NEWS RELEASE

# Selumetinib Granted U.S. Breakthrough Therapy Designation in Neurofibromatosis Type 1

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Designation Based on Phase 2 SPRINT Trial in Pediatric Patients with NF1 Plexiform Neurofibromas

Selumetinib Is a MEK 1/2 Inhibitor Being Co-Developed by AstraZeneca and Merck

KENILWORTH, N.J.--(**BUSINESS WIRE**)--AstraZeneca and Merck (NYSE: MRK), known as MSD outside the United States and Canada, today announced that the U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy Designation (BTD) for the investigational MEK 1/2 inhibitor selumetinib.

This designation is for the treatment of pediatric patients aged three years and older with neurofibromatosis type 1 (NF1) symptomatic and/or progressive, inoperable plexiform neurofibromas (PN), a rare, incurable genetic condition.

José Baselga, executive vice president, oncology, AstraZeneca, said, “Selumetinib shows promise in the treatment of NF1-related plexiform neurofibromas, a rare and debilitating disease with no approved medications to date. The Breakthrough Therapy Designation acknowledges the significant unmet need of these patients and the potential benefit of selumetinib in this setting.”

Dr. Roy Baynes, senior vice president and head of global clinical development, chief medical officer, Merck Research Laboratories, said, “This new designation validates our ongoing development of selumetinib. As a result of this, selumetinib has the potential to receive expedited regulatory review and we hope to bring this medicine to patients as soon as possible.”

The BTD is based on Phase 2 data from the SPRINT trial, evaluating selumetinib as an oral monotherapy in pediatric patients, aged three years or older with inoperable NF1-related PN. The results of the trial were presented by the National Cancer Institute (NCI) at the 2018 American Society of Clinical Oncology Annual Meeting.

BTD is designed to expedite the development and regulatory review of medicines that are intended to treat a serious condition and that have shown encouraging early clinical results, which may demonstrate substantial improvement on a clinically-significant endpoint over available medicines.

Selumetinib was granted Orphan Drug Designation for the treatment of NF1 by the FDA in February 2018 and the European Medicines Agency in August 2018.

## About Selumetinib

Selumetinib is an investigational MEK 1/2 inhibitor and potential new medicine licensed by AstraZeneca from Array BioPharma Inc. in 2003. AstraZeneca and Merck entered a co-development and co-commercialization agreement for selumetinib in 2017.

The NF1 gene provides instructions for making a protein called neurofibromin, which negatively regulates the RAS/MAPK pathway, helping to control cell growth, differentiation and survival. Mutations in the NF1 gene may result in dysregulations in RAS/RAF/MEK/ERK signaling, which can cause cells to grow, divide and copy themselves in an uncontrolled manner, and may result in tumor growth. Selumetinib inhibits the MEK enzyme in this pathway, potentially leading to inhibition of tumor growth.

Selumetinib is being assessed as a monotherapy and in combination with other treatments in ongoing trials.

## About the SPRINT Trial

The SPRINT trial is a U.S. Cancer Therapy Evaluation Program (CTEP) National Cancer Institute (NCI)-sponsored Phase 1/2 study. The Phase 1 study was designed to identify the optimal Phase 2 dosing regimen, and the results were published in the New England Journal of Medicine.

## About Neurofibromatosis Type 1 (NF1)

Neurofibromatosis type 1 (NF1) is an incurable genetic condition that affects one in 3,000 to 4,000 individuals. 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), skin pigmentation (so-called ‘cafe au lait spots’) and, in 20-50 percent of patients, tumors develop on the nerve sheaths (plexiform neurofibromas). These plexiform

neurofibromas can cause clinical issues such as pain, motor dysfunction, airway dysfunction, bowel/bladder dysfunction and disfigurement as well as having the potential to transform into malignant peripheral nerve sheath tumors (MPNST).

People with NF1 may experience a number of other complications such as learning difficulties, visual impairment, twisting and curvature of the spine, high blood pressure, and epilepsy. NF1 also increases a person's risk of developing other cancers, including malignant brain tumors, MPNST and leukemia. Symptoms begin during early childhood, with varying degrees of severity, and can reduce life expectancy by up to 15 years.

## About the AstraZeneca and Merck Strategic Oncology Collaboration

In July 2017, AstraZeneca and Merck, known as MSD outside the United States and Canada, announced a global strategic oncology collaboration to co-develop and co- commercialize certain oncology products, including investigational selumetinib, a MEK inhibitor. Working together, the companies will develop selumetinib in combination with other potential new medicines and as monotherapy. Independently, the companies will develop selumetinib in combination with their respective PD-L1 and PD-1 medicines.

## Merck's Focus on Cancer

Our goal is to translate breakthrough science into innovative oncology medicines to help people with cancer worldwide. At Merck, the potential to bring new hope to people with cancer drives our purpose and supporting accessibility to our cancer medicines is our commitment. As part of our focus on cancer, Merck is committed to exploring the potential of immuno-oncology with one of the largest development programs in the industry across more than 30 tumor types. We also continue to strengthen our portfolio through strategic acquisitions and are prioritizing the development of several promising oncology candidates with the potential to improve the treatment of advanced cancers. For more information about our oncology clinical trials, visit **www.merck.com/clinicaltrials**.

## About Merck

For more than a century, Merck, a leading global biopharmaceutical company known as MSD outside of the United States and Canada, has been inventing for life, bringing forward medicines and vaccines for many of the world's most challenging diseases. Through our prescription medicines, vaccines, biologic therapies and animal health products, we work with customers and operate in more than 140 countries to deliver innovative health solutions. We also demonstrate our commitment to increasing access to health care through far-reaching policies, programs and partnerships. Today, Merck continues to be at the forefront of research to advance the prevention and treatment of diseases that threaten people and communities around the world - including cancer, cardio-metabolic diseases, emerging animal diseases, Alzheimer's disease and infectious diseases including HIV and Ebola. For more

information, visit **www.merck.com** and connect with us on **Twitter**, **Facebook**, **Instagram**, **YouTube** and **LinkedIn**.

## Forward-Looking Statement of Merck & Co., Inc., Kenilworth, N.J., USA

This news release of Merck & Co., Inc., Kenilworth, N.J., USA (the "company") includes "forward-looking statements" within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of the company's management and are subject to significant risks and uncertainties. There can be no guarantees with respect to pipeline products that the products will receive the necessary regulatory approvals or that they will prove to be commercially successful. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.

Risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; the company's ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of the company's patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

The company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in the company's 2018 Annual Report on Form 10-K and the company's other filings with the Securities and Exchange Commission (SEC) available at the SEC's Internet site (**www.sec.gov**).

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