

# Sustained drug delivery system takes lung disease treatment to the next level

Every year, a vast amount of money is spent on developing new medications. However, less research funding is invested in improving the methods by which these medications are administered to patients to make them more efficient and increase treatment compliance. Dr Pattisapu Gangadharam (Dr Ganga) and Dr Nejat Düzgüneş, subsequently joined by Dr Kameswari (Kamu) Konduri, Dr Sandhya Nandedkar, Dr Ram Pattisapu, Dr Jogi Pattisapu and Dr Ganesh Konduri at VGSK Technologies Inc, are working on a game-changing sustained drug-delivery system. Their latest focus is a sustained and more efficient administration of the steroid medication budesonide, to effectively treat lung inflammation secondary to COVID-19 and other respiratory diseases. Notably, their ProLung™ system allows the administration of one dose, once a week, as a targeted therapy to the point of viral attachment in the lungs, protecting the lungs from significant inflammation.

Respiratory diseases, including asthma and coronavirus disease (COVID-19), are leading causes of morbidity and death around the world. Asthma affects 235 million people globally and is the most common chronic disease in children. The COVID-19 pandemic is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The SARS-CoV-2 virus often infects the cells lining the airways, known as type II pneumocytes, which it invades by adhering to a specific cell receptor: angiotensin-converting enzyme 2 (ACE-2). This viral invasion can lead to complications such as pneumonia and, in more severe cases, acute respiratory distress syndrome (ARDS). With the COVID-19 pandemic still gripping the world and its respiratory complications a leading cause of death, there is a vital need to develop or improve sustainable delivery systems for new and existing medications.

## PROLUNG™ SYSTEM

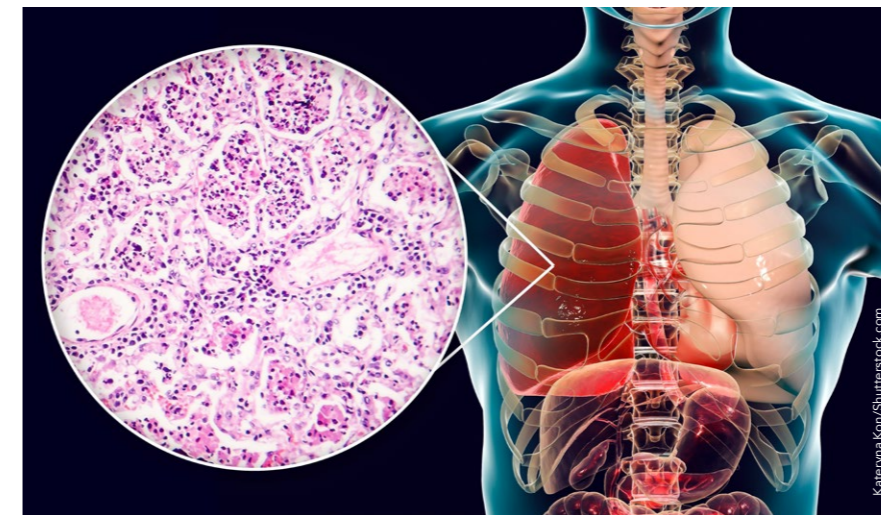
The ProLung™ system is a patented sustained technology platform developed by Drs Ganga, Duzgunes, and Konduri, and the team at VGSK Technologies Inc. This prolonged drug-delivery system neatly incorporates medications inside biochemical carrier structures. These structures are similar to naturally occurring substances found in cells; not only are they inert and non-toxic, they can also protect the lung tissues. Using the ProLung™ system and depending on the medication incorporated, these complex molecules can be designed to either remain in the lung tissues or cross the lung membrane and enter the blood circulation. This tailored delivery can thus promote medication efficacy.

When combined with a particular drug or peptide, the ProLung™ system decreases inflammation and the associated damage to the tissues. This offers a novel ability to treat a variety of diseases including asthma, with one dose administered once a week in a sustained manner. Several types of medications similar to those used to treat asthma and other respiratory diseases, such as anti-inflammatory medications (steroids, anti-inflammatory peptides (D-4F), antibiotics, and anti-viral medications) have all been successfully incorporated into the ProLung™ system. The actual medication is not changed, it is simply combined with the ProLung™ biochemical carrier structure to optimise medication delivery.

This newly developed technology can improve patient management by targeting areas with increased inflammation. It can also lead to significant reduction in treatment costs since it dramatically reduces the number of doses of medicine required to treat lung disease. Reducing the number of doses to a minimum tackles the challenge of drug toxicity and also improves patient compliance. Improving the potential for patients to complete their course of treatment in this way leads to improved patient outcomes.

## BUDESONIDE INCORPORATED IN PROLUNG™

Inhaled budesonide, a glucocorticoid, is a simple, safe, and inexpensive treatment for asthma, chronic obstructive pulmonary disease (COPD), and other respiratory diseases, including viral lung complications. It is an inhaled steroid, widely used not only to treat the respiratory symptoms, but also to reduce exacerbations of the respective disease. Laboratory studies show that



ProLung™-budesonide has a similar composition to the lung's own protective surfactant. Weekly administration of budesonide in this sustained carrier could play a protective role against SARS-CoV-2 infection.

inhaled budesonide among other steroids, causes a decrease in the number of ACE2 receptors in the airway cells, which are critical for cell invasion by the virus. Recent studies show that when given for a short period, budesonide can be an effective treatment of early COVID-19 in adults. In addition to reducing ACE2 receptors, it reduces the inflammation in the lungs and therefore the respiratory symptoms associated with the disease.

ProLung™-budesonide, which is budesonide incorporated into the ProLung™ system, has a unique lipid composition that helps to support the immune system, stabilise the lung epithelium (the cells lining the lungs), and decrease inflammation. All these factors have an important role in the presentation and progress of lung disease, including COVID-19. ProLung™-budesonide is effectively similar in composition to the lung's own protective surfactant (a complex of lipids and proteins lining the inside of the lungs). ProLung™-budesonide allows for weekly administration of budesonide in this sustained carrier. This could also have a protective role against SARS-CoV-2 infection.

The safety of ProLung™-budesonide has been tested thoroughly by conducting long-term safety and toxicity

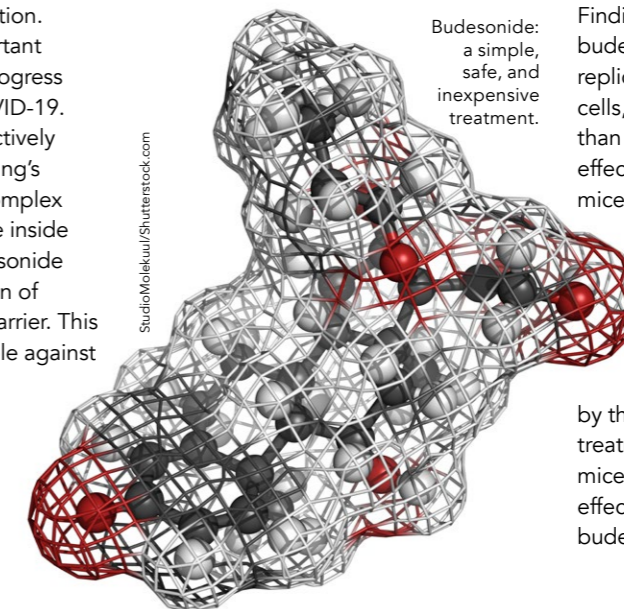
studies using an allergy animal model and repeat allergen challenges. These studies revealed low markers of allergic inflammation both in the lungs and

## The prolonged drug-delivery system, ProLung™, neatly incorporates medications inside biochemical carrier structures.

blood. There were also no issues with toxicity or severe allergic reactions.

### DOES PROLUNG™-BUDESONIDE PREVENT SARS-COV-2 FROM REPRODUCING?

In their most recent study, the VGSK team, in collaboration with NIH/NIAID, tested the effect of ProLung™-budesonide on SARS-CoV-2 virus replication.



Their hypothesis was that the combination of lipids and steroids such as budesonide could potentially improve COVID-19 symptoms by preventing the virus from replicating. The team infected Vero 76 cells (a well-characterised lineage of green monkey kidney cells often used in lab studies) with SARS-CoV-2. The effect of inhaled ProLung™-budesonide was also tested in a mouse model of lung inflammation.

The mice were divided into four groups: group (a) received aerosolised ProLung™-budesonide, weekly; group (b) plain budesonide, daily; (c) plain budesonide, weekly; and group (d) received empty ProLung™ carrier treatment (without budesonide), weekly. All groups were compared to untreated mice with significant lung inflammation, or normal mice using examination of their lung tissues and electron microscopy to evaluate lung inflammation and

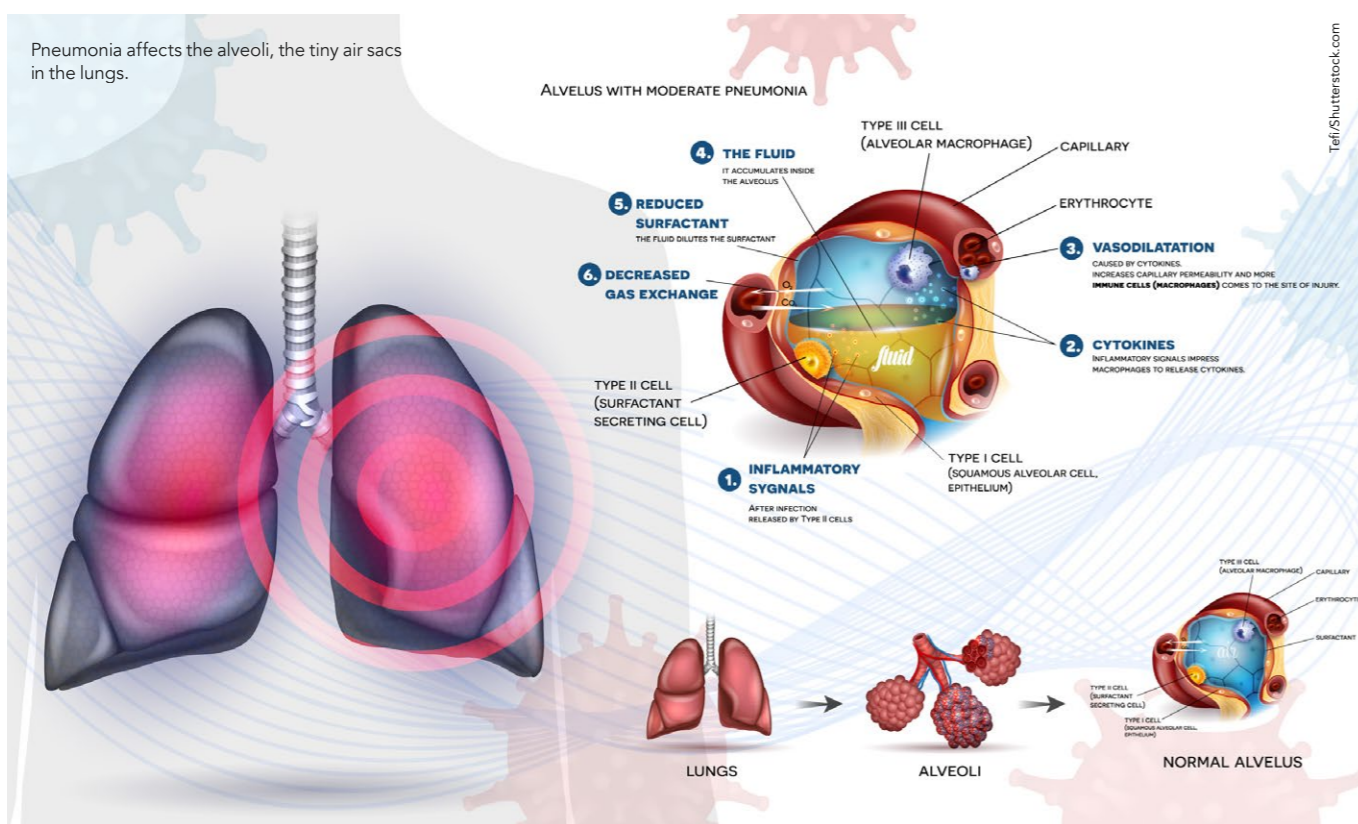
deposition of ProLung™-budesonide. Other study end-points included airway reactivity to methacholine challenge (to

determine airway resistance), and markers of inflammation such as numbers of inflammatory cells and measurement of eosinophil peroxidase levels (an enzyme secreted by immune cells to destroy invading microorganisms) in their lungs.

### PROLUNG™-BUDESONIDE PREVENTS SARS-COV-2 REPLICATION AND REDUCES INFLAMMATION

Findings showed that ProLung™-budesonide significantly reduced viral replication of SARS-CoV-2 in Vero 76 cells, and the effect was much stronger than a protease inhibitor (known to effectively block viral replication). The mice studies revealed low levels of inflammation after treatment with ProLung™-budesonide compared to the other study groups. It was shown to protect the lining of the lungs, which can prevent lung damage caused by the SARS-CoV-2 virus. Although daily treatment with plain budesonide in mice decreased lung inflammation, the effect did not last as long as ProLung™-budesonide treatment.

Pneumonia affects the alveoli, the tiny air sacs in the lungs.



Weekly treatment with plain budesonide did not show any significant decrease in inflammation. Since ProLung™-budesonide was found to localise to areas of the lung that the virus is known to attack, this treatment may also be important in preventing the virus from getting into the cells of the lungs.

In addition to the positive effects of ProLung™-budesonide on cells infected with SARS CoV-2 virus and reducing inflammation, its unique composition aids in stabilising the lung cells, suggesting that it may prevent SARS CoV-2 infection in the first place. ProLung™-budesonide has the potential to interrupt the interaction between type II pneumocytes (a basic type of lung cell that play a role in the immune system) and macrophages, as well as slow down the progression of lung inflammation observed in COVID-19. In addition, it may also aid lung stabilisation as it has been shown to significantly decrease airway hyper-responsiveness (thereby keeping the airways open) and help maintain lung function, secondary to its sustained steroid effect in combination with a similar composition to lung surfactant. The latter may also play a role with some of the factors of the immune

system. The above findings and properties suggest that the ProLung™-budesonide system could make a difference in the treatment of COVID-19 and its long-term lung complications, as well as other lung diseases.

#### FUTURE PROSPECTS

The novel ProLung™-budesonide delivery system could also be used to treat asthma, the most common chronic disease among children, as well as

improved patient compliance could have a big impact on outcomes for chronic respiratory diseases, and for 'long-haulers' post COVID-19, resulting in a reduction in complications and patient hospitalisations.

Excitingly, another potential use of ProLung™-budesonide could be its administration via the oral route, allowing drug delivery to the gastrointestinal system. VGSK is preparing to

**This exciting development could also open the door to developing innovative treatment regimes for a number of other diseases.**

other respiratory diseases. ProLung™-budesonide requires only one dose of inhaled steroid (budesonide) per week. This is preferable to current budesonide therapy which must be given daily over the course of one week, and could significantly increase levels of patient treatment compliance. It may also prove beneficial as a treatment for respiratory symptoms secondary to other diseases, or for treating severe acute respiratory distress. Notably,

launch the ProLung™ system for other modes of delivery such as sustained oral delivery and intra-nasal delivery. The team have also completed regulatory compliance studies for ProLung™-budesonide and are preparing submissions for clinical trials to test its effect on COVID-19 patients. This exciting development in the treatment of COVID-19 could also open the door to developing innovative treatment regimes for a number of other diseases.



# Behind the Research

## VGSK Technologies Inc

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### Research Objectives

VGSK Technologies Inc develops sustained delivery methods for multiple therapeutics.

### Detail

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#### Bio

The idea of a novel prolonged drug delivery system began with Dr Pattisapu Gangadharam (Dr Ganga), a pioneer in drug resistance and drug toxicity research for infectious diseases such as TB and cancer, with 50 years of research experience in improving patient compliance and overcoming drug resistance. Dr Ganga worked with Dr Nejat Düzgüneş on novel sustained

drug delivery systems, such as intra-dermal, intra-nasal, inhalational, as well implantable polymers. Dr Kamu Konduri, together with Dr Sandhya Nandedkar, Dr Ram Pattisapu, Dr Jogi Pattisapu and Dr Ganesh Konduri, have joined the collaboration, to develop sustained inhalational drug delivery system for inhaled steroids targeted to decrease inflammation and improve patient compliance for diseases such as asthma.

#### Funding

• This project was funded in part with federal funds from the Division of Microbiology and Infectious

Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Department of Health and Human Services, under contract number N01-AI-30048.  
 • Research was also partially funded by Children's Foundation Grant, Children's Hospital of Wisconsin, Milwaukee WI.

#### Collaborators

VGSK Technologies Inc has utilised the non-clinical and preclinical services programme offered by the National Institute of Allergy and Infectious Diseases.

### References

Konduri, KS, Pattisapu, R, Pattisapu, J, et al, (2021) ProLung™-budesonide Inhibits SARS-CoV-2 Replication and Reduces Lung Inflammation. *Arch Pharmacol Ther*, 3(2):52–65. doi:10.33696/pharmacol.3.028

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### Personal Response

**Do you plan to carry out studies to test the administration of ProLung™-budesonide orally? What diseases could this potentially benefit?**

Yes. We are working on oral therapy as a method to deliver a multitude of drugs in a sustained manner, such steroids for inflammatory diseases, antibiotics, some anti-cancer drugs, and other chronic disease states. We are evaluating drugs with the aim of reducing their toxicity by giving less doses in a sustained manner.

