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Investor News

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ESMO 2018 Congress (European Society for Medical Oncology)

Expanded larotrectinib data confirm findings on efficacy and safety in adult and pediatric patients with TRK fusion cancer across various tumor types

- Data presented across 122 adult and pediatric patients (55 patients from primary dataset plus supplementary dataset with 67 additional patients) with TRK fusion cancer across various tumor types
- Integrated dataset on larotrectinib demonstrated high overall response rate of 81 percent (63 percent partial responses and 17 percent complete responses), per investigator assessment
- For the initial 55 patients, ongoing responses at 12 months improved to 75 percent with longer follow-up; ongoing responses in the supplementary dataset were 81 percent at 12 months; median duration of response not reached at a respective follow-up of 17.6 and 7.4 months
- 84 percent of responding patients in the integrated dataset remained on treatment or underwent surgery for curative intent
- Larotrectinib showed favorable safety profile with majority of adverse events grade 1 or 2
- Larotrectinib is currently under regulatory review in the EU and U.S.

Leverkusen, Germany, October 21, 2018 – Results from an expanded dataset from clinical trials with larotrectinib, an investigational oral, CNS-active tropomyosin receptor kinase (TRK) inhibitor, in patients with TRK fusion cancer showed continued robust antitumor activity across different tumor types and in both adults and children. The updated data, which were presented in an oral session at the ESMO 2018 Congress (European Society for Medical Oncology), in Munich, Germany, include the primary dataset of 55 patients, published in the *New England Journal of Medicine*, as well as a

supplementary dataset of an additional 67 patients with a data cut-off date of July 30, 2018.

At the new data cut-off, larotrectinib demonstrated an overall response rate (ORR) of 80 percent in the primary dataset (n=55) and an ORR of 81 percent in a supplementary dataset (n=54, 13 patients continuing on study and awaiting initial response assessment), by investigator assessment. Across both datasets, the ORR was 81 percent, with a 63 percent of partial response (PR) rate and a 17 percent complete response (CR) rate. Patients in the primary dataset continued to improve on larotrectinib with CRs increasing from 16 to 18 percent and corresponding PRs decreasing from 64 to 62 percent based on investigator assessment. Complete and partial response rates in the supplementary dataset were 17 and 65 percent, respectively. Duration of response (DOR) at 12 months was 75 percent and 81 percent for the primary and supplementary datasets, respectively; with median follow-up of 17.6 and 7.4 months, median DOR had not yet been reached. Across the integrated dataset, as of the July 30, 2018 data cut-off date, 84 percent of responding patients remained on treatment or had undergone surgery with curative intent. Larotrectinib continued to be associated with a positive safety profile, with the majority of adverse events (AEs) being grade 1 or 2.

“It is exciting to see larotrectinib deliver responses to patients in these studies with TRK fusion cancer, across different ages, tumor sites of origin, or CNS involvement,” said Ulrik Lassen, M.D., Ph.D., Department of Oncology, Rigshospitalet, Copenhagen. “In the supplementary set, the response rate is nearly the same as in the primary set and duration of response has actually increased with longer patient follow-up. The larotrectinib experience provides strong clinical evidence supporting the development of single-purpose drugs against oncogenic driver targets, and underscores the importance of tumor genomic profiling capable of identifying *NTRK* gene fusions alongside other activating alterations.”

Bayer and Loxo Oncology, Inc., (NASDAQ: LOXO), a biopharmaceutical company from Stamford (Connecticut, U.S.), are jointly developing larotrectinib, which is being studied globally for the treatment of patients with TRK fusion cancer.

“These data from a large patient group with TRK fusion cancer are truly encouraging – bringing us one step further to delivering this treatment to patients,” said Dr. Scott Z. Fields, Senior Vice President and Head of Oncology Development at Bayer’s

Pharmaceutical Division. “We look forward to bringing this potential treatment option to adults and children with TRK fusion cancer as soon as possible.”

The U.S. Food and Drug Administration (FDA) has accepted the New Drug Application (NDA) submitted by Loxo Oncology, and granted Priority Review for larotrectinib for the treatment of adult and pediatric patients with locally advanced or metastatic solid tumors harboring a neurotrophic tyrosine receptor kinase (*NTRK*) gene fusion. The FDA has set a target action date of November 26, 2018, under the Prescription Drug User Fee Act (PDUFA). Bayer has submitted a Marketing Authorization Application (MAA) in the European Union (EU) and additional filings in other markets are underway.

Detailed results presented at ESMO 2018 Congress

The data presented include additional follow-up for the first 55 consecutively enrolled adult and pediatric patients with TRK fusion cancer treated across three clinical trials; a Phase I adult trial, the Phase II trial (NAVIGATE) and Phase I/II pediatric trial (SCOUT). These patients were the subject of the *New England Journal of Medicine* publication and constitute the primary analysis population supporting larotrectinib’s NDA filing. The presentation also includes data for the 67 patients subsequently enrolled. Presented data were based on a July 30, 2018 data cut-off date, providing approximately one year of additional follow-up for the primary analysis population.

The 122-patient integrated dataset includes both adult and pediatric patients, who ranged in age from approximately one month to 80 years in 24 different tumor types, including cancers of the salivary gland, thyroid, lung, colon, infantile fibrosarcoma and sarcomas. The datasets included patients with RECIST-evaluable disease enrolled to the three clinical trials, regardless of prior therapy or testing methodology used to establish their TRK fusion status. In the ESMO 2018 Congress presentation, response evaluations were based on investigator assessment.

In the ORR analysis of the integrated dataset (n=109), larotrectinib resulted in an ORR of 81 percent (63 percent PR and 17 percent CR). In this analysis, 84 percent of responding patients and 73 percent of all patients remained on treatment or had undergone surgery with curative intent. Patients in the primary dataset (n=55) continued to improve on larotrectinib with CRs increasing from 16 to 18 percent and corresponding PRs decreasing from 64 to 62 percent based on investigator assessment. Complete and partial response rates in the supplementary dataset (n=54) were 17 and 65 percent, respectively. The ORR analyses for the supplementary and integrated datasets included

nine patients with unconfirmed partial responses awaiting confirmatory response assessments; they did not include 13 patients who were continuing on study awaiting an initial response assessment.

The safety data presented encompassed the entire larotrectinib safety database in cancer patients (n=207). The majority of adverse events (AEs) recorded as grade 1 or 2. No treatment-related grade 3 or 4 AEs occurred in more than 5 percent of patients. Of the 122 patients with TRK fusion cancer, 11 patients (9 percent) required larotrectinib dose reductions. In every case, patients whose doses were reduced maintained their best response at the lower dose. One patient (<1 percent) discontinued larotrectinib due to an adverse event.

About larotrectinib

Larotrectinib is an investigational tropomyosin receptor kinase (TRK) inhibitor in clinical development for the treatment of patients with solid tumors that harbor a neurotrophic tyrosine receptor kinase (*NTRK*) gene fusion. Growing research suggests that the *NTRK* genes can become abnormally fused to other genes, producing a TRK fusion protein that can lead to the development of solid tumors across multiple sites of the body.

In November 2017, Bayer and Loxo Oncology entered into an exclusive global collaboration for the development and commercialization of larotrectinib and LOXO-195, a novel TRK inhibitor. Bayer and Loxo Oncology will jointly develop the two products with Loxo Oncology leading the ongoing clinical studies as well as the filing in the U.S., and Bayer leading ex-U.S. regulatory activities and worldwide commercial activities. In the U.S., Bayer and Loxo Oncology will co-promote the products.

For additional information about the larotrectinib clinical trials, please refer to www.clinicaltrials.gov or www.loxooncologytrials.com. Larotrectinib has not been approved by the U.S. Food and Drug Administration, the European Medicines Agency or any other health authority.

TRK fusion cancer

TRK fusion cancer occurs when a neurotrophic tyrosine receptor kinase (*NTRK*) gene fuses with another unrelated gene, producing an altered tropomyosin receptor kinase (TRK) protein. The altered protein, or TRK fusion protein, is constitutively active, triggering a signaling cascade. These proteins are a driver of the spread and growth of tumors in patients with TRK fusion cancer. TRK fusion cancer is not limited to certain

types of tumors, which means it can occur in any part of the body. TRK fusion cancer occurs in various adult and pediatric solid tumors with varying frequency, including appendiceal cancer, breast cancer, cholangiocarcinoma, colorectal cancer, GIST, infantile fibrosarcoma, lung cancer, mammary analogue secretory carcinoma of the salivary gland, melanoma, pancreatic cancer, thyroid cancer and various sarcomas.

Only specific tests can reliably detect TRK fusion cancer. Next-generation sequencing (NGS) can provide a comprehensive view of genomic alterations across a large number of genes. Fluorescence in situ hybridization (FISH) can also be used to test for TRK fusion cancer and immunohistochemistry (IHC) can be used to detect the presence of TRK proteins. For further information, go to www.trkcancer.com.

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 four marketed products and several other compounds 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 agriculture. Its products and services are designed to benefit people and improve their quality of life. At the same time, the Group aims to create value through innovation, growth and high earning power. Bayer is committed to the principles of sustainable development and to its social and ethical responsibilities as a corporate citizen. In fiscal 2017, the Group employed around 99,800 people and had sales of EUR 35.0 billion. Capital expenditures amounted to EUR 2.4 billion, R&D expenses to EUR 4.5 billion. For more information, go to www.bayer.com.

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Forward-Looking Statements
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