



**SCHOOL OF MEDICINE
DEPARTMENT OF MEDICINE
DIVISION OF PULMONARY AND CRITICAL CARE MEDICINE**

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August 6, 2007

Allen F. Gant
CEO and Chairman of the Board
BioMarck Pharmaceuticals
2619 St. Mary's Street
Raleigh, NC 27609

Dear Mr. Gant,

I am very pleased to have the opportunity to support Dr. Kenneth Adler, and to comment upon the high scientific quality and potential clinical impact of his research on airway mucus secretion. As a laboratory researcher in airways disease and a clinician caring for patients with these diseases, I have followed this research with great interest.

Chronic obstructive pulmonary disease currently afflicts more than 16 million Americans, and is the fourth leading cause of death in this country, accounting for over 100,000 deaths annually. The direct cost of caring for these patients in 2002 was estimated to be \$18 billion. Despite the recognized impact of COPD, progress in developing new and more effective treatments has been frustratingly slow. Drug management of COPD currently relies of an armamentarium derived largely from asthma treatment, and is widely recognized as inadequate.

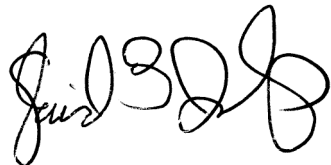
Among the clinical manifestations of COPD, a particularly troublesome one for both patients and physicians is increased mucus secretion. Moreover, mucus hypersecretion is a common problem for patients with other lung diseases, including asthma and bronchiectasis. Critically ill patients on mechanical ventilators also frequently suffer with increase secretions, prolonging their stay in intensive care units.

Despite the recognized importance of mucus hypersecretion, there is currently no treatment that addresses this. In part, this reflects our incomplete understanding of the cell biology of mucus secretion in the lungs. Dr. Adler has been a leader in this field for over two decades, and has made great progress in defining the proteins involved in the release of mucus from airway cells. Central to this process is the myristoylated alanine-rich C-kinase substrate, or MARCKS protein. A protein with a variety of functions, Dr. Adler was the first to recognize that MARCKS protein controls the release of mucus from airway epithelial cells. Among his publications on this topic is a landmark article in the highly prestigious journal *Nature Medicine* in 2004, showing that a peptide with the same sequence as part of the MARCKS protein blocked mucus secreting in the mouse. This highly innovative research provides the first truly novel approach to treatment of COPD, as well as other lung diseases characterized by mucus hypersecretion, since I have been involved in lung research. Moreover, in a subsequent publication, Dr. Adler demonstrated that this peptide prevented lung function changes in a mouse model

of asthma, supporting the exciting possibility that it could offer a new therapeutic strategy in human asthma.

It would be difficult to overemphasize the importance of this research, and of the necessity to move this into human subjects and patients as quickly as possible. This new approach has the potential to improve the health and quality of life for millions of patients with COPD and other lung diseases. Please feel free to contact me should you require additional information about this research.

Sincerely,

A handwritten signature in black ink, appearing to read "David B. Jacoby". The signature is fluid and cursive, with the first name "David" written in a smaller, more compact script than the last name "Jacoby".

David B. Jacoby, M.D.

Professor of Medicine, Physiology and Pharmacology, and Anesthesiology and Peri-Operative Medicine

Edwards Professor of Pulmonary Medicine

Deputy Director, Oregon Clinical and Translational Research Institute.

Chief, Pulmonary and Critical Care