



PORTAGE BIOTECH INC.

NEWS RELEASE

Portage Biotech Highlights First Patient Dosed in IMP-MEL Study of PORT-2 for the Treatment of Melanoma and Non-Small Cell Lung Cancer (NSCLC)

- *Novel iNKT agonist leads to a broad reprogramming of the innate and adaptive immune system to target cancer*
- *PORT-2 has the potential to re-sensitize checkpoint-resistant tumors to treatment with PD-1 antibodies*

Westport, Conn. – (August 5, 2021) – Portage Biotech Inc., (NASDAQ: PRTG) (“Portage” or the “Company”) a clinical-stage immuno-oncology company focused on the development of therapies targeting cancer treatment resistance, today announced that the first patient has been dosed in the Oxford-led IMP-MEL study, a Phase 1/2, open-label, dose-escalation and randomized expansion clinical trial assessing the safety, tolerability and efficacy of PORT-2, a liposome formulation of the invariant natural killer T-cell (iNKT) agonist IMM60 developed for the treatment of solid tumors.

Preclinical data for PORT-2 demonstrated good tolerability and a strong cancer-specific B- and T-cell response. It also showed a robust innate and adaptive immune response and an increase in expression of PD-L1 on cancer cells. Combining PORT-2 with checkpoint inhibitors led to increased immune activation and PD-L1 expression, suggesting rationale for enhanced activity of the combination treatment.

“PORT-2 offers a novel, targeted approach to address a variety of today’s most common cancers, many of which are often elusive or resistant to treatment. Preclinical data show that our iNKT agonist can stimulate a broad response from both the innate and adaptive immune systems, helping the body recognize and attack these cancers,” said Dr. Ian Walters, chief executive officer of Portage Biotech. “This first-in-human trial features a robust design with a multi-arm comparison against standard of care therapies currently used in the clinic, which we believe has the potential to accelerate our research as we evaluate the effectiveness of PORT-2 both as a monotherapy and in combination with PD-1 checkpoint inhibitors.

The IMP-MEL study is expected to enroll 100 patients at Oxford and other centers and will evaluate PORT-2 both as a monotherapy and in combination with approved PD-1 inhibitor Keytruda in the treatment of Melanoma and Non-Small Cell Lung Cancer (NSCLC).

“Checkpoint inhibitor therapies have enormous opportunity in the treatment of solid tumors, but unfortunately, many cancers develop a resistance to these therapies leaving many patients without adequate treatment options,” said Mark Middleton, Departmental Head of Oncology and Professor of Experimental Medicine at the University of Oxford. “We’re constantly seeking new therapies that are capable of addressing resistance and enabling a durable response in patients with cancer. Should PORT-2 prove successful, this novel iNKT agonist therapy could potentially

re-sensitize patients to checkpoint inhibitor treatment and could activate that durable immune response. It's a very exciting new avenue for oncology research.”

The IMP-MEL study is part of a comprehensive clinical development plan to evaluate Portage's iNKT agonist therapies, PORT-2 and PORT-3. PORT-3, which is a nanoparticle co-formulation of IMM60 and a NY-ESO-1 peptide antigen, is also currently being evaluated in a Phase 1 clinical trial initiated in April 2021 at Radboud University, Netherlands.

The IMP-MEL study is supported by the NIHR Biomedical Research Centre. The trial is actively recruiting at the University of Oxford, United Kingdom. For more information, please visit <https://www.isrctn.com> #ISRCTN80472712

About iNKT agonists PORT-2 and PORT-3

PORT-2 and PORT-3 contain small molecule agonists (IMM60) of invariant natural killer T-cells (iNKT cells) developed by the University of Oxford, which play an important role in anti-tumor immune responses. iNKT cells are a distinct class of T lymphocytes and recognize lipid antigens on the surface of the tumor. Our synthetic iNKT agonists are designed to optimally engage the T-cell receptor on the iNKT and facilitate its binding to dendritic cells, resulting in the secretion of a large amount of pro-inflammatory cytokines. This leads to the activation and expansion of important immune system components and primes and boosts an adaptive immune attack against cancer. We see that monotherapy treatment with iNKT agonists shows a heightened immune response and better cancer control in animal models that are resistant to PD-1 antibody treatment. Combination therapy with PD-1 antibodies is synergistic with iNKT agonists and restores sensitivity to PD-1 blockade. While treatment with iNKT agonists alone shows promising preclinical activity against cancer, data suggests that when an iNKT agonist is co-packaged with tumor-specific antigens, potency is increased by up to 5x. PORT-2 is a liposomal formulation of our IMM60 iNKT agonist while PORT-3 is a co-formulation of our IMM60 iNKT agonist with an NY-ESO-1 peptide vaccine, co-packaged into a nanoparticle.

About Portage Biotech Inc.

Portage is a clinical-stage immuno-oncology company advancing first-in-class therapies that target known checkpoint resistance pathways to improve long-term treatment response and quality of life in patients with evasive cancers. The Company's access to next-generation technologies coupled with a deep understanding of biological mechanisms enables the identification of the most promising clinical therapies and product development strategies that accelerate these medicines through the translational pipeline. Portage's portfolio consists of five diverse platforms, leveraging delivery by intratumorals, nanoparticles, liposomes, aptamers and virus-like particles. Within these five platforms, Portage has 10 products currently in development with multiple clinical readouts expected over the next 12-24 months. For more information, please visit www.portagebiotech.com, follow us on Twitter at [@PortageBiotech](https://twitter.com/PortageBiotech) or find us on LinkedIn at [Portage Biotech Inc.](https://www.linkedin.com/company/portage-biotech)

Forward-Looking Statements

This news release contains statements about the Company's information that are forward-looking in nature and, as a result, are subject to certain risks and uncertainties. Although the Company believes that the expectations reflected in these forward-looking statements are reasonable,

undue reliance should not be placed on them as actual results may differ materially from the forward-looking statements. The forward-looking statements contained in this news release are made as of the date hereof, and the Company undertakes no obligation to update publicly or revise any forward-looking statements or information, except as required by law.

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