

# *NeuTec Pharma plc*

## **Successful multi-national, confirmatory clinical trial of Mycograb<sup>□</sup> - breakthrough in the treatment of life-threatening fungal infections**

**12<sup>th</sup> July 2004 - Manchester, UK:** *NeuTec Pharma plc* ("*NeuTec*" or the "*Company*"), the biopharmaceutical company targeting drug-resistant, life-threatening infections, announces the successful achievement of clinical end points from a multinational, double-blind, placebo-controlled trial involving 10 European countries and the USA.

The trial was conducted in 139 patients with invasive candidiasis who received conventional treatment with a lipid-based formulation of amphotericin B combined with a five day course of either Mycograb<sup>®</sup> or placebo. Mycograb<sup>□</sup>, the *Company*'s lead product, is based on a naturally-occurring human antibody against hsp90 which defends the body against fungal infections. Candidiasis is the leading cause of serious fungal infection. Worldwide sales of antifungals were US\$2.6 billion in 2001 increasing to US\$2.9 billion in 2003.

### **Key points:**

- **Mycograb<sup>□</sup> positive clinical results:**
  - **Primary end point – 84% overall response rate vs 48% in placebo control group:** To be regarded as a success, patients had to show both a complete clinical response ("cure") and a mycological response (culture-confirmed clearance of the infection in the laboratory) at Day 10. The trial showed a highly statistically significant difference (*P* value < 0.001) in the overall response rates (clinical and mycological response) between the placebo control group and those receiving Mycograb<sup>□</sup>. The positive response rate of the group receiving mono-therapy was 48% compared to 84% in the group receiving Mycograb<sup>□</sup> with amphotericin B.
  - **Secondary end point** – In addition, a separate analysis of each of the two components (clinical response and mycological response) showed a highly statistically significant difference between the two groups (*P* value < 0.001).
  - **Secondary end point – less deaths due to candidal infection:** In the group receiving mono-therapy, candida-attributable mortality was 18%, whereas in the group receiving additional therapy with Mycograb<sup>®</sup> this fell to 4%, a statistically significant difference (*P* value < 0.025).
  - **Secondary end point – faster eradication of fungus:** A highly statistically significant difference between the two groups (*P* value < 0.001) occurred in the rate of culture-confirmed clearance of the infection (Mycograb<sup>□</sup> 3 days, mono-therapy 23 days).
- **Plans for European market authorisation:**

- On the basis of this study, *NeuTec* intends to submit an application for market authorisation in Europe for the following clinical indication - "Mycograb<sup>®</sup> in combination with amphotericin B for the treatment of invasive candidiasis in immunocompetent intensive care patients."
  - In anticipation of market authorisation for Mycograb<sup>®</sup>, *NeuTec* is now actively planning for the commercial launch of the product, including the recruitment of a senior sales and marketing manager and third party contract manufacture to build adequate stocks of Mycograb<sup>®</sup> for the commencement of European sales.
- **Further equity funding:**
    - Encouraged by the safety and efficacy profile showed by this clinical data on Mycograb<sup>®</sup> and the clear near term opportunities available to create significant shareholder value, *NeuTec* intends to raise additional equity funds of £20-25 million through a Placing and Open Offer to augment the existing cash balance of £7.9 million.

**Prof. James Burnie, Chief Executive Officer of *NeuTec*, commented:**

"This is the first time that combination therapy has been shown to improve the outcome of invasive candidiasis. It heralds a new era in the treatment of life-threatening infections in which a genetically recombinant antibody is used in combination with a traditional drug to combat infection.

We intend to use this study as the basis of an application to the EMEA for market authorisation in Europe. We are now aiming to build a small, focused, sales and marketing team in anticipation of the market launch of this product as well as accelerating the other programmes within the development portfolio, particularly into the US."

**For further details please contact:**

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**A presentation for analysts will be held today at 9.30am at Financial Dynamics. For further details, please contact Mo Noonan on 0207 831 3113.**

## **Successful multi-national, confirmatory clinical trial of Mycograb<sup>□</sup> in the treatment of life-threatening candidal infection.**

### **Clinical Trial Data - Mycograb<sup>□</sup>**

This confirmatory study involved 139 patients, approximately half of whom received Mycograb<sup>□</sup> plus liposomal amphotericin B (the “test group”) and half placebo plus liposomal amphotericin B (the “placebo group”). Of these, 117 were used in the assessment of efficacy, having excluded patients who did not receive any study drug, did not have proven culture-confirmed invasive candidiasis or had candidal endocarditis.

The primary test of efficacy was based on comparison of the frequency with which patients in the test group showed a complete clinical and mycological response by Day 10 compared to frequency in the placebo group. That is, a comparison was made at a fixed time point of the frequency of clinical cure and culture-confirmed eradication of the fungus. This showed a highly statistically significant difference ( $P$  value  $< 0.001$ ) between the two groups; those receiving Mycograb<sup>□</sup> showing a complete overall (clinical and mycological) response in 84% of cases (47 out of 56 patients) compared to 48% (29/61) in the placebo control group. Analysis of the two components of this test of efficacy showed a complete clinical response occurring in 86% (48/56) of patients receiving Mycograb<sup>□</sup> compared to 52% (32/61) in the placebo group, and a mycological response in 89% (50/56) of the Mycograb<sup>□</sup> treated group compared to 54% (33/61) in the placebo group. In each case this was a highly statistically significant difference ( $P$  value  $< 0.001$ ).

The frequency of deaths due to the candidal infection under treatment was as high as 18% (11/61) in the placebo group but fell to 4% (2/56) in the group receiving Mycograb<sup>□</sup>, this being derived from the number of candida-attributable deaths by Day 33 (4 weeks after completion of the 5 day course of treatment with Mycograb<sup>□</sup> or placebo). This difference achieved statistical significance ( $P$  value  $< 0.025$ ).

As a further, laboratory-based test of efficacy, the speed with which culture-confirmed eradication of the fungus was achieved was compared between the two groups. The rate of culture-confirmed eradication of the infection showed a highly statistically significant difference between the two groups ( $P$  value  $< 0.001$ ), the median time to last positive culture being 3 days for the test group, compared to 23 days for the placebo group (Kaplan-Meier).

## **Planned European market authorisation and commercial launch**

Following earlier discussions with the Scientific Advisory Working Group of the EMEA and because Mycograb<sup>□</sup> has Orphan Drug Status, *NeuTec* now plans to use the clinical data from this completed study to support an application for market authorisation in Europe in the following clinical indication - "Mycograb<sup>□</sup> in combination with amphotericin B for the treatment of invasive candidiasis in immunocompetent intensive care patients".

In anticipation of a commercial launch programme *NeuTec* is currently in discussions to recruit an experienced senior commercial, sales and marketing manager with a brief to commence the planning for the commercial launch of Mycograb<sup>□</sup> in Europe. The intention is to build a small dedicated sales force focused on the large hospital intensive care unit market in anticipation of the launch of Mycograb<sup>□</sup>.

Furthermore, so as to support the commercial launch of Mycograb<sup>□</sup> in Europe, the Company is currently engaged in advanced discussions with a number of third party contract manufacturers to secure the commercial manufacture of Mycograb<sup>□</sup>.

## **Clinical development programmes**

Encouraged by the above data, *NeuTec* intends to enter into discussions with the FDA regarding market authorisation of Mycograb<sup>□</sup> in the US, where again Mycograb<sup>□</sup> has Orphan Drug Status.

*NeuTec* has been evaluating the use of Mycograb<sup>□</sup> with other antifungal drugs against cryptococcal infections and invasive aspergillosis. The Company is currently planning additional studies in this regard with a view to broadening the licensed indications of Mycograb<sup>□</sup> to include other fungi.

Moreover, hsp90 is a target molecule in a range of cancers, which are another potential indication for Mycograb<sup>□</sup>. In vitro data obtained by *NeuTec* has suggested possible drug combinations which could improve outcome and offer therapeutic benefit over existing therapies in breast cancer. *NeuTec* believes there is significant potential value in Mycograb<sup>□</sup> for cancer indications and plans to pursue further studies in this area.

Aurograb<sup>®</sup>, the Company's second product, is currently in a double blind, placebo-controlled Phase III study involving up to 250 patients from at least six European countries to determine whether the overall response (clinical and bacterial) to Aurograb<sup>®</sup> plus vancomycin is greater than the overall response to placebo plus vancomycin in hospitalised patients with severe, deep-seated staphylococcal infections, particularly MRSA. *NeuTec* is currently planning to carry out additional trials to evaluate the efficacy of Aurograb<sup>®</sup> against the full spectrum of staphylococcal infections, and may extend these trials into the US.

## Further equity funding

Based on progress to date and encouraged by the clinical data of proven quality on Mycograb<sup>®</sup> and the clear near term opportunities available to create significant shareholder value, the Directors are currently assessing the equity markets for raising additional equity funds of £20-25 million through a potential Placing and Open Offer to augment the existing cash balance of £7.9 million.

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## Notes to Editors

**NeuTec Pharma plc** is a biopharmaceutical company formed in 1997 which specialises in the development of human genetically recombinant antibodies (“grabs”) to combat the growing menace of antibiotic-resistant infections. Antibodies are an important, naturally occurring, component of the body’s defence system against infectious diseases. The Company is developing a portfolio of antibody-based therapeutic products to treat these infections with particular emphasis on hospital-acquired infections. In the United States, nearly two million patients a year become infected while in hospital and, of these, approximately 90,000 died in 2002 as a result of their infection compared 13,300 patient deaths in 1992. Over 70 per cent. of the bacteria that cause hospital-acquired infections are resistant to at least one of the drugs most commonly used to treat them. As a result, patients with drug-resistant infections are more likely to have longer hospital stays and require treatment with second line drugs that may be less effective, more toxic and more expensive. Severe sepsis now causes as many deaths annually in the US as heart attacks, is especially common in the elderly and is likely to increase substantially as the elderly population grows.

NeuTec’s two leading products are Mycograb<sup>®</sup>, which targets invasive fungal infection, specifically invasive candidiasis, and Aurograb<sup>®</sup>, which targets *Staphylococcus aureus* including methicillin-resistant *Staphylococcus aureus* (“MRSA”). To date, the clinical trials of these products have been based on the products being given as part of combination therapy with existing antibiotics to improve the outcome and reduce the chance of drug-resistance occurring which can lead to clinical failure.

In addition, NeuTec has research programmes exploring the use of these products against other diseases together with development programmes for new “grab” based therapeutics.

### **Mycograb<sup>®</sup>**

Mycograb<sup>®</sup> is a “grab” against heat shock protein 90 m (“hsp90”) which has been developed for the treatment of invasive candidiasis (also known as systemic or disseminated candidiasis). This is a life-threatening fungal infection, due to species of the yeast *Candida*, which has an overall mortality of around 40 per cent. and a mortality which is a direct result of the *Candida* infection itself (“*Candida*-attributable mortality”) of about 10 per cent. In 1998, the projected average incidence of systemic fungal infection in the US was 306 per million of population with candidiasis accounting for 75 per cent. of cases. The estimated total direct cost of treatment was US\$2.6 billion and the average attributable cost per patient was US\$31,200. Worldwide sales of antifungals were US\$2.2 billion in 2001 increasing to US\$2.9 billion in 2003.

### **Aurograb<sup>®</sup>**

Since 2002, a consensus view has developed that MRSA is now the most important hospital-acquired infection.

According to the Centers for Disease Control in the US, some 100,000 people are hospitalised with this infection each year. In one year, the rates of blood cultures positive for *S. aureus* in the UK have risen from 17,876 (April 2001 to March 2002) to 18,403 (April 2002 to March 2003) with approximately 40 per cent. being due to MRSA. Over twice the number of patients with positive blood cultures due to MRSA die compared to those with MSSA (methicillin-sensitive *S. aureus*). Patients with MRSA infection had a six-fold higher mortality rate than comparable patients with no such infection. At the same time sales of antibiotics to treat Gram positive infections (*S. aureus* being the most dominant form) have risen from US\$706 million in 2001 to US\$908 million in 2003.