SYNOPSIS

Name of Sponsor/Company	Daiichi Sankyo Co., Ltd.
Name of Finished Product	INAVIR® DRY POWDER INHALER 20mg
Name of Active Ingredient	Laninamivir Octanoate Hydrate（JAN）
Title of St udy	A Phase 3 Study of CS-8958 − A randomized study of CS-8958 comparing two inhalers in patients with influenza virus infection −
Investigators	
Study Centre(s)	
Publication (reference)	Not published.
Studied Period	
Phase of Development	Phase 3
Objectives	The objective of this study is to assess and compare the efficacy, safety and pharmacokinetics of a single inhalation of CS-8958 40 mg between an inhaler for commercial use (TwinCaps) and an inhaler for investigational use in patients with type A or B influenza virus infection.
Methodology	A multicenter, randomized, open-label comparative study
Number of Patients (planned and analyzed)	Planned number of patients：140 subjects (70 in the TwinCaps group and 70 in the investigational use group) The target number of subjects required for pharmacokinetic evaluation was 10 for each group. Full analysis set (FAS): 182 subjects (90 in the TwinCaps group and 92 in the investigational use group)
Diagnosis and Main Criteria for Inclusion	Patients with type A or B influenza virus infection who met all of the following criteria: 1) Influenza virus-positive by an influenza rapid diagnostic kit, and diagnosed with influenza virus infection by the investigators 2) Body temperature (axillary) ≥ 37.5°C at the time of informed consent 3) Within 36 hours after the onset of any influenza symptoms (fever [feeling of fever], headache, myalgia/arthralgia, fatigue, chill/sweating, nasal symptoms, sore throat, cough) at the time of informed consent 4) Aged ≥ 20 years as of informed consent drug using the inhaler
Test Product, Dose and Mode	CS-8958-20TC

of Administration	CS-8958 Subjects received a single inhalation of CS-8958 40 mg using either TwinCaps or the investigational use inhalers.
Duration of Treatment	Single dose
Reference Therapy, Dose and Mode of Administration	None
Criteria for Evaluation	Primary Endpoint: Time to Alleviation of Influenza Illness
Statistical Method	Efficacy Analysis; Primary analysis: The TwinCaps and the investigational use groups were compared using the generalized Wilcoxon test.The median difference (the TwinCaps group − the investigational use group) and the 95% CI was calculated based on the generalized Wilcoxon test statistics. Safety Analysis; Adverse Events: The number of subjects and the incidence by treatment group were calculated for all adverse events and adverse events considered related to the study drug. They were also summarized by event and severity. The number of subjects with serious adverse events and adverse events considered related to the study drug and their incidences were calculated by treatment group.
Summary - Conclusion	Efficacy (primary endpoint): A Kaplan-Meier plot of the time to alleviation of influenza illness, the primary endpoint, showed that recovery from influenza illness was similar in the TwinCaps and the investigational use groups. The median time to alleviation of influenza illness was 72.0 hours in the TwinCaps group and 78.0 hours in the investigational use group. The median difference (95% CI) was −6.0 (−23.9 to 6.7) hours and the time to alleviation of influenza illness was comparable between the two groups. Safety: The incidence of adverse events was 20.9% (19/91) in the TwinCaps group and 12.1% (11/91) in the investigational use group.
Date of Report	August 30, 2011