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News Release

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ESMO Virtual Congress 2020:

New data reinforce strong clinical profile of Vitrakvi™ for patients of all ages with TRK Fusion Cancer including lung and thyroid tumors

- 78% overall response rate (ORR) and median progression-free survival (PFS) of more than 3 years (36.8 months) demonstrate extended benefit in updated data set of 175 adults and children
- Majority of adverse events were grade 1 or 2; no new safety signals identified
- Consistently high ORRs shown in lung and thyroid data subsets (71 and 75%, respectively) as well as long durability (estimated duration of response at 12 months of 88% and 95%, respectively)
- Among patients from integrated dataset with brain metastases (n=14), ORR was 71%, and 57% in patients with lung cancer with brain metastases (n=7)

Abstracts: 1955P, 1916P, 1289P

Berlin, September 17, 2020 – Updated clinical data for Vitrakvi™ (larotrectinib) reinforce the consistent and long-term efficacy as well as a favorable safety profile for the precision oncology drug in an integrated dataset of 175 adult and pediatric patients with tropomyosin receptor kinase (TRK) fusion cancer. In addition, new tumor-type specific sub-analyses in lung and thyroid cancer patients further emphasize these durable responses while showing a favorable safety profile. These results are being presented at the ESMO Virtual Congress 2020, to be held between September 19-21, 2020.

“The consistent and durable responses as well as the safety profile from the larotrectinib data are supportive in determining the appropriate treatment option for my patients with TRK fusion cancer,” said Professor Ray McDermott, St. Vincent University Hospital and Tallaght Hospital, Ireland. “These clinically meaningful responses underscore the urgency

for widespread *NTRK* testing to help identify patients who are most likely to benefit from earlier treatment with this therapy."

Adult and pediatric integrated data set

In an expanded data set with a longer follow-up (cut-off July 15, 2019) of 175 patients (116 adult and 59 pediatric) with TRK fusion cancer, Vitrakvi demonstrated a consistent, investigator-assessed overall response rate (ORR) of 78% (95% CI 71–84), with 19% complete responses, 59% partial responses, 13% with stable disease and 7% with progressive disease. The ORR in 14 patients with central nervous system (CNS) metastases was 71% (95% CI 42-92).

The median duration of response (DoR) was not estimable at a median follow-up of 13.5 months, with a 12-month DoR rate of 81% (95% CI 73-89). Median progression-free survival (PFS) was 36.8 months (95% CI 25.7-NE) after a median follow-up of 13.8 months, showing an extended benefit for patients when compared to previous analyses. Median overall survival (OS) was not reached after 15.3 months of follow-up; 12-month estimated median OS rate was 90% (95% CI 85-95) and 24-month estimated OS rate was 83% (95% CI 75-90). At the time of data cut-off, 100 patients (57%) were still on treatment and 32 patients (18%) continued treatment post-progression.

In the expanded safety population of 279 patients, with 34 patients being treated with Vitrakvi for more than 24 months, adverse events (AEs) were primarily grade 1 and 2, and no new safety signals were reported. Serious AEs related to Vitrakvi were reported in 5% (15/279) of patients; the most common serious grade 3/4 events were increased alanine aminotransferase, increased aspartate aminotransferase and nausea (n=2 each).

"Designed specifically to treat TRK fusion cancer, Vitrakvi is a meaningful advancement in the treatment of both adult and pediatric patients with TRK fusion cancer and represents a true paradigm shift in cancer care – where treatment is based on the oncogenic driver and not the tumor location," said Scott Z. Fields, M.D., Senior Vice President and Head of Oncology Development at Bayer's Pharmaceutical Division. "These data affirm Vitrakvi's robust clinical profile with the largest dataset and longest follow-up of any TRK inhibitor and reinforce our longstanding commitment to developing innovative treatments for patients."

Vitrakvi in lung and thyroid cancers

In a sub-analysis of 14 adult heavily pre-treated patients with metastatic lung cancer harboring an Neurotrophic Tyrosine Receptor Kinase (*NTRK)* gene fusion, the ORR stayed at 71% (95% CI 42-92) compared to previous analyses with an additional year of follow-up, with 1 complete response, 9 partial responses, 3 with stable diseases and 1 progressive disease. For patients with brain metastases (n=7), the ORR was 57% (95% CI 18-90). At a median follow-up of 12.9 months, median DoR was not estimable (95% CI 5.6-NE months). The estimated DoR at 12 months was 88%. At a median follow-up of 14.6 months, the median PFS had not been reached (95% CI 7.2–NE), and the estimated rate of PFS at 12 months or more was 69%. The median OS was not reached (95% CI 17.2-NE) at a median follow-up of 12.6 months and 91% of patients were alive at 12 months. Vitrakvi was well tolerated for the duration of treatment (2.1 to 39.6+ months) with three of seven patients with CNS metastases still on treatment at the time of data cut-off. Treatment-emergent AEs were primarily grade 1 and 2, supporting Vitrakvi's long-term favorable safety profile.

In a separate analysis of 28 adults and children with locally advanced or metastatic TRK fusion thyroid cancer, the ORR was 75% (95% CI 55-89), with 2 complete responses and 19 partial responses. The ORR was 29% for patients with anaplastic disease (N=7), a rare, aggressive subtype of thyroid cancer. For patients with differentiated histology (n=21), the ORR was 90%. All four patients with CNS metastases at baseline had a partial response, three of which are continuing treatment. While median DoR was not estimable (95% CI 14.8-NE months) at a median follow-up of 10.2 months, the estimated DoR at 12 months was 95% (95% CI 85-100). Median PFS was not estimable (95% CI 16.6-NE months) at a median follow up of 12.8 months; estimated PFS was 81% (95% CI 67–96) at 12 months and 70% (95% CI 45–94) at 18 months. The median OS was 27.8 months (95% CI 16.7-NE) with an estimated OS at 12 months of 92% (95% CI 82-100). For patients with anaplastic thyroid cancer, a median OS was 14.1 months (95% CI 2.6-NE); for patients with differentiated thyroid cancer, median OS was not reached. AEs were mostly grade 1 and 2, further demonstrating Vitrakvi's safety and tolerability.

Data for the integrated dataset were pooled from three larotrectinib clinical trials (NCT02122913, NCT02576431 and NCT02637687) in adult and pediatric patients with TRK fusion cancer. Data from the lung and thyroid cancer subsets were pooled from two larotrectinib clinical trials (NCT02122913 and NCT02576431).

About Vitrakvi™ (larotrectinib)

Vitrakvi™ (larotrectinib), a first-in-class oral TRK inhibitor, was exclusively designed to treat tumors that have a *NTRK* gene fusion. The compound has demonstrated high response rates and durable responses over three years in adults and children with TRK fusion cancer, including central nervous system (CNS) tumors. It has the largest dataset and longest follow-up data of any TRK inhibitor. The trials are still ongoing, with the dataset of 153 patients published in The Lancet Oncology and additional updates planned to be presented at upcoming scientific meetings.

Larotrectinib was approved in September 2019 in the European Union under the brand name Vitrakvi™ for the treatment of adult and pediatric patients with solid tumors that display a Neurotrophic Tyrosine Receptor Kinase (*NTRK*) gene fusion, who have a disease that is locally advanced, metastatic or where surgical resection is likely to result in severe morbidity, and who have no satisfactory treatment options. Vitrakvi has also received regulatory approval in many other markets around the world, including the U.S, Brazil and Canada. Filings in other regions are underway or planned.

Following the acquisition of Loxo Oncology by Eli Lilly and Company in February 2019, Bayer now possesses the exclusive rights to develop and commercialize larotrectinib worldwide, and also has exclusive rights to the investigational TRK inhibitor selitrectinib (BAY 2731954) which is currently in 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 act as oncogenic drivers promoting cell growth and survival, leading to TRK fusion cancer, regardless to 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 now expands to six marketed products and several other assets in various stages of clinical development. Bayer focuses its research activities on first-in-class innovations across the following scientific platforms: Oncogenic Signaling, Targeted Alpha Therapies, and Immuno-Oncology. Across the areas of focus, the portfolio includes several prostate cancer treatments on the market or in development, with the goal to extend survival while limiting side effects of treatment throughout the different stages of the disease. Another key focus at Bayer is on innovative precision oncology treatments, with an approved TRK inhibitor exclusively designed to treat tumors that have a *NTRK* gene fusion, the oncogenic driver of tumor growth and spread, and another TRK inhibitor advancing through the pipeline. The areas of focus 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 2019, the Group employed around 104,000 people and had sales of 43.5 billion euros. Capital expenditures amounted to 2.9 billion euros, R&D expenses to 5.3 billion euros. For more information, go to www.bayer.com.

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Forward-Looking Statements
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