University College London researcher Dr Martin Pule created spin-out company Autolus Ltd in 2014 to commercialise his innovative research to ‘programme’ immune cells to specifically target and destroy cancer cells. Autolus raised £30M in their first, or ‘series A’, funding round; the largest series A investment raised by a European biotechnology company. A subsequent round raised an additional £40M.

Pule, Senior Lecturer at the UCL Cancer Institute, is now running a clinical trial to test the efficacy of engineered T-cells in treating acute lymphoblastic leukaemia and is planning a second, focussed on neuroblastoma.

Pule’s synthetic biology research into logic-gated T-cells was supported by BBSRC

Selective and non-toxic treatments
“I have no doubt that in 20 years’ time highly engineered immune cells will be the mainstay of cancer therapy,” says Pule. “This will benefit patients since the scope of engineering possible will allow development of highly selective non-toxic treatments.”

Engineered T-cells offer a potent and targeted approach to treating cancer. T-cells form part of our immune systems, playing a variety of roles, including seeking out and destroying cells infected with viruses. To do so, the T-cells possess receptors on their surface, which recognise specific ‘antigens’ on their targets. By engineering T-cells to carry artificially-constructed proteins called CARs (chimeric antigen receptors), researchers can use T-cells to find and destroy cancerous cells.

The approach does have limitations, however. For the CAR T-cells to be effective, and to avoid the toxic side effects that occur if T-cells target healthy non-cancerous cells, the researchers need to identify a single unique antigen on
Autolus Ltd - Engineered immune cells for cancer therapy

The surface of the cancer cell, which the T-cells can then target. While a few types of cancer possess such a marker, the majority do not. To be effective against most cancers, T-cells would instead need to recognise a specific pattern of antigens (e.g. only targeting cells where antigens A and B are both present, or which possess antigen A but not B).

A logical solution
Over a decade of work, supported by funding from BBSRC and MRC, enabled Pule and his team to develop and test a method for generating CAR T-cells that could be programmed using basic logic operations more commonly found in computing and electronics. The research builds on Pule’s previous experience of engineering T-cells, for instance to express a ‘suicide’ gene that can be used to destroy the engineered cells should they cause a problem.

Using the logic-based approach, Pule’s CAR logic-gated T-cells can recognise cancer cells that could not be targeted using other methods. Recognising the need to protect his ideas before they could be developed commercially, Pule worked with UCL Business (UCLB), which manages technology development and commercialisation for UCL, to develop a suite of patents.

Once he had developed and protected the basis of the technology, Pule sought further investment to develop it for clinical application. “I recognized that the only way to secure sufficient funding which would allow rapid technological development was through a spin-off company. I spent a year pitching to many different VC funds which finally led to the establishment of Autolus,” says Pule.

Working with UCLB, and with funding from a BBSRC Sparking Impact award, Pule founded Autolus in September 2014 and raised £30M investment from venture capital firm Syncona Partners. This was the largest ever ‘series A’ financing round for a European biotechnology company.

A subsequent investment round in early 2016 enabled Autolus to raise a further £40M from Woodford Investment Management LLP and Perceptive Bioscience Investments Ltd2.

Universal T-cells
Pule is also collaborating with French biopharmaceuticals company Cellectis3 to develop a way to make the CAR logic-gated T-cells work in every patient. To avoid a patient’s immune system rejecting the therapy, the T-cells need to be extracted from the patient, engineered, and given back to that patient. This limits the broader application of the technology.

Cellectis has developed a genome editing technology called TALEN. Using TALEN, Pule plans to create generic T-cells that will not attack the patient’s own healthy cells and which are not attacked by the patient’s own immune system. This would enable companies to produce ‘universal’ CAR T-cells that could be used to treat any patient that required them.

IMPACT SUMMARY
UCL researchers have developed a novel method to programme engineered immune T-cells with simple ‘logic gates’ that enable them to target and destroy specific cancer cells. The logic gates allow the cells to be directed against cancers that cannot be targeted using other therapeutic approaches.

To develop the technology, the researchers established spin-out company Autolus and sought venture capital funding. Their first funding round, known as ‘series A’ funding, raised £30M investment, the largest series A funding ever raised by a European biotechnology company.

A second funding round in 2016 raised a further £40M.

A £412K BBSRC responsive mode grant supported the underpinning research, and a BBSRC Sparking Impact award enabled the researchers to pitch their ideas to venture capitalist investors.

REFERENCES
1 BB/J018899/1 – Synthetic Biologic Application to T-cell Engineering.
2 [Reference/webpage no longer available – January 2017]