



Bronchiolitis

Three successful pilot studies completed in infants



Nitric Oxide Market Dynamics for Bronchiolitis

Targeting US Bronchiolitis Patients

~144M

Total Births Worldwide in 2019¹

~2-3%

Infants hospitalized with bronchiolitis diagnosis²

~3.2M

Annual child bronchiolitis hospitalizations globally

There are no approved therapies for this unmet medical need

~4M

Total US Births in 2019³

~3%

Infants hospitalized with bronchiolitis diagnosis²

~120K

Annual child bronchiolitis hospitalizations in the US

Bronchiolitis Disease Overview

A leading cause of child mortality globally

The disease

- Acute inflammatory injury of the bronchioles usually caused by viral infection
- Usually affects children <2 years⁽¹⁾, with a peak in infants aged 3-6 months⁽¹⁾
- Leading cause of infant hospitalizations, accounting for >120,000 hospitalizations with a direct cost of at least \$550 million each year⁽¹⁾
- Most common cause is respiratory syncytial virus (RSV)⁽²⁾

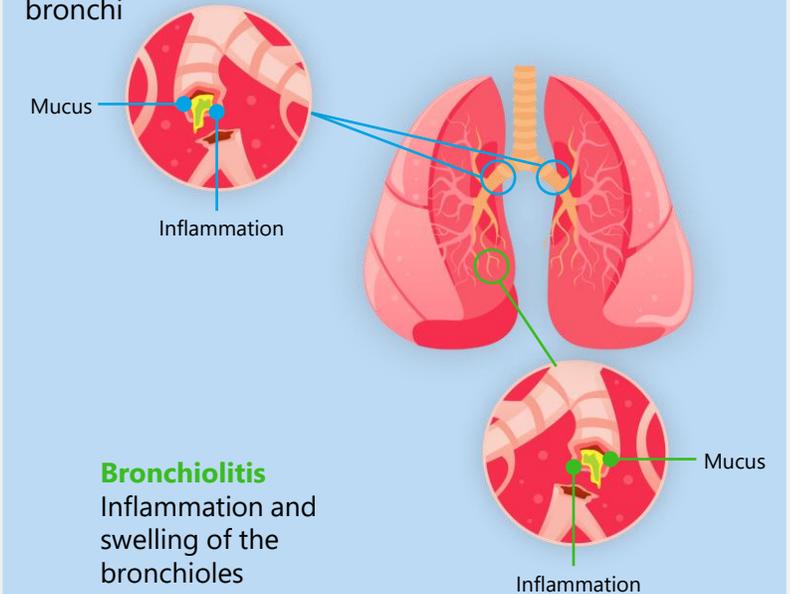
Benefits of nitric oxide

- Antiviral and Antibacterial mechanisms
 - Preclinical studies show high dose NO has antibacterial and antiviral properties⁽³⁻⁶⁾
- Pulmonary vasodilatory properties
 - FDA/EMA approved for ~20 years

Bronchitis is different from bronchiolitis⁽⁸⁾

Bronchitis

Inflammation and swelling of the bronchi



Bronchiolitis

Inflammation and swelling of the bronchioles

No drugs approved for the treatment of bronchiolitis⁽⁹⁾

1) Hasegawa K, Tsugawa Y, Brown DF, Mansbach JM, Camargo CA, Jr.: Trends in bronchiolitis hospitalizations in the United States, 2000-2009. *Pediatrics* 2013, 132(1):28-36.

2) Piedimonte G, et al. Respiratory syncytial virus infection and bronchiolitis. *Pediatr Rev.* 2014; 35(12):519-30

3) Ghaffari, A., et al. Efficacy of gaseous nitric oxide in the treatment of skin and soft tissue infections. *Wound Repair Regen.* 2007; 15(3):368-77.

4) Miller, C.C., et al. (2013) Inhaled nitric oxide decreases the bacterial load in a rat model of *Pseudomonas aeruginosa* pneumonia. *J Cyst Fibros* 12, 817-20.

5) Regev-Shoshani, G., et al. (2013) Prophylactic nitric oxide treatment reduces incidence of bovine respiratory disease complex in beef cattle arriving at a feedlot. *Res Vet Sci* 95, 606-611

6) Regev-Shoshani, G., et al. (2017) Non-inferiority of nitric oxide releasing intranasal spray compared to sub-therapeutic antibiotics to reduce incidence of undifferentiated fever and bovine respiratory disease complex in low to moderate risk beef cattle arriving at a commercial feedlot. *Prev Vet Med* 138, 162-169

7) <https://www.healthline.com/health/bronchiolitis-vs-bronchitis>

8) American Academy of Pediatrics

Two Completed and Published Pilot Bronchiolitis Trials

First two pilot bronchiolitis trials demonstrate reduction in hospital LOS



ORIGINAL ARTICLE: RESPIRATORY INFECTIONS

Nitric oxide inhalations in bronchiolitis: A pilot, randomized, double-blinded, controlled trial

Asher Tal✉, David Greenberg, Yossef Av-Gay, Inbal Golan-Tripto, Yael Feinstein, Shalom Ben-Shimol, Ron Dagan, Aviv D. Goldbart

First published: 27 November 2017 | <https://doi.org/10.1002/ppul.23905> | Citations: 1

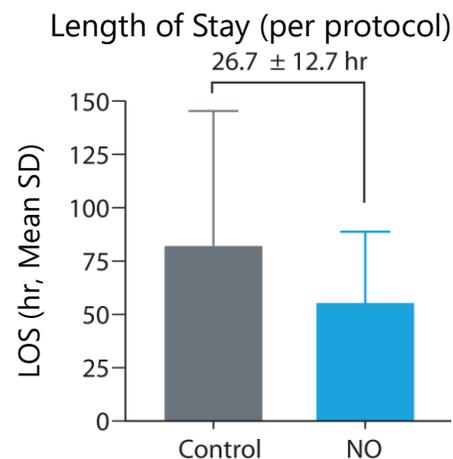
LOS did not differ between groups. However, in a post-hoc analysis of a subgroup of infants hospitalized for >24 h (n = 24), the median LOS was shorter in the nitric oxide (41.9 h) than in the control group (62.5 h) (P = 0.014).

**SCIENTIFIC
REPORTS**

nature research

Inhaled nitric oxide therapy in acute bronchiolitis: A multicenter randomized clinical trial

Aviv Goldbart^{1✉}, Inbal Golan-Tripto¹, Giora Pillar², Galit Livnat-Levanon², Ori Efrati³, Ronen Spiegel⁴, Ronit Lubetzky⁵, Moran Lavie⁵, Lior Carmon¹ & Amit Nahum¹



SCIENTIFIC REPORTS | (2020) 10:9605 | <https://doi.org/10.1038/s41598-020-66433-8>

Third Bronchiolitis Pilot Study Top Line Data

Statistical significance on both the primary and secondary endpoint at 150 ppm vs. placebo and vs. 85 ppm

	150 ppm vs. 85 ppm	150 ppm vs. SST	85 ppm vs. SST
Primary endpoint			
Time to Fit-to-Discharge (FTD)			
Hazard Ratio	2.11	2.32	0.90
95% CI	1.03, 4.31	1.01, 5.33	0.44, 1.81
P-value	0.041	0.049	NS
Secondary endpoint			
Hospital Length of Stay (LOS)			
Hazard Ratio	2.01	2.28	0.77
95% CI	1.01, 3.99	1.03, 5.06	0.40, 1.48
P-value	0.046	0.043	NS

Pivotal study delayed due to COVID-19 – Beyond Air is prepared to initiate in the fourth quarter of 2021 pandemic permitting