PRESS RELEASE
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Enterprise Therapeutics publishes paper on novel therapeutic approach for treatment of all cystic fibrosis patients

- *"TMEM16A Potentiation: A Novel Therapeutic Approach for the Treatment of Cystic Fibrosis" published in American Journal of Respiratory and Critical Care Medicine*
- *Paper demonstrates first in class TMEM16A chloride channel potentiators, to accelerate mucociliary clearance*
- *Co-authored by researchers from University of Sussex, University of North Carolina and University of Miami*

Brighton, UK, 08 January 2020: Enterprise Therapeutics Ltd (Enterprise), a biopharmaceutical company dedicated to the discovery and development of novel therapies to improve the lives of patients suffering with respiratory disease, today announced the publication of its first peer-reviewed paper. The open access paper, published in the American Journal of Respiratory and Critical Care Medicine[1], describes TMEM16A potentiation via ETX001 as a novel approach for the treatment of cystic fibrosis (CF). The research was conducted in collaboration with University of Sussex, University of North Carolina and University of Miami.

The paper, entitled "TMEM16A Potentiation: A Novel Therapeutic Approach for the Treatment of Cystic Fibrosis", demonstrates the ability of Enterprise's proprietary compound, ETX001, to enhance the activity of TMEM16A in human bronchial epithelial cells from CF patients, increasing epithelial fluid secretion and mucus clearance providing the first pre-clinical proof of principle for this approach.

CF is estimated to affect 75,000 patients globally and is caused by loss of function mutations in the anion channel, cystic fibrosis transmembrane conductance regulator (CFTR). Increasing anion conductance via CFTR modulation is a clinically validated approach for treating CF, however it does not treat ≥10% of patients with a combination of nonsense and other rare mutations. In addition, many patients eligible for CFTR repair therapy do not benefit from these therapies. TMEM16A potentiation offers a non-CFTR mediated approach for the treatment of CF and can be delivered as a monotherapy or in combination with other therapies such as CFTR repair.

Dr Henry Danahay, Head of Biology, Enterprise Therapeutics, and lead author of the paper, said: *"We have successfully demonstrated the positive effects of ETX001 on both airway fluid secretion and mucus clearance in CF patients. Given the percentage of the population of CF patients who are not genetically matched to existing CFTR repair therapies, this paper builds a strong case for testing TMEM16A potentiation in the clinic."*

Authors on the paper include Henry L Danahay (Enterprise Therapeutics), Sarah Lilley (Sussex Drug Discovery Centre, University of Sussex), Roy Fox (Sussex Drug Discovery Centre, University of Sussex), Holly Charlton (Sussex Drug Discovery Centre, University of Sussex), Juan Sabater (Mount Sinai Medical Centre, University of Miami), Brian Button (Department of Biochemistry & Biophysics, UNC Chapel Hill, North Carolina), Clive McCarthy (Enterprise Therapeutics), Stephen P Collingwood (Enterprise Therapeutics), and Martin Gosling (Enterprise Therapeutics, and Sussex Drug Discovery Centre, University of Sussex).

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[1]https://www.atsjournals.org/doi/abs/10.1164/rccm.201908-1641OC

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Notes for Editors

Photo: Dr Henry Danahay, Head of Biology, Enterprise Therapeutics

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About Enterprise Therapeutics www.enterprisetherapeutics.com
Enterprise Therapeutics is discovering and developing new therapies that target the underlying mechanisms of mucus congestion in the lungs, one of the main causes of difficulty in breathing and increased risk of infection in respiratory diseases such as cystic fibrosis and COPD. Reducing mucus congestion will reduce the frequency of lung infections and improve patient quality of life.

The Company's novel muco-regulatory therapies target ion channels TMEM16A and ENaC to increase the hydration and clearance of mucus. Enterprise has also identified novel targets and

compounds that reduce mucus production, an approach that complements mucus hydration therapies.

The Enterprise Therapeutics management team has significant expertise in drug discovery, drug development, respiratory biology and ion channel pharmacology. In April 2018 the Company closed an oversubscribed Series B funding round co-led by Versant Ventures and Novartis Venture Fund, with Forbion Capital Partners, Epidarex Capital and IP Group. In October 2019 the company received funding from the Cystic Fibrosis Foundation to advance TMEM16A through to clinical proof of concept in CF.

About Cystic Fibrosis (CF)
Cystic Fibrosis is the most common lethal genetic disease of Caucasians with more than 75,000 patients worldwide living with the disease. The average life expectancy of a CF patient, although improving, is approximately 40 years.