SYNOPSIS OF RESEARCH REPORT [redacted]
(PROTOCOL NV20236)

COMPANY: NAME OF FINISHED PRODUCT: NAME OF ACTIVE SUBSTANCE(S):	(FOR NATIONAL AUTHORITY USE ONLY)

TITLE OF THE STUDY / REPORT No. / DATE OF REPORT	An open-label multi-center trial of oseltamivir for the seasonal prophylaxis of influenza in children / Report No. [redacted] / May, 2008		
INVESTIGATORS / CENTERS AND COUNTRIES	[redacted] US US US Canada		
PUBLICATION (REFERENCE)	None		
PERIOD OF TRIAL	Dec 18, 2006 – May 23, 2007	CLINICAL PHASE	IIIb
OBJECTIVES	The primary objective of this study was to evaluate the safety of 6 weeks of seasonal prophylaxis of influenza with oseltamivir in children. Additionally, the effect of oseltamivir in preventing laboratory confirmed clinical influenza in children was evaluated.		
STUDY DESIGN	This was an open-label study to collect safety data on the use of oseltamivir for 6 weeks for the prevention of influenza in children during the influenza season.		
NUMBER OF SUBJECTS	52 subjects were enrolled		
DIAGNOSIS AND MAIN CRITERIA FOR INCLUSION	Children, 1 to 12 years of age who, in the opinion of their primary care physician, could benefit from seasonal prophylaxis during times when local surveillance indicated that influenza was present in the community. Children were negative for an influenza rapid diagnostic test at baseline and had no symptom suggestive of an influenza-like illness.		
TRIAL DRUG / STROKE (BATCH) No.	Oseltamivir Capsules Batch number: [redacted] Oseltamivir Powder (for suspension) Batch number: [redacted]		
DOSE / ROUTE / REGIMEN / DURATION	Oseltamivir dry powder (reconstituted to a concentration of 75 mg/ml) and 75 mg capsules. Children 1 - 12 years: Oseltamivir syrup ≤ 15 kg 30 mg once daily > 15 – 23 kg 45 mg once daily > 23 – 40 kg 60 mg once daily > 40 kg 75 mg once daily (syrup or capsules) Dose adjustments were not permitted. Oral dosing 6 weeks duration		
CRITERIA FOR EVALUATION			
EFFICACY:	Proportion of subjects with laboratory confirmed clinical influenza at any time post baseline up to and including the 70 day assessment.		
SAFETY:	Adverse events, physical examination, vital signs and clinical laboratory evaluations		
STATISTICAL METHODS	This study was conducted primarily to evaluate safety and therefore no formal statistical analysis was performed. The incidence of laboratory-confirmed clinical influenza and significant clinical events are descriptively summarized.		

METHODOLOGY:

Fifty-two children aged between 1 and 12 years were enrolled into this study if, in the opinion of the investigator, they were at risk for morbidity or mortality from influenza and could therefore benefit from seasonal prophylaxis. All subjects were negative for a rapid diagnostic test for influenza at baseline. Subjects received one daily dose of oseltamivir (dependent on weight) during a period of 6 weeks. Daily diary cards were supplied to the parents/guardians of the subjects to collect data on influenza symptoms, temperature and dosing times. The baseline assessment included a rapid diagnostic test for influenza virus shedding, nasal and throat swabs for viral shedding, safety lab assessments, serology, a physical examination (weight and height) and vital sign assessment. On Day 21,

SYNOPSIS OF RESEARCH REPORT [redacted] (PROTOCOL NV20236)

COMPANY: NAME OF FINISHED PRODUCT: NAME OF ACTIVE SUBSTANCE(S):	(FOR NATIONAL AUTHORITY USE ONLY)

weight was assessed, vital signs were measured and the diary card was reviewed. Safety labs were only reassessed at this visit if baseline levels were abnormal. Safety labs, serology, weight and vital signs were assessed and the diary card was reviewed on Day 42 of treatment. At the follow-up visit on Day 72, serology, weight and vital signs were assessed and the diary card was reviewed. Safety labs were assessed if Day 42 levels were abnormal. Subjects were encouraged to make illness visits at any time during the study if they had influenza-like symptoms whereby nasal and throat swabs were to be taken, vital signs and safety labs were to be assessed if indicated and the diary card was to be reviewed. Adverse events, secondary illnesses and treatments were recorded throughout the study, from Day 1 until Day 70.

EFFICACY RESULTS:

No cases of laboratory confirmed clinical influenza were confirmed. Three subjects had laboratory influenza confirmed by a ≥ 4-fold increase in antibody titer at the end of treatment assessment. A further 3 subjects had laboratory influenza confirmed by a ≥ 4-fold increase in antibody titer at the follow-up visit. Of the 6 subjects with laboratory confirmed influenza, 4 were asymptomatic and 2 experienced limited influenza symptoms, not meeting the criteria for clinical influenza.

Summary of Efficacy Results (ITT population)

Efficacy Parameter	YES (%)	NO (%)
Laboratory Confirmed Clinical Influenza (Fever, cough and coryza)	0	52
Laboratory Confirmed Clinical Influenza (Fever, cough and/or coryza)	0	52
Laboratory Confirmed Influenza	6 (12%)	46 (88%)
Asymptomatic Influenza	4 (8%)	48 (92%)
Influenza-like illness not caused by influenza virus (fever, cough and coryza)	3 (6%)	49 (94%)
Influenza-like illness not caused by influenza virus (fever, cough and/or coryza)	6 (12%)	46 (88%)

SAFETY RESULTS:

There were no unexpected safety concerns observed during the conduct of this study. There were no deaths or serious adverse events. Over the treatment period of 42 days, up to and including 2 days after last day of oseltamivir administration, 17/49 (35%) subjects reported 22 adverse events. The most common adverse events were gastrointestinal disorder (6 subjects), infection (6 subjects) and respiratory disorder (3 subjects). Twelve of the 22 adverse events were rated by the investigator as mild in intensity, 8 were rated as moderate and 2 events (toothache and otitis media) were rated as severe. The investigator considered 3 adverse events (1 moderate nausea, 1 mild nausea and 1 vomiting) probably related to treatment and 19 adverse events not related to treatment. Two subjects were withdrawn from the study due to adverse events. A 3-year-old male was withdrawn due to oral mucosal blistering, considered by the investigator as unrelated to treatment, and an 11-year-old female was withdrawn due to nausea which the investigator considered related to treatment.

Six subjects reported a further 6 adverse events (3 infections, including otitis media, tonsillitis and sinusitis, 1 joint injury, 1 headache and 1 wheezing) from the period > 2 days after stopping treatment up until the Day 70 follow-up.

CONCLUSIONS:

Once daily administration of oseltamivir (dose dependent on weight) to children aged between 1 and 12 years of age is well-tolerated.