SELUMETINIB GRANTED ORPHAN DRUG DESIGNATION IN THE US FOR ADJUVANT TREATMENT OF DIFFERENTIATED THYROID CANCER

AstraZeneca today announced that the US Food and Drug Administration (FDA) has granted Orphan Drug Designation for the investigational MEK 1/2 inhibitor, selumetinib (AZD6244, ARRY-142886) for adjuvant treatment of patients with stage III or IV differentiated thyroid cancer (DTC).

DTC is diagnosed in approximately 60,000 people in the US each year,[1] and radioactive iodine (RAI) is recommended for those with known/suspected metastases at diagnosis and those at high risk of recurrence.[2] A small proportion of patients do not benefit from currently available treatment with RAI because they do not express sufficient sodium/iodine symporter (NIS) which is important for RAI uptake into thyroid cells.[3,4] Selumetinib is being tested for its ability to increase expression of NIS with the potential to add a treatment option for patients who do not respond well to RAI.

Sean Bohen Executive Vice President, Global Medicines Development and Chief Medical Officer, at AstraZeneca, said: "Uptake of RAI is crucial for patients with thyroid cancer where no other therapies have proven beneficial. Selumetinib could significantly enhance currently available treatment options for these patients. The Orphan Drug Designation is an important achievement as we advance our development plans for this potential treatment in differentiated thyroid cancer."

The Orphan Drug Designation programme provides orphan status to drugs and biologics, which are defined as those intended for the safe and effective treatment, diagnosis or prevention of rare diseases or disorders that affect fewer than 200,000 people in the US.[5]

Selumetinib inhibits the MEK pathway in cancer cells to prevent tumour growth. It is being tested in the Phase III ASTRA trial in patients with DTC who are at high risk of recurrence.[6] In a Phase II study of selumetinib in patients with advanced thyroid cancer, clinically meaningful increases in iodine uptake and retention were seen in patients with thyroid cancer that was refractory to RAI.[7]

In addition to DTC, selumetinib is being tested in SELECT-1, a Phase III trial of patients with KRAS-mutant advanced non-small cell lung cancer (NSCLC) and in a Phase II registration trial of paediatric and adolescent patients with neurofibromatosis Type 1 in collaboration with the US National Cancer Institute.

About thyroid cancer

Cancer of the thyroid gland is diagnosed in approximately 60,000 people in the US each year.[1] Nearly 95% of patients have differentiated tumours with an associated five-year survival of over 90%.[2] DTC is usually treated by surgery and thyroxine hormone replacement therapy, and radioactive iodine treatment (RAI) is recommended for patients with known/suspected metastases at diagnosis and for those at high risk of recurrence.[2] Up to 30% of patients experience recurrence of DTC after initial treatment.[2]

Approximately 5-15% of patients with DTC do not respond to RAI.[3] Ten year survival in patients who fail to take up radioactive iodine into tumour cells is 10% compared to nearly 60%

in those with normal uptake.[8] Traditional chemotherapy has minimal efficacy in patients with metastatic DTC.[2]

About selumetinib

Selumetinib is an oral, potent, selective inhibitor of MEK, part of the mitogen-activated protein kinase (MAPK) pathway which is frequently activated in cancer, including those with the KRAS mutation, which is present in 20% of human cancers and 20-30% of non-small cell lung cancer tumours.

MAPK activation also inhibits expression of thyroid hormone biosynthesis genes, including the sodium/iodine symporter (NIS) which facilitates iodine uptake into cells.7 Pre-clinical studies have suggested that following MAPK inhibition, iodine uptake by thyroid tumour cells is regained.[7]

AstraZeneca acquired exclusive worldwide rights to selumetinib from Array BioPharma Inc. in 2003.

About the ASTRA trial

ASTRA is a Phase III randomised, double blind study which is comparing the complete remission rate following a 5-week course of selumetinib or placebo and single dose adjuvant radioactive iodine therapy in patients with differentiated thyroid cancer.[5]

About AstraZeneca in Oncology
AstraZeneca has a deep-rooted heritage in Oncology and offers a quickly growing portfolio of new medicines that has the potential to transform patients' lives and the Company's future. With at least 6 new medicines to be launched between 2014 and 2020 and a broad pipeline of small molecules and biologics in development, we are committed to advance New Oncology as one of AstraZeneca's six Growth Platforms focused on lung, ovarian, breast and blood cancers. In addition to our core capabilities, we actively pursue innovative partnerships and investments that accelerate the delivery of our strategy, as illustrated by our investment in Acerta Pharma in haematology.

By harnessing the power of four scientific platforms -- immuno-oncology, the genetic drivers of cancer and resistance, DNA damage response and antibody drug conjugates -- and by championing the development of personalised combinations, AstraZeneca has the vision to redefine cancer treatment and one day eliminate cancer as a cause of death.

About AstraZeneca

AstraZeneca is a global, innovation-driven biopharmaceutical business that focuses on the discovery, development and commercialisation of prescription medicines, primarily for the treatment of diseases in three main therapy areas - respiratory, inflammation, autoimmune disease (RIA), cardiovascular and metabolic disease (CVMD) and oncology - as well as in infection and neuroscience. AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. For more information please visit: www.astrazeneca.com

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Key: RIA - Respiratory, Inflammation and Autoimmunity, CVMD - Cardiovascular and Metabolic Disease,

ING - Infection, Neuroscience and Gastrointestinal

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