news release
xenova group plc

anti-smoking vaccine ta-nic
preliminary 12 month clinical trial results

slough, uk, 3 march 2005 – xenova group plc (nasdaq: xnova; london stock exchange: xen) today announced preliminary 12 month findings from the second phase i trial of ta-nic, the company’s therapeutic vaccine being developed for the treatment of nicotine addiction.

a total of 60 subjects who smoked between 10 and 75 cigarettes a day were recruited into the trial, divided into three cohorts. within each cohort of 20 smokers, 16 received the active vaccine and 4 received the placebo. the primary objectives of the study were to evaluate the safety, tolerability and immunogenicity vs. placebo of three doses of ta-nic – 50 µg, 250 µg and 1000 µg. the vaccine was administered by intramuscular injection at weeks 0, 2, 4, 6, 8 and 12 with a booster at 32 weeks.

secondary objectives included recording the number of cigarettes smoked per day, determining the time to first cigarette and the time to relapse following a quit attempt at week 12 and if necessary another quit attempt at week 32. these quit rates were then assessed again after 12 months.

initial 20 week immunogenicity data and other findings were reported in july 2004.

the data announced today show that

- 12 month self-reported quit rates\(^1\) were substantially greater amongst those receiving ta-nic than those receiving placebo. none of the participants receiving ta-nic or the placebo received counselling, nicotine replacement therapy or any other aid to quit smoking as part of the study.

  in the placebo group, 1 out of 12 participants (8%) reported being abstinent at their last visit or at 12 months compared with 3 out of 16 (19%) and 6 out of 16 (38%) in the two groups receiving the higher doses of ta-nic.

- additionally, the proportion of participants who successfully made a quit attempt was higher amongst those receiving ta-nic (95%) than amongst those receiving the placebo (73%).

- a booster, given at 32 weeks, produced a substantial and sustained increase in nicotine specific antibodies in both groups receiving the higher doses of ta-nic.

- immunogenicity data after 12 months follow up and the safety and tolerability profile support the 20 week findings announced in july 2004, and confirm the selection of the 250 µg dose for use in the phase ii and iii clinical trials.

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\(^1\) smokers who reported that they were no longer smoking at their last visit or at 12 months
Following these preliminary results and confirmation of the dose to be taken forward, Xenova expects to begin Phase II trials for TA-NIC this year with interim Phase II results expected in 2006.

David Oxlade, Chief Executive Officer of Xenova said: “Although this study was not primarily set up to assess the long term quit rates amongst smokers receiving TA-NIC, we are pleased to observe these promising findings and the confirmation of the selected dose for further clinical trials. There is an urgent need for a more effective treatment for nicotine addiction, with almost 5 million people dying each year from tobacco use and over 1 billion people globally still smoking,"

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Notes to Editors

**Smoking Statistics**
The World Health Organisation (WHO) notes that the tobacco epidemic is still expanding, especially in developing countries where currently 84% of smokers live. Tobacco use kills 4.9 million people each year and this toll is expected to double in the next 20 years. At current rates, the total number of tobacco users is expected to rise to 1.7 billion by 2025 from 1.3 billion now (May 2004).

**Smoking cessation**
Of the 1.3 billion smokers globally, it is estimated that some 4 million smokers each year in the UK attempt to quit, but that only 3-6% (or 1-2% of all smokers) are successful in giving up tobacco. Conventional treatment of nicotine addiction concentrates on psychosocial interventions (counselling, smoking cessation clinics) together with pharmacotherapy, including nicotine replacement therapy (NRT) and bupropion (Zyban®, GlaxoSmithKline). Even with effective behavioural and pharmacological therapies, many individuals dependant on nicotine fail in their attempts to remain abstinent, with smoking cessation rates of only approximately 10-20% at 1 year.

Inhaled nicotine is highly addictive. Absorption of nicotine from cigarette smoke through the lung is rapid, producing with each inhalation a high concentration arterial bolus of nicotine that reaches the brain within 10-16 seconds, faster than by intravenous injection. Nicotine is able to cross the blood brain barrier where it binds to acetyl-choline receptors, triggering the release of neurotransmitters, such as dopamine and serotonin. These give rise to positive feelings (pleasure, relaxation, lack of anxiety, suppressed appetite, improved concentration) which are reinforced with each cigarette.
Nicotine has a distribution half life of 15-20 minutes and a terminal half life in the blood of two hours. Smokers therefore experience a pattern of repetitive and transient high blood nicotine concentrations from each cigarette, with regular hourly cigarettes needed to maintain raised concentrations, and overnight blood levels dropping near to those of non-smokers. Smoking cessation is difficult to achieve due to the addictive properties of nicotine and the unpleasant withdrawal symptoms (irritability, lack of concentration, weight gain, nicotine craving).

**TA-NIC mode of action**

TA-NIC is a therapeutic vaccine in development for the treatment of nicotine addiction. Nicotine is a small molecule which, by itself, does not trigger an immune response. However, when nicotine is carried by an immunogenic protein it can prime the immune system to produce anti-nicotine antibodies. The active ingredient of TA-NIC vaccine is a protein conjugate: nicotine butyric acid (NBA) covalently linked to recombinant cholera toxin B (rCTB). rCTB was chosen as the carrier protein because it is known to be highly immunogenic and has been used for many years as a component of cholera vaccine. rCTB has been approved by the Swedish Medical Products Agency for use in an oral cholera vaccine that is marketed in Sweden and Norway and in 2003 was approved by the CPMP.

Nicotine is bound by the induced circulating anti-nicotine antibodies in the bloodstream and the resulting antigen-antibody complex is too large to cross the blood-brain barrier, so the pleasurable stimulus which usually accompanies smoking will be absent or reduced. Without this reward, the motivation to smoke again is reduced, preventing the reinforcement which is required to maintain the nicotine addiction.

**References:**

NICE Guidance on the use of nicotine replacement therapy (NRT) and bupropion for smoking cessation. March 2002


Xenova Group plc is a UK-based biopharmaceutical company focused on the development of novel drugs to treat cancer and addiction with a secondary focus in immunotherapy. The Company has a broad pipeline of product candidates in clinical development, including three cancer programmes: its lead product candidate TransMID™, for the treatment of high-grade glioma, is in Phase III trials, and its novel DNA targeting agents and XR303 are both in Phase I for cancer indications. Xenova is also developing two therapeutic vaccines for cocaine and nicotine addiction, which are in Phase II and Phase I trials respectively. Quoted on the London Stock Exchange (XEN) and on NASDAQ (XNVA), Xenova has approximately 75 full time employees in the UK and North America. (Reuters XEN.L; Bloomberg XEN LN).

For further information about Xenova and its products please visit the Xenova website at www.xenova.com and www.gbmtrial.com

*This press release contains “forward-looking statements,” including statements about the development and commercialization of products. Various risks may cause Xenova’s actual results to differ materially from those expressed or implied by the forward looking statements, including: adverse results and delays in our drug discovery and clinical development programs; failure to obtain effective patent protection for our discoveries; commercial limitations imposed by patents owned or controlled by third parties; failure to achieve product*
development or commercialization milestones on a timely basis or at all; our dependence upon strategic alliance partners to develop and commercialize products and services; difficulties or delays in obtaining regulatory approvals to market products and services resulting from our development efforts; the requirement for substantial on-going funding to conduct research and development and to expand commercialization activities; and product initiatives by competitors. For a further list and description of the risks and uncertainties we face, see our reports on file with the Securities and Exchange Commission. We disclaim any intention or obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.