PRESS RELEASE

For U.S audiences only

Blue Earth Diagnostics Highlights Clinical Utility of POSLUMA® (Flotufolastat F 18) PET and Post-scan Changes in Management in Patients with Suspected Recurrence of Prostate Cancer at ASCO GU

– Sub-analysis from Company's Phase 3 SPOTLIGHT trial examined impact of POSLUMA on treatment plans for recurrence after curative-intent primary therapy –

– Actionable information from POSLUMA imaging resulted in changes in management for 89% of patients with recurrent prostate cancer –

MONROE TOWNSHIP, N.J., and OXFORD, UK, January 25, 2024 – Blue Earth Diagnostics, a Bracco company and recognized leader in the development and commercialization of innovative positron emission tomography (PET) radiopharmaceuticals, today announced results from a sub-analysis of data from the Phase 3 SPOTLIGHT trial (NCT04186845) which investigated the use of POSLUMA® (flotufolastat F 18) PET in suspected biochemical recurrence of prostate cancer. The sub-analysis assessed the impact of POSLUMA on treatment plans for patients with recurrent prostate cancer after curative-intent primary therapy. POSLUMA® (flotufolastat F 18) injection (formerly referred to as ^{18}F-rhPSMA-7.3) is indicated for positron emission tomography (PET) of prostate-specific membrane antigen (PSMA) positive lesions in men with prostate cancer with suspected metastasis who are candidates for initial definitive therapy or with suspected recurrence based on elevated serum prostate-specific antigen (PSA) level.

Results highlights:

- Flotufolastat F 18 PET imaging was positive for recurrent prostate cancer in 84% (81/97) of patients in the sub-analysis.
- In 89% (86/97) of patients, management plans were changed following review of the flotufolastat F 18 PET scan results.
- 91% (78/86) of changes were considered major, defined as a change in the treatment modality.
- 75% (6/8) of patients whose plans were changed in favor of watchful waiting had a negative flotufolastat F 18 scan.
- All patients with management plans that were revised from salvage therapy to non-curative systemic therapy had distant/extrapelvic flotufolastat F 18-avid lesions.

"Recurrent prostate cancer presents challenges, and the ability to determine the extent and location of recurrent disease to inform appropriate clinical management is key for physicians and their patients, as up to 40% of patients who undergo radical prostatectomy, and up to 50% of patients who undergo radiation therapy will develop local or distant recurrences within 10 years," said Przemyslaw Twardowski, MD, Saint John's Cancer Institute at Providence Saint John's Health Center, Santa Monica, Calif., on behalf of the SPOTLIGHT Study Group. "The SPOTLIGHT study investigated the

diagnostic performance of POSLUMA PET imaging as a potential decision-making aid in assessing suspected biochemical recurrence of the disease. This sub-analysis further examined the impact of POSLUMA PET imaging on patients' management plans. Results showed that POSLUMA identified recurrence sites in the majority of patients, frequently resulting in major changes to previously planned management plans. Patient treatment based on visualization of POSLUMA-avid lesions has the potential to facilitate optimal targeting of recurrence sites and help patients avoid futile salvage therapy."

"We are very pleased to present these results to the oncology community at ASCO GU," said David E. Gauden, D.Phil., Chief Executive Officer of Blue Earth Diagnostics. "POSLUMA represents a new class of high-affinity PSMA-targeted radiopharmaceuticals based on novel radiohybrid technology, and provides physicians with clinically useful information based on its performance at low PSA levels, PSMA binding and low urinary bladder activity. Our product has been added to nationally recognized clinical oncology guidelines for prostate cancer, alongside and for all the same categories as the other currently FDA-approved PSMA PET radiopharmaceuticals. POSLUMA is labeled with the radioisotope fluorine-18 (^{18}F) to leverage high image quality and to enable broad, readily available geographic access for patients via the manufacturing and distribution network of our commercial U.S. manufacturer and distributor, PETNET Solutions Inc, A Siemens Healthineers Company."

The findings were discussed in a moderated poster presentation at the ASCO GU 2024 Genitourinary Cancers Symposium (ASCO GU) on January 25, 2024. "*Impact of ^{18}F-flotufolastat PET on management of patients with recurrent prostate cancer: Data from the SPOTLIGHT study,"* was presented by Przemyslaw Twardowski, MD, Saint John's Cancer Institute at Providence Saint John's Health Center, Santa Monica, Calif., on behalf of the SPOTLIGHT Study Group. Full session details are available in the ASCO GU online program here.

About the study

The sub-analysis of SPOTLIGHT data from the 389 patient study assessed the impact of flotufolastat F 18 on planned treatment after curative-intent primary therapy. The present analysis focused on patients who had a flotufolastat F 18 scan and sufficient data for management plan evaluation. Onsite investigators recorded patients' management plans before and after flotufolastat F 18 PET. Plans were then categorized as "no change," "major change,"" other change," "additional information required" or "intended plan not valid." A "major change" was defined as a change in treatment modality (e.g., salvage radiation to systemic therapy), while "other change" represented a change within a modality (e.g., modified radiation therapy field). All imaging data were then submitted for blinded image evaluation by 3 central readers.

- In total, 97 patients (median [range] PSA: 0.08 [0.09-134.6]] ng/mL) had an evaluable flotufolastat F 18 PET scan and sufficient data to evaluate management plan changes. Most patients, 86/97 (89%) had a change to their management plan post-scan. A "major change" was noted for 78 (80%) patients, while 8 (8.2%) had an "other change." Onsite imaging reads showed that both positive and negative flotufolastat F 18 scans influenced management planning. While 88% of revisions occurred after a positive scan, 75% of those whose management plans were revised to watchful waiting had negative scans. All patients with management plans revised from salvage therapy to non-curative systemic therapy had distant/extrapelvic flotufolastat F 18-avid lesions.
- No serious adverse reactions were attributed to flotufolastat F 18 in the SPOTLIGHT study. Overall, 16/389 (4.1%) patients had at least one treatment-emergent adverse event that was

considered possibly related/related to flotufolastat F 18. The most frequently reported events were: hypertension: 1.8% (n=7); diarrhea: 1.0% (n=4); injection site reaction: 0.5% (n=2), and headache: 0.5% (n=2).

About Radiohybrid Prostate-Specific Membrane Antigen (rhPSMA)

Radiohybrid Prostate-Specific Membrane Antigen (rhPSMA) compounds consist of a radiohybrid ("rh") Prostate-Specific Membrane Antigen-targeted receptor ligand which attaches to and is internalized by prostate cancer cells, and they may be radiolabeled with imaging isotopes for PET imaging, or with therapeutic isotopes for therapeutic use – providing the potential for creating a true theranostic technology. Radiohybrid technology and rhPSMA originated from the Technical University of Munich, Germany. Blue Earth Diagnostics acquired exclusive, worldwide rights to rhPSMA diagnostic imaging technology from Scintomics GmbH in 2018, and therapeutic rights in 2020, and sublicensed the therapeutic application to its sister company Blue Earth Therapeutics. Blue Earth Diagnostics received U.S. Food and Drug Administration approval for its radiohybrid PET diagnostic imaging product for use in prostate cancer in 2023. rhPSMA compounds for potential therapeutic use are investigational and have not received regulatory approval.

Indication and Important Safety Information About POSLUMA

INDICATION

POSLUMA® (flotufolastat F 18) injection is indicated for positron emission tomography (PET) of prostate-specific membrane antigen (PSMA) positive lesions in men with prostate cancer

- with suspected metastasis who are candidates for initial definitive therapy
- with suspected recurrence based on elevated serum prostate-specific antigen (PSA) level

IMPORTANT SAFETY INFORMATION

- Image interpretation errors can occur with POSLUMA PET. A negative image does not rule out the presence of prostate cancer and a positive image does not confirm the presence of prostate cancer. The performance of POSLUMA for imaging metastatic pelvic lymph nodes in patients prior to initial definitive therapy seems to be affected by serum PSA levels and risk grouping. The performance of POSLUMA for imaging patients with biochemical evidence of recurrence of prostate cancer seems to be affected by serum PSA levels. Flotufolastat F 18 uptake is not specific for prostate cancer and may occur in other types of cancer, in non-malignant processes, and in normal tissues. Clinical correlation, which may include histopathological evaluation, is recommended.
- Risk of Image Misinterpretation in Patients with Suspected Prostate Cancer Recurrence: The interpretation of POSLUMA PET may differ depending on imaging readers, particularly in the prostate/prostate bed region. Because of the associated risk of false positive interpretation, consider multidisciplinary consultation and histopathological confirmation when clinical decision-making hinges on flotufolastat F 18 uptake only in the prostate/prostate bed region or only on uptake interpreted as borderline.
- POSLUMA use contributes to a patient's overall long-term cumulative radiation exposure. Long-term cumulative radiation exposure is associated with an increased risk for cancer. Advise patients to hydrate before and after administration and to void frequently after administration. Ensure safe handling to minimize radiation exposure to the patient and health care providers.
- The adverse reactions reported in ≥0.4% of patients in clinical studies were diarrhea, blood pressure increase and injection site pain.

- Drug Interactions: androgen deprivation therapy (ADT) and other therapies targeting the androgen pathway, such as androgen receptor antagonists, may result in changes in uptake of flotufolastat F 18 in prostate cancer. The effect of these therapies on performance of POSLUMA PET has not been established.

To report suspected adverse reactions to POSLUMA, call 1-844-POSLUMA (1-844-767-5862) or contact FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Full POSLUMA prescribing information is available at www.posluma.com/prescribing-information.pdf.

About Blue Earth Diagnostics
Blue Earth Diagnostics, an indirect subsidiary of Bracco Imaging S.p.A., is a growing international molecular imaging company focused on delivering innovative, well-differentiated diagnostic solutions that inform patient care. Formed in 2014, the Company's success is driven by its management expertise and supported by a demonstrated track record of rapid development and commercialization of positron emission tomography (PET) radiopharmaceuticals. Blue Earth Diagnostics' expanding oncology portfolio encompasses a variety of disease states, including prostate cancer and neuro-oncology. Blue Earth Diagnostics is committed to the timely development and commercialization of precision radiopharmaceuticals for potential use in imaging and therapy. For more information, please 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 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. In 2021, Bracco Imaging established Blue Earth Therapeutics as a separate, cutting-edge biotechnology vehicle to develop radiopharmaceutical therapies. Visit: www.braccoimaging.com.

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