PRESS RELEASE:
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Blue Earth Therapeutics initiates Phase 2 Clinical Trial evaluating the efficacy and safety of Lutetium (^{177}Lu) rhPSMA-10.1 Injection in metastatic castrate resistant prostate cancer

- *(177Lu) rhPSMA-10.1 injection, engineered to improve delivery of radiation to cancer lesions, recently showed promising data in a phase 1 trial[1]*
- *The goal of the phase 2 study is to further assess this improved profile, together with testing of optimised dosing regimens*
- *First patients have received doses of (177Lu) rhPSMA-10.1 injection*
- *1st study results could be available as soon as H1 2026*

OXFORD, UK, 1 May 2025 – Blue Earth Therapeutics today announced further progress in development of its radiohybrid, lutetium-labelled, PSMA targeted, investigational radioligand therapy, with enrolment of the first two patients in a Phase 2 clinical trial. The primary measure of efficacy in the study will be the proportion of patients achieving a ≥50% reduction in PSA levels, as well as assessing radiographic progression-free survival and patient safety (NCT05413850).

The study is testing multiple dosing regimens that focus on delivering higher radiation doses when tumor burden is usually highest, at the beginning of treatment. This approach contrasts to pivotal studies of earlier radioligand therapies where the same dose was administered in every cycle[2] regardless of tumor burden. The study design aligns with the US FDA Project Optimus initiative where the goal is that drug developers optimize dosing early in a product's development to deliver the best possible benefit risk profile.

Loading doses will be delivered by either a) giving a higher dose in the first two treatment cycles, or b) shortening the time between administration of the first three doses to three weeks from the usual six weeks. The study is also designed to test the clinical benefit of administration of high total doses of administered radioactivity, up to 60GBq. The Phase 1 data confirmed a high ratio of uptake in tumor tissues vs. uptake in healthy tissues such as kidneys and salivary glands[1].

David Gauden DPhil, CEO of Blue Earth Therapeutics said, "This is an important step forward in the development of Lutetium (^{177}Lu) rhPSMA-10.1 injection and builds on the strong data seen in the Phase 1 clinical trial. Commencement of treatment of patients at full intended therapeutic dosing levels provides a great opportunity to assess the benefit this therapy can bring to patients. With up to 20 sites enrolling patients, we expect to see first results from the study early next year. We are grateful to the physicians and patients of Biogenix Molecular in Florida, who have just recruited the first patients for the study."

About metastatic prostate cancer
In 2025 it is estimated that there will be 50,055 new cases of metastatic prostate cancer in the United States (de novo diagnoses plus recurrence from earlier stage diagnoses).[3] Five-year survival for newly diagnosed metastatic prostate cancer is low, 36.6%.[4] While death rates from prostate cancer have declined over the past three decades[4], there is still considerable room to improve patient outcomes.

About Radiohybrid Prostate-Specific Membrane Antigen (rhPSMA)
rhPSMA compounds are referred to as radiohybrid ("rh"), as each molecule possesses four distinct domains. The first consists of a Prostate-Specific Membrane Antigen-targeted receptor ligand. It is attached to two labelling moieties which may be radiolabelled with diagnostic isotopes such as ^{18}F or ^{68}Ga for PET imaging, or with therapeutic isotopes such as ^{177}Lu or ^{225}Ac for radioligand therapy, all of which are joined together by a modifiable linker which can be used to modulate important pharmacokinetic characteristics. Radiohybrid PSMA offers the potential for targeted treatment for men with prostate cancer and originated at 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 has sublicensed the therapeutic application to its sister company Blue Earth Therapeutics.

About Blue Earth Therapeutics
Blue Earth Therapeutics is a clinical stage company dedicated to advancing next-generation targeted radiotherapeutics to treat patients who have cancer and has been incubated within the Bracco family of companies. Other investors joined with Bracco in a $76.5M Series A financing round in 2024. With proven management expertise across the spectrum of radiopharmaceutical and oncology drug development, as well as biotechnology start-up experience, the Company aims to innovate and improve upon current technologies and rapidly advance new targeted therapies for serious diseases. Blue Earth Therapeutics has an emerging pipeline initially focused on prostate cancer. For more information, please visit: https://www.blueearththerapeutics.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.

1. https://www.blueearththerapeutics.com/news
2. NCT04647526, NCT05204927, NCT04720157, NCT04689828
3. Gallichio L et al, JNCI J Natl Cancer Inst (2022) 114(11): djac158
4. SEER 22 database, https://seer.cancer.gov/statfacts/html/prost.html

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