PRESS RELEASE

The Lancet Publishes Results of Axumin® (Fluciclovine F 18) PET Imaging Study Demonstrating Improved Patient Outcomes in Patients with Recurrent Prostate Cancer

– Treatment informed by Axumin PET imaging significantly improved event-free-survival for men with recurrent prostate cancer at three and four years –

– Winship Cancer Institute of Emory University's EMPIRE-1 trial is first-of-its-kind randomized patient outcomes study of amino acid PET imaging in influencing a cancer control endpoint –

BURLINGTON, Mass. and OXFORD, UK, May 25, 2021 – Blue Earth Diagnostics, a Bracco company and recognized leader in the development and commercialization of innovative PET radiopharmaceuticals, is pleased to share news of the publication of a study from researchers at Winship Cancer Institute of Emory University (Winship) evaluating Axumin® (fluciclovine F 18) PET imaging in men with recurrent prostate cancer. The randomized, prospective study showed that Axumin-guided post-prostatectomy radiation therapy increased biochemical event-free survival rates in men with recurrent disease. Among 165 patients whose prostate cancer had returned following surgical removal of their prostate, 75.5% whose treatment integrated Axumin PET imaging were event-free after three years, compared to 63% for whom only conventional imaging techniques were used to plan treatment. The increased event-free survival rate persisted after four years of follow-up, at 75.5% vs. 51.2%, respectively. Provider-reported genitourinary or gastrointestinal side effects were similar between the two study groups. Axumin, a novel amino acid-based radiopharmaceutical, is FDA-approved for PET imaging in men with suspected prostate cancer recurrence based on elevated blood prostate specific antigen (PSA) levels following prior treatment.

The manuscript, "EMPIRE-1: Randomized Trial Comparing Conventional- vs Conventional plus Fluciclovine (18F) PET/CT Imaging-Guided Post-Prostatectomy Radiotherapy for Prostate Cancer," was published online in *The Lancet* on May 7, 2021 (DOI: https://doi.org/10.1016/S0140-6736(21)00581-X). The manuscript will also appear in an upcoming print issue. The EMPIRE-1 (Emory Molecular Prostate Imaging for Radiotherapy Enhancement) trial (NCT01666808) is the first randomized trial of men with recurrent prostate cancer to show that treatment based on advanced molecular imaging with ^{18}F-fluciclovine PET can improve event-free survival rates. The Phase 2/3 trial was led by Winship radiation oncologist and prostate cancer specialist, Ashesh B. Jani, MD, MSEE, FASTRO, and Winship nuclear medicine specialist David M. Schuster, MD, FACR.

"We are extremely pleased that these exciting results, from Emory University's independent study of how PET imaging with Axumin can influence radiation therapy treatment outcomes, have been made available to the physician community through publication in the well-respected medical journal, *The Lancet,"* said David Gauden, D. Phil., President of R&D and CSO of Blue Earth Diagnostics. "We sincerely congratulate the researchers on the design and execution of this important study. Axumin was invented at Emory to enable PET visualization of increased amino acid transport that occurs in prostate and other cancers. Blue Earth Diagnostics subsequently developed and advanced Axumin through U.S. and EU approvals for PET imaging of recurrent prostate cancer. Axumin PET imaging has informed healthcare decisions for more than 125,000 men with recurrent prostate cancer across the United States, where it

is available at 1,300 imaging centers and widely reimbursed. In Europe, Axumin availability and reimbursement continue to expand, with additional access anticipated this year. The commercial success of Axumin has set the stage for applying Blue Earth's proven expertise in developing and commercializing innovative radiopharmaceutical technology to new products and indications. We are committed to improving the lives of patients through innovative diagnostic solutions that empower the evolution of care for men with recurrent prostate cancer, and we look forward to helping even more patients in the future."

"The decision to offer post-prostatectomy radiation is complex, because conventional imaging can leave unanswered questions on the best approach for treatment planning," said co-principal investigator Ashesh B. Jani, MD, MSEE, FASTRO, Winship Cancer Institute of Emory University, Atlanta, Ga. "This research has found that integrating advanced PET imaging using ^{18}F-fluciclovine into the treatment planning process allows us to do a better job of selecting patients for radiation therapy, guiding radiation decisions and planning, and ultimately, keeping our patients' cancer under control. The group getting treatment guided by ^{18}F-fluciclovine PET had a 'cancer control rate' of 75.5% at both three and four years; the group receiving treatment guided by conventional imaging had a 'cancer control rate' of 63% at three years and 51.2% at four years."

"The question that we wanted to answer in this study was whether the treatment plan effect informed by ^{18}F-fluciclovine PET imaging had a positive effect in the lives of patients," said David M. Schuster, MD, FACR, Professor of Radiology and Imaging Sciences and Director of the Division of Nuclear Medicine and Molecular Imaging, Emory University. The EMPIRE-1 trial allowed us to determine whether using ^{18}F-fluciclovine PET imaging influences patient outcomes for the better, and the significant results confirm that it does."

Authors on the *The Lancet* manuscript were: Ashesh B. Jani, Eduard Schreibmann, Subir Goyal, Raghuveer Halkar, Bruce Hershatter, Peter J. Rossi, Joseph W. Shelton, Pretesh R. Patel, Karen M. Xu, Mark Goodman, Viraj Master, Shreyas S. Joshi, Omer Kucuk, Bradley Carthon, Mehmet A. Bilen, Sherrie Cooper, Bridget Fielder, Olayinka A. Abiodun-Ojo, Vishal R. Dhere, and David M. Schuster. All authors are affiliated with Winship Cancer Institute of Emory University, Atlanta, Georgia.

About the EMPIRE-1 trial

The EMPIRE-1 (Emory Molecular Prostate Imaging for Radiotherapy Enhancement) trial (NCT01666808) study was a single-center-open-label, Phase 2/3, randomized controlled trial. It enrolled 165 patients (median age 61 years; inter-quartile range 55-68 years) whose cancer recurred after having undergone prostatectomies, but who later showed abnormal PSA blood test scores, indicating that their cancer had returned. All patients underwent conventional imaging (bone scan, CT or MRI) for initial treatment planning. Patients were then randomized 1:1 into two groups: the first receiving radiation therapy based on the initial treatment plans; the second receiving ^{18}F-fluciclovine PET scans with treatment re-evaluated based on those findings. After three years, the study showed patients who were treated based on incorporating the ^{18}F-fluciclovine PET imaging results had a higher event*-free survival rate ($p=0.003$), which persisted after four years (75.5% in the ^{18}F-fluciclovine PET imaging arm, versus 51.2% in the conventional arm; $p<0.0001$). Provider-reported genitourinary or gastrointestinal side effects were similar between the two study groups.

*Events defined as biochemical or clinical recurrence or progression, or initiation of systemic therapy.

NOTE: This content is intended to provide information about Blue Earth Diagnostics' business in the United States and Europe. Approval status and product label for Axumin varies by country worldwide.

For U.S. Readers:

U.S. 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 U.S. Axumin prescribing information is available at:

https://www.axumin.com/prescribing-information.pdf.

For UK and European Readers:

Full European Axumin ▼ (fluciclovine (^{18}F)) Summary of Product Characteristics is available at:

https://www.ema.europa.eu/en/medicines/human/EPAR/axumin#product-information-section

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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