Promising Results From Novel 'Dual-Cell' Therapy Pancreatic Cancer Study

Highlights

- **First anti-cancer results from novel preclinical 'dual-cell' therapy drug published**
- **'Dual cell' effect refers to killing both cancer cells and their barrier cells to achieve a more profound anti-cancer treatment outcome**
- **Tumour cells decreased by up to 85% and barrier cells reduced by up to 87%**
- **Study conducted using cutting-edge model developed by UNSW Sydney**
- **Global need for pancreatic cancer treatments predicted to be a US$4 billion market**

Sydney 14 September 2022: Innovative biotech company **Noxopharm Limited (ASX:NOX)** is pleased to announce encouraging new preclinical data from its long-term collaboration with UNSW Sydney.

The results were reported this week at the prestigious American Association of Cancer Research (AACR) Special Conference on Pancreatic Cancer taking place in Boston, as a poster and video presentation.

The study involves Noxopharm's novel preclinical drug that attacks pancreatic cancer in a different and innovative way. Pancreatic cancer is especially difficult to treat because the tumours are surrounded by a dense barrier of cells that protects them from anti-cancer drugs, as well as from the body's immune system. These barrier cells also help the cancer spread to the rest of the body, adding to the challenge of developing treatments.

Noxopharm has conducted an 18-month study as part of an ongoing collaboration with UNSW to test a new drug developed by the company, known as CRO-67.

The major findings were that CRO-67 killed tumour cells as well as barrier cells in samples taken from six patients who had their tumours surgically removed.

Key Results

Patient samples were treated with CRO-67 at doses of 10, 20 and 50 micrograms per millilitre and a dose-response relationship was found, such that greater amounts of drug resulted in highly statistically significant effects.

At the highest dose level and when compared to untreated controls:

- The number of tumour cells decreased by 85% ($p < 0.0002$)
- The number of barrier cells decreased by 87% ($p < 0.0001$)
- Cell replication decreased by 73% ($p < 0.0001$)
- Overall cell death increased 6.2-fold ($p < 0.0001$)

Further details can be found in the appendix to this announcement.

Images: Fluorescence study showing living cells in blue and dead cells in green

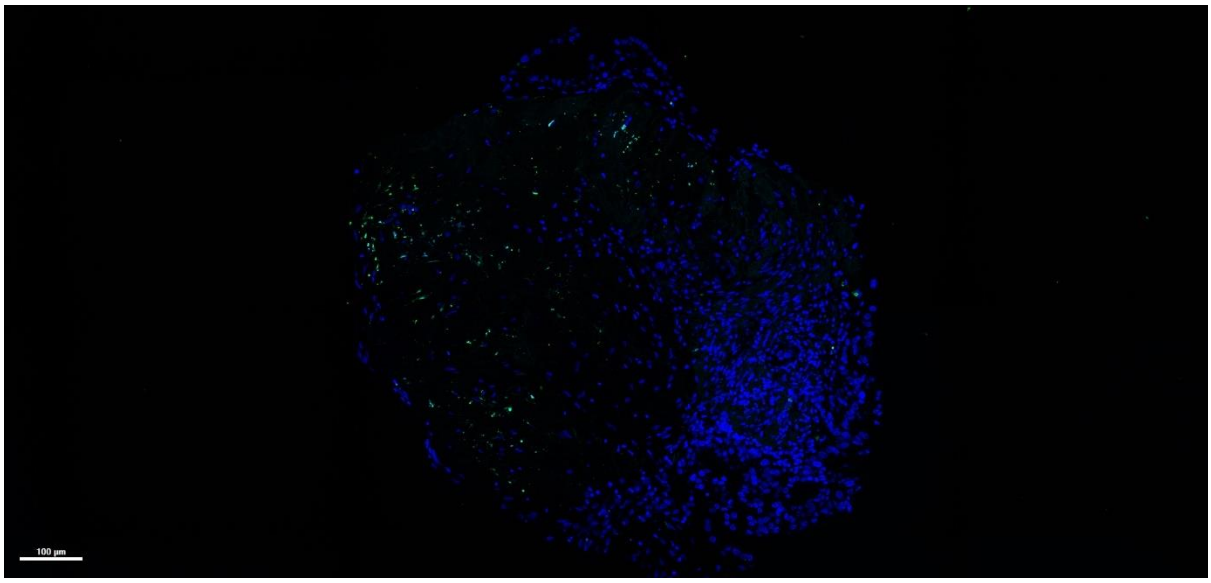

Image 1 – A representative tumour sample with no treatment. There are high numbers of living cells (blue) in the cancer tissue sample after 12 days without treatment.

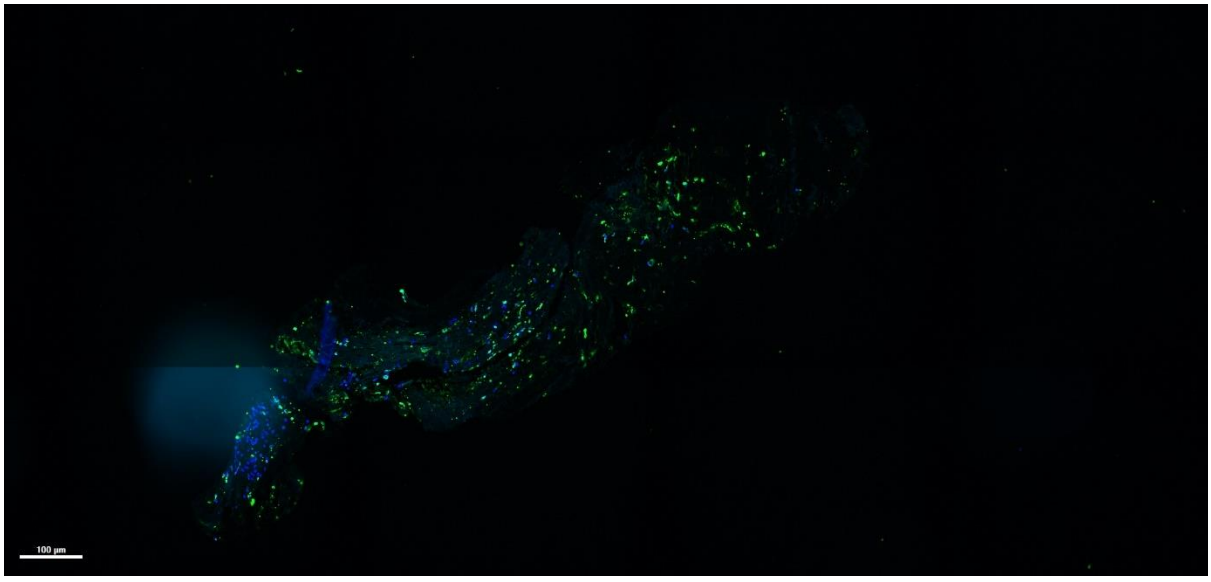

Image 2 – A representative tumour sample with CRO-67 treatment. After 12 days of treatment with CRO-67 there are predominantly dead cells (green) visible, and very few living cells (blue) remaining.

This unique ability to target both cell types could pave the way for a novel treatment that is being termed 'dual-cell' therapy, to acknowledge the distinctive properties of the new drug and its innovative way of attacking pancreatic cancer.

The study used a new cutting-edge model developed by UNSW that grows whole-tissue tumours and keeps pancreatic tumour cells as well as barrier cells alive in the laboratory for

12 days after they have been surgically removed from actual cancer patients. The tumour tissues were then treated with CRO-67 and studied under conditions as close as possible to real life.

There is an urgent need to develop more effective treatments for pancreatic cancer, which is set to become the second leading cause of cancer-related deaths in the US by 2030. It has a five-year survival rate of just 9% from the time of diagnosis.

Professor Phoebe Phillips from UNSW said: "The results demonstrated CRO-67 has potential to improve patient outcomes via a 'dual-cell' targeting activity that can attack tumour cells directly while also destroying the tumour's surrounding 'helper cells'. Traditional chemotherapeutics in this area have only targeted tumour cells and not the surrounding helper cells, and therefore their treatment effect is very limited."

Noxopharm CEO Dr Gisela Mautner said: "The development of new treatments is a core part of our expanded drug development strategy, and we are pleased that the Chroma™ platform is showing such promising initial results. What makes this study so exciting is that it is the closest you can get to studying human cancer in the laboratory before giving the drug to patients. It is still early days and there is a lot of work we need to do, but we are on an exciting path. The market for pancreatic cancer drugs is sizeable and clearly underserved, which presents a valuable opportunity for Noxopharm."

The study will now be followed by more tests on the therapeutic efficacy of CRO-67, as well as deeper analysis into the mechanisms by which CRO-67 exerts its 'dual-cell' targeting effects. Several additional studies will need to be performed to support the research required to move CRO-67 towards clinical trials.

In terms of commercial strategy, Noxopharm has filed comprehensive patent applications in order to protect the value of its intellectual property in this area.

The Chroma™ platform is one of two preclinical programs that support Noxopharm's science-driven strategy to develop and progress the most promising life-saving therapies. The second is the Sofra™ technology platform that focuses on inflammation and autoimmune diseases.

A timelapse video showing pancreatic cancer cells treated *in vitro* with CRO-67 is available here: https://youtu.be/6TbOixDq5Mc

Noxopharm – UNSW AACR Abstract:

Title: ***CRO-67 is a novel therapeutic for pancreatic cancer: implications for tumour and stromal reprogramming***

Authors: Kokkinos J[1], Sharbeen G[1], Haghighi KS[2], Youkhana J[1], Raina A[1], Pitiyarachchi O[1], Truong, Q[3], Wenholz, D[3,4], Laczka, O[3], Kumar, N[4], Goldstein D[1,2], Phillips PA[1].

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About Noxopharm

Noxopharm Limited (ASX:NOX) is an innovative Australian biotech company discovering and developing novel treatments for cancer and inflammation.

It has three active drug development programs: its clinical-stage drug candidate Veyonda®, plus two innovative technology platforms – Chroma™ (oncology) and Sofra™ (inflammation and autoimmunity), which provide the basis for active development of a growing pipeline of new proprietary drugs.

Noxopharm also has a major shareholding in the US biotech company Nyrada Inc (ASX:NYR), which is active in the areas of drug development for cardiovascular and neurological diseases.

To learn more, please visit: noxopharm.com

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Dr Gisela Mautner, CEO and Managing Director of Noxopharm, has approved the release of this document to the market on behalf of the Board of Directors.

Forward Looking Statements

This announcement may contain forward-looking statements. You can identify these statements by the fact they use words such as “aim”, “anticipate”, “assume”, “believe”, “continue”, “could”, “estimate”, “expect”, “intend”, “may”, “plan”, “predict”, “project”, “plan”, “should”, “target”, “will” or “would” or the negative of such terms or other similar expressions. Forward-looking statements are based on estimates, projections and assumptions made by Noxopharm about circumstances and events that have not yet taken place. Although Noxopharm believes the forward-looking statements to be reasonable, they are not certain. Forward-looking statements involve known and unknown risks, uncertainties and other factors that are in some cases beyond the Company’s control (including but not limited to the COVID-19 pandemic) that could cause the actual results, performance or achievements to differ materially from those expressed or implied by the forward-looking statement.

FACT SHEET

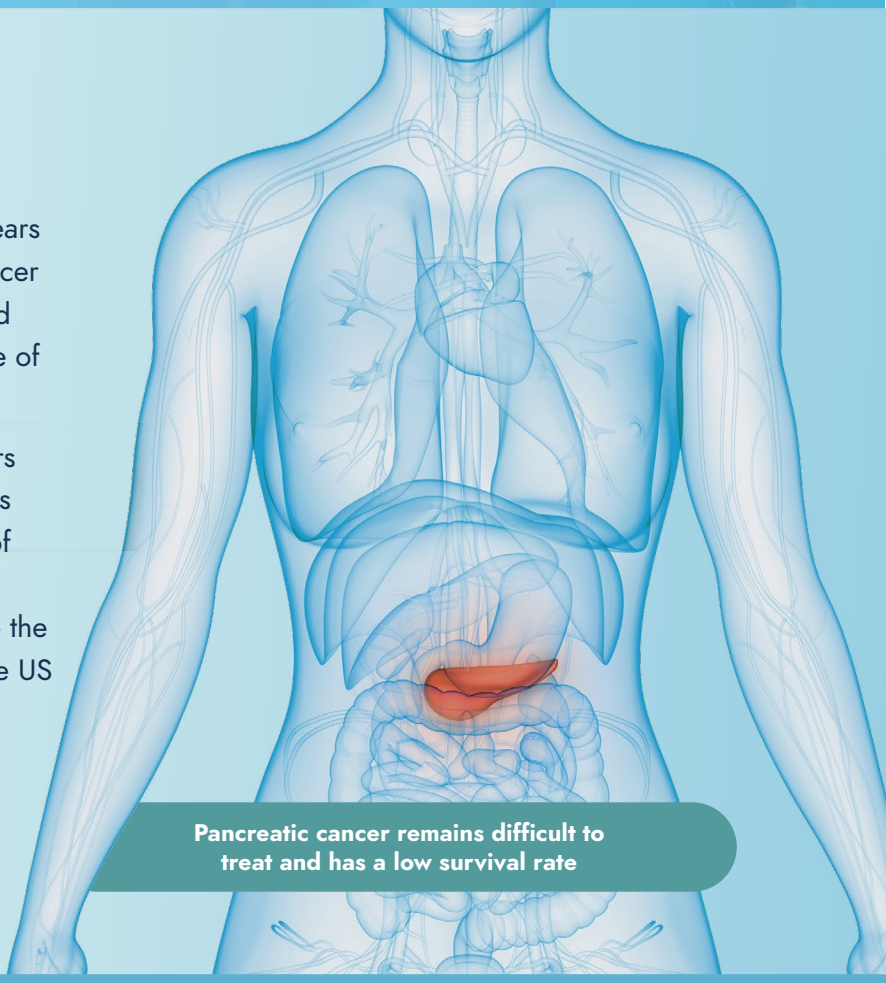
Noxopharm CRO-67

Dual-Cell Therapy for Pancreatic Cancer

Pancreatic Cancer

Pancreatic cancer is highly aggressive with low survival rates – only 9% of people survive five years after diagnosis[i]. It is the 7th leading cause of cancer death worldwide[ii], more common in industrialised countries, and currently is the third leading cause of cancer death in the United States[iii].

Despite an increased understanding of risk factors and improvements in diagnosis, treatment options are still limited. As a consequence, the number of pancreatic cancer cases is predicted to continue increasing, with pancreatic cancer set to become the 2nd leading cause of cancer related deaths in the US by 2030[iv].



Pancreatic cancer remains difficult to treat and has a low survival rate

The Challenge of Pancreatic Cancer

In cancer, there are cells that are found in layers surrounding tumours known as CAFs (cancer-associated fibroblasts). These CAFs create a barrier around the tumour, protecting it from treatment and promoting the growth and spread of the tumour.

A unique feature of pancreatic cancer is that the tumours are surrounded by a particularly dense barrier of CAFs. It has only relatively recently been discovered that this barrier layer is why pancreatic cancer tends to spread rapidly and is particularly difficult to treat[v].

With this new knowledge, Noxopharm has developed a ground-breaking dual-cell therapy approach to treating pancreatic cancer that focuses on attacking both the cancer cells and the CAFs forming the barrier around the tumour with a single novel drug candidate – CRO-67.

Noxopharm CRO-67

The Noxopharm proprietary drug candidate CRO-67 has been generated from Noxopharm's Chroma™ technology platform, which is focused primarily on developing oncology drug candidates.

CRO-67 was selected from an extensive drug library and showed the most promising results in a number of screening tests. It has been selected as the lead pancreatic cancer drug candidate due to its ability to act as a dual-cell therapy targeting both pancreatic tumour cells and the CAF (barrier) cells.

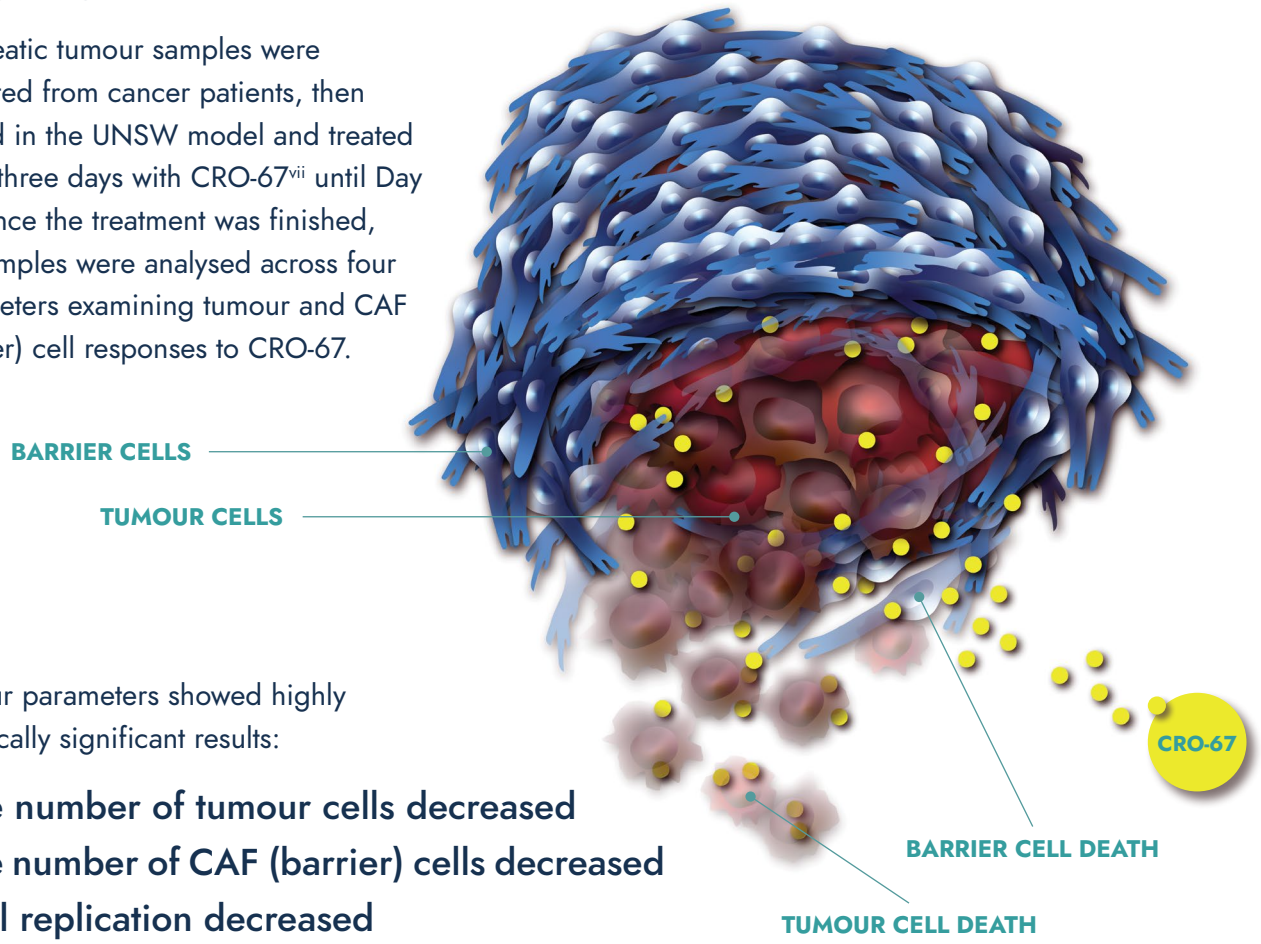
The UNSW Sydney Pancreatic Cancer Explant Model

UNSW Sydney has developed a world-first explant model where tumours and the surrounding tissue (including the barrier formed by CAFs) are surgically removed from cancer patients. Details on the model have been published in the highly regarded journal Nature: Scientific Reports[vi].

These samples are kept alive in the laboratory for 12 days where they continue to grow and behave as they would inside the body. This cutting-edge technology is the first time that the dual-cell ability of Noxopharm's drug candidate CRO-67 can be tested for an extended period in a model that closely replicates how pancreatic cancer behaves in the patient. Using this model, it was possible to measure the activity of CRO-67 against both the tumour and its surrounding barrier.

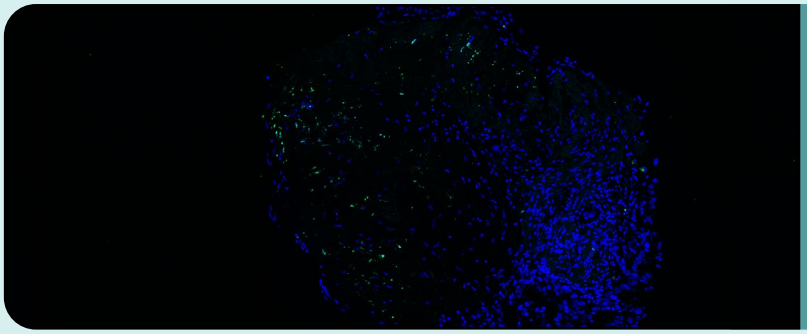
Results

Pancreatic tumour samples were collected from cancer patients, then placed in the UNSW model and treated every three days with CRO-67[vii] until Day 12. Once the treatment was finished, the samples were analysed across four parameters examining tumour and CAF (barrier) cell responses to CRO-67.



All four parameters showed highly statistically significant results:

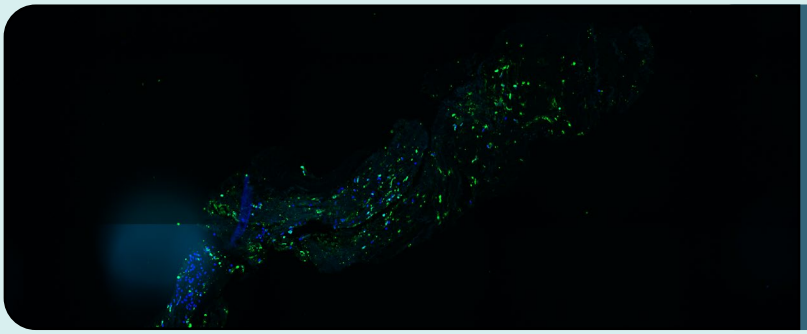
- The number of tumour cells decreased
- The number of CAF (barrier) cells decreased
- Cell replication decreased
- Cell-death increased



Representative tumour sample with no treatment

There are high numbers of living cells (blue) in the cancer tissue sample after 12 days without treatment.

Fluorescence study showing living cells in blue and dead cells in green.



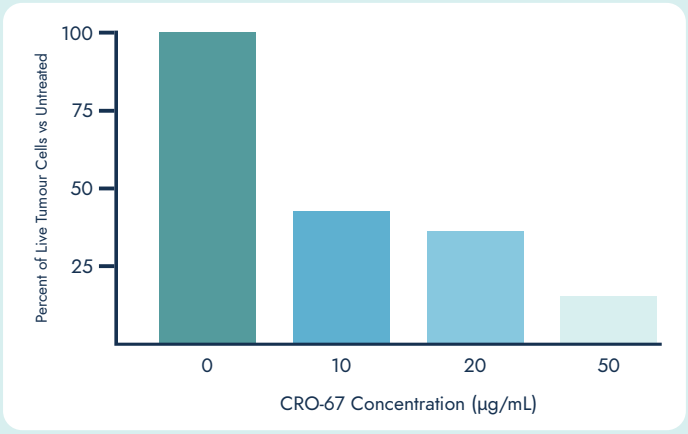
Representative tumour sample with CRO-67 treatment

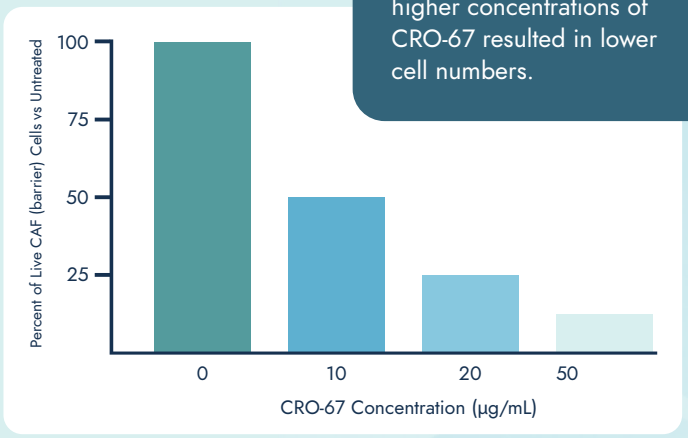
After 12 days treatment with CRO-67 there are predominantly dead cells (green) and very few living cells remaining.

	CRO-67 (µg/mL)	Average % Reduction vs Control	p-value
Tumour Cell Death	10	58%	0.003
	20	63%	0.0018
	50	85%	0.0002
Barrier Cell Death	10	51%	0.0018
	20	75%	<0.0001
	50	87%	<0.0001
Cell Replication	10	54%	<0.0001
	20	59%	<0.0001
	50	73%	<0.0001
	CRO-67 (µg/mL)	**Average % Increase vs Control**	**p-value**
Total Cell Death	10	298%	0.0123
	20	313%	0.0077
	50	621%	<0.0001

Significance p <0.05

Table and graphs showing the effect of increasing concentrations of CRO-67 on pancreatic tumour cell and CAF (barrier) cell numbers after 12 days of treatment. There is a clear treatment effect where higher concentrations of CRO-67 resulted in lower cell numbers.





This world-first study demonstrates CRO-67 as a novel dual-cell therapy, potently destroying both the tumour and its surrounding barrier. These highly promising results will now drive further studies to maximise the potential of this new approach to pancreatic cancer treatment.

REFERENCES

i. Rawla P, Sunkara T, Gaduputi V. Epidemiology of Pancreatic Cancer: Global Trends, Etiology and Risk Factors. World J Oncol. 2019 Feb;10(1):10-27. doi: 10.14740/wjon1166. Epub 2019 Feb 26. PMID: 30834048; PMCID: PMC6396775.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6396775/

ii. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394–424. doi: 10.3322/caac.21492.

https://pubmed.ncbi.nlm.nih.gov/30207593/

iii. Siegel, RL, Miller, KD, Fuchs, HE, Jemal, A. Cancer statistics, 2022. CA Cancer J Clin. 2022. https://doi.org/10.3322/caac.21708

https://acsjournals.onlinelibrary.wiley.com/doi/full/10.3322/caac.21708

iv. Rahib L, Smith BD, Aizenberg R, Rosenzweig AB, Fleshman JM, Matrisian LM. Projecting cancer incidence and deaths to 2030: the unexpected burden of thyroid, liver, and pancreas cancers in the United States. Cancer Res. 2014 Jun 1;74(11):2913-21. doi: 10.1158/0008-5472.CAN-14-0155. Erratum in: Cancer Res. 2014 Jul 15;74(14):4006. PMID: 24840647.

https://pubmed.ncbi.nlm.nih.gov/24840647/

v. Neesse A, Michl P, Frese KK, Feig C, Cook N, Jacobetz MA, Lolkema MP, Buchholz M, Olive KP, Gress TM, Tuveson DA. Stromal biology and therapy in pancreatic cancer. Gut. 2011;60:861–880

https://pubmed.ncbi.nlm.nih.gov/20966025/

vi. Kokkinos J, Sharbeen G, Haghighi KS, Ignacio RMC, Kopecky C, Gonzales-Aloy E, Youkhana J, Timpson P, Pereira BA, Ritchie S, Pandzic E, Boyer C, Davis TP, Butler LM, Goldstein D, McCarroll JA, Phillips PA. Ex vivo culture of intact human patient derived pancreatic tumour tissue. Sci Rep 11, 1944 (2021).

https://doi.org/10.1038/s41598-021-81299-0

vii. Kokkinos J, Sharbeen G, Haghighi KS, Youkhana J, Raina A, Pitiyarachchi O, Truong, Q, Wenholz, D, Laczka, O, Kumar, N, Goldstein D, Phillips PA. CRO-67 is a novel therapeutic for pancreatic cancer: implications for tumour and stromal reprogramming

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