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Koselugo approved in the US for adults with neurofibromatosis type 1

Approval based on KOMET Phase III trial results which showed 20% overall response rate in tumour size reduction

Alexion, AstraZeneca Rare Disease's *Koselugo* (selumetinib), an oral, selective MEK inhibitor, has been approved in the US for the treatment of adult patients with neurofibromatosis type 1 (NF1) who have symptomatic, inoperable plexiform neurofibromas (PN).[1]

The approval by the US Food and Drug Administration (FDA) was based on positive results from KOMET, the largest and only placebo-controlled global Phase III trial in this patient population. Data were presented at the 2025 American Society of Clinical Oncology (ASCO) Annual Meeting and published in *The Lancet*.[2]

NF1 is a rare, progressive, genetic condition usually diagnosed in early childhood, but often progressing into adulthood, that can impact every organ system.[3,4] Up to 50% of people living with NF1 may develop a type of non-malignant tumour called PN that may affect the brain, spinal cord and nerves.[4,5] PN may appear later in a person's life and can grow and become large, leading to pain, disfigurement and muscle weakness, among other debilitating symptoms.[4,5]

Prof. Pierre Wolkenstein, MD, PhD, Head of the Department of Dermatology at Henri Mondor Hospital, APHP, Paris East University (UPEC), and Investigator of the KOMET trial, said: "The KOMET Phase III trial, which builds on the established clinical profile of *Koselugo* and its real-world use in paediatric patients, underscores its potential to address the substantial and oftentimes progressive clinical burdens associated with PN in adulthood. This approval reaffirms the role of *Koselugo* as a strong option for the treatment of adult and paediatric patients with NF1 PN."

Marc Dunoyer, Chief Executive Officer, Alexion, said: "This expanded approval of *Koselugo* in adults with NF1 PN, together with the recently approved granule formulation for young children aged one year and older, enables much-needed continuity of care and supports patients across the disease journey in the US. As the first approved therapy in NF1 PN, backed by more than a decade of clinical evidence, *Koselugo* has transformed the treatment standard for this rare disease."

Annette Bakker, PhD, Chief Executive Officer, Children's Tumor Foundation, said: "We celebrate this FDA approval of *Koselugo* for adults with NF1 plexiform neurofibromas-a major step forward for NF patients everywhere. *Koselugo* has already changed what is possible for children with NF1, and now adults will benefit from that same progress. It is proof that NF research is delivering real results and opening the door to even more treatment options. This milestone shows what can be achieved when scientists, clinicians, industry and the NF community work together with one focus: getting effective treatments to patients faster."

In the primary analysis of the KOMET Phase III trial, *Koselugo* showed a statistically significant and clinically meaningful overall response rate (ORR) of 20% (n=14/71, 95% confidence interval [CI]: 11, 31) compared to 5% with placebo (n=4/74, 95% CI: 2, 13; p=0.011) by cycle 16, with 86% of patients on *Koselugo* having an observed duration of response (DOR) of at least 6 months. After 12 cycles, patients on placebo were switched to *Koselugo* and patients on *Koselugo* remained on treatment for an additional 12 cycles.[1]

The safety of *Koselugo* in the KOMET Phase III trial was consistent with its known profile and established use in paediatric patients.[2]

Koselugo has been recently approved in the EU, Japan and other countries for the treatment of adult patients with NF1 who have symptomatic, inoperable PN based on data from the KOMET Phase III trial, and additional regulatory reviews are ongoing. In the US, *Koselugo* granules have recently been approved for paediatric patients one year of age and older with NF1 PN.

Notes

NF1

NF1 is a rare, progressive, genetic condition that is caused by a spontaneous or inherited mutation in the NF1 gene.[3,4] NF1 is associated with a variety of symptoms, including soft lumps on and under the skin (cutaneous neurofibromas) and, in up to 50% of patients, tumours called plexiform neurofibromas (PN) may develop on the nerve sheaths.[4,5] These PN can cause clinical issues such as disfigurement, motor dysfunction, pain, airway dysfunction, visual impairment and bladder or bowel dysfunction.[4,5]

KOMET

KOMET is a global Phase III randomised, double-blind, placebo-controlled, multicentre trial designed to evaluate the efficacy and safety of *Koselugo* in adults with NF1 who have symptomatic, inoperable PN. The trial enrolled 145 adults from 13 countries across North America, South America, Europe, Asia and Australia, with participants' baseline characteristics, including gender and distribution of PN, reflective of the global adult NF1 patient population. Patients were enrolled and randomised to receive *Koselugo* or placebo (1:1) for 12 28-day cycles. Participants were required to have diagnosis of NF1, at least one symptomatic, inoperable PN measurable by volumetric MRI analysis, chronic PN pain score documented during screening, adequate organ and marrow function and stable chronic PN pain medication use at enrolment.[2,6]

The primary endpoint is confirmed overall response rate (ORR) by cycle 16 as assessed by ICR. ORR is defined as the percentage of patients with confirmed complete response (disappearance of PNs) or partial response (at least 20% reduction in tumour volume). Secondary endpoints include improved PN-related pain and health-related quality of life (HRQoL) at cycle 12.[2,6]

After 12 cycles, patients on placebo were switched to *Koselugo* and patients on *Koselugo* remained on treatment for an additional 12 cycles. Patients who had the opportunity to complete 24 cycles of treatment have the option to participate in a long-term extension period and continue to receive *Koselugo*.[2,6]

Koselugo

Koselugo (selumetinib) is a kinase inhibitor that blocks specific enzymes (MEK1 and MEK2), which are involved in stimulating cells to grow. In NF1, these enzymes are overactive, causing tumour cells to grow in an unregulated way creating so-called plexiform neurofibromas (PN). By blocking these enzymes, *Koselugo* slows down the growth of tumour cells and, therefore, the PN growth.

Koselugo is approved in the US, EU, Japan, China and other countries for the treatment of certain paediatric patients with NF1 who have symptomatic, inoperable PN.

Koselugo is approved in the US, EU, Japan and other countries for the treatment of adult patients with NF1 who have symptomatic, inoperable PN, and additional regulatory reviews are ongoing.

Koselugo has been granted Orphan Drug Designation in the US, EU, Japan and other countries for the treatment of NF1.

Alexion
Alexion, AstraZeneca Rare Disease, is focused on serving patients and families affected by rare diseases and devastating conditions through the discovery, development and delivery of life-changing medicines. A pioneering leader in rare disease for more than three decades, Alexion was the first to translate the complex biology of the complement system into transformative medicines, and today it continues to build a diversified pipeline across disease areas with significant unmet need, using an array of innovative modalities. As part of AstraZeneca, Alexion is continually expanding its global geographic footprint to serve more rare disease patients around the world. It is headquartered in Boston, US.

AstraZeneca
AstraZeneca (LSE/STO/Nasdaq: AZN) is a global, science-led biopharmaceutical company that focuses on the discovery, development, and commercialisation of prescription medicines in Oncology, Rare Diseases, and BioPharmaceuticals, including Cardiovascular, Renal & Metabolism, and Respiratory & Immunology. Based in Cambridge, UK, AstraZeneca's innovative medicines are sold in more than 125 countries and used by millions of patients worldwide. Please visit astrazeneca.com and follow the Company on Social Media @AstraZeneca.

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

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Matthew Bowden
Company Secretary
AstraZeneca PLC