BLUE EARTH DIAGNOSTICS ANNOUNCES PUBLICATION OF READER TRAINING STUDY RESULTS FOR AXUMINTM (FLUCICLOVINE F 18) PET IMAGING OF MEN WITH RECURRENT PROSTATE CANCER

May 3, 2017

OXFORD, U.K. and BURLINGTON, Mass. – May 3, 2016 – Blue Earth Diagnostics, a molecular imaging diagnostics company, announced the peer-reviewed publication of results from the reader training component of Axumin Phase 3 registration data that evaluated the impact of reader training on the blinded, independent evaluation of Axumin (fluciclovine F 18) images. Axumin is a novel, FDA-approved molecular imaging agent indicated for use in positron emission tomography (PET) imaging in men with suspected prostate cancer recurrence based on elevated blood levels of prostate specific antigen (PSA) following prior treatment. Results of this study, based on PET/CT (computed tomography) images from the Axumin image database at Emory University, Atlanta, Ga., demonstrated that, with standardized Axumin reader training, previously naïve readers were able to achieve acceptable diagnostic performance and reproducibility when using Axumin PET/CT images to re-stage patients with biochemically recurrent prostate cancer.

The manuscript, "Reader training for the re-staging of biochemically recurrent prostate cancer using fluciclovine (^{18}F) PET/CT," was accepted by *The Journal of Nuclear Medicine* and is now available online: *J Nucl Med* 2017; doi: 10.2967/jnumed.116.188375. The manuscript will also appear in an upcoming print issue. Lead authors are M. Miller of Blue Earth Diagnostics, Oxford, UK; L. Kostakoglu of Icahn School of Medicine at Mount Sinai, New York, NY; D. Pryma, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pa. and J. Yu of Fox Chase Cancer Center, Philadelphia, Pa. Significant contributions to the reader training study were provided by the Society of Nuclear Medicine and Molecular Imaging's Clinical Trial Network and the American College of Radiology.

"This Phase 3 study demonstrated that reader training is effective in enabling physicians new to Axumin PET/CT image interpretation to replicate results from an expert center," said Jonathan Allis, D. Phil., CEO of Blue Earth Diagnostics Ltd. "Axumin use in the United States continues to expand from expert technical centers into general clinical use. In addition to this increasing U.S. commercial availability and access, Blue Earth Diagnostics Inc., in collaboration with the SNMMI's Nuclear Medicine Clinical Trial Group, continues to provide reader training in image acquisition and interpretation to new users of Axumin as part of our commitment to helping men with recurrent prostate cancer."

"Commonly used imaging techniques for the identification of suspected recurrent prostate cancer are limited in the information they provide, leaving physicians with difficult medical

challenges in defining appropriate care for their patients," said Lale Kostakoglu, MD, MPH, Professor of Radiology and Chief of Nuclear Medicine, Icahn School of Medicine at Mount Sinai, New York, NY. "This study demonstrated that Axumin reader training enabled overall consistent image interpretation at the patient level and for regional sites of recurrence. In my experience, PET/CT imaging with Axumin effectively detects and localizes recurrent disease, which can help guide my patient management decisions."

About the Axumin™ Phase 3 Reader Training Study

This Phase 3 study assessed the ability of readers without prior experience in reading Axumin PET/CT images ("naïve readers") to interpret images from men with biochemically recurrent prostate cancer with acceptable diagnostic performance and reproducibility. Primary objectives were to establish individual readers' diagnostic performance and the overall interpretation (2/3 reader concordance) compared to standard of truth data (histopathology (i.e., biopsy) and/or clinical follow-up) and to evaluate reproducibility of interpretation among the readers. Standardized image interpretation methodology was established in conjunction with the SNMMI Clinical Trials Network, with the blinded independent evaluation conducted at the American College of Radiology Clinical Research Center.

Axumin images and standard of truth data from 110 patients with biochemically recurrent prostate cancer were collected from Emory University, Atlanta, Ga. Three independent readers were trained using standardized interpretation methodology, who then evaluated Axumin images in a blinded manner. Analyses of 121 images were conducted at several levels: lesion; prostate region (prostate, including prostate bed and seminal vesicles) and extraprostatic (including all lymph nodes, bone or soft tissue metastases); and patient.

Results demonstrated that the overall ability of the readers to classify Axumin uptake as malignant at the lesion level had a Positive Predictive Value (PPV) of 71% (98/139). The PPV at the region level was 73% (53/73) for the prostate region and 92% (24/26) for the extraprostatic region. The PPV at the patient level was 79% (68/86). The Readers' PPV and Negative Predictive Value (NPV) were broadly consistent for the regions that were measureable, with each other and with the onsite read. Overall Sensitivity (SEN) at the patient level was 92% (68/74). The SEN at the region level was 91% (53/58) for the prostate region and 86% (24/28) for the extraprostatic region; and 64% at the lesion level. Importantly, readers in this study were able to identify areas of recurrent cancer on fluciclovine (18F) PET/CT images with comparable accuracy to fluciclovine-experienced readers who had access to histopathological findings and subject data, as reported in the literature (Bach-Gansmo T, et al. *J Urol* 2017;197:676-83).

Though interpretation errors can occur and clinical correlation is still recommended, the authors concluded that standardized interpretation methodology and a specific training program for evaluating Axumin images enables naïve readers to achieve acceptable

diagnostic performance and reproducibility when staging recurrent prostate cancer. Blue Earth Diagnostics provided financial support for the study.

For the latest information on Axumin image interpretation training, please contact Blue Earth Diagnostics, Inc.'s Medical Information Hotline at medinfo@blueearthdx.com or 1-855-AXUMIN1 (298-6461); Option 3 or visit SNMMI's Nuclear Medicine Clinical Trial Group: www.snmmi.org/research/index.aspx?navItemNumber=673

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 www.axumin.com.

About Axumin™ (fluciclovine F 18)

Axumin (fluciclovine F 18) injection is a novel product indicated for use in positron emission tomography (PET) imaging to identify suspected sites of prostate cancer recurrence in men. Recurrence of prostate cancer is suspected by an increase in prostate specific antigen (PSA) levels following prior treatment. PET imaging with Axumin may identify the location and extent of such recurrence. Axumin was developed to enable visualization of the increased amino acid transport that occurs in many cancers, including prostate cancer. It consists of a synthetic amino acid that is preferentially taken up by prostate cancer cells compared with surrounding normal tissues, and is labeled with the radioisotope F 18 for PET imaging. Fluciclovine F 18 was invented at Emory University in Atlanta, Ga., with much of the fundamental clinical development work carried out by physicians at Emory University's Department of Radiology and Imaging Sciences. Axumin was approved by the U.S. Food and Drug Administration in May 2016, following Priority Review, and is the first product commercialized by Blue Earth Diagnostics, which licensed the product from GE Healthcare. The molecule is being investigated by Blue Earth Diagnostics for other potential cancer indications, such as glioma.

About Prostate / Recurrent Prostate Cancer

Prostate cancer is the second leading cause of cancer death in men in the United States. While most primary prostate cancer can be successfully treated, the disease recurs in approximately one-third of patients. In some patients recurrent disease is detectable only by a rise in prostate specific antigen (PSA) levels, yet the location of the recurrence cannot consistently be located by conventional imaging, potentially impacting subsequent management of these patients.

About Blue Earth Diagnostics

Blue Earth Diagnostics is a molecular imaging diagnostics company focused on the development and commercialization of novel PET imaging agents 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 recognized experts in the clinical development and commercialization of innovative nuclear medicine products. The company's first approved and commercially available product is Axumin™ (fluciclovine F 18), a novel molecular imaging agent for use in PET imaging to detect and localize prostate cancer in men experiencing suspected biochemical recurrence. Blue Earth Diagnostics is funded by Syncona Limited, an investment company listed on the London Stock Exchange (LON: SYNC). For more information, visit www.blueearthdiagnostics.com.

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