



# CYSTIC FIBROSIS

## GLOSSARY OF TERMS

**CYSTIC FIBROSIS (CF)** – A life-threatening, genetic disease for which there is no cure. It affects approximately 70,000 people worldwide: 30,000 in the United States,<sup>1</sup> nearly 3,800 in Canada,<sup>2</sup> 35,000 in Europe,<sup>3</sup> and 2,500 in Australia.<sup>3</sup> CF is caused by defective cystic fibrosis transmembrane conductance regulator (CFTR) proteins that result from mutations in the *CFTR* gene.<sup>4,5</sup> These proteins are essential to regulating the flow of salt and water into and out of cells in a number of organs, including the lungs. When the proteins don't work properly or don't exist, abnormally thick, sticky mucus accumulates and can cause chronic lung infections and progressive lung damage.<sup>6</sup>

**CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATOR (CFTR)** – The *CFTR* gene controls production of CFTR protein; the CFTR protein regulates the flow of salt and water into and out of cells. Defective CFTR proteins that result from mutations in the *CFTR* gene cause CF.<sup>6</sup>

**CFTR MUTATION** – A genetic mutation that can affect the *number* (e.g., trafficking) and *function* (e.g., gating) of CFTR protein channels at the cell surface.<sup>7</sup>

**F508DEL** – The most common *CFTR* mutation, found in nearly 90 percent of people living with CF. The CFTR protein is defective and does not generally reach the cell surface.<sup>7</sup>

**GATING MUTATION** – A *CFTR* gene mutation that prevents the CFTR protein from opening or working (gating) properly on the cell surface. The most common example of a gating mutation is G551D.<sup>7</sup>

**G551D** – A CF gating mutation found in approximately 1,200 people in the United States, 1,000 in the EU and 180 in Ireland, where the defect is most prevalent.<sup>9</sup> This gating mutation prevents the protein from working properly on the cell surface.<sup>7</sup>

**CFTR MODULATORS** – A class of medicines and medicines in development that targets the underlying cause of CF and is designed to treat a protein defect found in specific subsets of people with CF.<sup>10</sup>

- **Correctors** – A type of medicine in development that aims to increase *CFTR* function by increasing the movement (trafficking) of CFTR to the cell surface.<sup>10</sup> These molecules target the CFTR protein defects caused by the more common F508del *CFTR* mutation,<sup>7,10</sup> which is found in an estimated 90 percent of people living with CF.<sup>8</sup>
- **Potentiators** – A type of medicine and medicines in development which aim to help the CFTR protein function more normally once it reaches the cell surface.<sup>10</sup> Healthy CFTR function helps regulate the flow of salt and water into and out of cells.<sup>11</sup>

**RARE DISEASE** – A disease or disorder that affects fewer than 200,000 people in the United States as classified by the National Institutes of Health.<sup>12</sup> These diseases affect approximately 30 million Americans.<sup>12</sup> (also referred to as “*orphan disease*”)

## CLINICAL TRIAL ENDPOINTS

- **FEV<sub>1</sub>/lung function** – Forced expiratory volume in one second, or lung function.<sup>13,14</sup> Lung function is assessed with a standard test that measures the amount of air a person can exhale in one second (FEV<sub>1</sub>).<sup>13,14</sup>
- **Patient-Reported Outcomes** – The Cystic Fibrosis Questionnaire – Revised (CFQ-R) is a validated patient-reported outcomes tool used to measure the impact of an investigational product’s impact on study participants’ overall health, daily life, perceived well-being and symptoms.<sup>13,14</sup> A ≥4-point change from baseline in CFQ-R is considered clinically meaningful.
- **Sweat Chloride Concentration** – The amount of chloride in sweat is measured using a standard test. Elevated sweat chloride is a diagnostic characteristic of CF, and sweat chloride is a marker of CFTR protein dysfunction. A reduction in sweat chloride is considered to be a marker of improved CFTR function.<sup>13,14</sup>
- **Pulmonary exacerbation** – A period when lung disease worsens and requires intravenous antibiotics and/or hospitalization.<sup>13,14</sup>

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