

First Indication: Pulmonary Hypertension (PH) Overview

NO is an established therapeutic option for patients suffering from Pulmonary Hypertension worldwide

Pulmonary Hypertension Overview

- Life-threatening condition from increased pulmonary vascular resistance resulting in decreased pulmonary blood flow
- Generally not diagnosed until multi-organ system function is affected
- NO is the de facto standard of care for PH in the hospital setting

Benefits of NO in Treatment of PH⁽²⁾

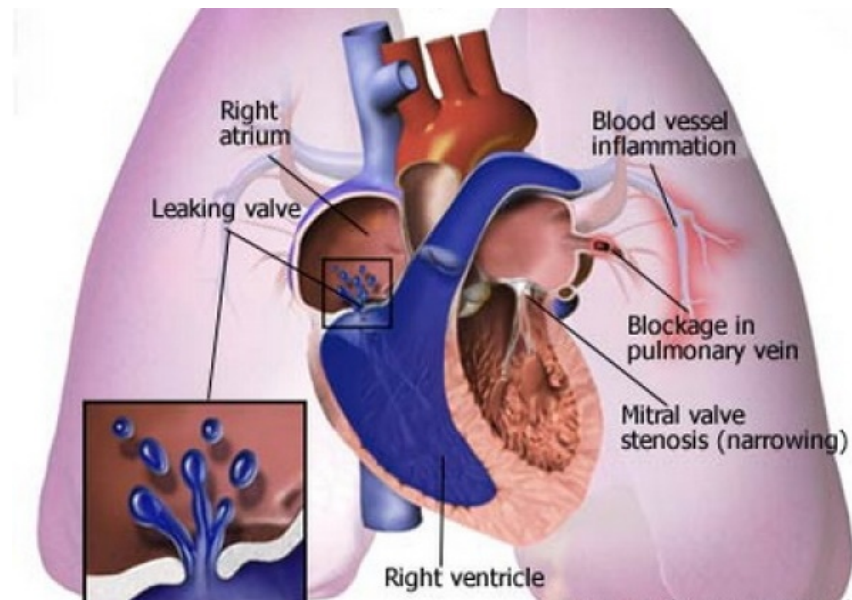
- NO has been used as a long-term therapeutic option for patients with pulmonary hypertension
 - Approved in the U.S. by the FDA in 1999 for PPHN⁽³⁾
 - Approved in the EU in 2001 for PPHN⁽³⁾ and cardiac surgery
- Inhaled NO causes increase in the concentration level of intracellular Cyclic Guanosine Monophosphate (cGMP) and an activation of the soluble guanylate cyclase
 - Causes smooth muscle relaxation, which increases blood flow to the lungs and decreases the workload on the right ventricle.

Effects of Pulmonary Hypertension⁽¹⁾

Narrowing of the Pulmonary Arteries



Failure of Right Ventricle

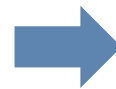


(1) "Pediatric Pulmonary Hypertension" – Guidelines from the American heart Association and American Thoracic Society
(2) Pulmonary Hypertension News – "Pulmonary Hypertension and Nitric Oxide"
(3) Persistent Pulmonary Hypertension of the Newborn

Nitric Oxide US market



- ❖ Approved indication: persistent pulmonary hypertension of the newborn (PPHN)
- ❖ FY 2018 Mallinckrodt reported INOmax sales >\$500m and 1Q19 sales >\$140m¹
- ❖ Praxair expected to enter the market in 2019
 - Praxair system is cylinder based, like INOmax
 - Anticipate rational price decline
- ❖ AIT will expand the market
 - ~800 hospitals have NO today¹ – AIT's AirNOvent will allow NO use by hospitals unable to use a cylinder system
 - > 1,000 NICUs in the US today²
 - Increase use with a lower cost and ease of use vs. cylinder systems
 - Volume expansion with AirNOvent expected to offset price decline
- ❖ The Bottom Line is that all the problems associated with NO cylinders disappear



TYPICAL NO CYLINDER PROFILE IN THE US:

Height 45", Diameter 7.5", **Weight ~45 lbs** (Weight for 2 cylinders on cart w/delivery system is **~175 lbs**)

APPROXIMATE COMMERCIAL GENERATOR PROFILE:

Height 14", Width 17", Depth 13", **Weight 20 lbs** (Weight on cart with back-up system is **50 lbs**)

(1) MNK Company Reports

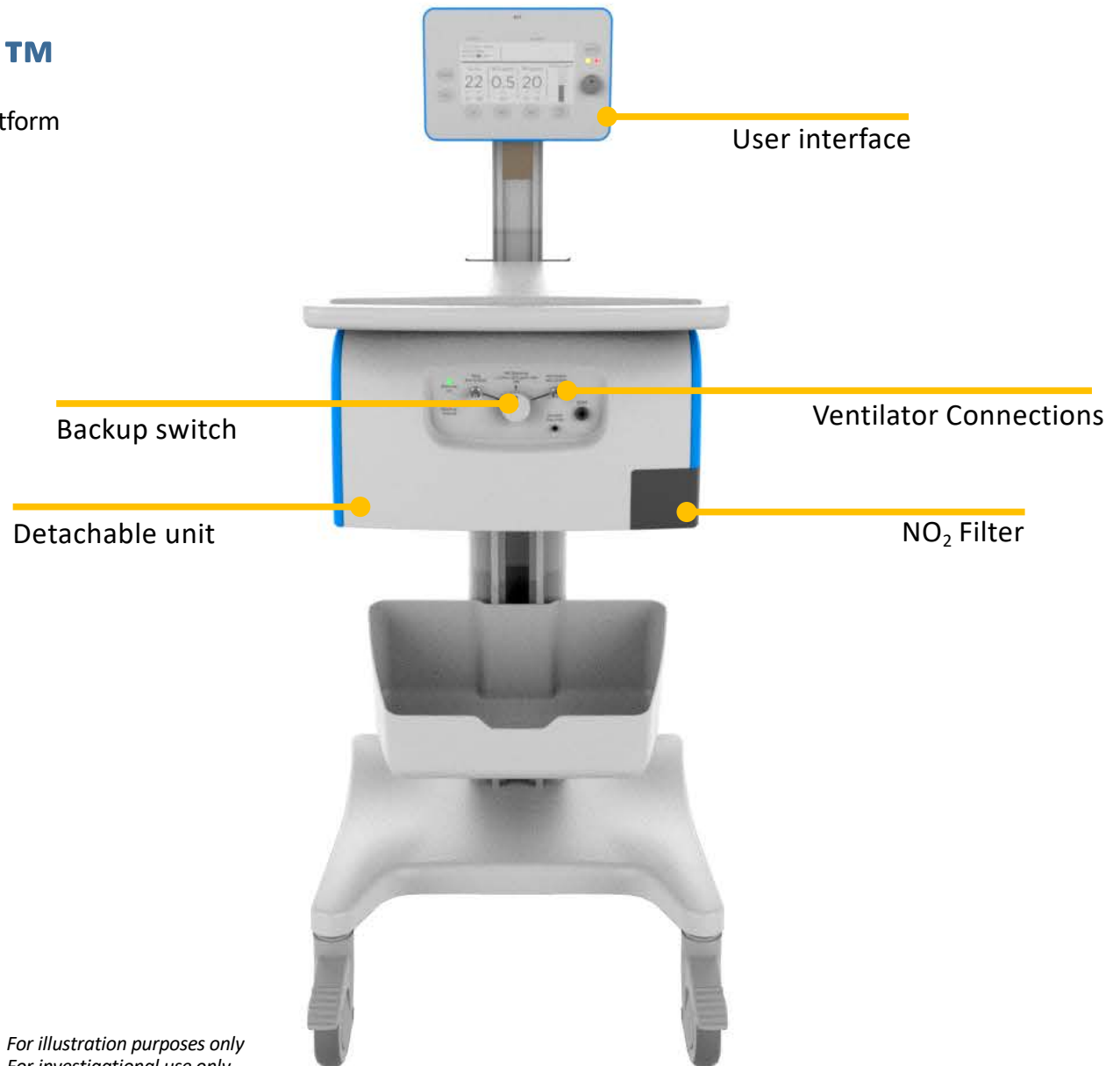
(2) American Academy of Pediatrics, American Hospital Association

AirNOvent™

Cylinder Free Nitric Oxide Therapeutic Platform

The next generation phasic flow nitric oxide delivery system. The cylinder free system will be used for the treatment of pulmonary hypertension for certain ventilated patients, dependent on approvals in each country, in the hospital setting.*

* For investigational use only.



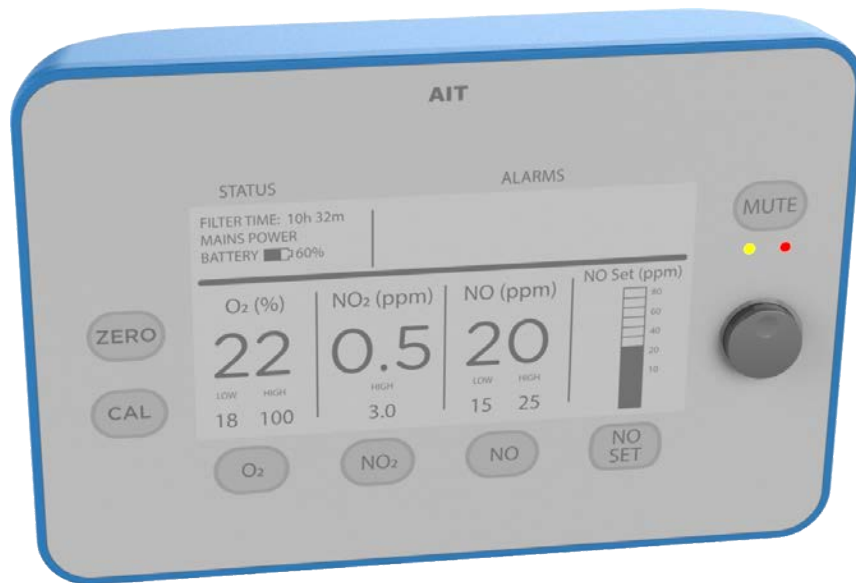
Width: ~24 inches
Depth: ~ 28 inches
Height: ~5 feet
Weight: ~50 lbs

*For illustration purposes only
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AirNOvent™

Cylinder Free Nitric Oxide Therapeutic Platform

Don't want the cart? NO problem!



User Interface

Detachable Unit
Provides flexibility in various hospital settings



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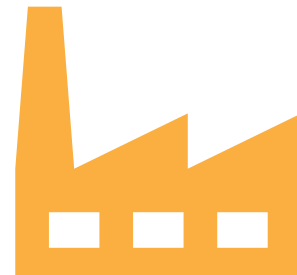
* AirNOvent may not be the final commercial product name; AirNOvent is the ventilator compatible version of our NO Generator and Delivery System

Losing the High-Pressure Cylinder is a Significant Gain

Hospitals will have significant cost & logistics Advantages

-  – Improved operating economics for the hospital
-  – No significant capital investment required for hospitals new to NO
-  – No burdensome inventory and storage requirements
-  – NO supplied as a non-hypoxic gas mixture
-  – No purging procedures or additional safety measures due to NO₂ buildup
-  – NO now available to hospitals unable to use NO cylinder systems today
-  – Reduced training burden
-  – Pregnant staff members not impacted

Our device will have significant cost Advantages



AIT does not have any expenses associated with a **manufacturing facility** for nitric oxide



AIT does not have any expenses associated with **logistics** related to nitric oxide cylinders

Key Terms

- ❖ In January 2019 AIT licensed commercial rights to its ventilator compatible NO Generator and Delivery System (AirNOvent*) to Circassia Pharmaceuticals for the United States and China markets
 - Specifically for all indications in the hospital setting using \leq NO 80 ppm

- ❖ \$32.55 million in potential Total Milestones and 15-20% Royalty
 - \$10.5 million received to date

- ❖ Royalties to AIT on Gross Profit
 - 5% on the first \$50 million in the US (one time)
 - 5% on the first \$20 million in China (one time)
 - 15% up to \$100m annually (US & China combined)
 - 20% above \$100m annually (US and China combined)
 - Gross profit defined as net sales less the cost of AirNOvent, NO₂ filters and accessories
 - Circassia will pay cost plus for the AirNOvent, NO₂ filters and accessories

- ❖ PMA filing with FDA is anticipated in the Summer of 2019

- ❖ US commercial launch planned First Half 2020

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Circassia: world-class specialty biopharma company, backed by Astra Zeneca



Snapshot

Circassia Pharmaceuticals plc

Status: Public company traded on AIM: CIR | Stock Price (05/1/2019): £0.315

About: Specialty pharmaceutical company founded in 2006. Focused on respiratory diseases based out of the UK.

IPO date: Mar 2014

Market Cap (02/28/2019): £120 M | **Sales (2018):** £48.3 M

Loss (2018): £25.9 M | **Cash in Hand (Dec. 31, 2018):** £40.7 M

Commercial Team: US = ~200; China ~100 | **Total Employees:** ~400

Major Shareholders Invesco Asset mgmt., Woodford Investment mgmt., AstraZeneca own about 67% combined
Direct Sales Force in United States, China and certain European Countries.

Area of Expertise	Strategic Fit with AirNOvent
Respiratory	<ul style="list-style-type: none"> ❖ NIOX (2018 sales £27.4m) <ul style="list-style-type: none"> ○ Used for asthma management ❖ Tudorza (Aclidinium bromide) {2018 sales £20.9m} <ul style="list-style-type: none"> ○ indicated for the long-term, maintenance treatment of bronchospasm associated with COPD, including chronic bronchitis and emphysema ❖ Duaklir (Aclidinium bromide & formoterol fumarate) {2H19 launch} <ul style="list-style-type: none"> ○ Indicated for the maintenance treatment of patients with chronic obstructive pulmonary disorder (COPD)
Nitric Oxide	<ul style="list-style-type: none"> ❖ NIOX is a nitric oxide measurement system for monitoring airway inflammation
AirNOvent will be a meaningful product	<ul style="list-style-type: none"> ❖ 2018 Circassia company revenues £48.3m ❖ Launching Duaklir 2H19 in the US ❖ Currently a small hospital presence ❖ Just rolling out commercial infrastructure in China
Exposure to US hospitals	<ul style="list-style-type: none"> ❖ NIOX is detailed in the hospital and there is overlap in the US with top hospitals that use NO today