

News Release

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September 8, 2022

Not intended for UK-based media

Xevinapant Five-Year Data Show Survival Rate Nearly Doubled in Patients with Unresected LA SCCHN, When Added to Standard of Care

- **First randomized trial in decades to show significant improvement in overall survival in patients with LA SCCHN, reinforcing the transformative potential of xevinapant over standard of care in the curative setting**
- **Patients treated with xevinapant plus CRT almost twice as likely to be alive at five years (53% vs 28%) in Phase II study**
- **Two ongoing Phase III clinical trials of xevinapant in this setting, TrilynX and XRay Vision, are currently recruiting, with more than 250 centers worldwide**

Darmstadt, Germany, September 8, 2022 – Merck KGaA, Darmstadt, Germany, a leading science and technology company, today announced that the IAP (inhibitor of apoptosis protein) inhibitor xevinapant (formerly known as Debio 1143) plus chemoradiotherapy (CRT) markedly improved long-term efficacy outcomes in patients with unresected locally advanced squamous cell carcinoma of the head and neck (LA SCCHN) compared with placebo plus CRT. The addition of xevinapant more than halved the risk of death over five years compared with placebo. These late-breaking data from the 96-patient Phase II trial will be presented during the mini-oral session on head and neck cancer on September 10, 2022 at 10:55 AM CEST (Abstract #LBA33) at the European Society of Medical Oncology Congress 2022.

“There is a clear need for improved treatment options for patients with unresected locally advanced head and neck cancer. Chemoradiotherapy has served as the standard of care in this setting for the past several decades, yet half of patients treated with CRT see their cancer return, whether locally or as metastatic disease,”



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said Prof. Jean Bourhis, M.D., Ph.D., Department Head of Radio-Oncology at the University Hospital of Lausanne and lead investigator of the study. "The five-year results from this randomized Phase II study are the first to show improved efficacy outcomes over standard of care for these patients and suggest the potential for xevinapant to increase the proportion of patients who achieve cure following definitive therapy."

In this analysis, overall survival (OS) was evaluated at five years after the last patient was randomized; median follow-up was 60.1 months (range, 7.1-70.5 months) in the xevinapant arm and 39.2 months (range, 4.8-71.2 months) in the placebo arm. The data show:

- Xevinapant more than halved the risk of death over five years of follow-up compared with placebo (adjusted HR, 0.47 [95% CI, 0.27-0.84]; nominal $p=0.0101$).
- Median OS was prolonged with xevinapant (median not reached; 95% CI, 40.3 months-not evaluable) versus placebo (36.1 months; 95% CI, 21.8-46.7 months).
- Treatment with xevinapant nearly doubled OS, with a 53% (95% CI, 37-66%) probability of survival after five years compared with 28% (95% CI, 15-42%) with placebo.

As previously reported, the addition of xevinapant to CRT was well-tolerated and consistent with the safety profile of CRT alone with approximately two years of follow-up. Adverse events of grade 3 or higher were reported in 41 (85%) of 48 patients in the xevinapant group and 41 (87%) of 47 patients in the placebo group. The most common grade 3 or higher treatment-emergent adverse events among patients who received xevinapant plus CRT that occurred in more than 15% of patients were dysphagia (50%), anemia (35%), mucositis (31%), and neutropenia (23%).¹ Follow-up analysis at three years showed similar safety.²

"Head and neck cancer is a devastating disease that often has a profound impact on a patient's ability to eat, communicate and even sleep, yet there have been few treatment advances over the past 20 years," said Amanda Hollinger, Executive Director, Head and Neck Cancer Alliance. "We are hopeful that these findings may pave the way for a new approach that can improve outcomes."

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Previously reported results from the randomized, double-blind Phase II study showed the addition of xevinapant to standard-of-care CRT provided a statistically significant improvement in locoregional control rate at 18 months, the primary endpoint, versus placebo and CRT in patients with unresected LA SCCHN (54% [95% CI, 39 to 69] versus 33% [95% CI, 20 to 48]; odds ratio 2.69 [95% CI, 1.13 to 6.42]; $p=0.026$). Primary results of the study were published in *The Lancet Oncology*.¹

"The opportunity to develop an oncology medicine in a curative setting is a rare privilege, especially for a hard-to-treat disease such as locally advanced head and neck cancer, where many patients cannot undergo surgery," said Victoria Zazulina, M.D., Head of Development Unit Oncology, for the Healthcare business of Merck KGaA, Darmstadt, Germany. "Based on these Phase II results, we are committed to exploring the potential value of xevinapant in the locally advanced setting through our ongoing Phase III program, as we pioneer the investigation of the apoptotic pathway as a novel treatment modality."

Based on the promising efficacy and safety profile seen in the Phase II trial, and the urgent need for new treatments, xevinapant is being evaluated in two ongoing Phase III clinical trials. The first is the international, randomized, double-blind, placebo-controlled [TrilynX](#) study (NCT04459715) to evaluate the efficacy and safety of xevinapant versus placebo when added to definitive CRT in patients with unresected LA SCCHN. The second is [XRay Vision](#) (NCT05386550), a randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of xevinapant versus placebo when added to adjuvant, post-operative radiotherapy in patients with resected LA SCCHN who are at high risk for relapse and are ineligible for cisplatin. Both TrilynX and XRay Vision are currently recruiting.

In February 2020, the U.S. Food and Drug Administration granted Breakthrough Therapy Designation to xevinapant (formerly under development with Debiopharm as Debio 1143) for treatment of patients with previously untreated LA SCCHN, in combination with current standard of care, based on results of the Phase II trial.

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About Head and Neck Cancer

Worldwide, head and neck cancer accounts for more than 870,000 cases and 440,000 deaths annually,³ making it the 8th most common cancer type. LA SCCHN is a highly debilitating disease that can lead to impaired breathing, swallowing, and speech as it progresses. Despite treatment with curative intent using standard-of-care CRT, approximately 50% of patients with LA SCCHN develop local recurrence and/or distant metastasis,⁴ which are usually detected within the first two years after completion of standard-of-care treatment, underscoring the need to identify new therapeutic approaches.

About Xevinapant

Xevinapant (formerly known as Debio 1143) is an investigational first-in-class potent oral small-molecule IAP (inhibitor of apoptosis protein) inhibitor for the treatment of LA SCCHN. In preclinical studies, xevinapant restored sensitivity to apoptosis in cancer cells, thereby enhancing the effects of chemotherapy and radiotherapy. Xevinapant, the most clinically advanced IAP inhibitor, improved efficacy outcomes in combination with chemoradiotherapy (CRT), including three-year progression-free survival and five-year survival, compared with placebo plus CRT in a Phase II study in patients with unresected LA SCCHN. In March 2021, Merck KGaA, Darmstadt, Germany, gained exclusive rights from Debiopharm to develop and commercialize xevinapant worldwide. Xevinapant is not approved for any use anywhere in the world.

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About Merck KGaA, Darmstadt, Germany

Merck KGaA, Darmstadt, Germany, a leading science and technology company, operates across life science, healthcare and electronics. Around 60,000 employees work to make a positive difference to millions of people's lives every day by creating more joyful and sustainable ways to live. From advancing gene editing technologies and discovering unique ways to treat the most challenging diseases to enabling the intelligence of devices – the company is everywhere. In 2021, Merck KGaA, Darmstadt, Germany, generated sales of € 19.7 billion in 66 countries.

The company holds the global rights to the name and trademark "Merck" internationally. The only exceptions are the United States and Canada, where the business sectors of Merck KGaA, Darmstadt, Germany, operate as MilliporeSigma in life science, EMD Serono in healthcare and EMD Electronics in electronics. Since its founding in 1668, scientific exploration and responsible entrepreneurship have been key to the company's technological and scientific advances. To this day, the founding family remains the majority owner of the publicly listed company.

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¹ Sun X-S, Tao Y, Le Tourneau C, et al. Debio 1143 and high-dose cisplatin chemoradiotherapy in high-risk locoregionally advanced squamous cell carcinoma of the head and neck: a double-blind, multicentre, randomised, phase 2 study. *Lancet Oncol.* 2020 Sep;21(9):1173-1187. doi: 10.1016/S1470-2045(20)30327-2. Epub 2020 Aug 3.

² Bourhis J, Sun X-S, Le Tourneau C, et al. 3-year follow-up results of the double-blind, randomized, phase II trial comparing concurrent high-dose cisplatin chemo-radiation plus xevinapant (Debio 1143) or placebo in high-risk patients with locally advanced squamous cell carcinoma of the head and neck. Oral presentation at: 2020 Virtual ESMO Congress.

³ Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2021 May;71(3):209-249. doi: 10.3322/caac.21660. Epub 2021 Feb 4.

⁴ Choong N, Vokes E. Expanding role of the medical oncologist in the management of head and neck cancer. *CA Cancer J Clin.* 2008 Jan-Feb;58(1):32-53. doi: 10.3322/CA.2007.0004. Epub 2007 Dec 20.