

Clinical trials of inhaled interferon beta-1a (SNG001) in COVID-19 patients in the home and hospital settings

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synairgen



Disclosures

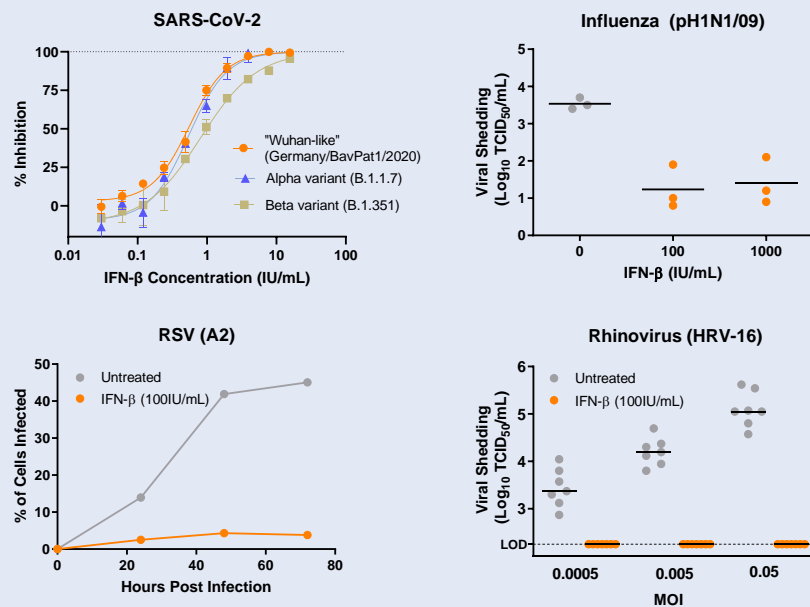
- Synairgen is a UK-based biotech company developing inhaled interferon beta (SNG001) as a treatment for severe viral lung infections
- Presenter
 - Employed by Synairgen
 - Owns shares and has share options



Rationale for Developing Inhaled Interferon beta (IFN- β) for Virus-induced Lower Respiratory Tract Illness

- IFN- β is a naturally occurring protein which orchestrates the body's antiviral defences
- Type I IFN deficiency is associated with severe viral lower respiratory tract illness
- Viruses suppress IFN- β production by cells to evade host immune response
- Antiviral activity demonstrated against key respiratory viruses including SARS-CoV-2

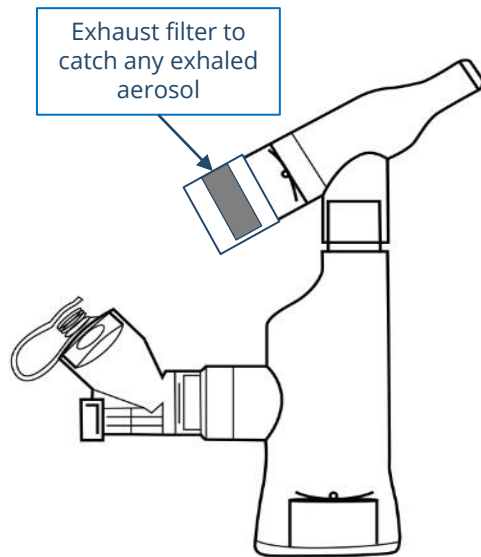
Antiviral activity of SNG001 (IFN- β) in cell based assays



Why inhaled?

The aim of administering SNG001 (Interferon beta-1a nebuliser solution) directly into the airways is to:

- Restore IFN- β levels at the site of infection in the lungs to drive antiviral responses to clear the virus
- Limit systemic exposure which can be associated with 'flu-like' symptoms when IFN- β is administered by injection



Aerogen Solo/Ultra

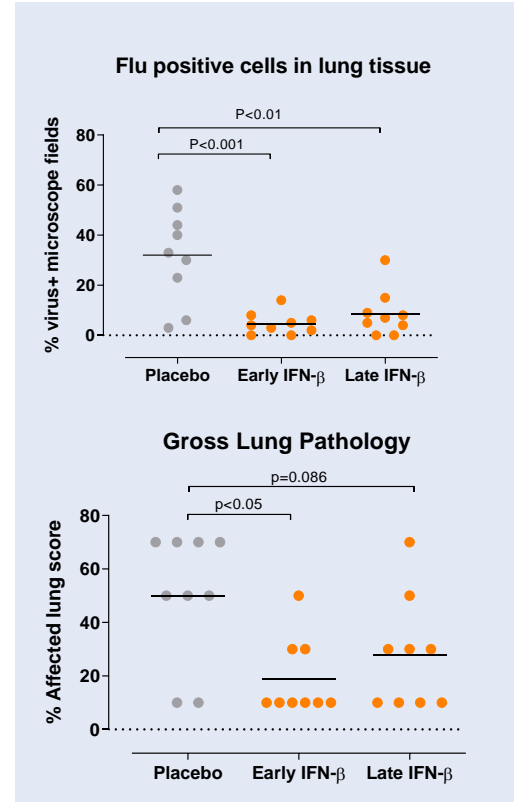
Pre- and Post-infection Treatment with Inhaled SNG001 in a Preclinical Model of Viral Pneumonia Driven by Pandemic H1N1

Challenge virus:

- pH1N1 (A/Netherlands/602/2009)
- 10^7 TCID50 units administered via intranasal and intratracheal routes

Drug delivery:

- Inhaled delivery using clinical device
- Dose relevant to clinical lung dose accounting for delivery efficiency

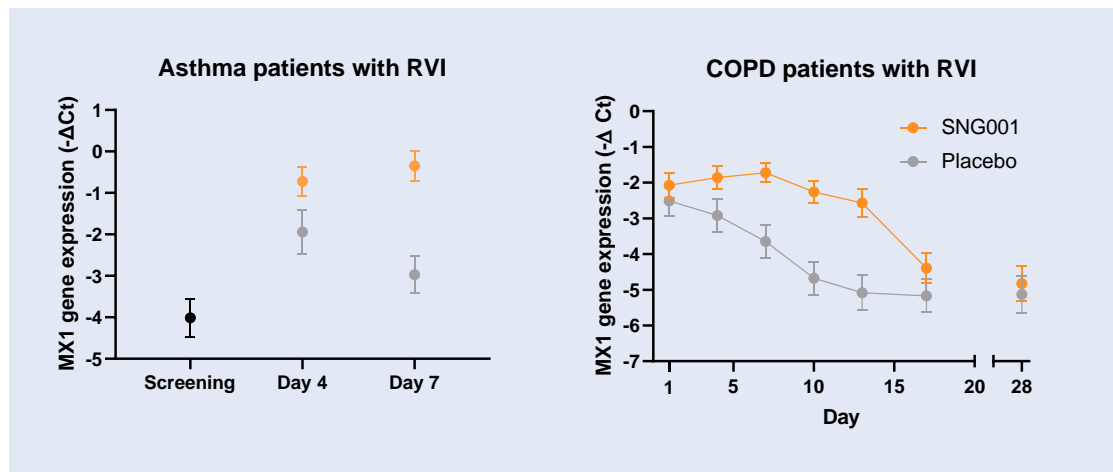


Randomised, double-blind, placebo-controlled clinical trials of SNG001(Interferon beta-1a nebuliser solution)

Study	Phase	Disease		Respiratory viral infection	Sponsor
SG004	Phase 1	Asthma		No	Synairgen
SG005	Phase 2	Asthma		Yes	Synairgen
INEXAS	Phase 2	Asthma		Yes	AstraZeneca
SG015	Phase 2	COPD	Part 1	No	Synairgen
			Part 2	Yes	Synairgen
SG016	Phase 2	Hospitalised COVID-19 Non-hospitalised COVID-19		Yes	Synairgen
ACTIV-2	Phase 2/3	Non-hospitalised COVID-19		Yes	NIH/NIAID
SG018 SPRINTER	Phase 3	Hospitalised COVID-19		Yes	Synairgen

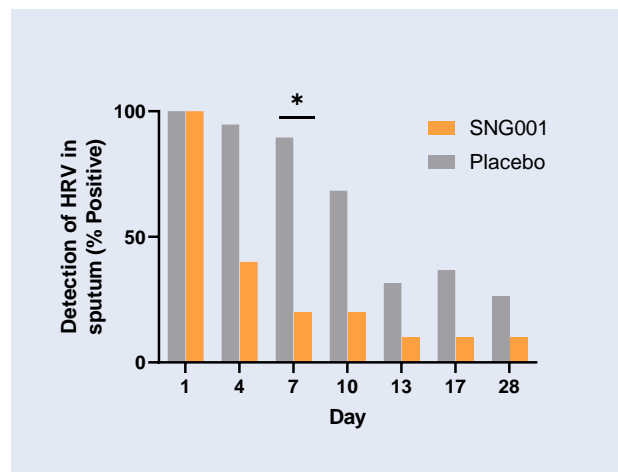
Clinical data supporting MoA: activation of lung antiviral defences (biomarkers) and accelerated viral clearance

Sputum cell gene expression of the IFN-dependent antiviral biomarker MX1



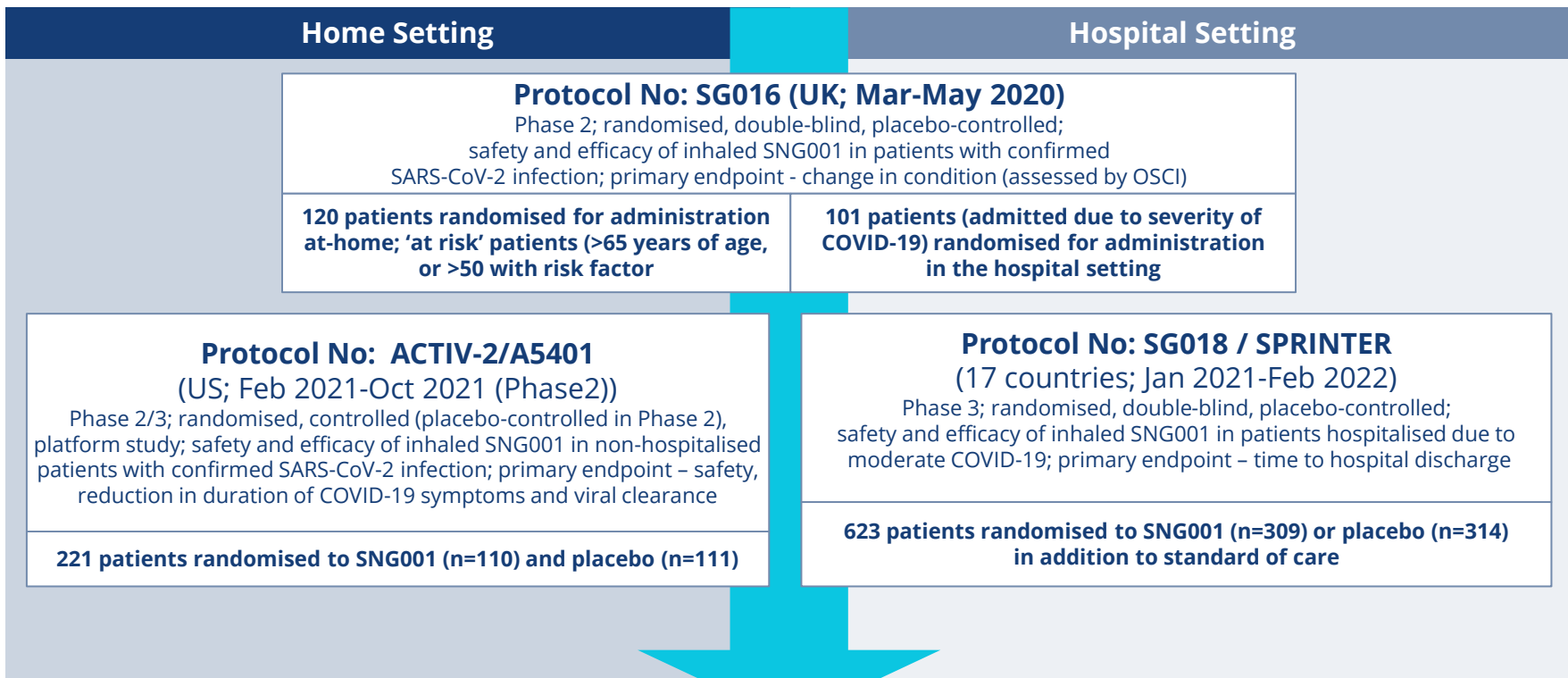
Djukanovic *et al.* (2014) AJRCCM 15;190(2):145-54

Viral clearance from the lungs (sputum)



Monk *et al.* (2023) Nebulized interferon beta-1a (SNG001) in the treatment of viral exacerbations of COPD. Submitted for publication

Clinical Development of SNG001 in COVID-19



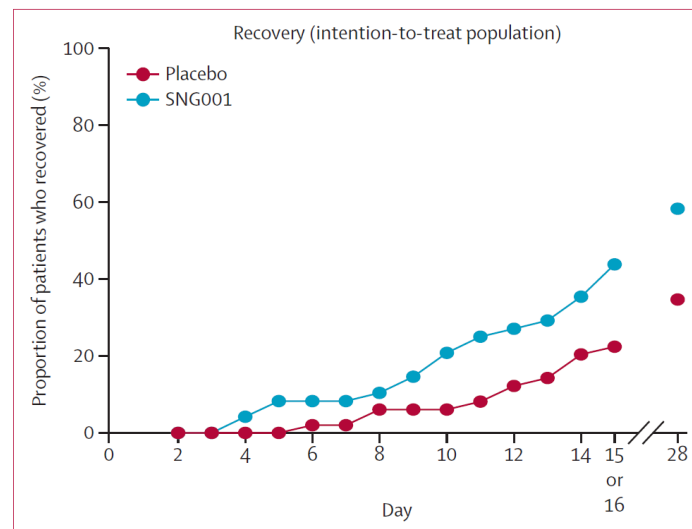
Phase 2 Results in Hospital Setting Supported Progression to SPRINTER Phase 3 Trial

Analysis of the WHO OSCI during the dosing period

	Intention-to-treat population		Per-protocol population	
	Ratio (95% CI)	p value	Ratio (95% CI)	p value
Odds of improvement on the OSCI	OR 2.32 (1.07-5.04)	0.033	OR 2.80 (1.21-6.52)	0.017
Time to severe disease or death (OSCI ≥ 5)	HR 0.50 (0.18-1.38)	0.179	Not calculated	..
Odds of severe disease or death (OSCI ≥ 5)	OR 0.28 (0.07-1.08)	0.064*	OR 0.18 (0.04-0.93)	0.041*
Time to intubation or death (OSCI ≥ 6)	HR 0.38 (0.09-1.65)	0.198	Not calculated	..
Odds of intubation or death (OSCI ≥ 6)	OR 0.42 (0.09-1.83)	0.246*	OR 0.31 (0.05-1.79)	0.189*
Time to recovery	HR 2.19 (1.03-4.69)	0.043	HR 2.29 (1.07-4.91)	0.033
Odds of recovery	OR 3.19 (1.24-8.24)	0.017	OR 3.18 (1.21-8.39)	0.019
Time to hospital discharge	HR 1.37 (0.85-2.20)	0.196	HR 1.53 (0.96-2.42)	0.072
Odds of hospital discharge	OR 1.63 (0.61-4.35)	0.330	OR 2.14 (0.64-7.12)	0.215

Table 3: Analysis of the WHO OSCI during the dosing period

Recovery (intention-to-treat population)



Monk *et al.* (2021) Safety and efficacy of inhaled nebulised interferon beta-1a (SNG001) for treatment of SARS-CoV-2 infection: a randomised, double-blind, placebo-controlled, phase 2 trial. *Lancet Respir Med*; 9(2):196-206

SPRINTER (SG018) Phase 3 Trial Design

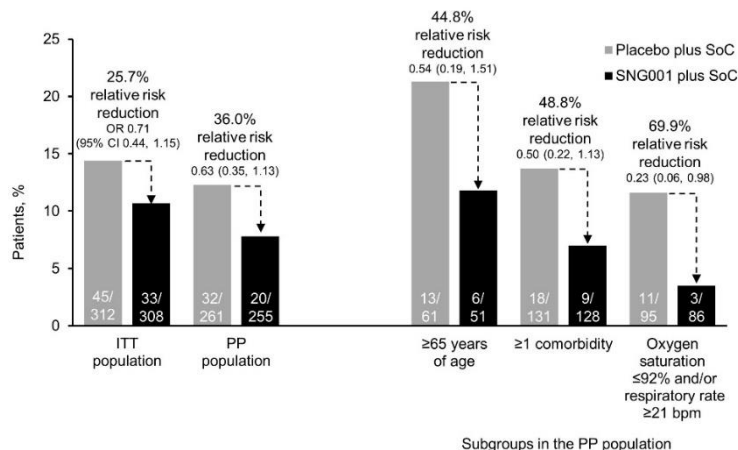


Study Title	A randomised, double-blind, placebo-controlled, Phase 3 trial to determine the efficacy and safety of inhaled SNG001 for the treatment of patients hospitalised due to moderate COVID-19
Primary Endpoints	Time to hospital discharge Time to recovery to 'No Limitation of Activities' up to Day 28
Key Secondary Endpoints	Progression to severe disease or death within 35 days Progression to intubation or death within 35 days Death within 35 days
Setting	Patients hospitalised due to COVID-19 requiring supplemental oxygen by mask or nasal prongs
Number of Patients	610+ patients
Dosing Regimen	<p>SNG001(15.6 MIU interferon beta-1a) or placebo (randomised 1:1) delivered by Aerogen Solo/Ultra vibrating mesh nebuliser with a filter on the exhalation port, once-a-day for up to 14 days on top of standard of care</p> <ul style="list-style-type: none">• The trial was conducted in 17 countries including Argentina, Belgium, Brazil, Colombia, France, Germany, India, Israel, Italy, Mexico, Netherlands, Portugal, Romania, Serbia, Spain, United Kingdom and United States• Recruitment completed: 623 patients randomised between January and November 2021

Summary of Efficacy and Safety (SPRINTER)

- The study did not meet its primary efficacy endpoints looking at hospital discharge and recovery
- There was an encouraging signal for the key secondary endpoint of prevention of progression to severe disease or death
- SNG001 was well tolerated

Progression to severe disease or death

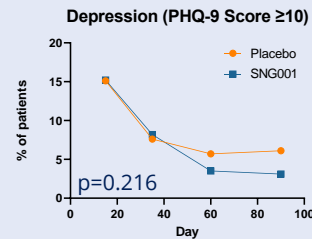
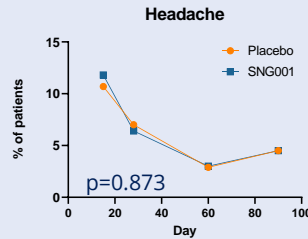
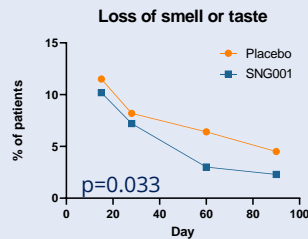
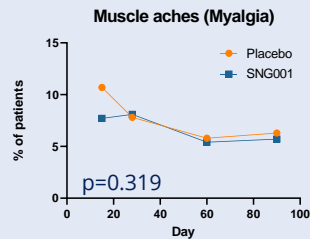
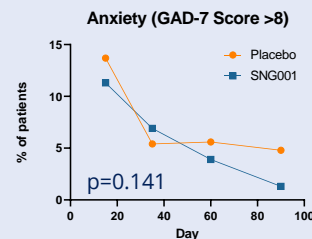
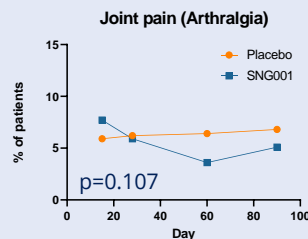
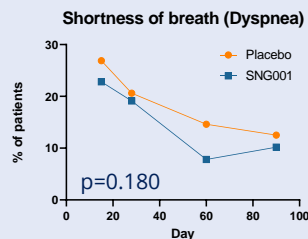
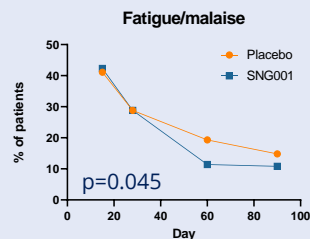


Monk *et al.* (2023) Nebulised interferon- β 1a (SNG001) in hospitalised COVID-19: SPRINTER phase III study. ERJ Open Res. 2023;9(2):00605-2022

Assessment of Long COVID (SPRINTER)

- Looking at fatigue (35% RRR), the predominant symptom of long COVID, and mental health, there is an intriguing positive signal in the SNG001 group

Long COVID symptoms



Statistical analysis: Comparison of the proportion of patients with symptoms or score on Day 60 and/or 90 using a Chi-Square test provided all counts are >5, otherwise a Fisher's Exact Test is used.

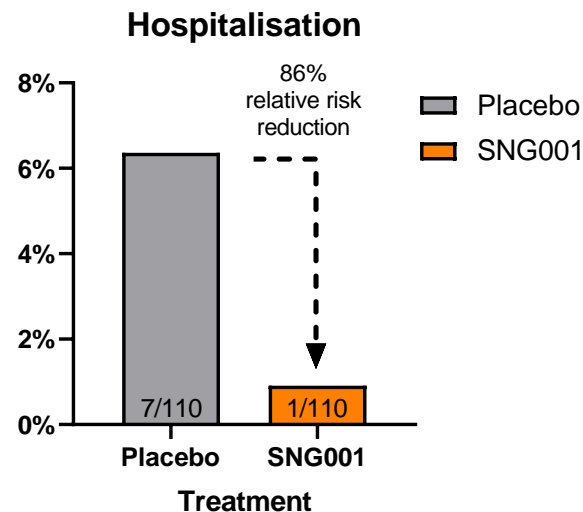
*No overall difference in FACIT-F, BPI or EQ5D VAS scores

ACTIV-2 (A5401) Phase 2 Trial Design

Study Title	Phase 2/3 Adaptive Platform Treatment Trial for Outpatients with COVID-19 (Adapt Out COVID)
Primary Objectives	Safety Duration of symptoms Viral clearance (nasopharyngeal swabs)
Setting	Symptomatic, non-hospitalised adults with COVID-19
Number of Patients	110 participants per investigational agent (and 110 on placebo) recruited across 25 US sites
Dosing Regimen	SNG001(15.6 MIU interferon beta-1a) or placebo (randomised 1:1) delivered by Aerogen Solo/Ultra vibrating mesh nebuliser with a filter on the exhalation port, once-a-day for up to 14 days on top of standard of care

Summary of Efficacy and Safety (ACTIV-2)

- Primary endpoints
 - No statistically significant differences with respect to safety, symptom resolution, or virology
- Fewer participants treated with SNG001 were hospitalized
 - 86% RRR (p=0.07; Two-sided Fisher's exact test)
 - There were no deaths in either arm
 - Placebo 2/58 (3.4%) versus SNG001 0/56 (0%) hospitalised in Synairgen's Phase 2 study (SG016)
- SNG001 was well tolerated
- DSMB recommended progression to Phase 3 in October 2021



SNG001: Substantial Clinical Database Indicating Favourable Local and Systemic Tolerability

- **Substantial clinical safety data base** from **7** clinical trials (predominantly randomised, double-blind, placebo-controlled) in range of populations including non-hospitalised and hospitalised patients;
- **Total of 750 patients treated with SNG001**, majority of which had confirmed or suspected respiratory viral infections (rhinovirus (RV), influenza, coronavirus, SARS-CoV-2, etc.)
- **515** patients had COVID-19; **67** had COPD; and **168** patients had Asthma
- **Favourable safety profile**; generally fewer patients on SNG001 reporting any adverse event or any serious adverse event versus patients on placebo. No specific safety signals seen.
- **Well tolerated locally (lung)**; lack of significant systemic tolerability concerns consistent with local delivery and **negligible systemic exposure (or ADAs)** to SNG001 after inhalation

Summary

- There remains a strong rationale for developing inhaled IFN- β as a broad-spectrum antiviral for severe viral lung infections
- Clinical trial results, including favourable safety profile, support continued investigation of SNG001 in trials in COVID-19 and against seasonal cold and flu viruses evaluating:
 - Prevention of hospitalisation in at risk patients in the home setting
 - Prevention of progression and/or mortality in at risk hospitalised patients
 - Prevention of the development of post viral symptoms e.g. long COVID

Acknowledgements

Thank you to everyone that contributed to our clinical trials:

- All patients
- All trial sites and investigators
- All vendors including Parexel, Data Magik, Veramed and tranScrip
- All members of the Synairgen oversight team
- ACTIV-2 Study Team

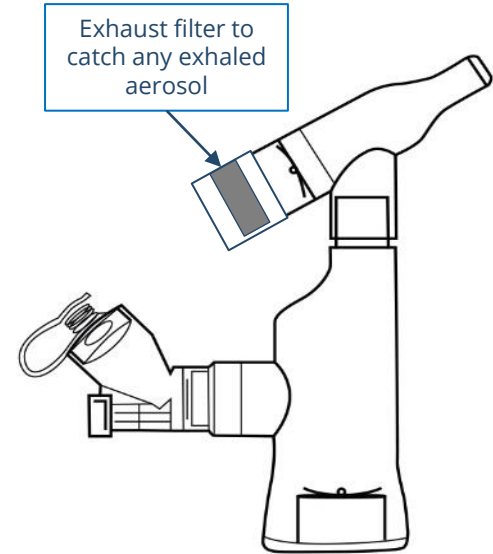
Thank you

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SNG001 (Interferon- β -1a Nebuliser Solution)

- Near neutral pH (pH 6.5); minimal excipients, no mannitol or HSA
- 3-year shelf-life
- IFN- β activity is maintained post-aerosolisation using specific vibrating mesh nebulisers
- Lung antiviral biomarkers upregulated following inhaled delivery of SNG001
- Well tolerated in clinical studies



Aerogen Solo/Ultra

Baseline Demographics (SPRINTER)

		Placebo (n=314)	SNG001 (n=309)
Age	Mean (SD)	53.7 (14.4)	52.0 (15.2)
Sex	Male	208 (66.2%)	203 (65.7%)
	Female	106 (33.8%)	106 (34.3%)
Race	White	220 (70.1%)	226 (73.1%)
	Non-white	60 (19.1%)	54 (17.5%)
	Missing	34 (10.8%)	29 (9.4%)
BMI (kg/m ²)	≥30	131 (41.7%)	112 (36.2%)
Baseline comorbidities	Any	158 (50.3%)	156 (50.5%)
Smoking history	Current smoker	18 (5.7%)	12 (3.9%)
Prior duration of symptoms	Median	9 days	9 days
COVID-19 Vaccination	No prior vaccination	224 (71.3%)	231 (74.8%)
	Partially vaccinated	30 (9.6%)	24 (7.8%)
	Fully vaccinated	60 (19.1%)	54 (17.5%)
COVID-19 treatments	Systemic corticosteroids	275 (87.6%)	267 (86.4%)
	Remdesivir	64 (20.4%)	54 (17.5%)

Improvements in SOC may have 'closed' window to show treatment effects on primary endpoints in SPRINTER trial

