PRESS RELEASE • PRESS RELEASE • PRESS RELEASE

Major milestone achieved: the Phase IIa clinical trial in rheumatoid arthritis meets its endpoint

- *Further demonstration of the excellent safety profile of the TNF-Kinoid*
- *Identification of 2 doses and an administration schedule that are immunogenic*
- *Evidence of therapeutic activity in patients who have lost response to anti-TNF biologics*

The trial constitutes further confirmation of the Kinoids' potential as active immunotherapies to treat inflammatory and auto-immune diseases

Paris, France, January 5, 2012 - Neovacs (Alternext Paris: ALNEV), a biotech company focused on the development of active immunotherapies to treat autoimmune and inflammatory diseases, today announced the full results for its TNF-K-003 clinical trial with TNF-Kinoid in rheumatoid arthritis (RA), the third indication targeted by Neovacs. The efficacy and safety of the TNF-Kinoid were studied in RA patients who had become resistant to anti-TNF biologics, including anti-TNF monoclonal antibodies. The full results confirm TNF-Kinoid's excellent safety profile, its ability to induce antibodies to TNF and a trend towards the relief of disease symptoms.

"We are very happy with the results of this study in rheumatoid arthritis - a serious and invalidating disease. These new data confirm TNF-Kinoid's promising clinical activity in RA patients when they lose response to monoclonal antibodies", commented Professor Marie-Christophe Boissier, Head of the Rheumatology Department at Avicenne University Medical Center in Bobigny,France.

The TNF-K-003 Phase IIa study of Neovacs' TNF-Kinoid in RA is a double-blind, placebo-controlled, randomized clinical trial in patients having received at least one anti-TNF treatment prior to inclusion. The trial's main objective was to establish the best dose and the best administration schedule, based on immune response to the Kinoid.
The full results dealt with 40 patients recruited:

- ✓ in the intermediate results already reported, 6 patients received the 90 mcg dose, 12 patients received the 180 mcg dose and 6 patients received placebo.
- ✓ in the final cohort of 16 patients in the study, 12 received the 360 mcg dose and 4 received placebo.

Two immunization regimens were tested: two injections with a four-week interval and three injections administered on days 0, 7 and 28.

It is important to note that the patients included in this study no longer responded to at least one anti-TNF biologic. Some of them were on their second or even third anti-TNF after failure of the previous treatments. This multiple TNF-failure patient population is increasing very rapidly and is known to be frequently refractory to subsequent treatments.

The study's primary endpoint was to identify an effective dose and administration regimen. The immune response 3 months after immunization was as follows: with the 90 mcg dose, only 50 % of the patients developed anti-TNF antibodies, so the dose was weakly immunogenic. At a dose of 180 mcg, the proportion was 75 % and at a dose of 360 mcg, the proportion was 91%, suggesting a dose effect. Of

note, the rate of seroconversion with the three dose administration schedule was 100% with the 180 and 360 mcg doses, while it was 67% in the two dose group.

The full study results published today also confirm the very good safety profile of the TNF-Kinoid: no patient withdrew from the study because of an adverse event and no Kinoid-related serious adverse events were reported.

Encouraging efficacy data

Given that not all dose/schedule combinations were reliably immunogenic, exploratory analyses of clinical efficacy and biomarkers were conducted comparing patients in whom the Kinoid induced antibody to TNF with those that did not. The study demonstrated an improvement in the RA symptoms in patients who had developed anti-TNF antibodies. This was evidenced by (i) a moderate-to-good clinical response according to the EULAR criteria (a decrease of at least 0.6 in the Disease Activity Score (DAS28*) and a final DAS28 score ≤ 5.1), (ii) a decrease in the mean DAS28 score and (iii) a decrease in the serum level of C reactive protein (CRP, a marker of inflammation).

1. In 21**patients out of 24 who had measurable anti-TNF antibodies over the first 84 days, 48% had a moderate-to-good clinical response (i.e. a drop of at least 0.6 point in the DAS28); this compared with only 31% of the 16 patients who did not develop anti-TNF antibodies.
2. The mean decrease in the DAS28 was 0.8 point in patients who developed anti-TNF antibodies but only 0.5 in the patients without anti-TNF antibodies.
3. A mean decrease of 14% in the CRP level was measured in patients who developed anti-TNF antibodies, whereas the mean CRP level increased by 5% in patients without anti-TNF antibodies.

"TNF-Kinoid has confirmed its potential as a promising new therapeutic option for RA patients who no longer respond to anti-TNF drugs. The development of TNF-Kinoid is progressing very well and the study's success further validates our innovative Kinoid technology, building on the positive results obtained in Crohn's disease (with TNF-Kinoid) and in lupus (with IFNα-Kinoid)", emphasized Guy-Charles Fanneau de La Horie, CEO of Neovacs.

The primary objective of the TNF-K-003 study was to define the optimal dose and administration regimen for subsequent testing in a Phase IIb study. Clinical efficacy was a secondary endpoint of the study. The trial is part of the Oséo-funded TRACKER project, in collaboration with the company biomedical diagnostics.

*DAS 28 : The composite index measuring RA disease activity designed by EULAR (European League Against Rheumatism). DAS 28 takes into account both pain and the level of swelling at 28 joints.
** The DAS28 score was not collected in three patients at Day 84.

About Neovacs

Neovacs is a biotechnology company focused on an active immunotherapy technology platform (Kinoids) with applications in autoimmune and inflammatory diseases. On the basis of the company's proprietary technology for inducing a polyclonal immune response (covered by five patent families that run until at least 2023), Neovacs is focusing its development efforts on two active immunotherapies: TNF-Kinoid is being developed for the treatment of TNF-mediated autoimmune diseases such as rheumatoid arthritis and Crohn's disease, whereas IFNα-Kinoid is being developed for the indication of lupus. The goal of the Kinoid approach is to enable patients to have access to safe treatments with efficacy that is sustained in these life-long diseases.

For more information on Neovacs, visit www.neovacs.com

Contacts

Press – ALIZE RP
Caroline Carmagnol
+33 (0)1 42 68 86 43
caroline@alizerp.com.com

Neovacs
Florence Hocdée-Leroy
+33 (0) 1 53 10 93 14
fhocdeeleroy@neovacs.com

Investors – NewCap
Axelle Vuillermet
+ 33 (0) 1 44 71 94 93
avuillermet@newcap.fr

Notes for journalists

Rheumatoid arthritis

Rheumatoid arthritis (RA) is a major public health issue; it is the most frequent, serious chronic inflammatory rheumatic disease and affects between 0.3% and 1% of the worldwide population: over 7 million people in the world's 7 largest pharmaceutical markets (source: Datamonitor, 2009). In recent years, population ageing has increased the number of RA sufferers. The disease attacks all the joints in the body (e.g. the feet, hands, knees, ankles, wrists, shoulders, hips and elbows) and is characterized by a combination of joint pain, morning stiffness and a type of joint swelling known as synovitis. Today's monoclonal antibody treatments are based on passive immunotherapy and frequently lose their efficacy over time. Consequently there remains a major need for therapies with sustained efficacy.

About TNFα-dependent auto-immune diseases

TNFα-mediated diseases affect the bones and joints (RA, ankylosing arthritis, psoriatic arthritis) the digestive tract (Crohn's Disease, ulcerative colitis) and the skin (psoriasis). In the seven major developed countries alone (USA, Japan, Germany, France, UK, Italy and Spain), there are 9.3 million people with bone and joint diseases, 2.1 million with digestive diseases and 16.5 million with psoriasis (Source: Datamonitor 2007).

A major unmet medical need in RA

It has been estimated than from 2012 onwards, the number of patients having to switch treatments will exceed the number of patients receiving their first anti-TNF biologic treatment (source: Datamonitor).

Neovacs' response: a next generation treatment beyond monoclonals

Dr Pierre Vandepapeliere (Neovacs' Director of Clinical Development) emphasizes that "*Over the last decade, monoclonal antibodies have transformed the treatment of inflammatory diseases. These treatments are the product of a different approach: instead of stimulating the patient's immune system to produce antibodies, monoclonal antibodies are synthesized in mammalian cell lines. One problem with this approach is that these antibodies are foreign to the patient and risk being identified as such by the patient's immune system which may, after a while, reject them. This explains why one often sees a loss of therapeutic benefit from these drugs over time*."

The Kinoid technology differs significantly from the monoclonal antibody approach. Dr Vandepapeliere adds that "*with an active immunotherapy approach, the antibodies are generated by the patient's own immune system and are recognized as self. Furthermore, monoclonal antibodies only target a small part of the TNF (known as an epitope), whereas the antibodies produced by therapeutic vaccination are polyclonal and target several different parts of the cytokine; this leads to greater efficacy for the same quantity of antibody. These are two reasons why Kinoids are less likely to prompt the development of resistance and treatment failure."*

Finally, a further major advantage for patients is that Neovacs' product candidates only require administration by intra-muscular injection every three to six months. Current monoclonal antibodies require administration every two to four weeks if subcutaneous or monthly or every other month if delivered by IV infusion. As Dr Vandepapeliere notes "*This is a huge advantage in terms of convenience and comfort for patients, which will produce better compliance and ultimately lower costs*".

Neovacs is developing two active immunotherapies based on the Kinoid technology: the TNF-Kinoid and the IFNα-Kinoid. The TNF-Kinoid is being developed in 2 indications:

- ✓ In Phase II in Crohn's Disease, with the results expected in the second quarter of 2012. The results observed in Phase I/II were very promising, with in particular a high and long-lived level of efficacy.
- ✓ In Phase IIa in rheumatoid arthritis. The results of this study are reported in this press release.

Key facts about monoclonal antibodies

> Marketed anti-TNF drugs had over $20bn in total sales in 2010 :
  - Enbrel®, Remicade®, Humira®, Cimzia®

> There is a growing problem of treatment failure to these products :
    - Up to 50% treatment failure after one year of therapy
    - Burdensome administration and expensive > 12 000€ /patient/year in Europe
    - An ongoing need for novel therapies