

PRESS RELEASE:
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Blue Earth Therapeutics Presents Modelling Data Supporting Early Dose Intensification of Lutetium (¹⁷⁷Lu) rhPSMA-10.1 Injection in mCRPC

- *Modelling of front-loading administered radioactivity in PSMA targeted radioligand therapy (RLT) improves cumulative tumour-absorbed radiation dose compared to a flat dosing regimen, without a proportional increase in normal organ-absorbed radiation dose or in total administered radioactivity.*
- *Front-loaded dosing starting with 10GBq administered radioactivity raised tumour-absorbed radiation doses by 15% vs. an equivalent amount of total radioactivity in a flat dosing regimen.*
- *With 14.8GBq as the front-loaded dose, tumour-absorbed radiation dose increased by 34% vs. the flat dosing regimen, again with equivalent administered radioactivity.*
- *Front-loaded regimens are being evaluated for clinical efficacy and safety in a Phase 2 trial.*

Oxford, UK – 7 October 2025 – Blue Earth Therapeutics today announced new modelling results demonstrating that front-loaded dosing of its radiohybrid lutetium labelled, PSMA targeted, investigational radioligand therapy Lutetium (¹⁷⁷Lu) rhPSMA-10.1 Injection may increase cumulative tumour absorbed radiation dose without a proportional increase in normal organ exposure or total administered radioactivity. These findings are being presented at the European Association of Nuclear Medicine (EANM) Annual Meeting (poster EPS-187) and have been used to shape the design of the Phase 2 portion of the Phase 1/2 clinical trial (NCT05413850). The model was built from patient data from the Phase 1 portion of the trial.

In the Phase 1 study, tumor absorbed radiation doses in cycles 2 and 3 declined by 37% and 56% respectively from cycle 1¹. In contrast, healthy organ-absorbed doses remain broadly the same across cycles. In the model, maximum cumulative administered radioactivity was defined by the current limit of 23 Gy absorbed dose to kidneys. With the Phase 1 trial showing 0.30 Gy/GBq absorbed dose to the kidneys, administration of up to 60GBq or more was possible.

The model assessed three dosing scenarios, all with dosing at six-weekly intervals:

1. 10 GBq in cycles 1 and 2, followed by five cycles of 7.4 GBq
2. 14.8 GBq in cycles 1 and 2, followed by four cycles of 7.4 GBq
3. 7.4 GBq in each of cycles 1-8 (flat dosing)

The model extrapolated the reductions in tumour-absorbed radiation doses across each of cycles 4-8 using data available from cycles 1-3 and predicted the cumulative tumour absorbed radiation dose for each dosing scenario. The results showed that the front-loaded regimens

both increase tumour-absorbed radiation dose; by 15% for regimen #1 and by 34% for regimen #2 vs. a flat dosing regimen (#3).

Commenting on the results, Dr Dan Stevens, Blue Earth Therapeutics' Chief Medical Officer, said, "There is increasing interest in exploring alternative dosing schedules for radiopharmaceutical therapies to try and optimise the potential for clinical benefit. We are taking observed data from our Phase 1 and attempting to apply this scientifically in testing different front-loading approaches in our ongoing Phase 2 study. The data collected should allow us to assess the potential benefit and any risks."

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).² Five-year survival for newly diagnosed metastatic prostate cancer is low, 36.6%.³ While death rates from prostate cancer have declined over the past three decades³, 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 ¹⁸F or ⁶⁸Ga for PET imaging, or with therapeutic isotopes such as ¹⁷⁷Lu or ²²⁵Ac 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. Nagarajah, J., Kim, H., Nordquist, L. et al. Organ and tumour dosimetry of ¹⁷⁷Lu-rhPSMA-10.1, a novel PSMA-targeted therapy: results from a Phase I trial. *Eur J Nucl Med Mol Imaging* (2025)
2. Gallichio L et al, *JNCI J Natl Cancer Inst* (2022) 114(11): djac158
3. SEER 22 database, <https://seer.cancer.gov/statfacts/html/prost.html>

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