



## ASX AND MEDIA RELEASE

### Peplin's Positive Phase IIb AK Trial Result Details

- **Advancement to Phase III development:** Short treatment course of three days and 0.015% concentration planned for actinic (solar) keratosis lesions on the face and scalp in Phase III trials
- **Trial Results:**
  - Median reduction in overall lesion count of 84.5% and total clearance rate of 50.0%
  - Local skin responses to drug peaked at Day 4 and returned to pre-treatment levels by Day 15

**EMERYVILLE, California and BRISBANE, Australia, 6 March 2009 Peplin, Inc.** (ASX:PLI) today announced further results of its Phase IIb actinic (solar) keratosis (AK) Australian and US trial for lesions on the head, which comprise face and scalp, and the selection of a Phase III dose for its lead product candidate PEP005 (ingenol mebutate) Gel.

Based on positive results from the Phase IIb AK trial (PEP005-015), a 0.015% concentration of PEP005 (ingenol mebutate) Gel applied once daily for three consecutive days is planned to advance to Phase III development. This concentration and dosing regimen provided a median reduction in overall lesion count of 84.5%, a total clearance rate in the intent to treat population equal to 50.0% (p-value = <0.001) and a partial clearance rate of 71.9% (p-value = <0.001). The local skin responses (LSRs) peaked at Day 4 and returned to baseline by Day 15 for all treatment groups.

AK is a common pre-cancerous skin condition caused by sun exposure. The face is the most common area for sun damage and the most common area for AKs, which can develop into skin cancers if left untreated.

Tom Wiggins, Chairman and CEO, said, "This comprehensive analysis of our trial provides additional support for the potential of PEP005 Gel to help physicians and patients dissatisfied with the current AK treatment options. No current product on the market has a short course of therapy as well as proven safety and efficacy for both head and non-head lesions. The potential value that PEP005 Gel offers patients is considerable."

Assuming a successful End-of-Phase II meeting with the U.S. Food and Drug Administration (FDA) on May 20, 2009, Peplin plans to use this dosing regimen to initiate subsequent Phase III clinical trials for patients with AK lesions on the head in the second quarter of 2009. Peplin recently completed enrolment in its first Phase III trial, REGION-I, for PEP005 Gel for AK lesions on non-head locations. REGION-I is

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being conducted under a Special Protocol Assessment with the FDA with results expected in the first half of 2009.

### **PEP005-015 Trial Details**

**Design and treatment method:** PEP005-015 was an eight-arm, 240-patient, US and Australian multi-centre, randomised, double-blind, vehicle-controlled, dose-ranging clinical trial. It was designed to evaluate the safety and efficacy of each of three concentrations (0.005%, 0.010% or 0.015%) and two treatment regimens (once a day for two or three consecutive days) for Peplin's patented product, PEP005 Gel in patients with AK lesions on the head (face and scalp). Patients were centrally randomised to treatment and stratified across treatment groups based on treatment area location (face or scalp). Enrolment was controlled so that approximately 20% of patients were treated on the scalp and approximately 80% of the patients were treated on the face. This field-directed therapy was applied to a 25 cm<sup>2</sup> contiguous AK treatment area containing four to eight clinically typical AK lesions.

**Evaluation criteria:** This Phase IIb trial aimed to evaluate the safety and efficacy of Peplin's proprietary product, PEP005 (ingenol mebutate) Gel, in patients with AK lesions on the head. The primary efficacy objective was *complete clearance* of AK lesions. *Complete clearance* was defined as the proportion of patients at the Day 57 visit with no clinically visible AK lesions in the selected treatment area.

The secondary objective was *partial clearance* of AK lesions. *Partial clearance* was defined as the proportion of patients at the Day 57 visit with a 75% or greater reduction in the number of AK lesions identified at Baseline in the selected treatment area.

The primary safety evaluation included:

- Incidence of adverse events (AEs) and serious adverse events (SAEs) recorded throughout the study
- Incidence and grade of local skin responses (LSRs), and changes in pigmentation and scarring following study medication application
- Dosing compliance/tolerance defined as the proportion of patients completing the assigned treatment regimen (2 or 3 day treatment)

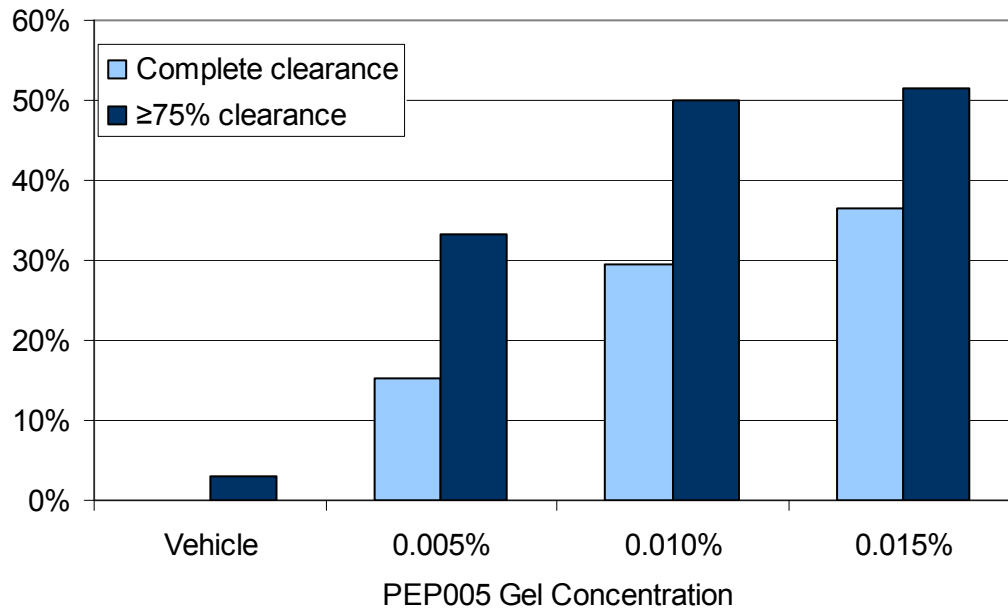
**Patients:** A total of 265 patients were randomised into the study and included in the intent to treat (ITT) population. 264 patients received at least one application of study medication and were included in the safety population. Fifteen patients were excluded from per protocol efficacy analyses, leaving 250 patients to be included in the per protocol population.

The majority of patients in this study were male and all patients enrolled were Caucasian. There were no apparent differences among treatment groups with respect to age, gender, time since AK diagnosis, baseline lesion counts or extent of lesions on the face or scalp.

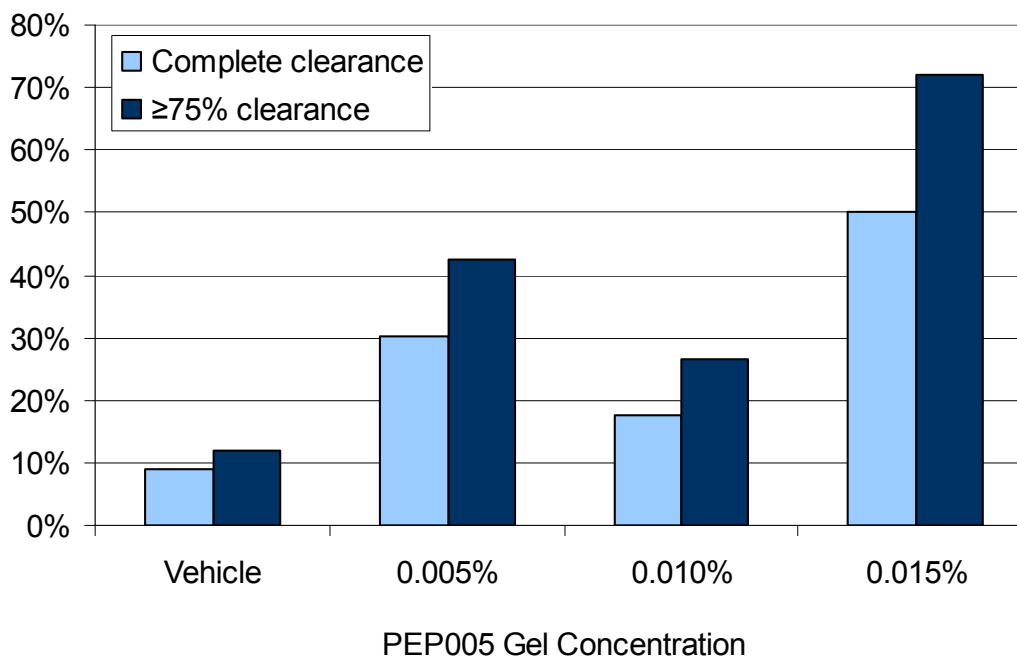
### **PEP005-015 Results**

**Efficacy:** A 0.015% concentration of PEP005 (ingenol mebutate) Gel applied once daily for three consecutive days (selected dose) resulted in a total clearance rate in the intent to treat population equal to 50.0% (p-value=<0.001) and a partial clearance rate of 71.9% (p-value= <0.001). The selected dose provided a median reduction in overall lesion count of 84.5%.

**FIGURE 1: Two-Day Clearance Rates – Intent to Treat Population**



**FIGURE 2: Three-Day Clearance Rates – Intent to Treat Population**



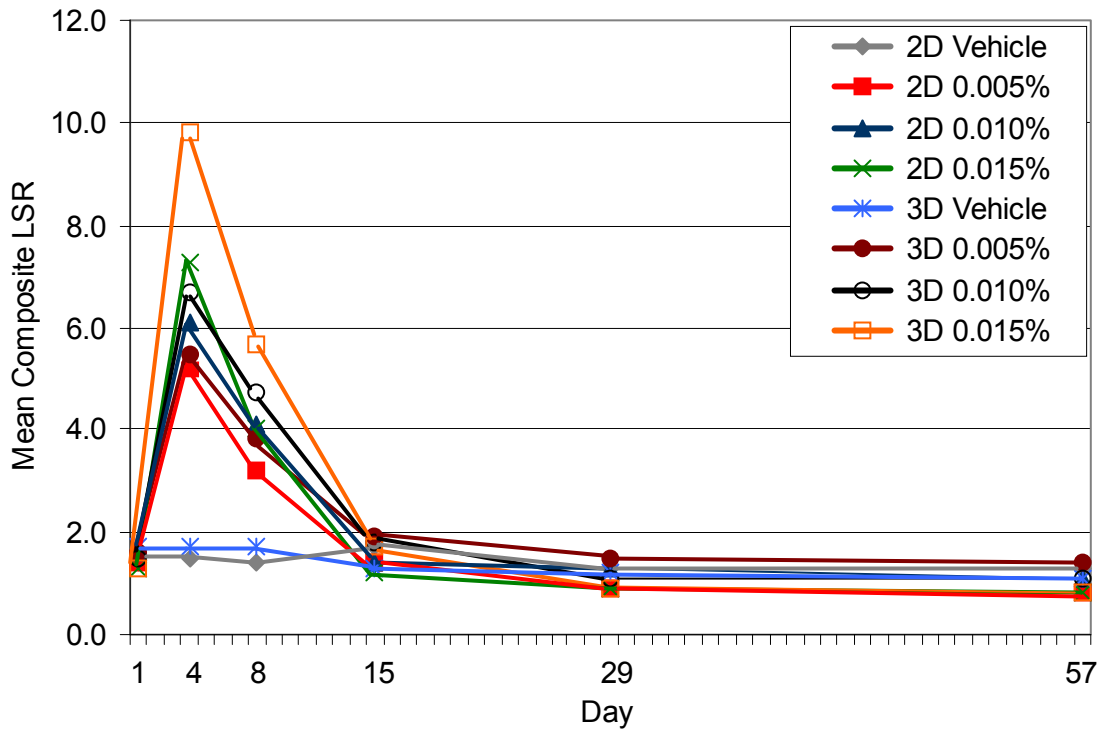
**Safety:** The drug suggested a favourable profile. There were no treatment-related SAEs, and AEs were generally mild to moderate in severity and resolved by Day 57. The most common treatment-related AEs, occurring within the treatment area, appeared to be application site irritation and pruritus. Other treatment-related AEs included peri-orbital swelling or swelling around the eye/eyelids, adjacent to the treatment area. In all cases, the treatment-related events resolved without further sequelae.

The local skin responses (LSRs) assessed in this study are as follows:

- erythema
- flaking/scaling
- crusting
- swelling
- vesiculation/pustulation
- erosion/ulceration

Each response was evaluated on a scale of 0 - 4 and then the mean composite score across responses is calculated.

**FIGURE 3: Composite Local Skin Response**



Pigmentation and Scarring: Thirty-nine patients showed an improvement in hyperpigmentation and nineteen showed improvement in hypopigmentation. Three patients reported a mild increase in hyperpigmentation and seven patients reported a mild increase in hypopigmentation. In addition, three patients reporting changes in scarring were all improved compared to the baseline assessments.

**Further information:**

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## **ABOUT PEPLIN**

Peplin is a development stage specialty pharmaceutical company focused on advancing and commercialising innovative medical dermatology products. Peplin is currently developing PEP005 (ingenol mebutate), which is the first in a new class of compounds and which is derived from the sap of *Euphorbia peplus*, or *E. peplus*, a rapidly growing, readily available plant commonly referred to as petty spurge or radium weed. *E. peplus* has a long history of traditional use for a variety of conditions, including the topical self-treatment of various skin disorders, including skin cancer and pre-cancerous skin lesions. Peplin's lead product candidate is a patient-applied topical gel containing ingenol mebutate, a compound the use of which Peplin has patented for the treatment of actinic (solar) keratosis, or AK. This product candidate is currently in Phase III clinical trials (trial known as REGION-I) and is referred to as PEP005 (ingenol mebutate) Gel.

## **ABOUT AK**

Actinic keratoses (AK), also known as solar keratosis or sun spots, is generally considered the most common pre-cancerous skin condition. AK usually appears as small, rough, scaly areas on the face, lips, ears, back of hands, forearms, scalp or neck. If left untreated, AK lesions may progress to a form of skin cancer called squamous cell carcinoma, or SCC. The Lewin Group, Inc., estimates that the total direct costs for AK in the United States was \$1.2 billion in 2004, and in 2002 there were approximately 8.2 million office visits for the treatment of AK. The Lewin Group also estimated that there were 58 million people in the United States living with AK in 2004. According to a May 2006 issue of *The Journal of Family Practice*, in northern hemisphere populations, 11% to 25% of adults have at least one AK lesion, compared with 40% to 60% of adults in Australia, which has the highest prevalence of AK worldwide.

## **FORWARD LOOKING STATEMENTS**

This press release contains "forward-looking statements" as defined under U.S. federal securities laws, including, but not limited to, Peplin's clinical development plan and timing of clinical trials referred to herein. These forward-looking statements can be identified through the use of words such as "anticipates," "expects," "intends," "plans," "believes," "seeks," "estimates," "may," "will," and variations of these words or similar expressions. Forward looking statements are based on management's current, preliminary expectations and actual results could differ materially as a result of various risks and uncertainties, including, but not limited to, delays in the completion of clinical trials resulting from, among other things, ambiguous or negative interim results, unforeseen safety issues, failure to conduct the clinical trials in accordance with regulatory requirements or clinical protocols, suspension or termination of a clinical trial by the FDA or other regulatory authorities, lack of adequate funding to continue a clinical trial and other important factors disclosed from time to time in Peplin's disclosures to the ASX. Forward-looking statements speak only as of the date they were made. No undue reliance should be placed on any forward-looking statements. Such information is subject to change, and we undertake no obligation to update such statements.