

# **Phase I Clinical Trial to Evaluate the Inhaled Safety and Tolerability of the Unique Antimicrobial OligoG Administered to Healthy Subjects**

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# Financial Disclosure

- I have the following financial arrangements to disclose:
  - ▶ The presenter represents the CRO that was contracted by the study sponsor (AlgiPharma AS) to plan, manage, analyze and interpret the clinical study. The financial contribution by AlgiPharma AS was strictly fee for service for conducting the study. Furthermore, I have no proprietary interest in the tested product, no equity interest in the sponsoring company and no significant payment (except fee for service) has been received.

# Cystic Fibrosis (CF)

- Pulmonary function compromised by elevated mucus viscosity
  - Secondary to defect in the Cystic Fibrosis Transmembrane Regulator (CFTR) protein
  - Viscosity associated with mucin polymer cross-linking
- Chronic pulmonary colonization of *Pseudomonas spp.* significant clinical problem
  - Biofilm expressing phenotype
- Required novel drug features would be
  - To promote sputum clearance
  - To increase the effectiveness of current antibiotics *in situ*

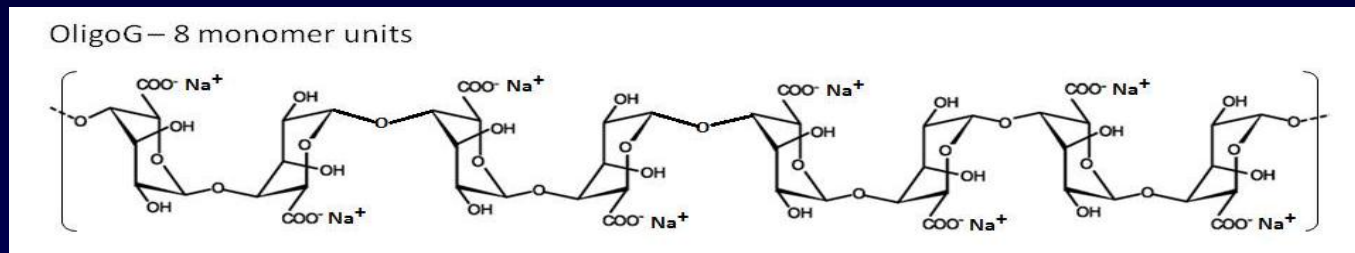
# Alginate oligosaccharide - OligoG

- Model systems and *ex vivo* studies on CF sputum indicate that OligoG
  - ▶ Reduces CF sputum viscosity and weakens microbial biofilms via inhibition of polymeric cross-linking
    - May increase pulmonary clearance of sputum
    - May promote diffusion of antimicrobial agents into microbial biofilms and augment their effectiveness
  - ▶ Antimicrobial properties (ICAAC Posters F1:1600-6)
    - Intrinsic antimicrobial effects of OligoG
    - Reduction in MICs for selected antibiotics
- Orphan Drug Medicinal Product Designation
  - ▶ EU 2007

# OligoG: Composition and Structure

- Sodium alginate

- ▶ Co-polymer of repeating guluronate & mannuronate monomers



- $(\text{NaC}_6\text{H}_7\text{O}_6)_n$
- $n = \#$  of monomer units

- OligoG

- ▶ Drug substance comprises 5-20 monomer units
- ▶ Sterile, isotonic solution
- ▶ Administered via inhalation

# Phase I Study: Experimental Design

- Single Centre, randomized, placebo controlled, dose escalation study
- 28 subjects
  - ▶ Single Dose (Cohort 0): n=4; 2 active, 2 placebo
    - Cohort 0: 1.5 ml single dose (90 mg) with 3-day observation period
  - ▶ Multiple Dose (Cohorts 1, 2 and 3): n=8; 6 active, 2 placebo
    - Cohort 1: 1.5 ml OD (90 mg/day) for 3 days
    - Cohort 2: 4.5 ml OD (270 mg/day) for 3 days
    - Cohort 3: 4.5 ml BID (540 mg/day) for 3 days
- Sidestream Plus/Portaneb aerosol delivery system (Phillips Respironics)
  - OligoG 6% solution (i.e. 60 mg/ml)
  - Placebo 0.9% NaCl

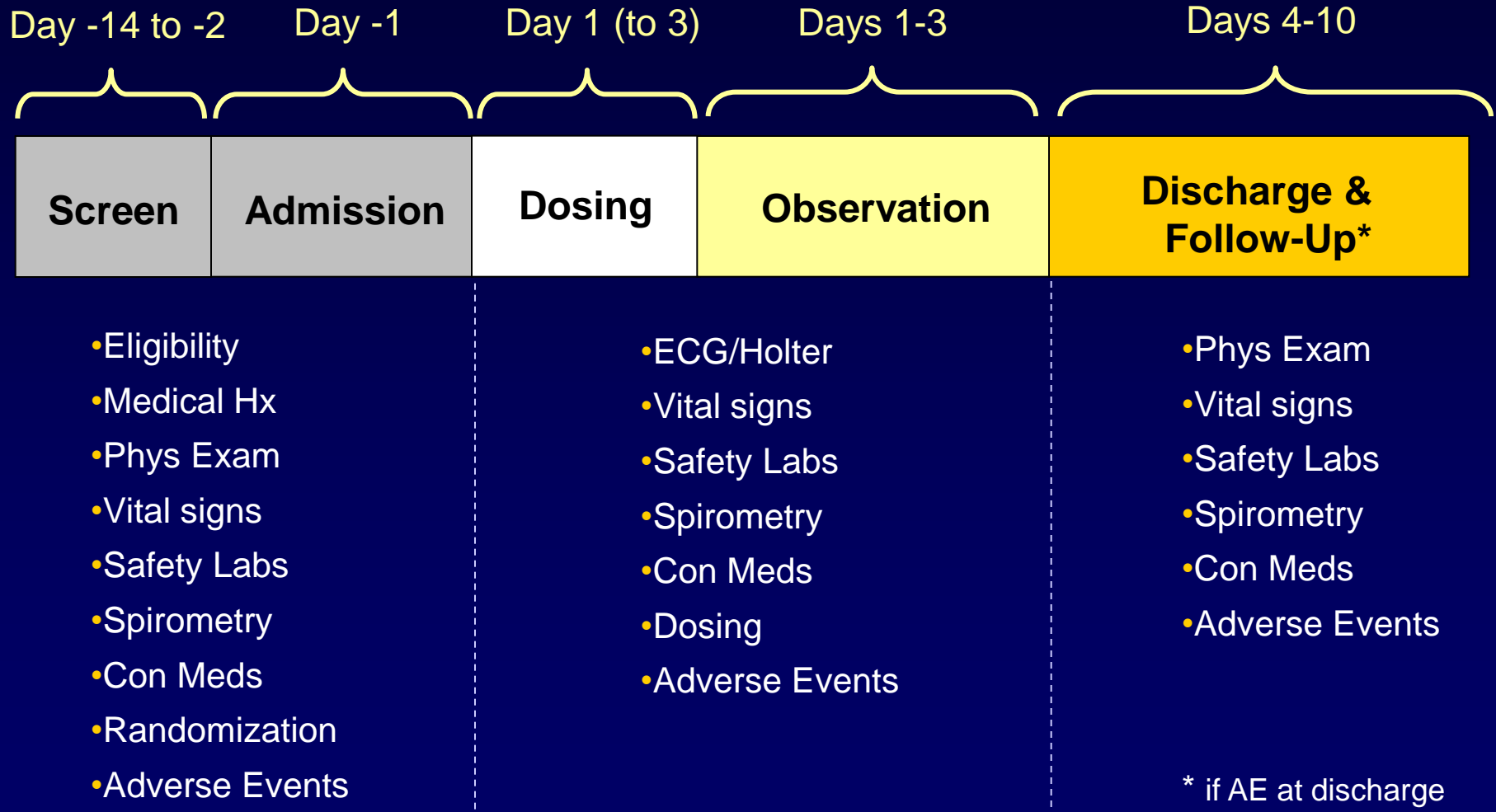
# Phase I Study: Objectives

- Primary
  - ▶ Safety and local tolerability of single and multiple dose administration of OligoG in healthy volunteers
    - pulmonary function
    - pulmonary adverse events
- Secondary
  - ▶ Other, overall safety
    - physical examination
    - vital signs
    - pulse oximetry
    - ECG
    - haematology and clinical chemistry
    - pharmacokinetics

# Phase I Study: Key Eligibility Criteria

- Healthy, male subjects aged 18 to 65 years
- Normal pulmonary function
  - ▶ FEV1  $\geq$  80% of predicted (for age, sex, height and race)
  - ▶ FEV1/FVC ratio  $\geq$  0.7
- Body Mass Index (BMI) of 18.0 – 29.9 kg/m<sup>2</sup>
- No history of any clinically relevant chronic respiratory disorder
- No history of smoking within 12 months prior to Day 1
- No inhaled drugs within 30 days prior to Day 1
- No systemic drugs within 14 days prior to Day 1
- No known allergic reactions or hypersensitivity to any component of the study medication

# Phase I Study: Visit Schedule



# Phase I Study: Baseline Subject Parameters

- All Cohorts were well-balanced by key baseline parameters

		OligoG					Placebo
Dose [mg/d]		90 SD	90	270	540		
Number		2	6	6	6	8	
Race	Caucasian	Number	2	6	6	6	8
		(%)	(100)	(100)	(100)	(100)	(100)
Age [years]		Number	2	6	6	6	8
		Mean (SD)	46.31 (2.14)	36.96 (14.33)	31.78 (8.09)	36.33 (13.42)	27.72 (6.25)
Weight [kg]		Number	2	6	6	6	8
		Mean (SD)	75.60 (4.38)	79.15 (15.17)	85.70 (4.53)	82.23 (10.02)	82.54 (7.61)
BMI [kg/m <sup>2</sup> ]		Number	2	6	6	6	8
		Mean (SD)	25.16 (2.48)	24.89 (2.89)	26.83 (1.59)	25.83 (2.88)	26.18 (2.51)

# Phase I Study: Adverse events

Cohort	0	1	2	3
	2A, 2P	6A, 2P	6A, 2P	6A, 2P
OligoG (A)	-	-	Headache 4 <sup>*a</sup>	Dry cough 2 <sup>**</sup> Headache 1 <sup>**</sup>
Placebo (P)	-	-	Headache 1 <sup>*</sup>	Incr CRP 1 <sup>***</sup> Hand tingling 1 <sup>*</sup>

All AEs were mild and have been resolved without any sequelae or any use of con med

\* Unlikely related to study medication

\*\* Possibly or probably related to study medication

\*\*\* Transiently

<sup>a</sup> 3 of the events in the same subject

# Phase I Study: Pharmacokinetic Analysis

- Plasma OligoG concentrations were determined via Liquid Chromatography with Tandem Mass Spectrometry detection (LC-MS-MS)
- Limit of Quantification (LOQ) was  $0.83 \mu\text{g}\cdot\text{ml}^{-1}$
- Plasma OligoG concentrations were below the LOQ at all timepoints for all subjects

# Phase I Study: Conclusions

- Inhaled OligoG is well tolerated when administered for up to 270 mg BID for 3 days
- No SAEs, no deaths or discontinuations
- All AEs were mild and transient
  - ▶ Equal distribution between OligoG and placebo
- No clinically significant changes in:
  - ▶ Safety laboratory parameters
  - ▶ Vital signs
  - ▶ ECG
  - ▶ Spirometry parameters
- No systemic uptake following administration via inhalation
- Supports the continued clinical development of OligoG into patients

# OligoG Development: Next Steps

- Phase IIa clinical trial in adult CF chronically colonised with *P. aeruginosa*
  - Planned for Q1, 2011
  - Europe, 1-2 countries
- Randomized, placebo-controlled, crossover design
- 1-2 dose levels of OligoG versus placebo BID for 28 days
- Endpoints
  - Safety and local tolerability
  - Microbiological outcomes
  - Pulmonary function
  - Respiratory symptoms

# References and Contact

- EudraCT no.: 2009-009330-33
- [www.clintrials.gov](http://www.clintrials.gov): NCT00970346
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**Thank you for your attention!**