NEOPHORE
DYNAMIC NEOANTIGEN EVOLUTION

NeoPhore Scientific Founders Publish Breakthrough Immuno-oncology Discoveries in Nature

Collaboration by company and founders will offer further insights into DNA repair and cancer immunity

29th November 2017, Cambridge, UK – The internationally recognised scientific journal Nature has published innovative cancer research by NeoPhore Ltd founders Professor Alberto Bardelli and Giovanni Germano PhD at the University of Torino, revealing findings that further establish and validate NeoPhore's distinctive therapeutic concept of creating first-in-class small molecule drugs to stimulate the immune system and attack cancer in a fundamental and disruptive way. The paper is entitled "*Inactivation of DNA repair triggers neoantigen generation and impairs tumour growth*" and can be found here: http://dx.doi.org/10.1038/nature24673

Clinical and now lab data suggest that many cancers with defective DNA repair appear to be highly sensitive to immune surveillance, including when the immune system is modified with agents that disrupt immune "checkpoints". The Nature paper establishes a simple, yet paradoxical, principle that NeoPhore aims to exploit for cancer therapy - inhibition of the body's DNA damage mismatch repair machinery can be exploited to continuously stimulate the creation of new cancer neoantigens in tumours, which in turn triggers a broad and effective immune response to disease. This new therapeutic approach, which aims to spark cancer immunity, could be applied to the majority of patients whose 'cold' tumours do not exhibit high natural levels of tumour antigens. While checkpoint and other cancer immunity therapies currently work well in certain mutationally 'hot' cancers (such as melanoma), NeoPhore's approach could expand use of these therapeutics to much larger patient populations.

NeoPhore co-founder Professor Alberto Bardelli, said: "*Our results suggest that inactivation of DNA mismatch repair causes a dynamic hyper-mutation status that increases tumour neoantigens, which in turn, triggers immune surveillance that can be further enhanced by immune-modulators such as checkpoint inhibitors. Overall, these data indicate a potential way for converting immune-refractory patients into sensitive cases."*

NeoPhore co-founder Dr Giovanni Germano, said: "*We started this project based on striking results obtained by immune therapies in mismatch repair deficient tumours, and wondered if we could develop preclinical models to better understand the mechanistic bases of those unprecedented clinical results. We were excited to observe for the first time that evoking dynamic neoantigen profiles triggered immune-surveillance in lab studies. In light of our findings, we believe blocking mismatch repair is an attractive therapeutic mechanism, and*

we are continuing research to further prove the genetics and pharmacology behind this key phenomenon."

NeoPhore, a spin-out from PhoreMost Ltd backed by Sixth Element Capital, today also announces its collaboration with the founders Professor Bardelli and Dr Germano at the University of Torino to develop first-in-class therapies to the unique targets arising from their research.

NeoPhore's drugs are designed to revive sensitivity and create lasting efficacy in non-immunogenic and immunogenic cancer types, particularly in combination with immune checkpoint drugs. Their mechanism and activity is differentiated from many competing strategies for combination immune-oncology therapy: NeoPhore's drugs are first-in-class inhibitors of mismatch DNA-repair, which clinical, genetic and laboratory evidence suggest is a fundamental approach to increase cancer immunity.

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For further information:

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NOTES TO EDITORS

NeoPhore Ltd

NeoPhore, based in Cambridge, UK is focused on the discovery and development of novel small molecule therapies to treat cancer through stimulation of the immune system. Cancer neoantigens are known to stimulate the immune system and potentially be a weak spot in a tumour cell's defence mechanisms. The Company's approach targets genetic mechanisms that both clinical and lab studies suggest will promote neoantigen creation and diversity across numerous cancers. Using these insights, the Company aims to generate next-generation immuno-oncology therapeutics to improve clinical outcomes for cancer patients. NeoPhore was spun-out of PhoreMost Ltd and is backed by Sixth Element Capital LLP, a UK based fund manager established to manage investments for the £70 million CRT Pioneer Fund.