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Scientists identify FLIP Inhibitors for cancer treatment

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Queen's University Belfast and Domainex are pleased to announce that their joint project team has successfully identified novel first-in-class small molecule inhibitors of the anti-apoptotic protein FLIP. The team has generated data suggesting multiple therapeutic opportunities for a FLIP inhibitor in both the single agent and combination settings and is now seeking a commercial partner for further development of the novel inhibitors.

The team is presenting the FLIP inhibitor programme at the AACR annual meeting in Atlanta on 31 March 2019 (New Molecular Targets poster session, poster 382 /14). The poster showcases the on-target effects of the inhibitors, their drug-like properties, their potency against B Cell Lymphomas, triple negative breast cancer and *KRAS* and *EGFR* mutant non-small cell lung cancer, and their potential for combination with chemotherapy, immune oncology agents and EGFR-targeted therapeutics.

The next phase of the programme will comprise selection of a pre-clinical development candidate and completion of pre-clinical activities. Profs Dan Longley (Biology lead) and Tim Harrison (Med Chem lead) are attending the AACR meeting and will be actively engaging in discussions with potential partners at the meeting.

This FLIP programme has been funded by the Wellcome Trust and has focussed on the identification and optimisation of novel first-in-class small molecule FLIP-FADD protein-protein interaction inhibitors. FLIP is a non-redundant inhibitor of Caspase 8 and functional FLIP allows tumour cells to evade cell death and promotes tumour growth and therapy resistance. The novel FLIP inhibitors activate Caspase 8 and have shown efficacy in a number of pre-clinical models including clinically challenging *KRAS* and *EGFR* mutant non-small cell lung cancer.