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FDA approves first ever treatment for neurofibromatosis

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The U.S. Food and Drug Administration (FDA) has approved Koselugo (selumetinib) for use in patients with inoperable plexiform neurofibromas, a common manifestation in the disease neurofibromatosis type one (NF1). The FDA's approval of AstraZeneca's and MSD (Merck)'s submission is a major milestone for patients living with neurofibromatosis (NF), a genetic disorder that causes tumors to grow on nerves throughout the body. Affecting 1 in 3,000 people of all populations equally, this announcement is the first ever approved treatment for NF, and portends the potential for the development of treatment options for all NF patients.

Koselugo's approval follows comprehensive clinical testing of the drug in patients at the National Cancer Institute (NCI), a division of the National Institutes of Health (NIH). In those clinical trials, over 70% of NF patients with inoperable plexiform neurofibromas saw tumor size reduction anywhere from 20-60% in size. In addition to both visible and actual tumor reduction, patients reported higher-quality physical function, reduced pain, improved mobility, and enhanced emotional and psychological status.

The first use of MEK inhibitors as a potential treatment for NF tumors came from early-stage discoveries by Children's Tumor Foundation (CTF)-funded researchers, who showed that MEK inhibitors could significantly affect NF tumor size. Positive early clinical results were first reported at CTF's annual scientific NF Conference in 2015, as well as in subsequent publications in the *New England Journal of Medicine* in

2016 and 2020.

Collaborative efforts among the NCI, the NIH, the NFRP-CDMRP (Neurofibromatosis Research Program of the Congressionally Directed Medical Research Programs), NTAP (Neurofibromatosis Therapeutic Acceleration Program), and CTF ensured that this 'MEK Story' proceeded expeditiously through proactive and strategic coordination, guaranteeing efficient use of donor/investor funding, including from the federal government.

Another hallmark of this path to approval has been the inclusion of patients throughout the process, including the first ever 'NF listening session' held at the FDA in 2019.

Many other MEK inhibitors are also now in clinical trial, including mirdametinib from SpringWorks Therapeutics, a company which the Children's Tumor Foundation helped spin off from Pfizer.

"We are so excited for the entire NF community today! This announcement from the FDA about Koselugo (selumetinib) is a tremendous step towards our ultimate dream—approved treatments for all forms of neurofibromatosis," said Annette Bakker, Ph.D., President of the Children's Tumor Foundation. "We believe that FDA approval of this treatment helps not only a subset of NF1 patients, it opens the door to increased interest in all forms of NF by pharmaceutical companies. We are already experiencing it—the number of companies interested in NF1, NF2, and schwannomatosis is growing rapidly."

More information: Andrea M. Gross et al. Selumetinib in Children with Inoperable Plexiform Neurofibromas, *New England Journal of Medicine* (2020). DOI: 10.1056/NEJMoa1912735

Provided by Children's Tumor Foundation