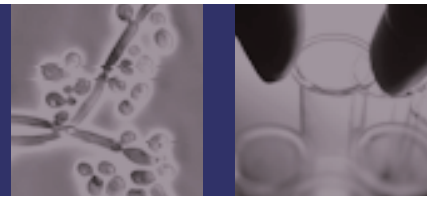


# PAC-113

## NOVEL ANTI-FUNGAL FOR IMMUNOCOMPROMISED PATIENTS



### MEDICAL NEED FOR NEW & EFFECTIVE ANTI-FUNGAL

PAC-113, an anti-fungal for the treatment of oral Candidiasis infections, completed a Phase IIb clinical program in mid 2008.

Opportunistic growth of *Candida* occurs in people with defective immune systems, or as a result of salivary dysfunction, and can be life-threatening if not treated. *Candida albicans* is the most common fungal pathogen among immune-compromised, hospitalized patients, accounting for roughly 50-60% of all bloodstream fungal isolates. Localized *Candida* infections, if untreated, can spread from the primary site of infection through the blood stream to cause a disseminated infection. Disseminated fungal infections are associated with a high mortality rate.

Current treatments for *Candida* infections are either only marginally efficacious, have poor patient compliance characteristics, can cause serious side effects, can lead to drug-resistance and/or have multiple drug interaction issues.

Nystatin  
Topical  
Modest efficacy  
Poor Palatability

Azoles  
Systemic/Topical  
Potential for resistance  
Drug interactions

Amphotericin B  
Systemic  
Severe side effects

### PAC-113 HAS A NOVEL MECHANISM OF ACTION

PAC-113 is a 12 amino-acid antimicrobial peptide derived from a naturally occurring histatin protein found in saliva. *In vitro* studies demonstrate that it has potent anti-fungal activity against the *Candida albicans*, including drug-resistant HIV patient isolates.

#### Modes of action:

1. PAC-113 is an amphipathic molecule that interacts with fungal cell membranes, altering permeability which causes cytoplasmic leakage and cell death.
2. PAC-113 also interacts with fungal mitochondria causing production of reactive oxygen species and fungal cell destruction. This activity is unique to histatin proteins.

In addition, PAC-113 is active against growing cells, stationary phase cells and fungal biofilms. Rapid fungal lysis of fungal cells in a wide range of growth states may affect a more rapid and complete clinical cure.

### PAC-113 HAS SUPERIOR PATIENT COMPLIANCE CHARACTERISTICS

The PAC-113 formulation is a sugar-free, pleasant tasting, non-viscous aqueous solution with a neutral pH. The prolonged half-life of PAC-113 in the saliva has the potential to extend the duration of the therapeutic effect.

### POSITIVE RESULTS

Pacgen recently reported positive proof of efficacy results from its Phase IIb trial of PAC-113 in the treatment of oral Candidiasis.

The Phase IIb clinical trial, which involved over 200 seropositive HIV patients, demonstrated that PAC-113 efficacy profile compares favorably to the efficacy of Nystatin, a current standard of care for topical treatment of oral Candidiasis.

### SOLID MARKET OPPORTUNITY

Pacgen estimates that the current worldwide market opportunity for a novel, safe and effective, oral Candidiasis therapy is US \$250 million.

In 2004, global sales of topical anti-fungal drugs represented nearly a US \$1.6 billion dollar market. The market for antifungal is projected to grow to US \$2.1 billion by 2009.

The growth of this market and demand for effective anti-fungals is driven by a rising incidence of immunocompromised patients populations including individuals with HIV, cancer, asthma and diabetes, among others.

## HIGH POTENCY ANTI-FUNGAL

PAC-113 has a Minimum Inhibitory Concentration (MIC) of 1.6 - 4.0 µg/ml against *Candida* spp. (vs fluconazole MIC of 16 - 32 µg/ml)

## EXCELLENT SAFETY PROFILE

Established clinical safety in over 600 subjects. Data shows that PAC-113 is well tolerated with no drug related serious adverse events.

Safety data was generated from Phase I/II and Phase IIb trials conducted by Pacgen.

Safety data was also generated from Phase I and Phase II trials conducted in the US by Periodontix Inc. (subsequently acquired by Demegen, Inc.) prior to PAC-113 being in-licensed by Pacgen in 2005. The studies conducted by Periodontix/Demegen were in oral rinse and gel formulation for prevention of bacterial periodontal disease.

## CLINICAL DEVELOPMENT PLAN FOR NOVEL ANTI-FUNGAL

PAC-113 is a peptide-based anti-fungal targeting oral *Candida* infections in immunocompromised patients and patients with salivary dysfunction.

### Phase IIb Study - Positive Results:

In June 2008 Pacgen reported topline results from its Phase IIb clinical trial evaluating the safety and efficacy of PAC-113. Results demonstrated that PAC-113 is generally safe, well tolerated, and is effective in the treatment of oral *Candida* infection with clinical cure rates comparable to the current standard of care.

### Study Design:

- PAC-113 mouthrinse vs. Nystatin oral suspension
- Randomized, examiner-blinded, parallel design clinical trial
- 14-day treatment phase with a 14-day follow-up period

### Treatment Arms:

Eligible subjects were randomized to one of the following treatment arms:

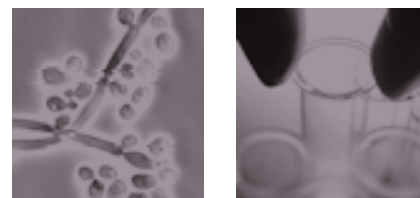
- a. 0.15% PAC-113 mouthrinse (5 mL, 4-times per day);
- b. 0.075% PAC-113 mouthrinse (5ml, 4 times per day);
- c. 0.0375% PAC-113 mouthrinse (5ml, 4 times per day);
- d. Nystatin oral suspension (5 mL, 4-times per day).

### Positive Results:

The optimal dose of PAC-113 demonstrated a 34% increase in primary endpoint efficacy level (complete clinical cure rate at Day 19) for the Per Protocol analysis as compared to Nystatin, and a 50% increase in the corresponding Intent to Treat analysis.

### Next Steps:

Pacgen plans to meet with the FDA to discuss its proposed Phase III clinical development plan. The Company is currently seeking collaboration and commercialization partner for PAC-113.



## TARGET PATIENT POPULATION

**Asthma:** Prolonged use of oral steroids causes a localized immunosuppression in the mouth, throat, and upper airways that leads to a high frequency of *Candidiasis* in asthma patients. Approximately half of the 15,000,000 asthmatics in the United States use inhaled steroids to manage their disease.

**Cancer:** *Candidiasis* occurs with high frequency in cancer patients due to either disease-related, or treatment-related immunosuppression. Both radiation and chemotherapy lead to a suppression of the immune system. The American Cancer Society statistics estimate 1.4 million new cases of cancer in 2005.

**Diabetes:** The Centers for Disease Control and Prevention report that there are about 21 million diabetics in the United States. Diabetics are predisposed to oral *Candidiasis* due in part to poor glycemic control providing a ready food source for *Candida* and in part to a reduction in immune function.

**HIV/AIDS:** The frequency of oral *Candidiasis* in AIDS patients varies with the disease state and is reflective of the underlying level of immune function. The frequency of OPC in HIV-infected individuals with good immune function is in the range of 7% to 48%, but rises to more than 90% in those with advanced disease. Furthermore, HIV patients frequently have a relapse of oral *Candidiasis* within 2 weeks to 3 months following completion of antifungal treatment. An estimated 1.1 million people are living with HIV/AIDS in the United States alone. In Asia, Japan and Western Europe, there are an additional 8.5 million HIV/AIDS patients.

**Xerostomia:** Dry mouth is a common side effect on a number of medications. Drugs causing this condition include many commonly used drugs such as: antidepressants, anticholinergics, antihypertensives, antipsychotics, anti-Parkinson agents, antihistamines, diuretics and sedatives. These medications are broadly prescribed exacerbate the development of *Candidiasis*.