Guerbet announces U.S. Food and Drug Administration (FDA) approval of Elucirem™ (Gadopiclenol)

- FDA approval of Elucirem™ (NDA 216986) was granted after priority review, a designation assigned to applications for drugs that provide significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions compared to available therapies.

- In the approved indications, a contrast-enhanced MRI examination using Elucirem™ requires half the gadolinium dose of existing non-specific GBCAs (gadolinium-based contrast agents), addressing practitioners' concerns about gadolinium exposure.[1,2,3]

- Elucirem™ (Gadopiclenol) will be produced in the United States and France.

- Elucirem™ will be marketed by Guerbet in the United States in bottle and pre-filled syringe form.

Villepinte, France, September 21st 2022 – *Guerbet (FR0000032526 GBT), a global leader in medical imaging, announced today that the U.S. Food and Drug Administration (FDA) after priority review, approved Elucirem™ (Gadopiclenol), a new macrocyclic GBCA for use in contrast-enhanced magnetic resonance imaging (MRI).*

Elucirem™ (Gadopiclenol) is a new macrocyclic gadolinium-based contrast agent with high relaxivity indicated for use in adults and children aged 2 years and older, for contrast-enhanced magnetic resonance imaging (MRI). The product is used to detect and visualize lesions with abnormal vascularity in the central nervous system (brain, spine and associated tissues) and the body (head and neck, thorax, abdomen, pelvis, and musculoskeletal system). Please refer to the FDA approved Prescribing Information on Drugs@FDA.[4]

Gadopiclenol, the active substance of Elucirem™, has been designed with two sites for water molecule exchange to increase relaxivity and contrast, allowing to use it at half the conventional dose of gadolinium compared to other non-specific GBCAs.

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The efficacy and safety of Gadopiclenol have been assessed as part of Guerbet's clinical development plan, with marketing authorization being targeted worldwide (cf. phase III trial results below).
The FDA is the first health authority to have approved **Elucirem™**. It is currently in the process of examination by the European Medicines Agency via a centralized procedure.

"As a pioneer in MR imaging, thanks to the success of our first gadolinium-based macrocyclic contrast agent, we are delighted with the FDA approval of Elucirem™. This approval allows patients and practitioners to benefit from the innovations brought by Elucirem™"

David Hale, Chief Executive Officer of Guerbet Group

Phase III clinical trials for Elucirem™

The approval was primarily based on data from two Phase III studies completed in March 2021 which demonstrated that Elucirem™ leads to non-inferior results in brain and body MRI at half the gadolinium dose of Gadobutrol.[5,6] The endpoints were met in terms of the diagnostic benefit of injecting Gadopiclenol (0.05 mmol/kg) during MRI examinations, based on two criteria:
1/ the superiority of the examination with Gadopiclenol compared to the examination with no contrast agent;
and 2/ the non-inferiority of Gadopiclenol (0.05 mmol/kg) compared to Gadobutrol (0.1 mmol/kg) for the visualization and detection of lesions of the central nervous system and in the other anatomical areas studied.

No major safety signals were reported during the development of Gadopiclenol, and the adverse reactions reported during the two-Phase III studies were similar for both products administered. Please refer to the FDA approved Prescribing Information on Drugs@FDA.[7]

Details on these two clinical trials are available in the www.ClinicalTrials.gov database:
- Efficacy and Safety of Gadopiclenol for Central Nervous System (CNS) Magnetic Resonance Imaging (MRI) - Full Text View - ClinicalTrials.gov
- Efficacy and Safety of Gadopiclenol for Body Magnetic Resonance Imaging (MRI) - Full Text View - ClinicalTrials.gov

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Production of Elucirem™ (Gadopiclenol)

The production of Gadopiclenol will take place at one Guerbet's US and at three French plants. Those three French plants employ approximately 700 people in production and research & development.

About Gadopiclenol

Gadopiclenol, initially invented by Guerbet with subsequent contribution of Bracco intellectual property, is a new macrocyclic gadolinium-based contrast agent (GBCA) with high relaxivity. The efficacy and safety of Gadopiclenol have been evaluated in MRI of the Central Nervous System, head and neck, thorax, abdomen, pelvis and musculoskeletal system (refer to the approved USPI for full information). Details on Phase III clinical trials are available on www.ClinicalTrials.gov:

- *Efficacy and Safety of Gadopiclenol for Central Nervous System (CNS) Magnetic Resonance Imaging (MRI) Full Text View - ClinicalTrials.gov*
- *Efficacy and Safety of Gadopiclenol for Body Magnetic Resonance Imaging (MRI) - Full Text View - ClinicalTrials.gov*

Gadopiclenol is currently in the process of examination by the European Medicines Agency.

About Guerbet

At Guerbet, we build lasting relationships so that we enable people to live better. That is our purpose. We are a global leader in medical imaging, offering a comprehensive range of pharmaceutical products, medical devices, and digital and AI solutions for diagnostic and interventional imaging. As pioneers in contrast products for 95 years, with more than 2,600 employees worldwide, we continuously innovate and devote 8%-10% of our revenue to research and development in five centers in France, Israel, and the United States. Guerbet (GBT) is listed on Euronext Paris (segment B – mid caps) and generated €732 million in revenue in 2021. For more information, please visit www.guerbet.com.

About Guerbet and Bracco Imaging Collaboration

Guerbet and Bracco Imaging entered in December 2021 into a worldwide collaboration on Gadopiclenol manufacturing and research and development indicate. Gadopiclenol will be commercialized independently under separate brands. Both Guerbet and Bracco Imaging each own valuable intellectual property on Gadopiclenol. Furthermore, after an agreed transition period when Guerbet manufactures Gadopiclenol for both Guerbet and Bracco Imaging, both companies will manufacture Gadopiclenol active ingredient and finished product.

Forward-looking statements

This press release may contain statements of a forward-looking nature, based on assumptions and predictions made by the management of the Guerbet group. Various known and unknown risks, uncertainties and other factors could lead to marked differences between the future results, financial situation, development and performances of the company, and the estimates made here. These factors include those mentioned in the public reports of Guerbet, available on its website www.guerbet.com.The company assumes no responsibility whatsoever in relation to the updating of these forward-looking statements, or how they correspond to future events or developments.

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[1] *PRAC, European Medicines Agency, 2017*
[2] *FDA Drug Safety Communication, 2017*
[3] *Brunjes et al. Water Research, 2020*
[4] *https://www.accessdata.fda.gov*
[5] *https://www.clinicaltrials.gov/ct2/show/NCT03996447?term=Gadopiclénol&draw=2&rank=2*
[6] *https://www.clinicaltrials.gov/ct2/show/NCT03986138?term=Gadopiclénol&draw=2&rank=1*
[7] *https://www.accessdata.fda.gov*

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