



Bayer AG
Communications
51368 Leverkusen
Germany
Phone +49 214 30-1
media.bayer.com

News Release

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ASCO Annual Meeting 2021:

Long-term data on Vitrakvi™ (larotrectinib) confirm sustained clinical benefit of greater than four years in patients with TRK fusion cancer regardless of tumor type and age

- Larotrectinib achieved 75% (95% CI 68-81) overall response rate (ORR) and median duration of response (DoR) of 49.3 months (95% CI 27.3-not estimable [NE]) in expanded integrated dataset of 206 evaluable adults and children with TRK fusion cancer, which occurs when an *NTRK* gene fuses with another unrelated gene, across 21 different tumor types and regardless of age (range: 0.1-84 years) with longer follow-up at a median follow-up of 22.3 months
 - In tumor-specific analyses, larotrectinib demonstrated rapid and durable responses, and long disease control, among patients with lung and primary central nervous system (CNS) TRK fusion cancers
 - Intra-patient comparison showed majority of TRK fusion cancer patients experienced a meaningful clinical benefit with larotrectinib compared to their prior line of therapy
 - Majority of adverse events (AEs) were Grade 1 or 2 and no new safety signals were identified
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Abstracts: 3108, 9109, 2002, 3114

Berlin, May 19, 2021 – New data across four distinct analyses confirm the robust long-term clinical profile for the precision oncology treatment Vitrakvi™ (larotrectinib) from Bayer, including rapid and highly durable responses and a favorable safety profile, across TRK fusion cancer patients of all ages (range: 0.1-84 years) and multiple tumor types. The analyses include updated long-term efficacy and safety data in non-primary central nervous system (CNS) solid tumors, primary CNS tumors and lung cancer harboring a neurotrophic tyrosine receptor kinase (*NTRK*) gene fusion. In addition, an intra-patient pooled

retrospective analysis showed that the majority of TRK fusion cancer patients experienced a meaningful clinical benefit with larotrectinib. Larotrectinib has now demonstrated consistent high response rates and response durability of over four years based on the largest dataset and longest follow-up of any TRK inhibitor, at median follow-up of 22.3 months, for patients across all ages and with different tumor types with an *NTRK* gene fusion. These findings are being presented at the [2021 American Society of Clinical Oncology \(ASCO\) Annual Meeting](#) being held online June 4-8, 2021.

“This data adds to larotrectinib's growing clinical profile, supporting its use as an effective treatment option for adults and children with *NTRK* gene fusion positive tumors,” said David S. Hong, M.D., Professor of Investigational Cancer Therapeutics at the University of Texas MD Anderson Cancer Center. “These findings present a clear rationale for robust comprehensive genomic testing inclusive of *NTRK* 1/2/3 genes for patients to better understand what could be driving their cancer and appropriately match them with the right treatment approach.”

“Designed specifically to treat TRK fusion cancer, Vitrakvi represents a meaningful advancement in the treatment of both adult and pediatric patients with TRK fusion cancer, inhibiting the oncogenic driver that causes these tumors to spread and grow, regardless of where they originate in the body,” said Scott Z. Fields, M.D., Senior Vice President and Head of Oncology Development at Bayer. “These long-term data confirm the impressive efficacy and favorable safety profile of Vitrakvi and reinforce its use for patients with TRK fusion cancer and demonstrate our commitment to advancing the future of cancer care, while providing true value for patients and physicians.”

Larotrectinib adult and pediatric integrated dataset (Abstract 3108)

An expanded dataset with longer follow-up (cut-off July 20, 2020) with 206 evaluable adult and pediatric patients with TRK fusion cancer across 21 different tumor types showed an overall response rate (ORR) per investigator assessment of 75% (95% CI 68-81), including 22% complete responses (n=45). For evaluable patients with brain metastases (n=15), the ORR was 73% (95% CI 45-92). Among all evaluable patients, the median duration of response (DoR) was 49.3 months (95% CI 27.3-not estimable [NE]) at a median follow-up of 22.3 months. The median progression-free survival (PFS) was 35.4 months (95% CI 23.4-55.7) at a median follow-up of 20.3 months. Median overall survival

(OS) was not reached at a median follow-up of 22.3 months, and 36-month OS was 77% (95% CI 69-84).

The safety profile was consistent with that of the overall safety population previously reported and no new safety signals were identified. The majority of treatment-related adverse events (TRAEs) reported were primarily Grade 1 or 2, with 18% of patients reporting Grade 3 or 4 TRAEs. Two percent of patients discontinued larotrectinib due to TRAEs and no treatment-related deaths were reported.

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. This analysis did not include the primary CNS patient subset.

Larotrectinib in lung cancer with or without CNS metastases (Abstract 9109)

Updated data (cut-off July 20, 2020) on heavily pre-treated adult TRK fusion cancer patients with lung cancer, who had received a median of three prior therapies, showed larotrectinib to be highly active with rapid and durable responses, an extended survival benefit and a favorable long-term safety profile. Among 15 evaluable patients and based on investigator assessment, the confirmed ORR was 73% (95% CI 45-92), and among evaluable patients with baseline CNS metastases (n=8), the ORR was 63% (95% CI 25-91). In all evaluable patients (n=15), the 12-month rates for DoR and PFS were 81% and 65%, respectively. Median OS was 40.7 months (95% CI 17.2-NE) at a median follow-up of 16.2 months. TRAEs were reported in 16 patients, of which two patients experienced Grade 3 events. No patients discontinued larotrectinib due to TRAEs. These data were investigator-assessed and from patients enrolled in two clinical trials (NCT02576431, NCT02122913).

Larotrectinib in primary CNS tumors (Abstract 2002)

In another presentation (cut-off July 20, 2020) larotrectinib was assessed in 33 pediatric and adult patients with primary CNS tumors with an *NTRK* gene fusion, pooled from two clinical trials (NCT02637687, NCT02576431). The majority of patients (82%) with measurable disease experienced tumor shrinkage, with an ORR of 30% (CI 95% 16-49). The 24-week disease control rate was 73% (95% CI 54-87). The median PFS was 18.3 months (95% CI 6.7-NE) and median OS was not reached (95% CI 16.9-NE), both at a

median follow-up of 16.5 months, with a 12-month OS rate of 85% (95% CI 71-99). Grade 3 or 4 TRAEs occurred in three patients. No patients discontinued larotrectinib due to TRAEs.

Intra-patient comparison from larotrectinib clinical trials in TRK fusion cancer (Abstract 3114)

Additional larotrectinib data to be presented at the congress include an updated and extended retrospective growth modulation index (GMI) analysis limited to patients enrolled in larotrectinib trials with at least one prior line of therapy. GMI is a retrospective intra-patient comparison that uses the patient as their own control by comparing PFS on current therapy to time to progression or treatment failure (TTP) on the most recent prior therapy. A GMI ratio ≥ 1.33 has been used as a threshold for meaningful clinical activity. In an extended follow-up analysis of 122 patients (cut-off of July 2020), almost three-quarters of patients had a GMI ≥ 1.33 , including six of the nine patients who had a GMI ≤ 1.33 in a previous analysis. In an expanded dataset of 140 patients, 74% had a GMI ≥ 1.33 . The data were pooled from three larotrectinib clinical trials (NCT02122913, NCT02576431 and NCT02637687).

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.

Larotrectinib is approved under the brand name Vitrakvi™ in more than 40 countries around the world, including the U.S., countries of the European Union (EU), the UK and most recently in Japan. Filings in other regions are underway or planned. In the EU, the product 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.

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 selitrectinib (BAY 2731954) progressing through clinical development.

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 (secretory carcinoma of the salivary gland) 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 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: Oncogenic Signaling, 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, and another TRK inhibitor advancing through the pipeline. 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.

Contact for media inquiries:

Anna Koch, phone +49 30 468-15942

Email: anna.koch@bayer.com

Contact for investor inquiries:

Bayer Investor Relations Team, phone +49 214 30-72704

Email: ir@bayer.com

www.bayer.com/en/investors/ir-team

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Forward-Looking Statements

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