ASX Release

Oventus clinical study results and regulatory update

1. **Predictive algorithm developed to provide treatment solutions for Obstructive Sleep Apnea (OSA) patients, using O2Vent® technology as a first-line therapy instead of Continuous Positive Airway Pressure (CPAP)**
2. **Recent study demonstrates that O2Vent therapy, or combination therapy including O2Vent Optima and ExVent®, successfully treats 100% of patients without the need for CPAP**
3. **Confirmatory trial planned to support ExVent 510(k) clearance with US FDA**
4. **Oventus has reapplied (due to recoding) in the US for oral appliance reimbursement authorisation (PDAC) relating to government-funded health plans**

Brisbane, Australia 26 October 2021: Obstructive Sleep Apnea (OSA) therapeutics company, Oventus Medical Ltd or the Company (ASX: OVN) is pleased to provide an update on clinical trial and regulatory matters.

1. Predictive algorithm developed to provide treatment solutions for Obstructive Sleep Apnea (OSA) patients, using O2Vent® technology as a first-line therapy instead of Continuous Positive Airway Pressure (CPAP)

Background – Cooperative Research Centre Project (CRC-P) clinical study update

In 2017, Oventus was pleased to be announced as lead participant in a $2,950,000, three-year Cooperative Research Centres Programme (CRC-P), administered by AusIndustry, a division within the Australian Federal Government's Department of Industry, Innovation and Science. The hugely successful CRC-P project: *Targeted therapy for sleep apnoea: A novel personalised approach* has led to the development of a substantial body of clinical evidence in support of Oventus' sleep treatment platform.

In July 2021, recruitment was completed for the multi-site (Adelaide and Sydney) clinical study. Several project milestones have been achieved to date, run in conjunction with CRC-P partners, Neuroscience Research Australia, Flinders University, the Commonwealth Science and Industrial Research Organisation (CSIRO) and Oventus.

The **ultimate goal** of the study is to provide a targeted treatment solution for every OSA patient, using O2Vent Optima technology as a first-line therapy, instead of CPAP. This includes determining if treatment outcomes can be predicted, based on individual patient characteristics and individual causes of sleep apnea.

With recruitment for the study now closed, 112 participants were enrolled, 25 of which remain in various stages of follow-up. Final data collection is scheduled for Q4 CY 2021.

Clinical study outcomes to date

The partnership between Oventus and the CRC-P yielded earlier compelling clinical data showing that O2Vent technology improved treatment efficacy over traditional oral appliances by over 50%. When the ExVent EPAP valve was added, efficacy increased a further 30% and reduced the apnea hypopnea index (AHI) to below 10 events per hour for 45% of patients who had failed alternative therapies (as published in *SLEEP*, August 2019). This data has previously been reported and presented at the American Academy of Dental Sleep meeting (AADSM), June 2017, in Boston and at the Australasian Sleep Association's (ASA) "Sleep DownUnder" conference (October 2018).

2. Recent study demonstrates that O2Vent therapy, or combination therapy including O2Vent Optima and ExVent®, successfully treats 100% of patients without the need for CPAP

New clinical study outcomes and their significance

A historic limitation of oral appliance therapy has been the inconsistency of outcomes and the inability to determine, prior to prescribing oral appliance therapy, who would respond to treatment and who would not. The recently completed portion of the study had the following goals and findings:

- Looking at a range of factors, investigators sought to draw clear lines of causality between patient OSA characteristics, treatments, and outcomes, and from that data, develop a predictive algorithm for treatment success
- Patients were enrolled and offered O2Vent therapy alone, and then in some cases patients were also offered supplemental therapies including the Oventus ExVent (an Expiratory Positive Airway Pressure valve), positional therapy, oxygen and pharmaceutical agents
- Based on the analysis, the predictive algorithm successfully predicted which therapy or combination of therapies to offer each patient, enabling a 100% treatment success rate
- Investigators concluded that while further study is needed, this algorithm has the potential to arm clinicians with a tool to facilitate treatment selection and enhance successful, long-term OSA outcomes

Clinical study details- using Machine Learning in Algorithm Development

Out of the 112 patients enrolled in the three-year clinical study, 62 men and women with OSA (aged 29–71 years) were studied to investigate whether a clinically applicable predictive

algorithm could be developed using standard data points collected in a typical patient diagnostic process. Seven standard variables from a diagnostic sleep study, plus age and BMI were included in a machine learning analytical model designed to predict O2Vent therapy response and obstructive sleep apnea treatment resolution (e.g. AHI<5 events/hr).

Predictive algorithm: responders vs. non-responders

The model used data from the first 45 participants with 10-fold cross-validation. A blinded independent validation was then performed on the data from the remaining 17 participants. Mean accuracy of the model to predict responders vs. non-responders to Mandibular Advancement Splint therapy (using O2Vent Optima) using 10-fold cross-validation was 91±8%. All 17 individuals were correctly classified in this independent validation.

Predicting optimal combination therapy

In a therapeutic application of the model, eleven people with OSA, not fully resolved with O2Vent Optima alone (apnea-hypopnea index (AHI)>10 events/h) were recruited. Initially, OSA subtypes were assessed via a detailed diagnostic sleep test. Step one of combination therapy focused on anatomical interventions including O2Vent Optima therapy plus ExVent and a device to avoid sleeping face up (supine). Participants with residual OSA (the subjective complaint of excessive daytime sleepiness and AHI>10 events/h) following the test were then given one or more targeted supplemental therapies per the protocol. These included:

- Oxygen (4L/min) to reduce unstable respiratory control (high loop gain);
- 10mg zolpidem to increase arousal threshold; or
- 80/5mg atomoxetine-oxybutynin (ato-oxy) for poor pharyngeal muscle responsiveness.

Following the addition of supplemental therapies with O2Vent, OSA was successfully treated (AHI<10 events/h) in all participants. O2Vent Optima combined with ExVent and supine-avoidance therapy resolved OSA in ~65% of participants (O2Vent Optima alone vs. combination therapy: 17±4 vs. 5±3, events/h, n=7). For the remaining participants, OSA resolved with the addition of oxygen (n=2), one with 80/5mg ato-oxy and one other required both oxygen and 80/5mg ato-oxy.

Principal investigator Danny Eckert, Matthew Flinders Professor, College of Medicine and Public Health, Flinders University commented, *"As the first prospective trial to apply comprehensive phenotyping approaches to deliver targeted therapy based on each individual patients' specific causes of sleep apnea, this body of work represents a major advance for the field. These exciting findings pave the way for a precision medicine approach to sleep apnea care and management where the right therapy or therapies are provided to the patient up front rather than the current imprecise trial and error approach. This unique collaborative program between the Australian Government, industry and academia has facilitated the acceleration of this important objective that has the potential to help a large number of patients globally."*

Oventus Founder and CEO, Dr Chris Hart also commented, *"The findings from the CRC-P research have been genuinely groundbreaking. We can now utilise data points from a standard sleep study report to identify best candidates for O2Vent therapy. This can make the diagnosis and prescription process shorter, meaning we can treat patients with the right therapeutics the first time around.*

Where needed, we can add in ExVent as part of combination therapy protocols to treat all OSA patients without the need for CPAP. This is a remarkable achievement for Oventus and our CRC-P partners.

Oventus was founded on the premise of being able to treat OSA patients without the need for CPAP. We now have data to demonstrate that it is achievable using O2Vent technology. We are extremely excited by these findings and also very appreciative of the collaboration Oventus has enjoyed with Flinders University, Neuroscience Research Australia and the CSIRO."

3. Confirmatory trial planned to support ExVent 510(k) clearance with US FDA

Oventus recently received feedback from the US Food and Drug Administration (FDA) on its ExVent 510(k) application. The feedback outlined the clinical data requirements necessary to achieve 510(k) clearance. Oventus has accepted the FDA's feedback and believes the data generated by the study will be useful for documenting the benefits of ExVent to the US clinical audience.

The trial design includes recruiting up to 20 evaluable participants, who will be drawn from one of several US sites that already provide O2Vent therapy to their patients. The study will be single-arm (no control group) showing the effect of ExVent therapy on sleep apnea events over a 90-day period of use. Oventus is fortunate to have some of the most respected researchers in the field of dental sleep medicine assisting with the study. The Primary Investigator, Dr Richard Bogan, MD, FCCP, FAASM, President of Bogan Sleep Consultants, LLC commented, *"I'm pleased with the FDA's recommendations and look forward to being able to use ExVent in conjunction with O2Vent technology in my practice."*

4. Application submitted in the US for oral appliance reimbursement authorisation (PDAC) relating to government-funded health plans

In the US the pricing data analysis and coding (PDAC) contractors Palmetto GBA have recently recoded the previously approved O2Vent Optima oral appliance as A9270 (a non-covered item or service). Oventus has reapplied to the contractors for approval of the newly submitted O2Vent Optima version, designed for Medicare patients. In the meantime, this means that O2Vent Optima will not be able to be supplied to Medicare patients in its own right for reimbursement purposes. To date, Medicare patients have represented a very small percentage of US sales.

—ENDS—

For further information, please visit our website at www.o2vent.com or contact the individuals outlined below.

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About Oventus – see more at www.o2vent.com

Oventus is a Brisbane-based medical device company that is commercialising a unique treatment platform for obstructive sleep apnea (OSA) and snoring. The Company has a collaborative Sleep Physician/Dental strategy that streamlines patients' access to treatment.

Unlike other oral appliances, O2Vent Optima devices manage the entire upper airway via a unique and patented built-in airway. O2Vent Optima devices allow for airflow to the back of the mouth while maintaining an oral seal and stable jaw position, avoiding multiple obstructions from the nose, soft palate and tongue. The devices reduce airway collapsibility and manage mouth breathing while keeping the airway stable.

O2Vent Optima devices are designed for any patient that is deemed appropriate for oral appliance therapy, but especially beneficial for the many people that suffer with nasal congestion, obstruction and mouth breathing. The O2Vent Optima allows nasal breathing when the nose is unobstructed, but when obstruction is present, breathing is supplemented via the airway integrated in the appliance.

The ExVent®[1] is a valve accessory that fits into the open airway of the O2Vent Optima device, to augment traditional oral appliance therapy by stabilizing the airway. The ExVent valve contains air vents that open fully on inhalation for unobstructed airflow. The valve closes on exhalation, directing the air through the vents, creating the mild resistance or airway support required to keep the airway stable (known as PEEP, positive end expiratory pressure).

According to a report published by the Sleep Health Foundation Australia, an estimated 1.5 million Australians suffer with sleep disorders and more than half of these suffer with obstructive sleep apnea[2].

Continuous positive airway pressure (CPAP) is the most definitive medical therapy for obstructive sleep apnea, however many patients have difficulty tolerating CPAP[3]. Oral appliances have emerged as an alternative to CPAP for obstructive sleep apnea treatment[4]. The O2Vent Optima and ExVent provide a discreet and comfortable alternative to CPAP for the treatment of OSA.

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[1] Not yet cleared for sale in the US.

[2] Deloitte Access Economics. Reawakening Australia: the economic cost of sleep disorders in Australia, 2010. Canberra, Australia.

[3] Beecroft, et al. Oral continuous positive airway pressure for sleep apnea; effectiveness, patient preference, and adherence. Chest 124:2200–2208, 2003

[4] Sutherland, Kate, et al. "Oral appliance treatment for obstructive sleep apnea: an update." Journal of Clinical Sleep Medicine 10.2 (2014): 215-227.