

## Translation

### New Drug Application Filed for Recombinant Human Deoxyribonuclease I (rhDNase) “Pulmozyme”

July 15, 2011 (Tokyo) - Chugai Pharmaceutical Co., Ltd. [Main Office: Chuo-ku, Tokyo. President: Osamu Nagayama (hereafter, “Chugai”)] announced today that it has filed a new drug application to the Ministry of Health, Labour and Welfare (MHLW), for recombinant human deoxyribonuclease I (rhDNase) “Pulmozyme,” (generic name: dornase alfa, overseas product name: “Pulmozyme®,” marketed by F. Hoffmann-La Roche and Genentech), for the indication of “improvement of pulmonary function in patients with cystic fibrosis.”

As a result of the evaluation by the “Review Committee on Unapproved Drugs and Indications with High Medical Needs\*” held on April 18, it was concluded that it is reasonable that dornase alfa be filed for approval in this indication based on available data. In overseas clinical studies, administration of dornase alfa by inhalation is already confirmed to be effective for the improvement of pulmonary function and reduction of the risk of serious infection of the respiratory tract in cystic fibrosis patients, compared to placebo. Dornase alfa is now designated as an orphan drug by the MHLW.

Cystic fibrosis is a hereditary genetic disease afflicting about one in 2500 newborns in the US and Europe. On the contrary, in Japan, the incidence is only about one in 1.74 million and is a very rare disease. According to MHLW-supported research done in 2009, “Investigational study on refractory pancreatic disease,” there were 15 patients estimated in Japan in 2009. Cystic fibrosis is caused by genetic mutation of CFTR, a chloride ion-channel. There is no curative treatment for this disease, and typically, expectorants and bronchodilators are administered for respiratory tract disturbances, and antibiotics by inhalation or systemic treatment are used to treat infection.

Dornase alfa cleaves extracellular DNA in the mucus of cystic fibrosis patients, reducing the adhesiveness and viscoelasticity of the mucus, and facilitating expectoration of sputum, thereby improving pulmonary function and reducing the risk of serious infection of the respiratory tract. Overseas, it is approved in approximately 70 countries including the U.S. and Europe, and is administered to around 50 thousand patients per year, as one of the standard treatments for cystic fibrosis.

Chugai will make effort to ensure that patients will have early access to “Pulmozyme,” a new treatment option that will enable better control of respiratory symptoms in cystic fibrosis, a very rare and difficult to treat disease in Japan.

\* The “Review Committee on Unapproved Drugs and Indications with High Medical Needs” was established for the purpose of “enhancing development by pharmaceutical companies of drugs and indications that have been approved for use in western countries but not yet approved in Japan. Its activities include evaluating medical needs, confirming the appropriateness of an application based on evidence in the public domain and investigating the need for studies that should be additionally conducted”.