

C4X Discovery Holdings plc

(“C4XD”, “C4X Discovery” or the “Company”)

C4XD and Horizon Discovery enter exclusive partnership to develop next-generation synthetic lethality targets in oncology identified by Horizon’s CRISPR-Cas9 technology

17 December 2018 – C4X Discovery Holdings plc (AIM: C4XD), a pioneering drug discovery company, today announces that it has entered into an exclusive target discovery partnership with Horizon Discovery Group plc (“Horizon”, AIM: HZD), a global leader in the application of gene editing and gene modulation technologies. The partnership aims to validate novel synthetic lethal oncology targets that have been identified by Horizon’s cutting-edge CRISPR-Cas9 technology leading to the generation of potential new drugs for patients with limited effective treatments such as colorectal and lung cancer.

C4XD aims to apply its proprietary 4D shape-based chemistry technology (Conformetrix) to discover drug candidates directed against these high value, novel, synthetic lethality targets and out-license them to clinical development partners. This discovery partnership bolsters C4XD’s oncology pipeline, a high priority therapeutic area for the company.

The therapeutic concept of harnessing synthetic lethality in cancer with tumour-specific mutations has been demonstrated with the recent approval of the poly(ADP-ribose) polymerase (PARP) inhibitors Lynparza® Zejula® and Rubraca®. These drugs are effective in indications that are poorly served by immunotherapy drugs, such as checkpoint inhibitors, and have become an established treatment in ovarian cancer. They work by targeting a specific DNA repair pathway that cancer cells, with mutations such as BRCA, become over-reliant on. Inhibiting this critical DNA repair pathway causes the tumour cells to self-destruct, resulting in the terminology ‘synthetic lethality’. The pharmaceutical industry is now rushing to fill its clinical pipelines with investigational drugs, identified by empirical research, that might produce similar efficacy in cancers where PARP inhibitors are not effective.

However, recent advancements in the gene-editing tool, CRISPR-Cas9, has enabled systematic ‘functional genomic’ screening to identify novel synthetic lethal genes in cancer cells with specific mutations. Horizon has utilised its target discovery platform to conduct high quality CRISPR gene knock-out studies across multiple cancer cell lines, screening around ~3000 genes suitable as the basis for small molecule drug targets. This cutting-edge approach has identified a shortlist of ~20 novel, high value synthetic lethal genes following a secondary screen to further validate them as targets. The partnership has been established to complete the target validation package for these novel targets, leading to the initiation of drug discovery programmes by C4XD should it exercise its options on a target-by-target basis. C4XD will provide the funding for the work plan and Horizon will receive a share of all future revenues C4XD receives should any drug discovery programmes emerging from the partnership be out-licensed for clinical development.

Dr Craig Fox, Chief Scientific Officer of C4XD, said: *“PARP inhibitors are transforming the treatment of ovarian cancer, particularly in patients with BRCA mutations and so identifying the next generation of synthetic lethality drug targets is a key priority to develop new therapies for cancers patients who are not responsive to current treatments. This partnership with Horizon gives C4XD access to a comprehensive proprietary CRISPR screening dataset that has selected the most promising novel drug targets in colon and lung cancer. We look forward to working with the highly experienced team at Horizon to complete the target validation package for these novel genes and initiate drug discovery programmes to generate high value pre-clinical licensable assets for partnering.”*

Dr Jon Moore, Horizon's Chief Scientific Officer added: *"Drugging the cancer genome now requires new synthetic lethal therapies that can exploit the vulnerabilities in patient's tumours that are created by mutations in undruggable cancer driver genes. Horizon's internal research program has used powerful CRISPR technology to open a new window into how cancer cells are wired and has identified a cohort of novel targets. We are delighted to have secured this collaboration with C4X Discovery, which applies a powerful drug discovery engine to the first-in-class opportunities for transformational medicines represented by the targets Horizon has found and allows Horizon to share in the upside."*

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About C4X Discovery

C4X Discovery aims to become the world's most productive drug discovery engine by exploiting cutting edge technologies to design and create best-in-class small-molecule candidates targeting a range of high value therapeutic areas. The company's goal is to drive returns through early-stage revenue-generating deals with the pharmaceutical industry.

C4X Discovery has a state-of-the-art suite of proprietary technologies across the drug discovery process. The company's innovative DNA-based target identification platform (Taxonomy3[®]) utilises human genetic datasets to identify novel patient-specific targets leading to greater discovery

productivity and increased probability of clinical success. This is complemented by C4XD's novel drug design platform which comprises two innovative chemistry technologies, Conformetrix and Molplex, that combine 4D molecular shape analyses (based on experimental data) with best-in-class computational chemistry. This provides new and unprecedented insight into the behaviour of drug molecules, enabling the production of potent selective compounds faster and more cost effectively than the industry standard.

C4X Discovery is advancing its in-house pipeline that is primarily focused on the high value therapeutic areas of inflammation, neurodegeneration and cancer (including immuno-oncology) with a number of new drug candidates identified and further progress made towards the pre-clinical licensing discussions. In selecting new targets and executing new drug discovery programmes, C4X Discovery focuses on high-value disease areas that are the subject of significant licensing activity and will continue to also maximise value from opportunistic areas such as addiction and diabetes. The Company recently signed a licensing agreement with Indivior for a pre-clinical addiction programme worth up to \$294 million.

The Company was founded as a spin-out from the University of Manchester. It has a highly experienced management team and Board who have delivered significant value creation within the healthcare sector historically and have enabled C4XD to reach multiple value inflexion points since IPO. For additional information please go to: www.c4xdiscovery.com

About Horizon Discovery Group plc www.horizondiscovery.com

Horizon Discovery Group plc (LSE: HZD) ("Horizon") is a world leader in gene editing and gene modulation technologies. Horizon designs and engineers cells using its translational genomics platform, a highly precise and flexible suite of DNA editing tools (rAAV, ZFN, CRISPR and Transposon) and, following the acquisition of Dharmacon, Inc., its functional genomics platform comprising gene knockdown (RNAi) and gene expression (cDNA, ORF) tools, for research and clinical applications that advance human health. Horizon's platforms and capabilities enable researchers to alter almost any gene or modulate its function in human or mammalian cell lines.

Horizon offers an extensive range of catalogue products and related research services to support a greater understanding of the function of genes across all species and the genetic drivers of human disease and the development of personalized molecular, cell and gene therapies. These have been adopted by over 10,000 academic, drug discovery, drug manufacturing and clinical diagnostics customers around the globe, as well as in the Company's own R&D pipeline.

Horizon is headquartered in Cambridge, UK, and is listed on the London Stock Exchange's AIM market under the ticker "HZD."