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NOVOGEN'S NV-128 TARGETS THE mTOR PATHWAY TO BLOCK DIFFERENTIATION AND INDUCE CELL DEATH IN OVARIAN CANCER STEM CELLS

(Sydney Australia and New Canaan, Connecticut - 20 April, 2009) – Data just presented at the Annual Meeting of the American Association for Cancer Research in Denver has demonstrated that NV-128, a Novogen, Limited (ASX: NRT NASDAQ: NVGN) synthetic isoflavonoid compound, not only induces cell death in Ovarian Cancer Stem Cells (OCSCs), but also blocks their differentiation into structures which are required to support tumour growth.

In a poster presentation by Ayesha Alvero, MD, of Yale University School of Medicine, Department of Obstetrics, Gynecology and Reproductive Science, it was revealed that in addition to an inhibitory effect on OCSC growth, NV-128 displays a remarkable ability to inhibit differentiation of OCSCs into formation of new blood vessels.

The anti-proliferative effects were demonstrated to be achieved as a result of NV-128 inhibiting phosphorylation of the pro-survival mTOR pathway resulting in mitochondrial depolarisation and cell death. Time lapsed photographic morphometry revealed in graphic detail how NV-128 induces morphological changes in OCSCs after 24 hours, even when dosed as low as 1µg/ml with a progressive "clearing" of cytoplasm and condensation of nuclear material.

The effect of NV-128 on OCSC vessel formation was observed by plating OCSCs in high-density matrigel either without NV-128 (controls) or in the presence of 0.1 mg/ml NV-128 and observing for 48 hours. Whereas the control cultures showed differentiation of the stem cells into endothelial-type cells forming structurally intact blood vessels in the culture plates, cells cultured in the presence of NV-128 showed no differentiation and no structural elements were observed.

OCSCs represent a highly chemo-resistant cell population, allowing them to survive conventional chemotherapy. Thus these cells are considered to be the potential source of tumour induction and post-treatment recurrence.

The team from Yale University, headed by Professor Gil Mor, recently reported the identification and characterisation of OCSCs using the CD44 marker and demonstrated pronounced up-regulation of the mTOR survival pathway in these cells. They previously reported that NV-128 is able to specifically induce mTOR dephosphorylation resulting in inhibition of both mTORC1 and mTORC2 activity in mature ovarian cancer cells derived from established human cancers and cultured *in vitro*. In mice with human ovarian cancers established by grafting techniques (xenografts) NV-128 caused substantial cancer cell death, reducing tumour growth with no apparent toxic side-effects.

"We have now demonstrated that by inhibiting the mTOR pathway in both the cancer stem cells and the mature cancer cells, we are able to inhibit development of structural elements necessary for tumour development as well as limit the number of cancer cells," Professor Mor said. "These results open a new avenue for the development of better treatment modalities for ovarian cancer patients."

"We are encouraged by these data from animal studies showing a combination of anti-cancer activities of NV-128, coupled with an apparently high safety profile," said Professor Alan Husband, Group Director of Research for the Novogen group. "This anti-angiogenic effect, coupled with the absolute effects on

cell survival, demonstrate the potential for NV-128 to become a powerful new tool in prevention as well as treatment of cancer."

Novogen has previously reported on the parallel effects of NV-128 in non-small cell lung cancer models and the Company intends to pursue this, as well as ovarian cancer, as target indications.

Novogen is currently in advanced negotiations with its majority owned subsidiary, Marshall Edwards, Inc. (MEI), to out-license NV-128 to MEI for its clinical development as a potential cancer therapeutic. To view an online abstract relating to this study, go to <http://www.abstractsonline.com/viewer/?mkey=%7BD007B270%2DE8F6%2D492D%2D803B%2D7582CE7A0988%7D>

About NV-128

NV-128 does not rely on the traditional approach of caspase-mediated apoptosis, a death mechanism which is not effective in cancer cells that have become resistant to chemotherapy. Rather, NV-128 uncouples a signal transduction cascade which has a key role in driving protein translation and uncontrolled cancer cell proliferation. Further, NV-128 induces mitochondrial depolarisation via the novel mTOR pathway. In cancer cells, mTOR signals enhance tumour growth and may be associated with resistance to conventional therapies. Inhibition of the mTOR pathway appears to shut down many of these survival pathways, including proteins that protect the mitochondria of cancer cells. Animal studies have shown that NV-128 not only significantly retards tumour proliferation, inhibiting the progression of ovarian cancers-engrafted into mice, but produces this effect without apparent toxicity. This effect was shown to be due to caspase-independent pathways involving inhibition of the mTOR pathway. Unlike analogues of rapamycin, which target only mTORC1, NV-128's capacity to inhibit mTOR phosphorylation enables it to inhibit both mTORC1 and mTORC2 activity. This blocks growth factor-driven activation of AKT and the potential for development of chemoresistance.

About Novogen Limited

Novogen Limited (ASX: NRT; NASDAQ: NVGN) is an Australian biotechnology company based in Sydney, Australia, that is developing a range of oncology therapeutics from its proprietary flavonoid synthetic chemistry technology platform. More information on NV-128 and on the Novogen group of companies can be found at www.novogen.com.

Under U.S. law, a new drug cannot be marketed until it has been investigated in clinical trials and approved by the FDA as being safe and effective for the intended use. Statements included in this press release that are not historical in nature are "forward-looking statements" within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. You should be aware that our actual results could differ materially from those contained in the forward-looking statements, which are based on management's current expectations and are subject to a number of risks and uncertainties, including, but not limited to, our failure to successfully commercialize our product candidates; costs and delays in the development and/or FDA approval, or the failure to obtain such approval, of our product candidates; uncertainties in clinical trial results; our inability to maintain or enter into, and the risks resulting from our dependence upon, collaboration or contractual arrangements necessary for the development, manufacture, commercialization, marketing, sales and distribution of any products; competitive factors; our inability to protect our patents or proprietary rights and obtain necessary rights to third party patents and intellectual property to operate our business; our inability to operate our business without infringing the patents and proprietary rights of others; general economic conditions; the failure of any products to gain market acceptance; our inability to obtain any additional required financing; technological changes; government regulation; changes in industry practice; and one-time events. We do not intend to update any of these factors or to publicly announce the results of any revisions to these forward-looking statements.

ISSUED FOR	:	NOVOGEN LIMITED
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