Selumetinib granted orphan drug designation in Japan for neurofibromatosis type 1

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Designation follows recent US approval

with additional regulatory submissions underway

Phase II SPRINT trial showed selumetinib reduced tumour volume in paediatric patients with NF1 plexiform neurofibromas

AstraZeneca today announced that selumetinib has been granted orphan drug designation (ODD) in Japan for the treatment of neurofibromatosis type 1 (NF1), a rare and debilitating genetic disease.[1]

Selumetinib is co-developed and co-commercialised with MSD Inc., Kenilworth, N.J., US (MSD: known as Merck & Co., Inc. inside the US and Canada).

Some 30-50% of patients with NF1 experience plexiform neurofibromas (PN) - tumours growing along their nerve sheaths.[2] These PN can cause clinical issues such as disfigurement, motor dysfunction, pain, airway dysfunction, visual impairment and bowel/bladder dysfunction.[3]

The Japanese Ministry of Health, Labour and Welfare grants ODD to medicines intended for the treatment of diseases that affect fewer than 50,000 patients in Japan and for which there is a high unmet medical need.

José Baselga, Executive Vice President, Oncology R&D, said: "Neurofibromatosis type 1 can have a devastating impact on children and new medicines are urgently needed to help treat the resulting plexiform neurofibromas and associated clinical issues. Current options in most countries are limited and this designation is a significant step forward in bringing the first medicine for NF1 to paediatric patients in Japan."

Roy Baynes, Senior Vice President and Head of Global Clinical Development, Chief Medical Officer, MSD Research Laboratories, said: "Plexiform neurofibromas are one of the key manifestations of NF1 and can lead to pain and disfigurement. In the SPRINT trial, selumetinib was shown to reduce the size of these tumours in children. We are hopeful that we will be able to bring this treatment to this underserved paediatric patient community in Japan."

The National Cancer Institute (NCI) Cancer Therapy Evaluation Program (CTEP)-sponsored Phase I/II SPRINT Stratum 1 trial showed an overall response rate (ORR) of 66% (33 of 50 patients, confirmed partial response) in paediatric patients with NF1 PN when treated with selumetinib as a twice-daily oral monotherapy. ORR is defined as the percentage of patients with confirmed complete or partial response of at least 20% reduction in tumour volume.

AstraZeneca and MSD are jointly developing and commercialising selumetinib which was approved in the US in April 2020 under the medicine name *Koselugo* for the treatment of paediatric patients two years and older with NF1 and symptomatic, inoperable PN. A marketing authorisation application in NF1 PN was accepted for review by the European Medicines Agency earlier in the year and further global regulatory submissions are underway.

NF1

NF1 is a debilitating genetic disease that affects one in every 3,000 to 4,000 individuals.[1] It is caused by a spontaneous or inherited mutation in the NF1 gene and is associated with many symptoms, including soft lumps on and under the skin (cutaneous neurofibromas) and skin pigmentation (so-called 'café au lait' spots)[1] and, in 30-50% of patients, tumours develop on the nerve sheaths (plexiform neurofibromas).[2] These plexiform neurofibromas can cause clinical issues such as disfigurement, motor dysfunction, pain, airway dysfunction, visual impairment, and bladder/bowel dysfunction.[3] PN begin during early childhood, with varying degrees of severity, and can reduce life expectancy by 8 to 15 years.[1,4,5]

SPRINT

The SPRINT Stratum 1 Phase I/II trial was designed to evaluate the objective response rate and impact on patient-reported and functional outcomes in paediatric patients with NF1-related inoperable PNs treated with selumetinib monotherapy.[6] Results were published in *The New England Journal of Medicine.*[7] This trial sponsored by NCI CTEP was conducted under a Cooperative Research and Development Agreement between NCI and AstraZeneca with additional support from the Neurofibromatosis Therapeutic Acceleration Program (NTAP).

Selumetinib

Selumetinib (available in the US under the medicine name *Koselugo*) is an inhibitor of mitogen-activated protein kinase kinases 1 and 2 (MEK1/2).[6] MEK1/2 proteins are upstream regulators of the extracellular signal-related kinase (ERK) pathway. Both MEK and ERK are critical components of the RAS-regulated RAF-MEK-ERK pathway, which is often activated in different types of cancers.

Selumetinib was granted US FDA Breakthrough Therapy Designation in April 2019, Rare Pediatric Disease Designation in December 2019, Orphan Drug Designation in February 2018, EU orphan designation in August 2018 and Swissmedic orphan drug status in December 2018 for the treatment of paediatric patients with NF1 PN.

AstraZeneca and MSD Strategic Oncology Collaboration

In July 2017, AstraZeneca and Merck & Co., Inc., Kenilworth, NJ, US, known as MSD outside the United States and Canada, announced a global strategic oncology collaboration to co-develop and co-commercialise *Lynparza*, the world's first PARP inhibitor, and *Koselugo*, a MEK inhibitor, for multiple cancer types. Working together, the companies will develop *Lynparza* and *Koselugo* in combination with other potential new medicines and as monotherapies. Independently, the companies will develop *Lynparza* and *Koselugo* in combination with their respective PD-L1 and PD-1 medicines.

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 six new medicines launched between 2014 and 2020, and a broad pipeline of small molecules and biologics in development, the Company is committed to advance oncology as a key growth driver for AstraZeneca focused on lung, ovarian, breast and blood cancers. In addition to AstraZeneca's main capabilities, the Company is actively pursuing innovative partnerships and investments that accelerate the delivery of our strategy, as illustrated by the investment in Acerta Pharma in haematology.

By harnessing the power of four scientific platforms - Immuno-Oncology, Tumour Drivers 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.

AstraZeneca

AstraZeneca (LSE/STO/NYSE: AZN) is a global, science-led biopharmaceutical company that focuses on the discovery, development and commercialisation of prescription medicines, primarily for the treatment of diseases in three therapy areas - Oncology, Cardiovascular, Renal & Metabolism, and Respiratory & Immunology. Based in Cambridge, UK, AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. Please visit astrazeneca.com and follow the Company on Twitter @AstraZeneca.

Contacts

For details on how to contact the Investor Relations Team, please click here. For Media contacts, click here.

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