IN-006: An Inhalable SARS-CoV-2-Directed mAb

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Background

COVID-19 is predominantly a respiratory illness, with respiratory failure being the most frequent cause of mortality (~86% total). As SARS-CoV-2 spreads throughout the respiratory tract, daughter virions are shed almost exclusively into the airway mucus, making the virus difficult to reach with systemic therapies and necessitating large doses of drug when given by IV or IM. With the support of USAMRDC and MTEC, Inhalon demonstrated the safety and tolerability of IN-006, an inhaled treatment for COVID-19, in a recently completed Phase 1 clinical study. This study also demonstrated the feasibility of inhaled delivery which can overcome the limitations of other routes of administration.

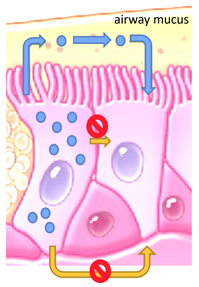
About Inhalon Biopharma: Inhalon is a clinical-stage, inhaled immunotherapy company developing prophylactic and therapeutic antibodies (mAb) for acute respiratory infections. Inhalon has a patented, proprietary muco-trapping mAb platform technology with broad IP coverage of inhaled mAb delivery. In addition to working on treatments and preventative measures for COVID-19, Inhalon is currently advancing the development of inhaled mAbs against respiratory syncytial virus (RSV), metapneumovirus (MPV), and influenza. Inhalon is a non-traditional contractor.

Spread of SARS-COV-2 in the Lung

Studies have shown that SARS-CoV-2, just like SARS-CoV-1, NL63 coronavirus, and other respiratory viruses, infects the airway epithelium via the apical membrane. More importantly, airway cells shed viruses back into the airways, which then propagate to the lower respiratory tract over time. Thus, direct delivery of mAbs into the lung will be far more effective at halting the spread of the infection, and require much lower doses of mAb, providing more immediate and effective antiviral activity.

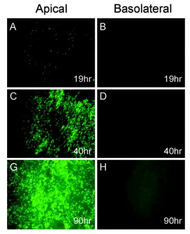
SARS, RSV, MPV, PIV spreads by shedding in the airway mucus

Infection does not spread from cell to cell or systemically



Lung Epithelium Cross-Section

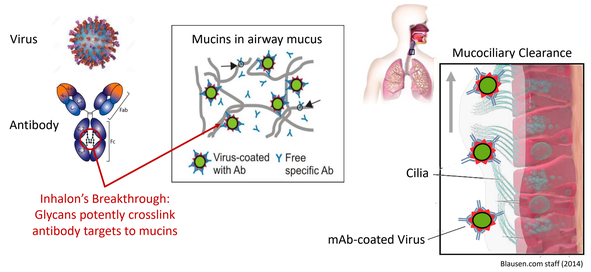
Respiratory viruses predominantly shed progeny back into airway mucus



Surface	PFU/mL
Apical	10^7
Basal	10^4

Small molecules and systemic mAbs cannot reach pathogens in the airway mucus

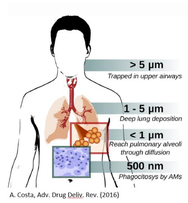
Inhalon's Inhaled Antibody Platform



Muco-trapping antibodies bind, neutralize, and trap virus. Trapped viruses are cleared from the lungs through normal mucociliary clearance.

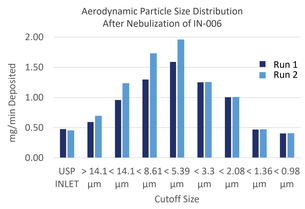
Nebulized Drug Delivery

Muco-trapping antibodies | Battery operated nebulizer | Inhale mist 3-5 minutes



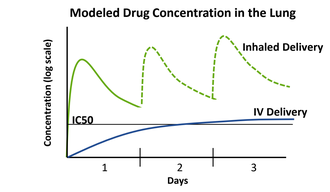
A. Costa, Adv. Drug Deliv. Rev. (2016)

Unlike nasal sprays, nebulization generates aerosols that deliver antibody throughout the entire respiratory tract

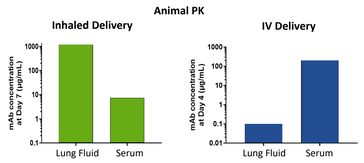


Low-cost handheld units generate aerosols with no loss of antibody activity for immediate protection of airways

Inhalation Delivers Far More Antibody into the Lung than IV Delivery



"Instantaneous" lung C_{max} achieved with inhalation vs. typically 2-3 days for i.v. administration

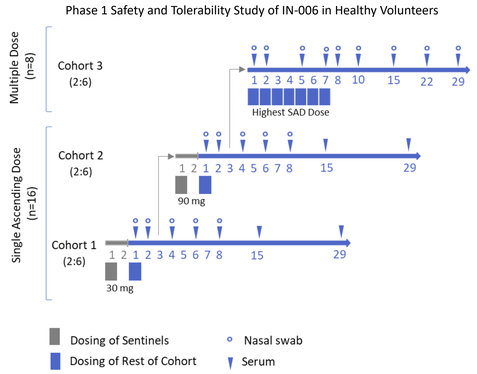


>10,000-fold higher concentration than with i.v. administration

bioRxiv 2022.02.27.482162: https://doi.org/10.1101/2022.02.27.482162

Inhaled IN-006 Phase 1 Clinical Study

Phase 1 Study Design



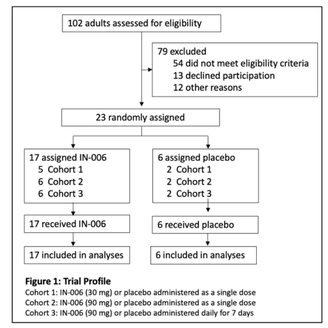


Figure 1: Trial Profile
Cohort 1: IN-006 (30 mg) or placebo administered as a single dose
Cohort 2: IN-006 (90 mg) or placebo administered as a single dose
Cohort 3: IN-006 (90 mg) or placebo administered daily for 7 days

IN-006, an inhaled formulation of regdanvimab, provided as a formulated liquid by Cellltrion, Inc.

Inhaled IN-006 Phase 1 Clinical Study

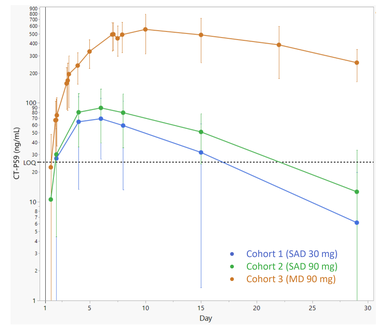
Phase 1 Safety Data

	IN-006 30 mg Single dose (n=5)	IN-006 90 mg Single dose (n=6)	IN-006 90 mg 7 daily doses (n=6)	All IN-006 (n=17)	Placebo (n=6)
Participants with any TEAE	3 (60%)	3 (50%)	4 (66.7%)	10 (58.8%)	2 (33.3%)
Participants with nebulization-related TEAE*	1 (20%)	0	1 (16.7%)	2 (11.8%)	0
Number of TEAEs	6	5	6	17	4
Number of participants with TEAEs by SOC and preferred term					
Nervous system disorders	2 (40%)	1 (16.7%)	2 (33.3%)	5 (29.4%)	2 (33.3%)
Dizziness	0	0	2 (33.3%)	2 (11.8%)	0
Dysgeusia	0	1 (16.7%)	0	1 (5.9%)	0
Headache	2 (40%)	0	0	2 (11.8%)	2 (33.3%)
Presyncope	0	1 (16.7%)	0	1 (5.9%)	0
Respiratory, thoracic and mediastinal disorders	1 (20%)	2 (33.3%)	1 (16.7%)	4 (23.5%)	0
Cough	1 (20%)	0	0	1 (5.9%)	0
Oropharyngeal pain	0	2 (33.3%)	0	2 (11.8%)	0
Throat irritation	0	0	1 (16.7%)	1 (5.9%)	0
Musculoskeletal and connective tissue disorders	0	0	1 (16.7%)	1 (5.9%)	0
Pain in extremity	0	0	1 (16.7%)	1 (5.9%)	0
General disorders and administration site conditions	0	1 (16.7%)	0	1 (5.9%)	1 (16.7%)
Complication associated with device**	0	1 (16.7%)	0	1 (5.9%)	0
Fatigue	0	0	0	0	1 (16.7%)
Investigations	1 (20%)	0	1 (16.7%)	2 (11.8%)	0
Forced expiratory volume decreased	0	0	1 (16.7%)	1 (5.9%)	0
Spirometry abnormal	1 (20%)	0	0	1 (5.9%)	0
Transaminases increased	1 (20%)	0	0	1 (5.9%)	0

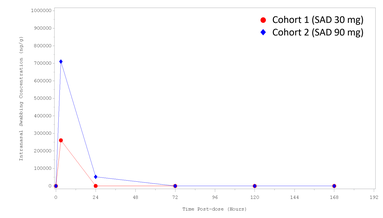
100% of subjects completed the study through Day 29. No SAEs observed. All AEs resolved without sequelae.

Inhaled IN-006 Phase 1 Clinical Study

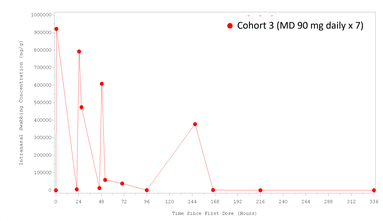
Phase 1 Pharmacokinetics Data



Cohort	Median Serum C_{max} (ng/mL)	Median Serum T_{max} (hours)
Cohort 1	72	122
Cohort 2	80	119
Cohort 3	529	191



Cohort	Median Nasal C_{max} (µg/mL)	Median Nasal T_{max} (hours)
Cohort 1	135	3
Cohort 2	367	3



Cohort	Median Nasal C_{max} (µg/mL)	Median Nasal T_{max} (hours)
Cohort 3 (Day 1)	716	0.6
Cohort 3 (Day 7)	366	3

Inhaled Cocktail Phase 3 Clinical Study

Title: To Evaluate the Safety and Efficacy of Inhaled CT-P63 and CT-P66 Combination Therapy in Symptomatic Patients With COVID-19 Not Requiring Supplemental Oxygen

Estimated Enrollment: 2,200 patients
Allocation: Randomized
Intervention/Treatment: CT-P63 and CT-P66 / Placebo
Primary Outcome Measure: Time to clinical recovery up to Day 14
Secondary Outcome Measure: Overall safety up to Day 90
Estimated Start Date: April 2022
Clinicaltrials.gov ID: NCT05224856

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