Noxopharm and U.S. National Cancer Institute to Collaborate on Promising New Approach to Treatment of Brain Cancer

Highlights

- **Noxopharm signs a materials Cooperative Research and Development Agreement (m-CRADA) with the U.S. National Cancer Institute**
- **Collaboration based on a new family of anti-cancer drugs designed by Noxopharm scientists with a unique dual anti-cancer action**
- **Dual action designed specifically for aggressive cancers including brain cancer and pancreatic cancer to block 'helper' signals from surrounding healthy tissue playing a key role in the aggressive cancer growth**
- **Initial asset in the Company's Cancer Research Pipeline Program.**

Sydney 9 August 2021: Australian clinical-stage drug development company Noxopharm Limited (ASX:NOX) announces a formal collaboration with the National Cancer Institute (NCI) within the U.S. National Institutes of Health (NIH) in the quest for more effective treatments of brain cancer.

The collaboration relates to a new family of molecules designed by Noxopharm scientists that combines the traditional role of chemotherapy drugs (killing cancer cells directly), with a unique ability to block 'helper' growth signals coming from neighbouring healthy cells. Those 'helper' signals from neighbouring stromal cells have emerged as an important contributor to the highly aggressive nature of certain cancers, notably cancers of the brain, pancreas and bile duct.

Finding drugs that block these 'helper' signals in a tumour's micro-environment has become a major new direction in oncology, offering the prospect of meaningful survival benefits in patients where effective treatment options continue to remain elusive. The challenge lies in blocking these signals without damaging their source, something even more vital in the case of the brain.

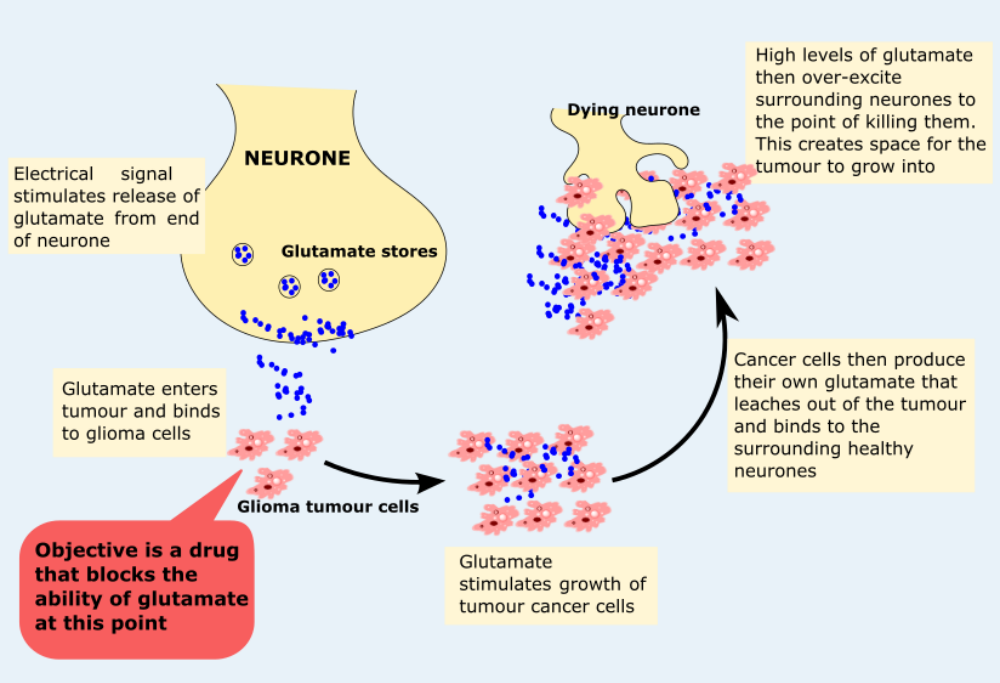
Noxopharm believes that it has achieved this objective in pre-clinical studies, combining potent killing of cancer cells with a secondary action that blocks the action of the 'helper' growth signals in a well-tolerated way. The objective is a drug that will convert aggressive brain cancers in adults and children into slow-growing cancers more able to be effectively managed by other treatments such as surgery and radiotherapy.

Brain cancer

The brain is composed mainly of neurones (cells carrying electrical impulses) and glial (support) cells in roughly equal numbers. The great majority of primary brain cancers derive from the brain's glial

cells and generally are devastating brain tumours with poor treatment options. Glioblastoma multiforme (GBM), the main form of brain cancer in adults, has a post-treatment 5-year survival rate as low as 4.7%.[1] Diffuse intrinsic pontine glioma (DIPG), a highly aggressive and usually fatal brain cancer in children, is even more devastating with a 5-year survival rate of only 2%.[2]

The main 'helper' signal in the case of gliomas is the brain's main neurotransmitter chemical, glutamate. This inappropriate use of glutamate serves two purposes in brain cancer: the first is that glutamate is fed from the neurones into the tumour where it stimulates the growth of the cancer cells[3]; the second is that the activated cancer cells appear to then go on to produce their own glutamate in large amounts, killing surrounding healthy neurones by over-exciting them to make room for expansion of the rapidly growing tumour.[4]



Adapted from Natarajan and Venneti. 2019. Glutamine Metabolism in Brain Tumors. Cancers, 11:1628.

The new Noxopharm drugs kill brain cancer cells directly in a similar way to idronoxil. However, an additional design feature has been added that blocks the ability of the cancer cells to respond to glutamate, and to do so in a way that preserves general brain function.

Comments

Mioara Larion principal investigator at the Neuro-Oncology Branch at NCI, said: "We are enthusiastic about this collaboration that aims to find new targeted molecular therapies for patients affected by diseases in the central nervous system, particularly brain cancers."

Noxopharm CEO, Graham Kelly PhD, said, "The principle of this approach is applicable to a wide variety of highly aggressive cancers. Brain cancer is our first program, and a separate pancreatic cancer program is underway with details to be announced shortly."

This program sits within the Company's Cancer Research Pipeline Program, one of the Company's 4-Pillars R&D programs.

Veyonda

Cancer treatment enhancement

Cancer Research Pipeline

Cancer growth factor inhibitors

Veyonda

Septic shock

pharmorage

Chronic inflammatory diseases/autoimmune diseases

Glossary

Glutamate: an amino acid. Serves as the main neurotransmitter in the brain. Also converted into glutamine which serves as a source of energy in cancer cells when glucose stores are exhausted.

Neurone: electrically excitable cell that communicates with other cells, and is responsible for all neurological functions of the brain.

Stromal cells: also known as mesenchymal cells. Self-replicating cells capable of turning into a variety of tissues, particularly connective tissue.

References:

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2. **Hoffman L.M et al (2016)** *Hg-75 clinical, radiological, and histogenetic characteristics of long-term survivors of diffuse intrinsic pontine glioma: a collaborative report from the international and SIOP-E DIPG registries.* Neuro-Oncology 18, iii65-iii66. doi: 10.1093/neuonc/now073.105
3. **Corsi L et al (2019)** *Glutamate receptor and glioblastoma multiforme: an 'old' routs for new perspectives*. Int J Mol Sci 20: 1796 doi: 10.3390/ijms20071796
4. **Sontheimer H (2008)** *A role for glutamate in growth and invasion of primary brain tumours*. J Neurochem 105:287-95. DOI:10.1111/j.1471-4159.2008.05301.x
5. **Huang J et al (2019**) *Isocitrate Dehydrogenase Mutations in Glioma: From Basic Discovery to Therapeutics Development*. Front Oncol 9:506. doi: 10.3389/fonc.2019.00506.

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

About the new drug family

The family of new chemical entities discovered by Noxopharm derives from the same drug technology platform that delivered idronoxil (Veyonda®) and comes from a more recent drug discovery program looking at the design of drugs specifically for the treatment of highly aggressive cancers (brain, pancreatic and bile duct cancers).

About the National Cancer Institute (NCI)

The National Cancer Institute (NCI), with an annual budget of approximately US$43 billion, is the U.S. federal government's principal agency for cancer research and training. Established under the National Cancer Institute Act of 1937, NCI is part of the National Institutes of Health (NIH). NCI's mission is to lead, conduct, and support cancer research across the nation to advance scientific knowledge and help all people live longer, healthier lives.

About the collaboration

The collaboration with the Neuro-Oncology Branch of the NCI brings three key assets to the project: (i) a strong research interest in the role of sphingolipids in brain cancer cell function, (ii) considerable expertise in mutations closely related to the occurrence and development of gliomas by promoting the formation of the tumour microenvironment[5], and (iii) NCI mouse models injected intra-cranially with patient-derived glioma cells will be used to test the effect of treatment with Noxopharm drugs as a proof-of-concept step in the process of bringing a drug into the clinic.

The collaboration is designed to help identify the lead candidate compounds and to confirm the hypothesised anti-cancer activity and mechanism of action of the Noxopharm compounds. The compounds remain the property of Noxopharm.

About Noxopharm

Noxopharm Limited (ASX:NOX) is an Australian clinical-stage drug development company focused on the treatment of cancer and cytokine release syndrome (septic shock).

Veyonda® is the Company's first pipe-line drug candidate currently in Phase 2 clinical trialling. Veyonda® has two main drug actions – a moderating effect on the ceramide/sphingosine-1-phosphate balance and inhibition of STING signalling. Activity against the former target contributes to its dual-acting oncotoxic and immunomodulatory functions designed to enhance the effectiveness and safety of standard oncology treatments, i.e., chemotherapies, radiation therapies and immune checkpoint inhibitors. Activity against the latter target provides an anti-inflammatory effect, as well as contributing to an anti-cancer action, but also potentially blocking septic shock.

Noxopharm is running comprehensive drug discovery programs in both oncology and inflammation, and is the major shareholder of US biotechnology company, Nyrada Inc (ASX:NYR), active in the areas of drug development for cardiovascular and neurological diseases.

To learn more, please visit: noxopharm.com

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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.