PRESS RELEASE:
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Blue Earth Therapeutics Reports Key Results from Lutetium (^{177}*Lu*) rhPSMA-10.1 Injection Phase 1 Clinical Trial

- *Data from the Phase 1 trial in metastatic prostate cancer suggest potential for highly optimized pharmacokinetics*
- *Improved tumour: normal organ ratios may allow the delivery of significantly higher tumor absorbed radiation doses than first generation agents when dosing up to accepted normal organ dose limits*
- *Phase 2 trial design will seek to maximise radiation doses to tumor and extend the duration of therapy, with first metastatic castrate resistant prostate cancer patients expected to enroll this quarter*

OXFORD, UK, 13 March 2025 – Blue Earth Therapeutics today announced further promising developments for its radiohybrid lutetium labelled, PSMA targeted, investigational radioligand therapy. Radiation dosimetry and pharmacokinetic data from the 13 metastatic castrate resistant prostate cancer patients enrolled in the Phase 1 portion of a Phase 1/2 clinical trial (NCT05413850) of Lutetium (^{177}Lu) rhPSMA-10.1 Injection showed proportionately higher absorbed radiation doses in tumours than in critical healthy tissues such as the kidneys. The data compares favourably to published data on first-generation PSMA-targeted radioligand therapies.[1,2]

The Phase 1 data shows that Lutetium (^{177}Lu) rhPSMA-10.1 Injection has high ratios for absorbed radiation dose to tumours vs. dose to healthy tissues, with a measured mean tumour to salivary gland ratio of 73 and tumour to kidney ratio of 32. Median absorbed radiation dose to tumours defined by SPECT imaging was 8.9 Gy for each GBq of administered radioactivity. Mean absorbed radiation dose to the kidneys was 0.27 Gy/GBq; to salivary glands, 0.13Gy/GBq.

Underlying these results, the mean biological half-life in tumors for the Lutetium (^{177}Lu) rhPSMA-10.1 Injection was 338 hours. When paired with the 6.7-day physical half-life of ^{177}Lu, this gives an effective mean half-life of 91.4 hours. This allows delivery of radiation to tumors over many days: one and a half to twice the reported data for established agents in this class[1]. This prolonged retention of the drug in tumors without proportionate increases to retention in normal tissues helps to explain the positive radiation dosimetry data.

Following recent consultation with regulatory authorities, and sharing of the preliminary data, this now opens the way for the Phase 2 portion of the Phase 1/2 trial to test innovative dosing regimens, with the goal of optimising outcomes for patients. This Phase 2 portion of the study will explore the following dosing concepts:

1. Administration of significantly higher overall injected radioactivity in comparison to recent Phase 3 clinical trials of other PSMA-targeted radioligand therapies
2. Front loading of administered radioactivity in early cycles; and
3. Extending the duration of administration of radioactivity beyond 36 weeks to provide longer time on treatment.

In combination with the promising Phase 1 data for Lutetium (^{177}Lu) rhPSMA-10.1 Injection, these design factors should further support the aim of maximizing treatment response and therefore may enable delivery of better outcomes for patients. The Phase 2 portion of the study is expected to start this quarter.

David Gauden DPhil, CEO of Blue Earth Therapeutics said, "The Phase 1 data provides strong validation of the innovative approach taken on optimizing radioligand therapy by Blue Earth Therapeutics and the inventors of the rhPSMA technology. The relative ratios of tumour to healthy organ absorbed radiation doses are key metrics in establishing a better profile of the risks and potential benefits of radioligand therapies. With radioligand therapies, normal organ toxicity considerations gate the total amount of radioactivity that can be administered, so the more of the radioactivity that accumulates in tumours, the better. Our goal is to substantially increase the potential for prostate cancer patients to benefit compared to available radioligand therapy, and completion of this study moves us closer to making that goal a reality."

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 radiolabeled 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. 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. Schuchardt, Christiane, et al. Journal of Nuclear Medicine 63.8 (2022): 1199-1207
2. Ells, Zachary, et al. "Dosimetry of [177Lu] Lu-PSMA–Targeted Radiopharmaceutical Therapies in Patients with Prostate Cancer: A Comparative Systematic Review and Meta analysis." *Journal of Nuclear Medicine* (2024)
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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