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News Release

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ESMO Congress 2021:

Latest analyses of Vitrakvi (larotrectinib) reaffirm powerful efficacy and tolerability profile for both adult and pediatric patients with TRK fusion cancer

- In an updated analysis on the adult subset of non-central nervous system (CNS) TRK fusion cancer patients from three larotrectinib clinical trials, a high overall response rate (ORR) of 67% with a median duration of response (mDoR) of 49.3 months was observed as well as an extended progression-free survival (PFS; median of 25.8 months) as assessed by investigators
 - Post hoc sub-analysis of investigator-assessed ORR, DoR and PFS of patients (n=218) show uniformly high ORRs in patients regardless of prior treatment or performance status; highest response rates observed in patients receiving first-line larotrectinib (81%) and being Eastern Cooperative Oncology Group performance status (ECOG PS) 0 (85%)
 - Safety profile for larotrectinib continues to be consistent with that previously published; analysis on the incidence of fractures in larotrectinib trials shows no fracture related to larotrectinib based on investigator assessment
 - E-Poster published of a matching-adjusted indirect comparison (MAIC) evaluating efficacy (overall survival [OS], PFS, ORR including complete responses and DoR) and safety observed in clinical trials with larotrectinib compared to entrectinib. MAIC is an alternative method for comparative data when a head-to-head randomized control trial (RCT) is not available and/or possible, like for TRK fusion cancer which is an ultra-rare disease
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Abstracts: 535P, 534P, 536P, 104P

Berlin, September 16, 2021 – Data from four distinct analyses for Vitrakvi™ (larotrectinib) showcase its sustained clinical benefit for patients with solid tumors harboring an *NTRK* gene fusion (also known as TRK fusion cancer). An updated analysis with longer follow-up (data cut-off July 20, 2020) among 130 evaluable from a total of 140 adult patients across 20 different non-central nervous system (CNS) tumor types confirms the robust and highly durable tumor-agnostic efficacy with extended survival benefits in adult patients with TRK fusion cancer, including those with CNS metastases. A post-hoc subgroup analysis of investigator-assessed overall response rate (ORR), duration of response (DoR) and progression-free survival (PFS) stratifying adult and pediatric patients (n=218) by prior lines of therapy and baseline performance status shows that larotrectinib benefitted patients across those criteria with the highest response rates observed in patients receiving first-line larotrectinib (ORR=81%; 95% CI 69–91; n=58) and being Eastern Cooperative Oncology Group performance status (ECOG PS) 0 (ORR=85%; 95% CI 77–91; n=114). A matching-adjusted indirect comparison (MAIC) evaluating efficacy endpoints such as overall survival (OS), PFS, ORR, complete responses and DoR as well as safety observed in clinical trials with larotrectinib and entrectinib confirmed the impact of larotrectinib for TRK fusion cancer patients. Separately, a safety analysis on the incidence of fractures in adult and pediatric patients add to the body of evidence for the compound. These results are being presented at the [ESMO Congress 2021](#), to be held between September 16-21, 2021.

“As we continue to see ongoing analyses of larotrectinib across a wide range of solid tumors and ages, its consistent results in *NTRK* fusion-positive cancers support its efficacy and safety in adults and children”, said Alexander Drilon, M.D., Medical Oncologist and Chief of Early Drug Development Service at Memorial Sloan Kettering Cancer Center*. “These data reinforce the importance of early comprehensive genomic testing to uncover actionable oncogenic drivers, including *NTRK* gene fusions, to help identify patients who are most likely to benefit from a targeted treatment approach.”

“The first regulatory approval of Vitrakvi nearly three years ago represented a paradigm shift in how we treat cancer, by inhibiting the oncogenic driver that is causing a solid tumor to grow and spread rather than the location where it originates,” said Scott Z. Fields, M.D., Senior Vice President and Head of Oncology Development at the Pharmaceuticals Division of Bayer. “The long-term data for Vitrakvi continues to support

consistent responses and a similar safety profile seen with the addition of new patients and with longer follow-up. These findings reinforce the importance of precision oncology medicines as a meaningful advancement in cancer care and are compelling to justify the use of larotrectinib as early as possible in TRK fusion cancer patients.”

Larotrectinib efficacy and safety in adult patients with tropomyosin receptor kinase (TRK) fusion cancer (Abstract 535P)

In an updated subgroup analysis with longer follow-up (data cut-off July 20, 2020) in 140 adult patients with non-CNS TRK fusion cancer across 20 different tumor types, larotrectinib continued to demonstrate durable efficacy. Among 130 evaluable patients, the ORR was 67% (95% CI 58–75) per investigator assessment, including 12% complete responses and 55% partial responses. Among the evaluable patients with CNS metastases (n=15), ORR was 73% (95% CI 45–92). Among all patients, the median duration of response (DoR) was 49.3 months (95% CI 26.3–Not Estimable [NE]) at a median follow-up of 23.2 months. Median PFS was 25.8 months (95% CI 12.7–51.1) at a median follow-up of 22.1 months. At a median follow-up of 24.0 months, median OS had not been reached; the 36-month OS rate was 66% (95% CI 56–77).

The safety profile for larotrectinib continues to be consistent with previous analyses; no new safety signals were identified. The majority of treatment-related adverse events (TRAEs) were Grade 1 and 2, and Grade 3–4 TRAEs occurred in 17 patients (12%). Data were pooled from three clinical trials (NCT02122913, NCT02637687, NCT02576431).

Larotrectinib in non-CNS TRK fusion cancer patients: outcomes by prior therapy and performance status (Abstract 534P)

In a post-hoc subgroup analysis with adult and pediatric patients (n=218; data cut-off July 20, 2020), patients were evaluated based on treatment history and baseline performance status. A total of 216 patients were evaluated based on prior line of systemic therapy and 218 patients were evaluated based on performance status as defined by Eastern Cooperative Oncology Group (ECOG PS) or equivalent Lansky/Karnofsky performance status for pediatric patients. Investigator-assessed treatment response rates were highest in patients who had no previous systemic treatment (ORR=81%; 95% CI 69–91; n=58) or with a baseline ECOG PS of 0 (ORR = 85%; 95% CI 77–91; n=114); however, all patients showed a clinical benefit from larotrectinib across varying degrees of pre-treatment and

ECOG PS. In patients who received larotrectinib following one line of systemic therapy (n=59), the ORR was 73% (95% CI 60–84), compared to 69% (95% CI 53–82) following two lines (n=42), and 75% (95% CI 62–86) following three or more lines (n=57). In patients with an ECOG PS of 1 (n=78), the ORR was 66% (95% CI 54–77), followed by 61% (95% CI 39–80; n=23) with an ECOG PS of 2, and 33% (95% CI 1–91; n=3) with an ECOG PS of 3. Across all patients, ORR was 75% (95% CI 68–81) and median DoR was 49.3 months (95% CI 27.3–NE). Median PFS was 35.4 months (95% CI 23.4–55.7) and the 36-month-OS rate was 77% (95% CI 69–84). Data were pooled from three clinical trials (NCT02122913, NCT02637687, NCT02576431).

Incidence of fractures in TRK fusion cancer patients treated with Larotrectinib (Abstract 536P)

In a pooled analysis of 331 patients (n=214 adult, 117 pediatric) with solid and CNS tumors treated with larotrectinib, the incidence of fractures, which can be an event of concern in oncology patients, was analyzed. Fractures were mainly Grade 1 or 2 (n=12 adult fractures, n=8 pediatric fractures) and were associated with trauma (fall) or were tumor-related, and no patients discontinued treatment due to a fracture. Treatment-emergent fractures of all grades were reported in 7% (n=15) of adult and 7.7% (n=9) of pediatric patients, which is within the expected range for patients with solid tumors. No fractures were considered to be larotrectinib-related by Investigator. Data were pooled from three clinical trials (NCT02122913, NCT02637687, NCT02576431).

Matching-Adjusted Indirect Comparison for Treatment of *NTRK* fusion cancer with Larotrectinib versus Entrectinib (Abstract 104P)

A matching-adjusted indirect comparison (MAIC) of data from clinical trials with larotrectinib (data cut-off July 2020) and entrectinib (data cut-off October 2018) analyzed the efficacy endpoints overall survival, progression-free survival, overall response rates including complete responses and duration of response and safety observed in these trials, matching patients based on available common baseline characteristics (gender, age, race, ECOG score, select tumor types, metastatic disease, *NTRK* gene, CNS metastases, number of prior lines of therapy) which are known or suspected to be confounding factors for the efficacy and safety outcomes of interest. Although cross-trial comparisons are subject to limitations, MAIC is an alternative method for comparative data when a head-to-head randomized control trial (RCT) is not available and/or possible,

such as in the case of TRK fusion cancer in part due to the rarity of the disease. The analysis provides further, more granular insights on the efficacy and safety outcomes between the clinical trials with these treatments. Data were pooled from three larotrectinib clinical trials (NCT02122913, NCT02637687, NCT02576431) and three entrectinib studies (ALKA-372-001, STARTRK-1 and STARTRK-2).

About Vitrakvi™ (larotrectinib)

Vitrakvi™ (larotrectinib), a first-in-class oral TRK inhibitor, was exclusively designed to treat tumors that have an *NTRK* gene fusion. The compound has demonstrated high response rates and highly durable responses of over four 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 latest dataset published in *The Lancet Oncology* and additional updates planned to be presented at upcoming scientific meetings.

In the EU, Vitrakvi is approved 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 the U.S, Brazil, Japan, 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 has obtained the exclusive licensing rights for the global development and commercialization, including in the U.S., for larotrectinib.

About TRK Fusion Cancer

TRK fusion cancer occurs when an *NTRK* gene fuses with another unrelated gene, producing a chimeric TRK protein. The altered protein, or TRK fusion protein, becomes constitutively active or overexpressed, triggering a signaling cascade. These TRK fusion proteins are oncogenic drivers promoting cell growth and survival, leading to TRK fusion cancer. 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 (including secretory carcinoma of the salivary gland) and pediatric cancers (infantile fibrosarcoma and other soft tissue sarcomas).

About Oncology at Bayer

Bayer is committed to delivering science for a better life by advancing a portfolio of innovative treatments. The company has the passion and determination to develop innovative medicines that help improve and extend the lives of people living with cancer. The oncology franchise at Bayer includes six marketed products across various indications and several compounds in different stages of clinical development. Bayer focuses its research activities on first-in-class innovations across the following scientific platforms: Precision Molecular Oncology, Targeted Alpha Therapies, and Immuno-Oncology. Across the areas of focus, we have several prostate cancer treatments on the market or in development, with the goal of extending 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 an *NTRK* gene fusion, the oncogenic driver of tumor growth and spread. The company's approach to research 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 help people and planet thrive by supporting efforts to master the major challenges presented by a growing and aging global population. Bayer is committed to drive sustainable development and generate a positive impact with its businesses. At the same time, the Group aims to increase its earning power and create value through innovation and growth. The Bayer brand stands for trust, reliability and quality throughout the world. In fiscal 2020, the Group employed around 100,000 people and had sales of 41.4 billion euros. R&D expenses before special items amounted to 4.9 billion euros. For more information, go to www.bayer.com.

**Dr. Drilon has provided speaking and consulting services to Bayer.*

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Forward-Looking Statements

This release may contain forward-looking statements based on current assumptions and forecasts made by Bayer management. Various known and unknown risks, uncertainties and other factors could lead to material differences between the actual future results, financial situation, development or performance of the company and the estimates given here. These factors include those discussed in Bayer's public reports which are available on the Bayer website at www.bayer.com. The company assumes no liability whatsoever to update these forward-looking statements or to conform them to future events or developments.