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New approach to developing cystic fibrosis treatments may have wider applications

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Earlier this year, the Food and Drug Administration (FDA) approved Symdeko (tezacaftor/ivacaftor) tablets for the treatment of certain cystic fibrosis (CF) patients 12 years and older. These patients are homozygous for the F508del mutation or have at least one mutation in the CF transmembrane conductance regulator (CFTR) gene that is responsive to tezacaftor/ivacaftor based on in vitro data and/or clinical evidence.

This approval built on the FDA's experience with ivacaftor.

Durmowicz AG, et al. (*Ann Am Thorac Soc*. 2018;15:1-2) described a novel approach to expanding the ivacaftor patient population to include relatively rare CFTR mutations using in vitro chloride ion transport data. This evaluation considered the accuracy and precision of the in vitro assay system, the current understanding of CF and ivacaftor clinical data.

FDA draft guidance titled "Developing Targeted Therapies in Low-Frequency Molecular Subsets of a Disease," published in December 2017 (http://bit.ly/2JOhdYL), describes recommendations on how to group patients with different molecular alterations for eligibility in clinical trials. It also delineates general approaches to evaluating the benefits and risks of targeted therapies within a clinically defined disease in which some molecular alterations occur at low frequencies, such as CF and other genetic diseases.

These resources provide new regulatory approaches that may be used to support the efficacy of drugs for other rare inherited diseases where the genetics, disease pathophysiology and drug's mechanism of action are well-delineated.