# US Patent Office has issued a patent covering the use of trimethylangelicin in Cystic Fibrosis

**Milan (Italy), April 15th,2016** – Rare Partners Srl Impresa Sociale announces that the United States Patent and Trademark Office has issued on March 15th the US Patent number 9283206 covering the use of trimethylangelicin (TMA) as CFTR Corrector in Bronchial Epithelial Cells. The patent's inventors Giulio Cabrini, Valeria Casavola and Roberto Gambari are leading academic scientists with a strong publication record in the field of cystic fibrosis. The patent's rights belong to Azienda Ospedaliera Universitaria di Verona, Università degli Studi di Bari, Università degli Studi di Ferrara and to Rare Partners. An Orphan Drug Designation for TMA for the treatment of Cystic Fibrosis has been already granted by the European Medicines Agency to Rare Partners in 2013.

Marco Prosdocimi, Managing Director of Rare Partners, says that "this important result was made possible by the collaboration we established with a network of outstanding Italian scientists: Giulio Cabrini (University Hospital of Verona), Valeria Casavola (University of Bari) and Roberto Gambari (University of Ferrara). Securing IP protection is an essential step in the process of making available to rare disease patients new products and we are confident that this result will increase attractiveness of collaboration with us as a way to advance discovery results toward clinical application.

Giulio Cabrini says that "clinical trials testing the first CFTR correctors that are presently available is revealing that the individual response is variable within the cystic fibrosis patients carrying the most common CF gene mutation and that association of a CFTR corrector with a CFTR potentiator can result in unexpected interferences. Thus, the discovery of further novel drugs correcting the defective CFTR protein is mandatory to make a set of drugs available to fit the individual response of the patients affected by cystic fibrosis".



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Valeria Casavola adds that "the efficacy of TMA as corrector of the mutated CFTR protein affecting the majority of CF patients has been now validated in an external internationally recognized North-American research group. This made also possible to identify the site of interaction of TMA with the mutated CFTR protein, starting to collect pieces of information relevant to understand the mechanism of action of TMA in CF and to design further improved TMA analogues."

Roberto Gambari also comments that "in order to bring a molecule so promising for the cure of the majority of CF patients from the stage of preclinical evidence to the chemist's bench, our collaborative network is now planning to strongly involve the pharmaceutical industry on the different issues required to allow the clinical application of TMA as a drug. On the other hand, this achievement demonstrates the interest on this particular class of molecules and will encourage further research efforts focusing of the development of novel analogues".

## About Rare Partners

Rare Partners is a non profit biopharmaceutical company devoted to the development of new therapies and diagnostics in the field of rare diseases. The company was founded in Milan on March 2010 and registered in Italy as “Impresa Sociale”. The basic idea of Rare Partners is to match non profit financial resources (public and private) with industrial drug development expertise, provided by the company’s organization together with a strong network of consultants. Rare Partners currently has product candidates in the fields of Cystic Fibrosis and of Thalassemia.

## About Cystic Fibrosis

Cystic fibrosis is a life-threatening, genetic disease. In the European Union population its prevalence is estimated between 7 and 13 cases over 100,000, in particular is estimated at 7.4 cases over 100,000 in the latest issue (March 2016) of Orphanet Report Series on



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the prevalence of rare diseases. A defect in the CFTR gene causes the body to produce abnormally thick, sticky mucus that leads to chronic lung infections and impairs digestion. Lung complications represent the most serious manifestation of the disease and the reason for the high mortality rate amongst patients.

## About TMA (4,6,4'–trimethylangelicin)

TMA was originally synthesized in the 80s within an R&D project carried on in the psoriasis area. Recently Giulio Cabrini (Department of Pathology and Diagnostics, University Hospital of Verona), Valeria Casavola (Department of Biosciences, Biotechnologies and Biopharmaceutics, University of Bari) and Roberto Gambari (Department of Life Sciences and Biotechnology, University of Ferrara), with their coworkers, discovered that TMA exerts 3 different actions on cells of the respiratory system, each one potentially able to improve clinical status of the patients. First, TMA was shown to inhibit IL-8 gene transcription mainly by intervening on driving the recruitment of activated transcription factors on IL-8 gene promoter. Furthermore, TMA was also tested on CFTR and found to potentiate F508del-CFTR-dependent chloride efflux. Finally, TMA was found to be able to correct F508del-CFTR activity. TMA is expected to provide a relevant benefit to patients, not shared by other treatments, for the peculiarity of this triple action, potentially able to reduce at the same time accumulation of thick and sticky mucus by inducing chloride secretion (activation and correction of CFTR) as well reducing inflammatory status of the respiratory tree (inhibition of IL-8).

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