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PRESS RELEASE

CORPORATE MEDIA RELATIONS

New anti-thrombotic product demonstrates superior benefits

Results of major international VTE prevention phase III program show superior benefits of the pentasaccharide Org31540/SR90107A

Arnhem/Oss, the Netherlands, 5 December 2000 – The results of four Phase III clinical trials show that the pentasaccharide Org31540/SR90107A provides a superior benefit over a low molecular weight heparin (comparator) in preventing deep-vein thrombosis (DVT) in major orthopedic surgery patients, with an overall relative risk reduction of 50% and a similar safety profile. These promising results of the international Phase III clinical trial program on the pentasaccharide Org31540/SR90107A, were presented yesterday at the 42nd annual meeting of the American Society of Hematology in San Francisco.

The four phase III trials in the prevention of venous thromboembolism (VTE) following major orthopedic surgery involved over 7,000 major orthopedic surgery patients in Europe, Latin America, Australia, Canada and the United States, and represented the largest phase III clinical development program ever performed in this indication. The program consisted of four multicenter, prospective, double blind, randomized trials all of which compared Org31540/SR90107A with the comparator in the prevention of VTE:

- **EPHESUS**: following elective hip replacement surgery;
- **PENTATHLON 2000**: following elective hip replacement surgery;
- **PENTHIFRA**: following hip fracture surgery;
- **PENTAMAKS**: following elective major knee surgery.

A major improvement in the efficacy of VTE prophylaxis following major orthopedic surgery

Patients undergoing major orthopedic surgery are at high risk of venous thromboembolic events. Prophylaxis is thus required to prevent deep-vein thrombosis (DVT) and pulmonary embolism (PE). Despite the prevention provided by current therapies, there are still unmet medical needs in terms of efficacy.
The clinical data generated by the four studies show that the new compound Org31540/SR90107A provides a major improvement in terms of efficacy in the prevention of VTE following orthopedic surgery. Versus the comparator, Org31540/SR90107A reduced incidence of both total and proximal DVT by 50%.

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In the four studies constituting the Phase III program, the same dose regimen of Org31540/SR90107A (2.5mg once daily started post-operatively) was compared to the standard, approved regimens of the comparator. The benefit of Org31540/SR90107A was consistent whatever the type of surgery, the type of anesthesia and the regimens of the comparator, and regardless of patients' gender, age and weight. The benefit of Org31540/SR90107A was also consistent whatever the location of deep-vein thrombosis (DVT), i.e. proximal, distal or both.

Org31540/SR90107A is thus the first antithrombotic agent to demonstrate a significant benefit over the comparator for the prevention of VTE in all three types of orthopedic surgery: hip fracture, hip replacement and knee surgery.

A well tolerated antithrombotic agent

The safety profile of Org31540/SR90107A is similar to that of the comparator. Mortality rates for any cause were similar in the two groups.

Bleeding rates within the two groups were also similar for the most clinically relevant bleeding criteria: fatal bleeding; bleeding in critical organs; and bleeding leading to intervention. Patients requiring a transfusion of more than or equal to 2 units and/or with a decrease of hemoglobin greater than or equal to 2g/dl, represented 2.3% of patients in the Org31540/SR90107A group and 1.4% of patients in the comparator group. Total incidence of other bleedings (minor) was similar in the two groups.

Org31540/SR90107A is the first agent of a new class of antithrombotics: selective factor Xa inhibitors. An original, entirely synthetic compound, Org31540/SR90107A was discovered and is being co-developed by Sanofi-Synthélabo and Organon in the prophylaxis and treatment of venous and arterial thromboembolic diseases.

Background information

In September 2000, Organon signed an agreement with the French pharmaceutical company Sanofi-Synthélabo to commercialize and manufacture the new drug. In the United States, Canada and Mexico, joint ventures will market the drug via both companies' sales and distribution organizations in each of these countries. Organon and Sanofi will each hold 50% of the joint ventures, which will be consolidated proportionally.

In Europe and the rest of the world (excluding Japan), where Sanofi-Synthélabo has considerable experience in the antithrombotics market, Sanofi will have the sole responsibility for the marketing and sale of the product. Sanofi-Synthélabo will make milestone payments related to the approval of the product in the targeted indications. In addition, Organon will receive royalties on sales generated in Europe and the rest of the world.

Note for the editor

N.V. Organon, Akzo Nobel's human healthcare business, develops and produces pharmaceutical products in the fields such as gynecology, psychiatry, athero-thrombosis, and autoimmune diseases. Organon employs more than 11,700 employees worldwide and invests over 17% of its sales income in its drug discovery and development programs.

Akzo Nobel, based in the Netherlands, serves customers throughout the world with healthcare products, coatings and chemicals. Consolidated sales for 1999 (excluding Acordis) totaled some EUR 12 billion (USD 13 billion, GBP 8 billion).
The Company currently employs 68,000 people in 75 countries.
Financial results for the year 2000 will be announced on February 23, 2001.

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