The European Agency for the Evaluation of Medicinal Products
Pre-authorisation Evaluation of Medicines for Human Use

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Please note that this product was withdrawn from the Community Register of designated Orphan Medicinal Products in April 2003 on request from the sponsor.

COMMITTEE FOR ORPHAN MEDICINAL PRODUCTS

PUBLIC SUMMARY OF POSITIVE OPINION FOR ORPHAN DESIGNATION OF anti-CD147 murine monoclonal IgM for the treatment of Graft versus Host Disease

On 14 November 2002, orphan designation (EU/3/02/123) was granted by the European Commission to SangStat UK Limited, United Kingdom, for anti-CD147 murine monoclonal IgM for the treatment of Graft versus Host Disease.

What is Graft versus Host Disease?
The bone marrow is the spongy tissue inside the large bones in the body. The bone marrow makes red blood cells (which carry oxygen and other materials to all tissues of the body), white blood cells (which fight infection), and platelets (which make the blood clot). Bone marrow transplantation (replacing with healthy marrow) is a treatment used against certain diseases of the bone marrow. A frequent complication of bone marrow transplantation is the development of a disease called Graft versus Host Disease (GvHD). This disease involves a reaction between the donor cells and the recipient's native tissues leading to injury of the recipient's tissues. GvHD occurs in acute and chronic form. The organs most commonly affected in acute GvHD are the stomach and the intestines, the skin, and the liver. Chronic GvHD involves a much wider range of tissues than the acute form. The condition is chronically debilitating and life-threatening.

What are the methods of treatment available?
The methods of treatment authorised for GvHD in the Community, at the time of submission of the application for orphan designation, consisted of certain steroid hormones (corticosteroids) administered at high doses. Other therapies include drugs that inhibit the immune response (immunosuppressants). Anti-CD147 murine monoclonal IgM might be of potential significant benefit for the treatment of GvHD, particularly in terms of a selective action against those cells that are responsible for the disease. This assumption remains to be proven. This will be necessary to maintain the orphan status.

What is the estimated number of patients affected by the condition* ?
According to the information provided by the sponsor, graft versus host disease was considered to affect about 8,000 persons in the European Union.

How is this medicinal product expected to act?
Anti-CD147 murine monoclonal IgM is an antibody. Antibodies are proteins which specifically recognise and attach themselves to certain foreign substances, such as proteins found on the surface of cancer cells or bacteria. In the case of this antibody, the target is a protein (CD-147) that is found on those cells of the immune system that are activated, thereby causing the graft versus host disease. The

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antibody is expected to bind to these cells and to induce their destruction. Cells, which are not involved in the immune reaction and, therefore, not activated at this time, would be preserved.

What is the stage of development of this medicinal product?
At the time of submission of the application for orphan designation, clinical trials in patients with GvHD were ongoing.

Anti-CD147 murine monoclonal IgM had not been marketed anywhere worldwide for GvHD, at the time of submission. Orphan designation of anti-CD147 murine monoclonal IgM had been granted by the United States Food and Drug Administration (FDA) for the treatment of acute GvHD.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 09 October 2002 a positive opinion recommending the grant of the above-mentioned designation.

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Opinions on orphan medicinal products designations are based on the following cumulative criteria: (i) the seriousness of the condition, (ii) the existence or not of alternative methods of diagnosis, prevention or treatment and (iii) either the rarity of the condition (considered to affect not more than five in ten thousand persons in the Community) or the insufficient return of development investments.

Designated orphan medicinal products are still investigational products, which have been considered for designation on the basis of potential activity. An orphan designation is not a marketing authorisation. As a consequence, demonstration of the quality, safety and efficacy will be necessary before this product can be granted a marketing authorisation.

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*Disclaimer: The number of patients affected by the condition is estimated and assessed for the purpose of the designation, for a European Community population of 377,000,000 (Eurostat 2001) and may differ from the true number of patients affected by the condition. This estimate is based on available information and calculations presented by the sponsor at the time of the application.