predicted based on the drug's mechanism of action. All but three subjects completed the two day course of therapy.

Local skin responses typically resolved within four weeks.

**Efficacy:** The primary evaluation of efficacy is the histological clearance rate as confirmed by complete excision of the tumour site at the end of the study (Day 57 or Day 85) and histological confirmation of absence of tumour tissue. 36% of tumours (n=9) were histologically cleared. A secondary evaluation of efficacy was clinical assessment of tumour clearance. 64% of tumours (n=16) were clinically cleared. Of the 22 patients that completed the two day course of therapy, 31.8% (n=7) were histologically cleared and 68.2% (n=15) were clinically cleared.

### **Implications**

The results of this trial confirm Peplin's expectations for PEP005 Topical's safety. The data obtained from this study are consistent with previously reported studies which evaluated PEP005 Topical for the treatment of superficial and nodular forms of basal cell carcinoma. Peplin believes these data are further evidence of the favourable safety profile for PEP005 Topical in the treatment of non-melanoma forms of skin cancer (basal cell and squamous cell carcinomas).

The observed favourable safety profile of two days treatment at 0.05%, the concentration used in this study and the highest concentration used in earlier studies, gives Peplin confidence that it could explore the activity of PEP005 Topical in the treatment of non-melanoma skin cancer at a higher concentration.

Peplin has developed a dose escalation strategy to optimize the dosing of PEP005 Topical to potentially deliver higher tumour clearance rates. Peplin has recently initiated a US clinical trial (PEP005-009) which will assess several dose levels of PEP005, using a dose escalation format. This trial has the goal of optimising the dose of PEP005 Topical for the treatment of superficial basal cell carcinoma (sBCC). The 009 trial is expected to define the maximum tolerated dose (MTD) of PEP005 Topical gel when applied to a sBCC either with one application or two applications of drug, one week apart. It is being conducted under Peplin's open IND application with FDA.

Peplin believes SCC and BCC are malignant tissue and require the careful intervention of a trained clinician. Accordingly Peplin intends to develop PEP005 Topical for non melanoma skin cancer as a clinician applied prescription therapeutic product. Conversely actinic (solar) keratosis is a pre-cancerous lesion and Peplin expects to develop PEP005 Topical for AK as a convenient patient applied take home prescription medication.

### **ABOUT PEPLIN**

Peplin is focused on the development and commercialisation of medical dermatology products and in particular a novel topical product to treat skin cancer and pre-cancerous lesions. Peplin's lead compound is PEP005, the first in a new class of investigational agents. Peplin's lead product has shown significant promise in phase II clinical trials for the treatment of actinic (solar) keratosis (AK), a very common pre-cancerous lesion and basal cell carcinoma (BCC), the most common form of skin cancer. Peplin believes the unique benefits of its lead product may include a very short course of therapy and a transient and favourable side effect profile. Peplin's product development activities are supported by the Australian Federal Government under its Pharmaceuticals Partnerships Program.

Peplin's earlier stage pipeline is targeted at leukemia (a blood borne cancer) using its lead compound PEP005 in an intravenous formulation (PEP005 IV) and bladder cancer using an intracavitary or intravesical formulation (PEP005 IC). PEP005 has demonstrated selective and potent anti-leukemia activity in pre-clinical disease models. PEP005 induces apoptosis in leukemia cells via the activation of PKC delta. Peplin holds global proprietary rights for PEP005 and related molecules.

### **ABOUT ACTINIC KERATOSIS**

AK is a common skin condition characterised by rough, red, scaly patches, crusts or sores on the top layer of skin. If left untreated AKs can progress to squamous cell carcinoma, an invasive skin cancer that can be fatal. AKs usually develop on the face, lips, ears, scalp, neck, forearms and back of hands - areas that are most commonly exposed to the sun.

AKs are the most common pre-cancerous skin lesions worldwide affecting 50% of Caucasians over the age of 40 years with the average patient having 6-8 lesions. The treatment of AKs is the most common dermatologic procedure performed in the out-patient setting. Based on a 2005 study by The Lewin Group, Inc. for The Society for Investigative Dermatology and The American Academy of Dermatology Association, in the US there were 8.2 million treatments of AK in 2004. According to this study 58 million Americans have AK. The cost to the US healthcare system of treating AK is US\$1.2 billion annually. The worldwide prevalence of AK is highest in Australia.

Current treatment alternatives comprise surgical techniques (primarily cryotherapy) and topical medications (e.g. 5-fluorouracil, imiquimod and diclofenac). Current treatment approaches can cause scarring and hypopigmentation at the treatment site, can be inconvenient or may require long treatment duration for effect.

### **ABOUT SKIN CANCER**

Skin cancer encompasses a number of diseases, including basal cell carcinoma (BCC), squamous cell carcinoma (SCC) and melanoma. BCC is the most common form of skin cancer, representing about 80% of all skin cancers. SCCs represent approximately 16%, while melanoma a further 4%. BCCs and SCCs together are referred to as non-melanoma skin cancer and typically develop on sun exposed parts of the body and are more prevalent in older Caucasians with a history of sun exposure.

Based on a 2005 study by The Lewin Group, Inc. for The Society for Investigative Dermatology and The American Academy of Dermatology Association, there are approximately 1.2 million new cases of non-melanoma skin cancer diagnosed every year of which 200,000 are new cases of SCC, of which 1,300-2,300 will result in fatality. The cost to the US healthcare system of treating non-melanoma skin cancer is US\$1.4 billion annually.

The worldwide prevalence of skin cancer is highest in Australia where it accounts for 80% of all new cancer cases diagnosed here each year. According to the Cancer Council of Australia 256,000 Australians were treated for BCC in 2002. Together, basal cell and squamous cell carcinoma are the most costly cancers in Australia, accounting for \$232 million in treatment costs per year.