

## News Release

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# **Merck KGaA, Darmstadt, Germany, Builds on Leadership in Head and Neck Cancer Through Worldwide Licensing Agreement with Debiopharm for Pivotal-Stage Xevinapant**

- **Xevinapant is the first Inhibitor of Apoptosis Proteins antagonist with FDA Breakthrough Therapy Designation for previously untreated locally advanced squamous cell carcinoma of the head and neck, in combination with current standard of care**
- **A Phase II trial reported that xevinapant plus chemoradiotherapy reduced risk of death by 51% vs standard of care in this patient population; Phase III TrilynX study initiated in September 2020**
- **Merck KGaA, Darmstadt, Germany, gains exclusive global development and commercialization rights; Debiopharm to receive € 188 million upfront and up to € 710 million in regulatory and commercial milestones, as well as royalty payments**

Darmstadt, Germany, March 1, 2021– Merck KGaA, Darmstadt, Germany, a leading science and technology company, today announced a worldwide in-licensing agreement with Debiopharm, Lausanne, Switzerland, for the development and commercialization of xevinapant (Debio 1143). Xevinapant, a potent oral Inhibitor of Apoptosis Proteins (IAP) antagonist, is the only medicine in its class in late-stage clinical development and has the potential to be first in class. Xevinapant is currently being investigated in the [Phase III TrilynX study](#) for previously untreated high-risk

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locally advanced squamous cell carcinoma of the head and neck (LA SCCHN), in combination with platinum-based chemotherapy and standard fractionation intensity-modulated radiotherapy.

“As a leading science and technology company, we are constantly evolving our three business sectors to ensure we are best-positioned to create sustainable value. This includes the addition of highly promising technologies, such as the in-licensing of xevinapant. This late-stage asset complements our Healthcare pipeline, which will be one of our key growth drivers in the coming years,” said Stefan Oschmann, Chairman of the Executive Board and CEO of Merck KGaA, Darmstadt, Germany.

“By bringing our expertise and heritage in head and neck cancer to the development of xevinapant, we have the opportunity to explore an important new treatment option in an area of high unmet need where other approaches, including immunotherapy, have seen limited success. The promising long-term efficacy of xevinapant in the Phase II trial suggests that antagonism of IAP has the potential to be a transformative approach in this cancer,” said Peter Guenter, Member of the Executive Board of Merck KGaA, Darmstadt, Germany, and CEO Healthcare. “Looking forward, we will continue to pursue opportunities to augment the in-house innovations in our oncology portfolio with new solutions for patients with cancer.”

Under the terms of the licensing agreement, Merck KGaA, Darmstadt, Germany, gains exclusive rights to develop and commercialize xevinapant worldwide, including in the U.S. Merck KGaA, Darmstadt, Germany, will co-fund with Debiopharm the ongoing Phase III registrational TrilynX study, a global double-blind, placebo-controlled, 700-patient randomized clinical trial to evaluate the efficacy and safety of xevinapant vs. placebo when added to definitive chemoradiotherapy (CRT) in cisplatin-eligible patients with high-risk LA SCCHN. Merck KGaA, Darmstadt, Germany, also will initiate a second global Phase III study to evaluate xevinapant in patients with LA SCCHN who are unable to tolerate high-dose cisplatin in combination with radiotherapy. The agreement also includes development rights for preclinical follow-on compounds to xevinapant. Debiopharm will receive € 188 million in upfront payments and up to € 710 million in regulatory and commercial milestones, as well as royalty payments. The parties anticipate the closing of the transaction in early Q2 2021.

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"The data for xevinapant to date show its potential to enhance the standard of care in this curative setting for head and neck cancer, addressing a significant unmet medical need for patients with this disease," said Bertrand Ducrey, Chief Executive Officer of Debiopharm. "Our partner is exceptionally qualified to advance xevinapant, given their extensive knowledge in head and neck cancer and their commercial oncology capabilities around the world."

"Locally advanced head and neck cancer is uniquely debilitating, often impairing the ability to swallow, speak and breathe. With the current standard treatments, at least half of patients will relapse, typically within the first two years. Based on the efficacy seen in the Phase II study, in which adding xevinapant to CRT cut the risk of death by half, this investigational medicine has the potential to offer a much-needed new standard of care," said Prof. Jean Bourhis, Department Head of Radio-Oncology at the University Hospital of Lausanne and lead investigator of the Phase III TrilynX study.

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 21% point improvement in locoregional control rate at 18 months, the primary endpoint, vs. placebo and CRT in patients with high-risk LA SCCHN (54% [95% CI: 39 to 69] vs. 33% [95% CI: 20 to 48]; odds ratio 2.69 [95% CI: 1.13 to 6.42];  $p=0.026$ ). A significant progression-free survival (PFS) benefit was also observed vs. the control arm after a two-year follow-up period (HR=0.37, 95% CI: 0.18 to 0.76;  $p=0.0069$ ).<sup>1</sup> At three years of follow-up, xevinapant plus CRT showed a statistically significant 51% reduction in the risk of death versus placebo plus CRT (HR=0.49, 95% CI: 0.26 to 0.92;  $p=0.0261$ ). About two-thirds of patients in the xevinapant arm were alive at three years, compared with 51% in the control arm. Statistically significant improvements in PFS and duration of response were also sustained at three years.<sup>2</sup> Xevinapant showed a predictable and manageable safety profile without substantial additional toxicity to standard CRT.<sup>1,2</sup> Primary results of the study were published in *The Lancet Oncology*, and the three-year follow-up data were presented at the European Society for Medical Oncology (ESMO) Virtual Congress 2020.

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In February 2020, the U.S. Food and Drug Administration (FDA) granted Breakthrough Therapy Designation to xevinapant for treatment of patients with previously untreated LA SCCHN, in combination with current standard of care, platinum-based chemotherapy and standard fractionation intensity-modulated radiotherapy, based on the Phase II results.

### **About Head and Neck Cancer**

Worldwide, head and neck cancer accounts for more than 650,000 cases and 330,000 deaths annually, making it the 6th most common cancer type.<sup>3</sup> LA SCCHN is a highly debilitating disease that can lead to impaired breathing, swallowing, and speech as it progresses.<sup>4</sup> Despite standard-of-care CRT, at least 40% to 60% of patients with LA SCCHN develop locoregional or distant relapses, which are usually detected within the first two years of treatment, underscoring the need to identify new therapeutic approaches.<sup>5</sup>

### **About Xevinapant**

Xevinapant (Debio 1143) is a potentially first-in-class potent oral antagonist of IAPs (Inhibitor of Apoptosis Proteins). In preclinical studies, xevinapant restores sensitivity to apoptosis in cancer cells, thereby depriving them of one of their major resistance mechanisms. As the most clinically advanced IAP antagonist, xevinapant has established proof of efficacy in combination with chemoradiotherapy (CRT) in patients with high-risk locally advanced squamous cell carcinoma of the head and neck (LA SCCHN), with a clinically significant and sustained clinical benefit compared with CRT alone.

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### **About Merck KGaA, Darmstadt, Germany**

Merck KGaA, Darmstadt, Germany, a leading science and technology company, operates across healthcare, life science and performance materials. Around 58,000 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 2019, Merck KGaA, Darmstadt, Germany, generated sales of € 16.2 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 EMD Serono in healthcare, MilliporeSigma in life science, and EMD Performance Materials. Since its founding 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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<sup>1</sup> Sun XS, 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; 21: 1173-1187.

<sup>2</sup> Bourhis J, Sun XS, Le Tourneau C, et al. Phase II comparing concurrent high-dose cisplatin chemotherapy plus Debio 1143 (xevinapant) or placebo in high-risk patients with locally advanced squamous cell carcinoma of the head and neck. Abstract presented at ESMO 2020 (Virtual conference).

<sup>3</sup> Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2018; 68 (6): 394-424.

<sup>4</sup> Johnson DE, Burtness B, Leemans CR, et al. Head and neck squamous cell carcinoma. *Nat Rev Dis Primers*. 2020 Nov 26;6(1):92.

<sup>5</sup> Machiels, J-P, Leemans, CR, Golusinski, W, et al. Squamous cell carcinoma of the oral cavity, larynx, oropharynx and hypopharynx: EHNS-ESMO-ESTRO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2020 Nov;31(11);1462-1475.