

## A Small Molecules for the Treatment of Sleep-Disordered Breathing

### SUMMARY

L-propargylglycine (L-PAG) is a small molecule that normalizes breathing patterns in sleep-disordered breathing without the need for mechanical respiratory aid devices. New L-PAG derivatives are being developed to further enhance the efficacy of the molecule.

### KEY RESULTS

In a rat model and genetic mouse model of sleep apnea, subjects demonstrated normalized breathing patterns when treated with L-PAG compared to subjects that received saline.

### ADVANTAGES

- Efficacious small compound.
- Does not require external breathing device.
- Normalizes breathing patterns within hours of administration.

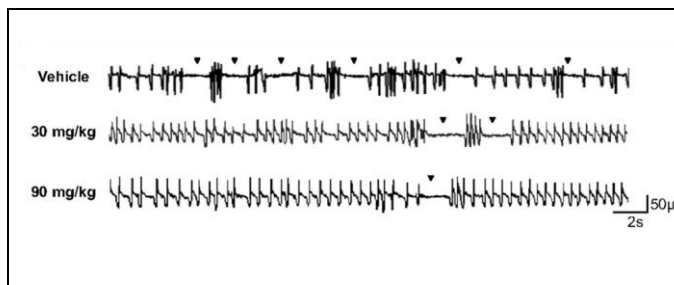
### APPLICATIONS

- Treatment of sleep-disordered breathing.
- Treatment of patients for whom mechanical breathing aids are not suitable.
- Potential first-line treatment for sleep apnea.

### TECHNICAL DESCRIPTION

Sleep apnea is a type of sleep-disordered breathing where a patient has difficulties breathing during sleep or the patient has partial or complete blockage of the airway during sleep. Dr. Nanduri Prabhakar and his team have identified the mechanism underlying sleep apneas, which involve key enzymes in sensing and production of oxygen, carbon dioxide, and hydrogen sulfide gas. In sleep apnea, oxygen levels are extremely reduced due to increased hydrogen sulfide production by the enzyme, cystathionine-γ-lyase (CSE) in the carotid body, a cluster of chemoreceptors located near the carotid artery. By blocking CSE activity using the small molecule, L-PAG, Dr. Prabhakar demonstrated a reduction in hydrogen sulfide levels and a return of normal breathing rates using rat and murine models of sleep apnea. Furthermore, the effects of L-PAG were observed within hours of administration. Dr. Prabhakar and his collaborators are applying medicinal chemistry approaches to further optimize L-PAG, and new compounds are being developed. Current treatments of sleep-disordered breathing rely on bulky external devices such as continuous positive airway pressure (CPAP) devices. Therefore, L-PAG is an attractive solution for treating apneas that would not rely on CPAP devices, and would be a potential treatment for patients who are not compatible with CPAP.

*Mice treated with L-PAG exhibit normal breathing patterns*



*Breathing patterns of genetic mouse models of sleep apnea, apneas indicated by arrows, treated with saline (top), or increasing doses of L-PAG (30 mg/kg, 90 mg/kg). Mice treated with L-PAG exhibited reduced apneas and regular breathing intervals at higher dose.*

REFERENCE  
UCHI 1935, 2632

DEVELOPMENT STAGE  
Pre-clinical

THERAPEUTIC AREAS  
Sleep-disordered breathing  
Sleep Apnea  
Obstructive Sleep Apnea

PUBLICATION  
[Peng et al. 2014. PNAS](#)  
[Peng et al. 2017. PNAS](#)

INTELLECTUAL PROPERTY  
[US 13/640,711](#)  
Provisional filed on new compounds

INVENTOR(S)  
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*Dr. Prabhakar is a leading authority in the field of hypoxia as a consequence of sleep-disordered breathing manifested as recurrent apneas.*

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