



## Chugai Presents Interim Analysis Data of Phase I/II Study of SKY59, anti-C5 antibody in PNH at ASH

-- SKY59 shows tolerability and efficacy in patient subjects --

TOKYO, December 6, 2018 – [Chugai Pharmaceutical Co., Ltd.](#) (TOKYO: 4519) today announced that the interim analysis data of the phase I/II study COMPOSER study (NCT03157635) of anti-C5 antibody SKY59, an investigational drug administered subcutaneously\* for Paroxysmal Nocturnal Hemoglobinuria (PNH) in patient subjects, was presented at the 60th American Society of Hematology (ASH) Annual Meeting held in San Diego, the United States.

The main results of the interim analysis are as follows:

- SKY59 is well tolerated and no related severe adverse events were confirmed for all PNH patients treated
  - Mild to moderate adverse events observed were infections, musculoskeletal pains, headaches, skin rashes and others
- Complete complement inhibition was achieved for all PNH patients treated
- Good control of intravascular hemolysis was shown for all PNH patients treated
  - Reduction of lactate dehydrogenase (LDH) was shown in treatment naïve patients (Part 2)
  - Maintenance of low LDH levels was shown in patients switching from eculizumab to SKY59 (Part 3)

\* First treatment will be dosed intravenously, and the maintenance therapy will be dosed subcutaneously.

### **COMPOSER Study**

#### **Summary:**

A phase I/II global, multicenter, open-label study to assess the safety and efficacy, pharmacokinetics, and pharmacodynamics of SKY59 in healthy volunteers and in patients with PNH.

#### **Primary Endpoints (Patients subjects: Parts 2 and 3):**

Safety and tolerability of SKY59, pharmacodynamic effect of multiple doses of SKY59 on complement activity in patients.

#### **Select Secondary Endpoints (Patients subjects: Parts 2 and 3):**

Change in LDH, change in free hemoglobin, proportion of patients with stabilized hemoglobin levels, proportion of transfusion free patients.

### Study Design:

This study consists of three parts; Part 1 is healthy volunteers and Part 2 and Part 3 are PNH patients. At the interim analysis, Part 1 and Part 2 were completed and Part 3 was ongoing. The number of patients in Part 3 was 16 at the interim analysis.

Part 1: Healthy volunteers (N=15)	Single ascending dose study Healthy volunteers were randomized to receive a single dose of 75mg, or 125mg IV, or a single dose of 100mg SC, respectively.
Part 2: Treatment-naïve patients including two C5 SNP** patients (N=10)	Intra-patient single ascending dose study Patients received IV dose of 375mg, 500mg, and 1000mg of SKY59 on day 1, 8 and 22, respectively, followed by weekly dose of SKY59 of 170mg SC starting on day 36.
Part 3: PNH patients who had been on eculizumab for at least 3 months (N=18)	Multiple-dose study Patients received an IV loading dose of 1000mg SKY59 on day 1, 2 weeks after their last eculizumab dose, and were randomized to receive 170mg SC QW (injection volume 1mL), 340mg SC Q2W (injection volume 2mL) or 680mg SC Q4W (injection volume 4mL) of SKY59 starting on day 8.

\*\* Single Nucleotide Polymorphism

### About Paroxysmal Nocturnal Hemoglobinuria (PNH)

Paroxysmal nocturnal hemoglobinuria (PNH) is an acquired clonal disorder of hemopoietic stem cells with an acquired mutation in the PIG-A gene characterized by the destruction of red blood cells (hemolytic anemia) by the complement system, a part of the body's innate immune system. PNH can often occur in or interact with patient with an acquired bone marrow failure disease where aplastic anemia (AA) is typical. Thrombosis is a characteristic complication of PNH even though only a few cases ( $\leq 10\%$ ) are reported in Japan. It is reported that a small number of patients with PNH would develop acute leukemia (3%).

Source: Japan Intractable Diseases Information Center (<http://www.nanbyou.or.jp/entry/3784>)

### About SKY59

SKY59 is an anti-C5 recycling antibody created using Chugai's innovative Sequential Monoclonal Antibody Recycling Technology (SMART). [Chugai Pharmabody Research Pte. Ltd](#) in Singapore, a research center which specializes in exploring Chugai's proprietary antibody engineering technology, engaged in the early development of SKY59. The Recycling Antibody is engineered to have a pH-dependence at the antigen binding part so that a single antibody molecule can bind to an antigen multiple times, thus having a longer half-life compared with a conventional antibody. SKY59 is designed to target C5, a key component of the complement system, and is expected to control complement activity. The molecule's subcutaneous administration, enabled by SMART, would significantly reduce the treatment burden for patients with PNH and their caregivers.

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