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Annual Meeting of the American Society of Clinical Oncology (ASCO) 2019:

New data on larotrectinib efficacy in patients with TRK fusion cancer and primary CNS tumors or brain metastases presented at ASCO 2019

- In five TRK fusion cancer patients with brain metastases across different tumor histologies, the overall response rate was 60%, with disease control achieved in all patients
- In 14 adult and pediatric patients with TRK fusion cancer with primary central nervous system (CNS) tumors (including high grade gliomas), the overall response rate was 36% including two complete responses
- 71% of evaluable patients with primary CNS tumors experienced disease control for 24 weeks or more
- First prospective analysis of the activity of larotrectinib in patients with TRK fusion cancer and intracranial disease, including first data ever presented for a TRK inhibitor in adult primary CNS TRK fusion cancer

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Abstract: 2006

Leverkusen, Germany, June 3, 2019 – A new analysis from clinical trials in patients with TRK fusion cancer and brain metastases or primary tumors of the central nervous system (CNS) confirm the strong activity of larotrectinib in both adults and children. In TRK fusion cancer patients with intracranial disease, the compound achieved responses and durable disease control, across age or tumor histology.

The analysis included 14 evaluable patients with primary CNS tumors, including cases of glioma, glioblastoma, glioneural tumors, and astrocytoma, the overall response rate (ORR) was 36% (n=5; 95% CI: 13-65) with two complete responses (CR) and three partial responses (PR). In all other patients (64%, n=9), stable disease was achieved. For 71% of patients with primary CNS tumors, disease control (defined as CR plus PR plus Stable

Disease, SD) was achieved for 24 weeks or more. In evaluable patients with *NTRK* gene fusion positive solid tumors with brain metastases (n=5), the ORR was 60% (n=3 PRs; 95% CI: 15-95), and stable disease was achieved in 40% (n=2) of patients. These data were presented in an oral presentation at ASCO on June 3, 2019 (*Abstract 2006, Session: Central Nervous System Tumors; Monday, June 3, 3:15PM – 3:27PM (CDT), Room: S102)*

“Taken in their entirety, these data further confirm the activity of larotrectinib in patients with TRK fusion cancer regardless of tumor type and age, including those who present with brain metastases or primary CNS tumors,” said Alexander Drilon, M.D., principal investigator and Research Director of the Early Drug Development Service at Memorial Sloan Kettering Cancer Center. “The rapid and durable responses observed with larotrectinib in patients in these analyses are encouraging.”

“These data are important as we continue to see efficacy with Larotrectinib in TRK fusion cancer across different tumor types and ages,” said Scott Z. Fields, M.D., Senior Vice President and Head of Oncology Development at Bayer’s Pharmaceuticals Division.

Data on larotrectinib in CNS tumors presented at ASCO

Twenty four patients with intracranial disease were identified from three clinical studies (adult Phase I trial, NCT02122913, one patient; Pediatric Phase I trial SCOUT, NCT02637687, 12 patients; and the adult/adolescent Phase II basket trial NAVIGATE, NCT02576431, 11 patients). Eighteen patients presented with primary CNS tumors (data cut-off February 19, 2019), of which 14 were evaluable, and six patients had brain metastases, of which five were evaluable (data cut-off July 30, 2018). Safety data from additional presentations reported at ASCO are consistent with previous publications, with the majority of adverse events (AEs) being grade 1 or 2.

Of the five evaluable patients with brain metastases, three had a partial response and two achieved stable disease based on investigator assessment by RECIST (Response Evaluation Criteria In Solid Tumors) 1.1. Four patients remained on treatment at the time of data cut-off, with treatment durations ranging up to 18.4 months.

In the 14 evaluable patients with primary CNS tumors, two patients (14%) achieved a complete response and three patients (21%) had a partial response. In all other patients

(64%, n=9), stable disease was achieved based on investigator assessment by RECIST 1.1 or RANO (Response Assessment in Neuro-Oncology). The disease control rate (DCR, defined as CR plus PR plus SD for 24 weeks or more), was 71%, respectively. Thirteen patients remained on treatment at time of data cut-off, with treatment durations ranging up to 16.6 months.

About Larotrectinib

Larotrectinib (Vitrakvi®) was approved by the U.S. Food and Drug Administration (FDA) in November 2018 for the treatment of adult and pediatric patients with an *NTRK* gene fusion without a known acquired resistance mutation that are either metastatic or where surgical resection will likely result in severe morbidity, and have no satisfactory alternative treatments or that have progressed following treatment. In the U.S., larotrectinib was approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. Bayer has submitted a Marketing Authorization Application (MAA) in the European Union and additional filings in other regions are underway or planned.

Following the acquisition of Loxo Oncology by Eli Lilly and Company in February 2019, Bayer has obtained the exclusive licensing rights for the global development and commercialization, including in the U.S., for larotrectinib and the investigational TRK inhibitor BAY 2731954 (previously LOXO-195) progressing through clinical development.

About TRK Fusion Cancer

TRK fusion cancer occurs when an *NTRK* gene fuses with another unrelated gene, producing an altered TRK protein. The altered protein, or TRK fusion protein, becomes constitutively active or overexpressed, triggering a signaling cascade. These TRK fusion proteins can act as an oncogenic driver, promoting cell proliferation and survival in tumor cell lines, leading to TRK fusion cancer, regardless of where it originates in the body. TRK fusion cancer is not limited to certain types of tissues and can occur in any part of the body. TRK fusion cancer occurs in various adult and pediatric solid tumors with varying frequency, including lung, thyroid, GI cancers (colon, cholangiocarcinoma, pancreatic and appendiceal), sarcoma, CNS cancers (glioma and glioblastoma), salivary gland cancers (mammary analogue secretory carcinoma) and pediatric cancers (infantile fibrosarcoma and soft tissue sarcoma).

About Oncology at Bayer

Bayer is committed to delivering science for a better life by advancing a portfolio of innovative treatments. The oncology franchise at Bayer includes five marketed products and several other assets in various stages of clinical development. Together, these products reflect the company's approach to research, which prioritizes targets and pathways with the potential to impact the way that cancer is treated.

About Bayer

Bayer is a global enterprise with core competencies in the life science fields of health care and nutrition. Its products and services are designed to benefit people by supporting efforts to overcome the major challenges presented by a growing and aging global population. At the same time, the Group aims to increase its earning power and create value through innovation and growth. Bayer is committed to the principles of sustainable development, and the Bayer brand stands for trust, reliability and quality throughout the world. In fiscal 2018, the Group employed around 117,000 people and had sales of 39.6 billion euros. Capital expenditures amounted to 2.6 billion euros, R&D expenses to 5.2 billion euros. For more information, go to www.bayer.com.

Bayer Investor Relations Team

Bayer AG
Investor Relations
51368 Leverkusen, Germany
E-mail: ir@bayer.com
Internet: http://www.investor.bayer.com