



**FOR IMMEDIATE RELEASE**

**Lantheus Enters into Strategic Collaboration with CarThera for Use of Microbubbles in Combination with SonoCloud® System for Treatment of Glioblastoma**

***Agreement Supports Lantheus' Microbubble Franchise Growth Strategy and Expansion into Oncology***

NORTH BILLERICA, Mass., December 9, 2019 - Lantheus Holdings, Inc. (the "Company") (NASDAQ: LNTH), parent company of Lantheus Medical Imaging, Inc. ("LMI"), a global leader in the development, manufacture and commercialization of innovative diagnostic imaging agents and products, today announced it has entered into a strategic commercial supply agreement with CarThera® for the use of Lantheus' microbubbles in combination with SonoCloud®, a proprietary implantable device in development for the treatment of recurrent glioblastoma (rGBM). Glioblastoma is a lethal and devastating form of brain cancer with median survival of 15 months after diagnosis<sup>1</sup>. The collaboration directly aligns with key Lantheus growth strategies of pursuing new applications for its microbubble franchise and expansion into oncology.

Under the commercial supply agreement, Lantheus' microbubbles will be used as a component in CarThera's SonoCloud® System, which uses low-intensity pulsed ultrasound (LIPU) specifically designed to open the blood-brain barrier to facilitate more effective delivery of chemotherapy to tumors. As part of the agreement, CarThera will be responsible for regulatory filings and approvals in the U.S., Europe and rest of world as well as commercialization of SonoCloud®. Lantheus will supply its microbubble vials (the ultrasound resonator) and activation devices at a predetermined transfer price. Additionally, Lantheus will receive royalties on the SonoCloud® kit product sales upon regulatory approval.

"We are excited to collaborate with CarThera to extend our microbubble franchise into the oncology field to target glioblastoma, an aggressive type of brain cancer with significant unmet medical need," said Mary Anne Heino, President and Chief Executive Officer of Lantheus. "Our collaboration leverages both companies' strengths to bring novel solutions to the healthcare community. As the use of microbubbles in diagnostic and therapeutic applications gains more interest around the world, our collaboration with CarThera demonstrates our commitment to drive Lantheus' microbubble into new disease areas with great potential for significant improvement in patient outcomes."

"We are delighted to enter into this collaboration with Lantheus for the development of our SonoCloud ultrasound-based medical device," said Frederic Sottolini, Chief Executive Officer of

CarThera. “With Lantheus’ expertise in the field of microbubbles combined with CarThera’s novel and proprietary ultrasound technology, we see the potential for a long-term, highly successful collaboration. We are excited to work with Lantheus to advance our promising SonoCloud technology with the goal of improving treatment and prognosis of patients with glioblastoma, a debilitating, and all too often, fatal disease.”

CarThera’s SonoCloud-9 System is currently being evaluated in a Phase IIa clinical trial with a Phase IIb/III pivotal clinical trial to follow. The objective of this trial to evaluate the safety and efficacy of repeated opening of the blood brain barrier using the SonoCloud-9, its next-generation implantable ultrasound device designed to cover the entire tumor and surrounding infiltrative areas. Twenty-one patients will undergo repeated blood brain barrier opening with the SonoCloud-9 prior to infusion of carboplatin at clinical sites in France (Paris, Lyon, Marseille, Angers) and the United-States (MD Anderson Cancer Center in Houston, Northwestern Memorial Hospital in Chicago).

### **About Glioblastoma**

Roughly 12,000 people are diagnosed per year with glioblastoma in the U.S.<sup>2</sup>, and incidence is growing more than 1% per year<sup>3</sup>. Worldwide, annual incidence is as high as 5 in 100,000 people, and roughly 225,000 people die from the disease each year.<sup>4</sup>

The first line treatment for most glioblastoma patients is surgical resection of the tumor. After a healing period from surgery, patients will then typically undergo radiation and chemotherapy treatment cycles.<sup>5</sup> The main goal of surgery is to remove as much GBM tumor as possible without impacting surrounding normal brain tissue that is critical for normal neurological function (such as motor skills, speaking and walking ability, etc.). However, GBMs are commonly surrounded by a reservoir of migrating, infiltrating tumor cells that invade surrounding tissue, making it virtually impossible to remove the cancer entirely. Surgery does help to reduce the amount of solid tumor tissue within the brain and thus can reduce intracranial pressure. The surgical debulking of tumor can prolong life and improve the quality of life for patients.<sup>5</sup> The treatment of this region surrounding the tumor using chemotherapy is challenging due to the limited penetration of agents into the brain owing to the highly protective blood-brain barrier, a layer of specialized endothelial cells. Research has shown the blood-brain barrier can be accessed using ultrasound in combination with systemic injection of an ultrasonically resonated microbubble.

### **About the SonoCloud System**

Earlier this year, CarThera published results from a Phase I/IIa clinical trial using SonoCloud-1 ultrasound implantable device to open the blood-brain barrier prior to carboplatin chemotherapy in patients with rGBM. Those results from 19 patients, published in the March 19, 2019 edition of journal *Clinical Cancer Research*, revealed a good safety profile and demonstrated the feasibility and promising potential of the SonoCloud® approach. Notably, the 11 rGBM patients who received

optimal pressure levels of ultrasound showed a median progression-free survival (PFS) of 4.11 months and a median overall survival (OS) of 12.94 months as compared to those patients who received a suboptimal dosage, in whom median PFS and OS were 2.73 months and 8.64 months, respectively.<sup>6</sup>

### **About CarThera®**

CarThera designs and develops innovative therapeutic ultrasound-based medical devices for treating brain disorders. The company is a spin-off from AP-HP, Greater Paris University Hospitals, the largest hospital group in Europe, and Sorbonne University. Since 2010, CarThera has been leveraging the inventions of Professor Alexandre Carpentier, a neurosurgeon at AP-HP who has achieved worldwide recognition for his innovative developments in treating brain disorders. CarThera developed SonoCloud, an intracranial ultrasound implant that temporarily opens the blood-brain barrier (BBB).

CarThera is based at the Brain and Spine Institute (Institut du Cerveau et de la Moelle épinière, ICM) in Paris, France, and has laboratories at the Bioparc Laënnec business incubator in Lyon, France. The company, led by Frederic Sottolini (CEO), works closely with the Laboratory of Therapeutic Applications of Ultrasound (Laboratoire Thérapie et Applications Ultrasonores, LabTAU, INSERM) in Lyon. Since its inception, the company has received support from the AP-HP, Sorbonne University, the ANR (Nationale Research Agency), France's Ministry of Research, the Ile-de-France region, the Bpifrance public investment bank, the Medicen Paris Region and Lyonbiopôle clusters. For more information, visit [www.carthera.eu](http://www.carthera.eu).

### **About Lantheus Holdings, Inc. and Lantheus Medical Imaging, Inc.**

Lantheus Holdings, Inc. is the parent company of LMI, a global leader in the development, manufacture and commercialization of innovative diagnostic imaging agents and products. The Company is headquartered in North Billerica, Massachusetts with offices in Puerto Rico and Canada. For more information, visit [www.lantheus.com](http://www.lantheus.com).

## Safe Harbor for Forward-Looking and Cautionary Statements

*This press release contains “forward-looking statements” as defined under U.S. federal securities laws, including statements about the Company’s future outlook. Forward-looking statements may be identified by their use of terms such as anticipate, believe, confident, could, has the potential to, estimate, expect, intend, may, plan, predict, project, target, will and other similar terms. Such forward-looking statements are subject to risks and uncertainties that could cause actual results to materially differ from those described in the forward-looking statements. Readers are cautioned not to place undue reliance on the forward-looking statements contained herein, which speak only as of the date hereof. The Company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future developments or otherwise, except as may be required by law. Risks and uncertainties that could cause the Company’s actual results to materially differ from those described in the forward-looking statements are discussed in the Company’s filings with the Securities and Exchange Commission (including those described in the Risk Factors section in the Company’s Annual Report on Form 10-K and its Quarterly Reports on Form 10-Q).*

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<sup>1</sup> Koshy M, Villano JL, Dolecek TA, Howard A, Mahmood U, Chmura SJ, et al. Improved survival time trends of glioblastoma using the SEER 17 population-based registries. *J Neuro Oncol.* 2012;107(1):207–12.

<sup>2</sup> American Brain Tumor Association: <http://www.abta.org/brain-tumor-information/types-of-tumors/glioblastoma.html>

<sup>3</sup> Focused Ultrasound Foundation: Glioblastoma Workshop, November 2015.

<sup>4</sup> Bush, N. A., Chang, S. M., and Berger, M. S. (2017). Current and future strategies for treatment of glioma. *Neurosurg. Rev.* 40, 1–14. doi: 10.1007/s10143-016-0709-8.

<sup>5</sup> American Association of Neurological Surgeons (AANS).

<sup>6</sup> Safety and Feasibility of Repeated and Transient Blood-Brain Barrier Disruption by Pulsed Ultrasound in Patients with Recurrent Glioblastoma. Ahmed Idbaih, Michael Canney, Lisa Belin, Carole Desseaux, Alexandre Vignot, Guillaume Bouchoux, Nicolas Asquier, Bruno Law-Ye, Delphine Leclercq, Anne Bissery, Yann De Rycke, Clementine Trosch, Laurent Capelle, Marc Sanson, Khe Hoang-Xuan, Caroline Dehais, Caroline Houillier, Florence Laigle-Donadey, Bertrand Mathon, Arthur André, Cyril Lafon, Jean-Yves Chapelon, Jean-Yves Delattre and Alexandre Carpentier. *Clinical Cancer Research*: March 19, 2019

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