Kither Biotech announces publication of new data in Science Translational Medicine

Data support the use of Kither Biotech's lead asset, KIT2014, in obstructive airway diseases

KIT2014 demonstrated a triple mechanism of action in reversing disease pathogenesis: enhancing functionality of CFTR channels and reducing bronchoconstriction and inflammation

Adds to evidence supporting the use of KIT2014 as a potential add-on therapy to current cystic fibrosis standard of care

Turin, Italy, 31 2022 – Kither Biotech ("Kither" or "the Company"), a biopharmaceutical company developing novel therapies for rare respiratory diseases, today announces the publication of a study in *Science Translational Medicine* describing the mechanism of action of its lead asset, KIT2014, and proof-of-concept data for its use for the treatment of chronic obstructive airway diseases (Ghigo et al., Sci. Transl. Med. 14, eabl6328 (2022)).

KIT2014 is a novel, cell-permeable peptide currently being investigated for the treatment of cystic fibrosis (CF) that works to modulate cyclic adenosine monophosphate (cAMP) levels inside cells. Increasing cAMP can reduce mucus accumulation, inflammation, and bronchoconstriction, issues that are inherent to cystic fibrosis. KIT2014 is currently being developed as an add-on to the current standard of care enabling improved efficacy by directly focusing on the most significant ailments of CF patients, delivered directly to the lungs as an inhaled therapy. The Company expects to begin a Phase 1/2A clinical trial of KIT2014 in 2023.

The data demonstrate the therapeutic potential of inhaled KIT2014 (referred to as PI3Kγ MP in the publication) to increase cAMP levels in pulmonary cells, alleviating the pathogenesis of several obstructive airway diseases, such as cystic fibrosis, asthma and COPD, through a triple mechanism of action: promoting bronchodilation, reducing lung inflammation, and enhancing the activity of the cystic fibrosis transmembrane conductance regulator (CFTR), the channel that triggers mucus hydration and clearance. In airway cells from patients with cystic fibrosis, a disease where CFTR dysfunction is particularly critical, KIT2014 was reported to enhance the effects of existing CFTR modulators by up to 80%.

Vincent Metzler, CEO at Kither Biotech, commented: *"The publication of these data in a prominent peer-reviewed journal represents an important step as we advance the development of KIT2014 for the treatment of cystic fibrosis as an add-on therapy to CFTR modulators. We are preparing for our Phase 1/2A clinical trial of KIT2014, as we move one step closer to potentially bringing this innovative therapy to patients with unmet need."*

Alessandra Ghigo, scientific co-founder at Kither Biotech and lead investigator, said*: "These new data validate KIT2014's ability to modulate cAMP signal transduction in the lungs, increasing the functionality of CFTR channels, as well as reducing inflammation and bronchoconstriction, properties which are potentially highly beneficial to patients with cystic fibrosis and other diseases like COPD and asthma. We are looking forward to commencing clinical trials for KIT2014."*

Emilio Hirsch, scientific co-founder at Kither Biotech and last author, added: *"Our data of KIT2014 showing an enhancement of the effect of existing CFTR modulators by 80% demonstrate the potential of*

this peptide, when administered as an inhalation therapy, to improve the condition of many patients still suffering from CF or other respiratory diseases."

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About Kither Biotech

Kither Biotech is a biopharma company founded by Prof. Alessandra Ghigo, Prof. Emilio Hirsch, Prof. Alberto Bardelli and Marco Kevin Malisani. The company aims to identify and develop new drug candidates for the treatment of rare pulmonary diseases, with specific focus on cystic fibrosis and idiopathic pulmonary fibrosis. Kither Biotech is a spin-off from the University of Turin and actively collaborates with the Molecular Biotechnology Center (University of Turin) and other research centres in the world. The company developed a pipeline of treatments currently under preclinical development, with programs in cystic fibrosis, idiopathic pulmonary fibrosis and other respiratory diseases. |www.kitherbiotech.com

About KIT2014

KIT2014 is a cell-permeable cAMP modulating peptide that disrupts the interaction of PI3Kgamma with its partner, protein kinase A (PKA), leading to type 3 and 4 phosphodiesterases (PDE3/4) inhibition and, in turn, to enhanced cAMP responses within the cell. KIT2014 is currently being investigated for the treatment of cystic fibrosis (CF) as an add-on inhalation therapy to the current standard of care, enabling improved efficacy by directly impacting mucus hypersecretion, airway inflammation and bronchoconstriction, the most significant ailments of CF patients. When inhaled, KIT2014 increases cAMP locally in bronchial epithelial cells to promote the opening of CFTR chloride channels, which are key to mucus hydration, while in lung smooth muscle and immune cells cAMP elevation limits bronchoconstriction and neutrophil infiltration. In CF patients, treatment with KIT2014 is believed to restore the function of CFTR mutants by potentiating the effects of CFTR modulators (Ghigo et al., Science Translational Medicine, in press).

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