PRESS RELEASE

Blue Earth Diagnostics Announces Dosing of Initial Patient in Phase 3 REVELATE Clinical Trial of ^{18}F-Fluciclovine PET Imaging for Detection of Recurrent Brain Metastases

– Clinical utility of Axumin® (fluciclovine F 18) being investigated in expanded areas of cancer imaging –

BURLINGTON, Mass. and OXFORD, UK, January 12, 2021 – Blue Earth Diagnostics, a Bracco company and recognized leader in the development and commercialization of innovative PET radiopharmaceuticals, today announced that the first patient has been dosed in its Phase 3 REVELATE clinical trial of ^{18}F-fluciclovine, a positron emission tomography (PET) imaging radiopharmaceutical being studied for potential use in detecting recurrent brain metastases. The REVELATE study is a Phase 3, multi-center, single-arm imaging study being conducted in the United States. Its purpose is to assess the diagnostic performance of ^{18}F-fluciclovine PET in detecting recurrent brain metastases in patients previously treated with radiation therapy. The first patient dosed in the study was at Yale University, New Haven, Conn., under the auspices of Dr. Mariam Aboian, Assistant Professor of Radiology.

Note: ^{18}F-fluciclovine, under the tradename Axumin® (fluciclovine F 18) injection, is an FDA-approved and commercially available molecular imaging radiopharmaceutical for use in PET imaging in men with suspected prostate cancer recurrence based on elevated blood prostate specific antigen (PSA) levels following prior treatment. The safety and efficacy of ^{18}F-fluciclovine PET imaging for the detection of recurrent brain metastases has not been established.

Blue Earth Diagnostics has two clinical studies underway to investigate the use of ^{18}F-fluciclovine PET in the detection of recurrent brain metastases. The Phase 2 PURSUE trial is designed to establish image interpretation criteria for ^{18}F-fluciclovine PET in detecting recurrent brain metastases. REVELATE is a Phase 3 study designed to evaluate its diagnostic performance in the detection of recurrent brain metastases in patients previously treated with radiation therapy. Further information about these trials, including a current list of clinical trial sites, can be found on www.clinicaltrials.gov (PURSUE, NCT04410367; REVELATE, NCT04410133).

“The mission of Blue Earth Diagnostics is to develop novel PET radiopharmaceuticals to address unmet medical needs and inform the management and care of patients with cancer. With these two clinical trials now underway, we are hopeful that our efforts may help patients with recurrent metastatic brain cancer,” said Jonathan Allis, D. Phil., Executive Chairman of Blue Earth Diagnostics. “Blue Earth Diagnostics’ initial focus for ^{18}F-fluciclovine has been on the successful development and commercialization of Axumin in the United States and Europe for the detection and localization of recurrent prostate cancer, where it has become widely adopted as the standard of care and commercially administered to more than 110,000 U.S. patients. Broadening our ^{18}F-fluciclovine franchise into neuro-oncology is part of our overall growth strategy for the company. This rapid advancement of ^{18}F-fluciclovine into Phase 3 clinical development marks a significant milestone for Blue Earth Diagnostics and is testimony to the proven expertise of the team.”

"Brain metastases occur in up to 40% of patients with cancer, and approximately 200,000 patients in the United States are affected by brain tumors each year," said Samuel T. Chao, MD, Department of Radiation Oncology, Cleveland Clinic; Professor at the Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, Ohio; and Coordinating Investigator on the REVELATE Phase 3 study. "Due to the severity of disease, accurate and timely evaluation of the presence or absence of recurrent disease is essential for informing treatment decisions, as well as facilitating much-needed research into effective therapies for these patients. Conventional magnetic resonance imaging (MRI) is considered the "gold standard" for patient follow-up, but is unable to reliably differentiate recurrent disease from necrotic (dead) tissue which can result from radiation therapy. This can present challenges for physicians in determining appropriate patient management and care. The Phase 3 REVELATE clinical study is designed to investigate the diagnostic performance of ^{18}F-fluciclovine PET imaging as a potential decision-making aid in assessing a patient's disease status, and we look forward to seeing the results of this clinical study."

"Guidelines and recommendations established by the Response Assessment in Neuro-Oncology (RANO) group recognize the limitations of conventional MRI. Recent recommendations in 2019 cite the potential utility of amino acid PET radiopharmaceuticals in distinguishing brain tissue changes after radiation therapy from recurrent brain metastases, while noting that data have been derived mainly from single center, retrospective studies. Consequently, a call for prospective multi-center studies has been re-iterated to validate these observations," said Peter Gardiner, MB ChB, MRCP, FFPM, Chief Medical Officer of Blue Earth Diagnostics. "In addition to its proven performance in the detection and localization of recurrent prostate cancer and, based on its mechanism of action, ^{18}F-fluciclovine holds potential clinical utility for the detection of other cancers. Being an amino acid-based PET radiopharmaceutical, ^{18}F-fluciclovine is designed to visualize the increased amino acid transport that occurs in malignant tumors, including in brain metastases that can recur after radiation therapy. The preferential uptake of ^{18}F-fluciclovine into cancer cells should enable this recurrent disease to be reliably detected."

About the REVELATE and PURSUE Clinical Trials in Brain Metastases

The REVELATE study ("Study to Establish the Diagnostic Performance of ^{18}F-fluciclovine PET in Detecting Recurrent Brain Metastases") is an open-label, single-arm, single-dose, prospective, multi-center Phase 3 study designed to establish the diagnostic performance of ^{18}F-fluciclovine PET in detecting recurrent brain metastases after radiation therapy. The study is planned to enroll approximately 150 patients at clinical sites in the United States. The primary endpoint of the REVELATE study is to assess the Negative Percent Agreement (NPA) and Positive Percent Agreement (PPA) of ^{18}F-fluciclovine PET in detecting recurrent brain metastases on a patient level. Secondary endpoints will assess the Positive Predictive Value (PPV) and Negative Predictive Value (NPV) of ^{18}F-fluciclovine PET for detecting recurrent brain metastases, among others. Additional information about the Phase 3 REVELATE trial is available at: www.clinicaltrials.gov (NCT04410133).

Blue Earth Diagnostics' PURSUE study ("Study to Establish Image Interpretation Criteria for ^{18}F-fluciclovine PET in Detecting Recurrent Brain Metastases") is an open-label, single-arm, single-dose, prospective, multi-center Phase 2b study designed to establish image interpretation criteria for ^{18}F-fluciclovine PET in detecting recurrent brain metastases after radiation therapy. The primary endpoint of the PURSUE study is to assess the diagnostic performance of various thresholds of ^{18}F-fluciclovine uptake in lesions based on visual reads versus histopathological analysis. It is anticipated to enroll approximately 40 patients at sites in the United States. More information about the PURSUE trial is available at: www.clinicaltrials.gov (NCT04410367).

About ^{18}F-Flucivlovine PET and Recurrent Brain Metastases

^{18}F-flucivlovine PET is a novel diagnostic imaging radiopharmaceutical for PET imaging to visualize the increased amino transport that occurs in malignant tumors. It consists of a synthetic amino acid that is preferentially taken up by cancer cells compared with surrounding normal tissues and is labeled with the radioisotope ^{18}F for PET imaging. ^{18}F-flucivlovine is under investigation by Blue Earth Diagnostics for potential use in adults for the detection of recurrent brain metastases in patients who have previously undergone radiation therapy. ^{18}F-fluciclovine, under the tradename Axumin® (fluciclovine F 18), is approved by the U.S. Food and Drug Administration (FDA) and in the EU for PET imaging in men with recurrent prostate cancer. ^{18}F-fluciclovine was invented at Emory University, in Atlanta, Ga., with much of the fundamental clinical development carried out by physicians at Emory University's Department of Radiology and Imaging Sciences. Blue Earth Diagnostics licensed ^{18}F-fluciclovine from GE Healthcare and is investigating the molecule for other potential cancer indications, including in neuro-oncology.

About Metastatic Brain Tumors

Brain metastases occur in up to 40% of patients with cancer, and are the most common intracranial tumor in adults. Approximately 200,000 patients in the United States are affected by brain tumors each year. The most frequent causes for metastatic spread to the brain arise from lung, breast, colorectal or kidney cancers or from melanoma.

Current treatment options for patients with metastatic brain tumors include surgery, and radiation therapy, which is sometimes combined with systemic treatment. Assessment of metastatic brain tumors typically involves magnetic resonance imaging (MRI). More than half of patients have at least one lesion increase in size on MRI following radiation therapy, which may indicate either recurrent disease or necrotic (dead) tissue resulting from the radiation therapy. Accurate and timely evaluation for the presence or absence of recurrent disease is essential for informing management decisions. However, diagnostic uncertainty exists, arising from limitations of MRI to reliably differentiate recurrent disease from necrotic tissue. This can present challenges for physicians in making determining appropriate patient management and care.

Indication and Important Safety Information About Axumin

INDICATION

Axumin® (fluciclovine F 18) injection is indicated for positron emission tomography (PET) imaging in men with suspected prostate cancer recurrence based on elevated blood prostate specific antigen (PSA) levels following prior treatment.

IMPORTANT SAFETY INFORMATION

- Image interpretation errors can occur with Axumin PET imaging. A negative image does not rule out recurrent prostate cancer and a positive image does not confirm its presence. The performance of Axumin seems to be affected by PSA levels. Axumin uptake may occur with other cancers and benign prostatic hypertrophy in primary prostate cancer. Clinical correlation, which may include histopathological evaluation, is recommended.
- Hypersensitivity reactions, including anaphylaxis, may occur in patients who receive Axumin. Emergency resuscitation equipment and personnel should be immediately available.
- Axumin use contributes to a patient's overall long-term cumulative radiation exposure, which is associated with an increased risk of cancer. Safe handling practices should be used to minimize radiation exposure to the patient and health care providers.

- Adverse reactions were reported in ≤ 1% of subjects during clinical studies with Axumin. The most common adverse reactions were injection site pain, injection site erythema and dysgeusia.

To report suspected adverse reactions to Axumin, call 1-855-AXUMIN1 (1-855-298-6461) or contact FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Full Axumin prescribing information is available at https://www.axumin.com/prescribing-information.pdf**.**

About Blue Earth Diagnostics

Blue Earth Diagnostics, a subsidiary of Bracco Imaging S.p.A., is a recognized leader in the development and commercialization of novel PET radiopharmaceuticals to inform clinical management and guide care for cancer patients in areas of unmet medical need. Formed in 2014, Blue Earth Diagnostics is led by proven experts in nuclear medicine, who have expanded and advanced its robust oncology portfolio. The company's first approved and commercially available product is Axumin® (fluciclovine F 18), a novel molecular imaging agent approved in the United States and European Union for use in PET imaging to detect and localize prostate cancer in men with suspected recurrence, based on elevated Prostate-Specific Antigen (PSA) levels. ^{18}F-fluciclovine has a broad range of other potential applications in cancer imaging and Blue Earth Diagnostics is investigating the molecule for other cancers, including in neuro-oncology. The company's pipeline includes innovative radiohybrid Prostate-Specific Membrane Antigen (rhPSMA)-targeted agents, a clinical-stage, investigational class of theranostic compounds with potential applications in both the imaging and treatment of prostate cancer. For more information, visit: www.blueearthdiagnostics.com.

About Bracco Imaging

Bracco Imaging S.p.A., part of the Bracco Group, is a world-leading diagnostic imaging provider. Headquartered in Milan, Italy, Bracco Imaging develops, manufactures and markets diagnostic imaging agents and solutions. It offers a product and solution portfolio for all key diagnostic imaging modalities: X-ray imaging (including Computed Tomography-CT, Interventional Radiology, and Cardiac Catheterization), Magnetic Resonance Imaging (MRI), Contrast Enhanced Ultrasound (CEUS), and Nuclear Medicine through radioactive tracers and novel PET imaging agents to inform clinical management and guide care for cancer patients in areas of unmet medical need. Our continually evolving portfolio is completed by a range of medical devices, advanced administration systems and dose-management software. In 2019 Bracco Imaging also enriched its product portfolio by expanding the range of oncology nuclear imaging solutions in the urology segment and other specialties with the acquisition of Blue Earth Diagnostics. Visit: www.braccoimaging.com.

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