PRESS RELEASE

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Blue Earth Diagnostics Announces Results of Post-hoc Analysis Assessing Impact of Urinary Activity on Interpretation of POSLUMA® (Flotufolastat F 18) Injection PET/CT in Prostate Cancer

– Based on data from prospective Phase 3 LIGHTHOUSE and SPOTLIGHT studies in newly diagnosed and recurrent prostate cancer –

MONROE TOWNSHIP, NJ, and OXFORD, UK, June 26, 2023 – Blue Earth Diagnostics, a Bracco company and recognized leader in the development and commercialization of innovative PET radiopharmaceuticals, today announced results of a post-hoc analysis assessing the impact of urinary activity on the interpretation of POSLUMA® (flotufolastat F 18) injection (formerly known as ^{18}F-rhPSMA-7.3) PET/CT in prostate cancer. The analysis was based on data from Blue Earth Diagnostics' prospective Phase 3 LIGHTHOUSE and SPOTLIGHT studies that evaluated the diagnostic performance and safety of POSLUMA in newly diagnosed and recurrent prostate cancer. The majority read results from 3 blinded readers assessing 712 evaluable POSLUMA scans showed that urinary activity did not influence disease assessment for the majority (96%, 682/712) of patients and that halo artifacts, that can potentially inhibit image assessment, occurred very rarely (0.3%, 2/712). The results as reported expanded on the initial data from a single reader that were detailed in the abstract. Recently approved by the U.S. FDA, POSLUMA 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. The results were reported at the Society of Nuclear Medicine and Molecular Imaging (SNMMI) Annual Meeting, held June 24 – 27, in Chicago, Ill.

"The ability to gather actionable information from PSMA PET scans is important for physicians to make informed decisions about patient management for men with prostate cancer," Phillip Kuo, MD, Ph.D., Departments of Medical Imaging, Medicine, and Biomedical Engineering. "Activity in the urinary bladder area is a common feature of PSMA-PET radiopharmaceuticals. It can potentially obscure tumors and lymph nodes in the prostate region, which is the most common site of recurrence, and interfere with accurate image interpretation. The data presented here build on early clinical experience and suggest that, among this large dataset from two Phase 3 prospective trials, POSLUMA urinary activity is relatively low and rarely impacts disease assessment."

"We are pleased to share these results about our new FDA-approved product, POSLUMA, with the imaging community at SNMMI," said David E. Gauden, D.Phil., Chief Executive Officer of Blue Earth Diagnostics. "POSLUMA represents a new class of PSMA-targeted PET radiopharmaceuticals based on novel radiohybrid technology. It is engineered to advance clinical decision-making by providing beneficial information for treatment planning in men with prostate cancer, which can lead to changes in patient management. In preclinical and Phase 1 studies, POSLUMA demonstrated a high binding affinity

for PSMA, with low urinary bladder activity, thus providing the potential for enhanced image evaluation in the prostate and regions near the ureters for patients with prostate cancer. We conducted this post-hoc analysis of PET scans from the Phase 3 LIGHTHOUSE and SPOTLIGHT studies to further investigate these earlier findings. We believe that POSLUMA's diagnostic performance, high-affinity PSMA binding and low urinary activity characteristics make it a valuable diagnostic tool that is radiolabeled with ^{18}F for high image quality and readily available patient access."

Results presented at SNMMI were based on 712 evaluable POSLUMA scans (348 newly diagnosed patients and 364 patients with recurrent prostate cancer from LIGHTHOUSE and SPOTLIGHT, respectively). Of the 718 eligible scans, 6 were excluded on the basis of cystectomy, renal failure or presence of a urinary catheter. Findings included quantitative analyses of activity in the urinary bladder, based on maximum and mean standardized uptake values (SUV_{max} and SUV_{mean}, respectively). Qualitative analyses conducted by 3 blinded, independent PET readers examined the impact of any urinary activity on the ability to assess the prostate/prostate bed and pelvic/retroperitoneal lymph nodes using a 3-point scale.

The median bladder SUV_{max} and SUV_{mean} for POSLUMA were 17.1 and 12.5, respectively. For the qualitative metrics, by majority read, it was possible to distinguish urinary activity from disease uptake in 96% (682/712) of patients. Halo artifacts impacting assessment around the ureters and bladder were only observed in 0.3% (2/712) of patients.

There were several limitations to the study, including that it was not designed as a head-to-head comparison with other PSMA-PET radiopharmaceuticals and that any comparisons with data from other radiopharmaceuticals reported in the literature should be made with caution. Another limitation was that reader agreement was not formally tested. It should also be noted that, per the Important Safety Information for POSLUMA, the interpretation of POSLUMA PET in patients with suspected prostate cancer recurrence may differ depending on imaging readers, particularly in the prostate/prostate bed region.

Results of the presentation, "Post-hoc analysis of the LIGHTHOUSE and SPOTLIGHT studies to assess the impact of urinary activity on interpretation of ^{18}F-rhPSMA-7.3," were presented at SNMMI on June 27, 2023, by Phillip Kuo, MD, Ph.D., Departments of Medical Imaging, Medicine, and Biomedical Engineering, University of Arizona, Tucson, Ariz. Full session details and the abstract are available in the SNMMI 2023 online program here.

Blue Earth Diagnostics' LIGHTHOUSE Phase 3 clinical trial (NC04186819) was a prospective, Phase 3, multi-center, single-arm, imaging study conducted in the United States and Europe to evaluate the safety and diagnostic performance of POSLUMA PET in men with newly diagnosed prostate cancer. Results have been presented at the 23rd Annual Scientific Meeting in Urologic Oncology (SUO) in December 2022[1] and at ASCO GU in February 2023.[2] The SPOTLIGHT trial (NCT04186845) was a Phase 3, multi-center, single-arm imaging study conducted in the United States and Europe to evaluate the safety and diagnostic performance of POSLUMA PET imaging in men with suspected prostate cancer recurrence based on elevated PSA following prior therapy. Results from the SPOTLIGHT study were published online on April 26, 2023 in the *Journal of Urology*: DOI: 10.1097/JU.0000000000003493.[3]

About POSLUMA® (flotufolastat F 18)

POSLUMA® (flotufolastat F 18) injection (formerly referred to as ^{18}F-rhPSMA-7.3) is an optimized, targeted radiohybrid diagnostic imaging agent 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. Precision PET imaging with POSLUMA can help identify the location and extent of prostate cancer, providing clinically valuable information to guide patient management. POSLUMA represents a new class of high-affinity PSMA-targeted PET radiopharmaceuticals based on novel radiohybrid technology and is labeled with the radioisotope ^{18}F to provide readily available patient access and leverage the high image quality of ^{18}F-labeled PSMA PET imaging to facilitate effective detection of disease. POSLUMA was approved by the U.S. Food and Drug Administration in May 2023.

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.

References

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[2] Chapin BF on behalf of Koontz B, LIGHTHOUSE Study Group. "Detection of true positive M1 lesions by ^{18}F-rhPSMA-7.3 PET in newly diagnosed prostate cancer: Results from the phase 3 prospective LIGHTHOUSE study," 2023 ASCO Genitourinary Cancers Symposium (ASCO GU), ASCO GU 2023. San Francisco, Calif.: https://meetings.asco.org/abstracts-presentations/217100, 2023.

[3] Jani AB, Ravizzini GC, Gartrell BA, et al. Diagnostic Performance and Safety of ^{18}F-rhPSMA-7.3 PET in Men with Suspected Prostate Cancer Recurrence: Results from a Phase 3, Prospective, Multicenter Study (SPOTLIGHT), *The Journal of Urology®* (2023), doi:10.1097/JU.0000000000003493.

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