ASX:NRT
NASDAQ:NVGN

Novogen Ltd
(Company)

ABN 37 063 259 754

Capital Structure

Ordinary Shares on issue:

483 M

Board of Directors

Mr John O'Connor
Chairman
Non-Executive Director

Mr Bryce Carmine
Deputy Chairman
Non-Executive Director

Dr James Garner
Chief Executive Officer
Managing Director

Mr Ian Phillips MNZM
Non-Executive Director

Mr Iain Ross
Non-Executive Director

Mr Steven Coffey
Non-Executive Director

MARKET RELEASE
10th April; 2017

NOVOGEN UPDATE ON PHASE II DEVELOPMENT PLANS FOR GDC-0084

- Phase II study is planned to enroll patients with glioblastoma multiforme (GBM), the most common and most aggressive form of primary brain cancer in adults, who are largely resistant to temozolomide, the most widely-used pharmaceutical treatment in this disease

- Trial is expected to be a randomized, two-arm design of approximately 200 patients, with commencement in the second half of calendar 2017

- Consultation with United States Food & Drug Administration (FDA) is planned to occur prior to initiation of study

Sydney, 10th April 2017 – Australian oncology-focused biotechnology company Novogen Limited (ASX: NRT; NASDAQ: NVGN) is pleased to provide an update for investors on progress with its lead program, GDC-0084, and plans for a phase II human trial which is scheduled to commence in calendar 2017.

An oral therapy under development for glioblastoma multiforme (GBM)

GDC-0084 is an orally-administered therapy which is under development as a treatment for glioblastoma multiforme (GBM), the most common and most aggressive form of brain cancer. GBM affects approximately 130,000 patients worldwide annually, and has one of the poorest outcomes of any cancer, with only 3-5% of patients alive five years after diagnosis. GDC-0084 is designed to inhibit tumor growth by targeting an important biochemical control mechanism that is thought to be critical to growth of the tumour.

GDC-0084 was licensed from Genentech, Inc, a member of the Roche Group, in October 2016. Genentech had completed a phase I clinical study in 47 patients with advanced brain cancer, which had shown the drug to be generally well-tolerated, and which provided signals of clinical efficacy that support further development.

Progress to date

Since the transaction, Novogen has completed transfer of the open Investigational New Drug (IND) application from Genentech to Novogen. For a drug in development, the IND is the key regulatory filing with the US Food & Drug Administration (FDA) which allows for the conduct of clinical trials.

Novogen has also taken possession of approximately 48.8kg of premanufactured drug substance that had been prepared by Genentech in anticipation of a phase II study. This material is now being formulated into oral capsules for use in the phase II clinical trial.

Novogen conducted an Advisory Board of expert neuro-oncologists in San Francisco, CA in January 2017, and has developed the phase II clinical trial design based on their input. Novogen has also benefited from consultation with its international Scientific Advisory Board which was established in September 2016.

Planned trial design

The phase II study is intended to measure the efficacy of GDC-0084 in patients. It is envisaged that the study will be conducted in patients who have been recently diagnosed with GBM, and who have undergone surgical resection and radiotherapy in accordance with usual treatment practice in this disease. This is a different, and less advanced population than the phase I study, which was conducted in patients with recurrent disease. The study will recruit only patients who have a confirmed unmethylated MGMT promoter, which is associated with limited response to temozolomide, the pharmacological standard of care for GBM.

The study will be a randomized, two-arm study with patients receiving either GDC-0084 or temozolomide as maintenance therapy after completion of standard radiotherapy treatment. Approximately 200 patients will be enrolled, with 100 patients in each arm. It is expected that the study will be open-label, which means that patients and clinicians will be aware of which drug is being administered, but the key efficacy assessments will be performed in a blinded fashion by independent adjudicators. The primary endpoint of the study will be progression-free survival (PFS), with patients followed for overall survival (OS).

PFS can be considered an acceptable endpoint for approval of oncology drugs by FDA.[1] In addition, FDA provides a mechanism known as accelerated approval which is designed to hasten the delivery of products appearing to provide a benefit for serious or life-threatening illnesses lacking satisfactory treatments, and which can allow for new drugs to be approved prior to completion of the requisite phase III trials. Avastin (bevacizumab) was initially approved by FDA for recurrent GBM following two single-arm phase II studies which enrolled 141 patients in total. It is Novogen's hope that GDC-0084 may also be considered by FDA for accelerated approval if the phase II study is successful, given the unmet medical need in this patient population.

[1] U.S. Department of Health and Human Services, Food and Drug Administration. Guidance for Industry: Clinical Trial Endpoints for the Approval of Cancer Drugs and Biologics (May 2007)

Novogen anticipates that the phase II study will commence in the second half of calendar 2017, and will take approximately 18 months to reach full recruitment, with PFS data available 12 months thereafter. It is expected that the study will recruit patients in the US, Australia, and several European countries.

Novogen plans to consult with the United States Food & Drug Administration (FDA) regarding its plans for GDC-0084, prior to initiating the study, and its approach may be modified if needed on the basis of FDA feedback.

Dr James Garner, Chief Executive Officer, said ‘‘glioblastoma remains an area of significant unmet need in the treatment of cancer. It is the most common and most aggressive malignant primary brain tumour in adults. The disease affects more than 12,000 patients per annum in the United States alone, and there have been few meaningful advances in treatment.

‘‘The patient group we are targeting represents a significant proportion of patients diagnosed with GBM. Unfortunately, median overall survival is very short at only about 12 months. We are hopeful that GDC-0084 could become a valuable new treatment option for these patients.’’

Novogen looks forward to sharing further updates as the trial progresses.

GDC-0084 phase II trial summary

The study will be a randomized, two-arm study with patients receiving either GDC-0084 or temozolomide. Recently diagnosed Glioblastoma multiforme (GBM) patients will enter the study after surgical resection and completion of radiotherapy. Approximately 200 patients will be enrolled, with 100 patients in each arm.

Objectives:	**Primary endpoint:** The primary endpoint of the study will be progression-free survival (PFS), with patients followed for overall survival (OS). **Secondary endpoints:** Secondary endpoints will include safety and tolerability, quality of life, and other measures of response.
Study design:	This is a phase II, multi-site, open label, monotherapy study, where around 100 patients will receive temozolomide, the current standard of care for first-line treatment of GBM, and around 100 patients will receive GDC-0084. Patients enrolled in the trial will be those who have a confirmed unmethylated MGMT promoter, which means they are considered to be effectively resistant to temozolomide. They will have undergone surgical resection and chemoradiotherapy in accordance with accepted treatment practice. GDC-0084 will be administered orally to patients at a dose of 45mg, which was identified in the phase I study as the most suitable dose for further studies.
Planned sample size:	It is expected that around 200 patients will be enrolled in the phase II study.
Treatment duration:	Patients in the comparator arm will be eligible to receive temozolomide for up to six months, which is the approved duration of treatment, while those in the experimental arm will be eligible to receive GDC-0084 for up to two years.

About GDC-0084

GDC-0084 is a small molecule inhibitor of the PI3K / AKT / mTOR pathway, which is distinguished from other molecules in the class by its ability to penetrate the blood-brain barrier. PI3K inhibitors have shown evidence of clinical activity in a broad range of tumour types, and one product in the class has reached market for several haematological malignancies. GDC-0084 was developed by Genentech, who completed a phase I study in patients with recurrent glioma, and was licensed to Novogen in October 2016. A phase II clinical trial is slated to begin in the second half of calendar 2017.

About Novogen Limited

Novogen Limited (ASX: NRT; NASDAQ: NVGN) is an emerging oncology-focused biotechnology company, based in Sydney, Australia. Novogen has a portfolio of development candidates, diversified across several distinct technologies, with the potential to yield first-in-class and best-in-class agents in a range of oncology indications.

The lead program is GDC-0084, a small molecule inhibitor of the PI3K / AKT / mTOR pathway, which is being developed to treat glioblastoma multiforme. Licensed from Genentech in late 2016, GDC-0084 is anticipated to enter phase II clinical trials in 2017. A second clinical program, TRXE-002-01 (Cantrixil) commenced a phase I clinical trial in ovarian cancer in December 2016. In addition, the company has several preclinical programs in active development, the largest of which is substantially funded by a CRC-P grant from the Australian Federal Government.

For more information, please visit: www.novogen.com