NeoVent: Global Low Cost, Low-Tech Respiratory Support for Infants

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ABSTRACT

Purpose

Severe respiratory illnesses in newborns are a leading cause of pediatric death worldwide, resulting in over 1 million deaths annually; 99% of these deaths occur in low- to middle-income countries. Bubble Continuous Positive Airway Pressure (bCPAP) is a simple, proven, and widely used therapy for infants in respiratory distress. However, infants with more serious respiratory illnesses need more advanced therapy, traditionally provided with a mechanical ventilator. In many settings, current treatment options for newborns with these severe illnesses are too expensive, require highly skilled operators, and fail during power outages that are common in the developing world.

Product

We aim to develop high-quality, low-cost, low-power, and easy-to-use respiratory equipment for patients in emerging markets. Our patent-pending

NeoVent is a one-connection add-on to existing bCPAP setups to provide the next level of care: noninvasive bilevel pressure ventilation. Our easy-to-use design has only one moving piece and does not require continuous electricity. As with a traditional ventilator, the clinician can use NeoVent to set two independent pressure levels and the rate cycling between them. We anticipate the NeoVent can be manufactured for less than 1/100th the manufacturing cost of traditional ventilators.

Next Steps

We have completed preclinical studies demonstrating device efficacy and are currently preparing to launch our first-in-human NeoVent safety study, followed by a larger study of efficacy. After clinical validation, we plan to wholesale the device as a one-connection add-on to companies with developed distribution channels and customer bases

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Conflicts of interest: Stephen John and Anna John are employees of Advanced Innovative Medical Technologies (AIM Tech).

that are selling complementary respiratory equipment. In addition, we anticipate partnering with international medical device distributors to conduct direct sales in target geographic locations.

After launching direct sales in countries where the device has been studied in clinical trials, we will subsequently scale in additional emerging markets.

Company Purpose

Advanced Innovative Medical Technologies (AIM Tech) seeks to develop high-quality, low-cost, low-power, and easy-to-use medical equipment that will enable clinicians to provide excellent medical care in resource-limited settings. Our initial product, NeoVent, is an easy-to-use respiratory device for achieving noninvasive pressure ventilation at a fraction of the cost of existing options.

Problem We Want to Solve

Severe respiratory illnesses in newborns are a leading cause of pediatric death worldwide, resulting in over 1 million deaths annually; 99% of these deaths occur in low- to middle-income countries.¹⁻³ Bubble Continuous Positive Airway Pressure (bCPAP) is a widely used, noninvasive therapy that provides continuous positive pressure to recruit and stabilize the infant's alveoli. It saves up to 70% of infants

in respiratory distress^{4,5}; the continuous positive pressure serves to recruit and stabilize the infant's alveoli. With bubble CPAP, the expiratory limb of tubing is submerged in water, hydrostatically setting the pressure in the entire circuit with what is effectively a "bubbling PEEP valve" (Figure 1). By altering the submerged depth of tubing, the clinician can adjust the pressure level in an intuitive and visual manner. (Pressures are typically reported in centimeters of water, reflecting the mechanism of operation.) This low-cost, low-tech solution is effectively used in both low- and high-resource settings.⁴

The remaining 30% of infants with more severe respiratory illnesses often need advanced respiratory therapy. These infants, with weaker musculature and less mature lungs, benefit from noninvasive ventilation such as bilevel positive airway pressure or nasal intermittent positive pressure ventilation.⁶ These treatments can be provided using expensive

FIGURE 1: Functional diagram of bubble CPAP

ventilators; however, in low-to-middle income countries, access to ventilator therapies like these are limited by cost, accessibility to technical expertise, and sporadic availability of electricity. In lieu of advanced therapies, hospitals must often provide parents with a bag and mask to manually ventilate their infant at the bedside. When they tire out, their child dies.

In addition to infant respiratory distress, millions of pediatric and adult patients suffer from acute respiratory distress due to conditions such as chronic obstructive pulmonary disease (COPD) or congestive heart failure (CHF). These patients also need pressure ventilation.^{7,8}

Product Solution

NeoVent (Figure 2) seeks to provide noninvasive breathing support for patients in moderate to severe respiratory distress. The clinician can use NeoVent to set two levels of pressure and the rate cycling between them, achieving an effect similar to

FIGURE 2: NeoVent

traditional dual-pressure ventilators. NeoVent utilizes the same operating principle as bubble CPAP; the pressure of the respiratory circuit is hydrostatically determined based on the submerged depth of the expiratory tubing and its bubbling exhaust. Unlike bubble CPAP, however, NeoVent harnesses the energy of the bubbles to cycle between two distinct levels of pressure (Figure 3). Briefly, the float collects bubbles, becomes buoyant, and rises. In the process, an attached sleeve seals the proximal bubbling holes and increases the effective submerged depth of pipe (and thus the pressure). The float then vents, loses buoyancy, and sinks, reopening the proximal bubbling holes and decreasing the effective submerged depth of pipe (and pressure). Adjusting the air-flow rate alters the rate at which the float fills, which in turn sets the cycles/minute. By utilizing pipes with differing distances between the proximal and distal holes, different pressure gradients (high pressure level—low pressure level) can be delivered to the patient. Thus, the valve affects a controllable dual pressure waveform.

FIGURE 3: Functional diagram of NeoVent, courtesy of Advanced Innovative Medical Technologies, LLC.

NeoVent is a one-connection add-on to the basic bCPAP circuit. After a clinician determines that the infant requires additional respiratory support based on the infant's clinical condition (possibly using clinical metrics like the Downes' score), they can transfer the infant to the next level of care in a matter of seconds (Figure 4). The bCPAP can be provided by fully integrated devices, some of which have their own internal battery backup power sources. In emerging markets, bCPAP is often provided utilizing a simpler, rudimentary setup consisting of an air pressure source (either cylinders of compressed air/oxygen or a battery-operated air pump), respiratory tubing with nasal prongs, and a water reservoir. The NeoVent requires no additional electrical power because it harnesses the waste energy of bCPAP.

Fundamentally, this dual pressure therapy ("Bi-PAP") can be effectively used in the treatment of many other respiratory conditions, including COPD, CHF, and obstructive sleep apnea. As a result, it is possible that NeoVent (with some modifications) could help millions of people in emerging markets who have these conditions and currently do not have access to treatments.

Competition and Differentiation

To our knowledge, NeoVent could be the first low-cost, nonelectric, noninvasive dual pressure ventilator to reach the market. NeoVent is a patent-pending technology.

Table 1 compares our product with alternative solutions currently used in neonatal care around the globe. (Note that while efficacy has not been studied, the device delivered pressure waveforms consistent with conventional non-invasive ventilation and bilevel-PAP therapies in infant manikins over thousands of cycles.¹²)

AIM Tech's experience working in and designing for emerging markets has led to our success to date and will continue to differentiate our company as we market NeoVent and develop future products. NeoVent was conceived and designed in response to team members who witnessed the need first-hand while living and working in a resource-limited setting. This led to a product that is adapted to the context where we intend to sell the device.

AIM Tech has also established important relationships with potential collaborators from industry and academia. We maintain ongoing relationships with clinicians from southeast Asia and Africa who have seen and are interested in the NeoVent. In 2016, 30 nurses in Nepal were trained in device function and setup. They were able to assemble the device in approximately one minute (mean 64.7 sec, SD 20.4 sec [S. J., A.J. et al, unpublished data 2016]) and switch between bCPAP and NeoVent in a few seconds (mean 3.61 sec, SD 2.26 sec [S. J., A.J. et al, unpublished data 2016]).

The device has been reviewed with positive feedback by pulmonologists, respiratory therapists, and pediatricians in the United States. Finally, we have engaged in preliminary discussions with

FIGURE 4: Clinical use of NeoVent

TABLE 1: Competitive Landscape for Noninvasive Pressure Ventilation*

	NeoVent	Traditional Ventilator	Bag Mask
Description	<i>Non-invasive dual pressure respiratory therapy device</i>	<i>Device with multiple modes of invasive, non-invasive therapy</i>	<i>Balloon bag attached to face mask used for manual ventilation</i>
Ease of use	✓ Simple	✗ Complex	✓ Simple
Clinical efficacy	✓ High	✓ High	✗ Low
Power source	✓ Waste energy of bCPAP	✗ Requires continuous electricity	✗ Powered manually
Can be used for	✓ hours-days	✓ hours-days	✗ minutes-hours
Price	✓ \$100	✗ \$10,000	✓ \$15

potential distribution partners based in the U.S. and abroad.

Market Analysis

Total Market: Developed Markets

When utilized with a bCPAP circuit, NeoVent enables patients to receive either continuous or dual-pressure ventilation. Globally, the continuous positive airway pressure (CPAP) device and traditional ventilator market is forecast to grow at a 4.2% CAGR (compound annual growth rate), reaching a market size of \$4.8 billion in 2021⁹. This market encompasses highly developed mechanical ventilators as well as simpler, noninvasive therapies such as bCPAP. Revenue for dual pressure devices specifically is forecast to reach a market size of \$600 million in 2021 (about 12% of the total market).⁹

Market Sizing Analysis: Emerging Markets

Maternal-neonatal health indicators in many Southeast Asia and African countries demonstrate a significant unmet need for our product in these regions. To better understand the market potential, we have collected data on the number of hospitals in each of our target countries. More than 26,000 hospitals, total, exist in the countries

we have identified as our top 10 markets. If we assume that 40 devices are sold to each hospital annually at a price point of \$100 per device, this translates to a \$104.6 million market annually.

Market Trends and Key Demand Drivers

The NeoVent capitalizes on several key trends in our target markets. In emerging markets, most major medical-device manufacturers have begun investing in developing “context-appropriate” medical devices that are low cost, low power, and easy to use. Globally, pulmonologists and respiratory therapists are increasingly selecting simple, non-invasive respiratory therapies over traditional invasive mechanical ventilation therapies.^{10,11}

Business Model

Revenue Model

In emerging markets, we plan to sell NeoVent to hospitals and other healthcare providers, wholesaling the device via medical-device distributors and strategic reseller partners.

Marketing and Sales Strategy

AIM Tech’s strategy is first to market NeoVent as an add-on to existing bCPAP setups in emerging

markets for infant, pediatric, and adult use. In these markets, we have three customer segments: (1) companies manufacturing and selling synergistic infant respiratory products and that serve as strategic reseller partners, (2) hospitals and healthcare networks, and (3) individual healthcare providers, such as skilled birth attendants and community health workers. We intend to scale by selling in sequence to each of these segments across multiple geographic locations.

Manufacturers: Companies currently manufacture and sell basic infant respiratory setups specifically designed for low-resource settings. Because NeoVent is a one-connection add-on to basic respiratory equipment such as bubble CPAP setups, we can utilize the existing sales and distribution channels in place at these manufacturers by developing strategic resale partnerships. Selling via these companies is the most efficient way for us to bring NeoVent to market in the near future.

Hospitals and Healthcare Networks: We intend to sell to these institutions in select geographic locations by using local distributors who will also provide service and technical support. We anticipate our first sales will take place in the countries where we will launch our safety and efficacy studies. Subsequently, we plan to scale throughout Southeast Asia and Africa. In both cases we will leverage our existing relationships with in-country accelerators and partners. Many hospitals and clinics in the developing world obtain the majority of their devices through local distributors; therefore, we plan to contract with multiple local distributors in our target markets, both directly and through international medical-device distributors. Our device will be a complementary sale to more basic respiratory equipment sold by these distributors.

Individual Healthcare Providers: After we have established market traction, we plan to further scale the device to more remote emerging market settings, selling to individual providers such as skilled birth attendants and community health workers. To reach these groups, we plan to leverage partnerships with nongovernmental organizations

(NGOs) that support individual community health providers and other maternal-neonatal health initiatives. These NGO partnerships will help us access these large user bases, and assist in providing training, service, and support. We believe that through these partnerships, we can unlock a large, untapped market with revenue potential that has not been captured in the global respiratory therapy market size and growth estimates mentioned above, thus greatly increasing our impact. These regions have unmet needs that represent a significant market opportunity for our device. For example, India alone has 2.1 million skilled birth attendants.

Traction and Company Status

Product Development and Manufacturing: We currently manufacture NeoVent prototypes via 3D printing and are transitioning to more scalable manufacturing in partnership with medical device manufacturers that comply with Good Manufacturing Practices (GMPs).

Preclinical Studies: We have quantified the reliability of our device in infant manikins, demonstrating an ability to deliver pressure waveforms comparable to those of traditional bilevel positive airway pressure therapies over thousands of cycles.¹²

Recognition: Since developing NeoVent in 2014, the technology has taken First Place in national design competitions, including the Collegiate Inventors Competition (<http://www.invent.org/challenge/past-winners/>), the James Dyson Award (<http://www.jamesdysonfoundation.com/news/neovent-wins-2015-us-james-dyson-award/>), VentureWell's BME Start (<https://venturewell.org/portfolio-item/neovent/>), and the Lemelson-MIT Student Prize (<http://lemelson.mit.edu/winners/joseph-barnett-and-stephen-john>). It has been presented at the Gate Foundation's "Grand Challenges in Global Health" meeting and the national conferences of the American Academy of Pediatrics and the Canadian Society of Respiratory Therapists. Additionally, AIM Tech took first place in the 2017 Michigan Business Challenge (Social Impact Track;

<http://socialimpact.umich.edu/michigan-business-challenge-impact-track-winner-announced/>) and first place in the 2017 Brown-Forman Cardinal Challenge (<https://insiderlouisville.com/business/startups/cardinal-challenge/>).

Company Next Steps

Safety Study: We have received Institutional Review Board (IRB) and Nepal Ministry of Health clearance to conduct a first-in-human feasibility and safety trial that we are launching in collaboration with the local hospital and a respiratory nonprofit organization. This study will serve to demonstrate device safety on a small scale and pave the way for larger follow-on studies.

Safety and Efficacy Trials: In collaboration with leading clinical researchers, we are planning to follow the initial safety study with a large, randomized control study of safety and efficacy. This study will build on safety to compare the physiologic efficacy of NeoVent vs the current gold standard, bCPAP. This will, in turn, set the stage for larger trials comparing mortality of infants in respiratory distress on NeoVent vs bCPAP to quantify the therapeutic benefit.

Regulatory Pathway: FDA clearance would allow us to sell in many southeast Asian and African countries. While the exact regulatory requirements vary across most emerging-market countries we are targeting, FDA clearance is widely accepted and would provide us access to multiple regions outside the US and limit country-specific requirements.

Device Design and Production: We are currently finalizing the design of NeoVent in preparation for manufacturing on a larger scale. AIM Tech's manufacturing strategy is to contract the manufacturing rather than manufacture our technology in house. In preparation for the initial contracting, we are currently being advised by several firms on material selection and other design and manufacturing decisions. We are also in the process of selecting a GMP-compliant manufacturing partner to assist in future device production.

Business Development and Sales in Emerging Markets: After receiving results from the safety study and initial results from the physiologic safety and efficacy trials, we plan to select a strategic resale partner. Our ideal partner will have existing market penetration in our target markets; provide training, service, and support for our device; and commit to growing sales of NeoVent. In parallel, we will hire in-country sales staff for our initial pilot markets who will be responsible for initiating pilots and establishing relationships with local distributors.

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