Novogen

Pipeline update

Anisina nixed, GDC-0084 on track for Phase II

Pharma & biotech

Novogen's recent market updates presented mixed news for investors. Recruitment in the Cantrixil Phase I is underway and preparations for the Phase II trial of GDC-0084 in glioblastoma are progressing well, although headline data are now likely in H1 CY20, 12 months later than we initially forecast. Mixed data from preclinical studies have seen development terminated for Anisina, which had been expected to enter the clinic in H217. While the termination of Anisina is disappointing, it is encouraging to see that management is taking a disciplined approach to assessing pipeline products. We now value Novogen between $66m ($3.39/ADR) and $111m ($5.74/ADR) under two different development scenarios for GDC-0084. Major milestones anticipated in 2017 include initiation of a Phase II trial of GDC-0084 and full enrolment in the Cantrixil Phase I.

Year end	Revenue (US$m)	PTP (US$m)	EPADR ($)	DPADR ($)	P/E (x)	Gross Yield (%)
06/15	1.2	(6.4)	(0.57)	0.0	N/A	N/A
06/16	2.8	(8.8)	(0.54)	0.0	N/A	N/A
06/17e	3.3	(9.4)	(0.51)	0.0	N/A	N/A
06/18e	7.2	(14.4)	(0.75)	0.0	N/A	N/A

Note: Converted at A$1/US$0.76 for the table above and throughout the note.

Cantrixil enters the clinic

The Phase I trial of Cantrixil in patients with recurrent or refractory ovarian cancer is expected to enroll up to 60 patients in the US and Australia and to be fully enrolled by Q417. While the primary aim is to assess dosage, safety and tolerability, radiological responses and biomarkers will be assessed for indications of efficacy.

GDC-0084 Phase II to commence H2 CY17

GDC-0084, which was in-licensed from Genentech in October 2016, was specifically designed to cross the blood-brain barrier and showed signals of potential clinical activity in a Phase I brain cancer trial conducted by Genentech. A Phase II trial in newly diagnosed glioblastoma (GBM) is expected to start in H217 and report top-line data in H1 CY20 (versus our prior estimate of H1 CY19).

Anisina terminated, new ATM program starts

The company has terminated development of Anisina following inconsistent efficacy and emerging toxicology findings in preclinical studies. Anisina had been slated to enter the clinic in H2 CY17. Novogen has initiated a separate anti-tropomyosin (ATM) drug discovery program supported by a $2m government grant.

Valuation: $66-$111m in two GDC-0084 scenarios

We revise our indicative valuation to reflect the termination of Anisina and to incorporate GDC-0084 under two different development scenarios: assuming post-Phase III approval of GDC-0084 in 2025, our valuation is $66m; assuming accelerated approval in 2021, our valuation is $111m. Our valuation prior to the GDC-0084 transaction and termination of the Anisina program was $86m ($4.95/ADR). Novogen had $14.1m cash at 31 December 2016 and we estimate that it may require $8m additional funding in FY18 and $12m in FY19.

25 May 2017

Price	**$0.85**
Market cap	**$16m**
	ADR/Ord conversion ratio 25/1
Net cash ($m) at 31 December 2016	14.1
ADRs in issue	19.3m
ADR Code	NVGN
ADR exchange	NASDAQ
Underlying exchange	ASX
Depository	BNY

ADR share price performance

52-week high/low	$2.17	$0.85

Business description

Novogen is an ASX- and NASDAQ-listed biotechnology company. It is developing GDC-0084 for brain cancer and its super-benzopyran (SBP) drug technology platform. SBPs show activity against cancer stem cells and are active across many different cancers.

Next events

FDA consultation re GDC-0084 Phase II design	Mid-2017
Initiate GDC-0084 Phase II	H217
Fully enroll Cantrixil Phase I	Q417

Analysts

Dennis Hulme +61 (0)2 9258 1161

Juan Pedro Serrate +44 (0)20 3681 2534

healthcare@edisongroup.com

Edison profile page

Investment summary

Company description: Two novel classes of anti-cancer drugs

Novogen is an Australian biotechnology company focused on oncology drug development. It is listed on both ASX (ASX:NRT) and NASDAQ (NASDAQ:NVGN). The company is developing two classes of anti-cancer compounds: GDC-0084, a Phase II-ready PI3K inhibitor licensed from Genentech that is being developed for GBM; and its SBP drugs, Cantrixil and Trilexium, which have shown strong preclinical efficacy in a range of cancers. A Phase I trial of Cantrixil in ovarian cancer is underway and a Phase II trial of GDC-0084 in GBM is expected to commence in H2 CY17. Novogen recently initiated an ATM drug discovery program, largely funded by a $2m government grant.

Valuation: $66-111m, $3.39-5.74 per ADR

We value Novogen between $66m and $111m. Our base case valuation of $66m assumes that GDC-0084 could be approved in 2025 after a confirmatory pivotal trial. Our alternative valuation of $111m is for a scenario where GDC-0084 seeks potential accelerated approval in 2021 after a single Phase II trial. Our base case valuation is equal to $3.39/ADR, or $3.23/ADR after diluting for options and convertible notes. Our valuation is based on a risk-adjusted NPV analysis, which includes net cash and our forecasts for GDC-0084, Cantrixil and Trilexium, with probability of success of 5-25% to reflect the stage of development of each product. Our undiluted base case valuation equals $0.18 per ASX-listed share current exchange rates.

Financials: Additional funds likely required in FY18

Novogen reported a net loss of $3.2m in H1 FY17 (six-month period ending 31 December 2016). R&D expenses for the period were $3.7m and administration expenses were $3.0m, including costs associated with the GDC-0084 transaction. We forecast R&D expenditure of $8.3m in FY17 and $17.1m in FY18. With $14.1m cash at 31 December 2016 and the Phase II trial of GDC-0084 estimated to cost $25m, Novogen will require additional funding to complete the trial. We estimate the funding requirement to be $8m in FY18 and $12m in FY19 (the FY19 funding requirement could potentially be met by out-licensing Cantrixil at the completion of the Phase I trial, if the outcome is positive).

Sensitivities

The key sensitivities for Novogen will be the success of its three lead drugs in clinical trials and funding risk. A crucial question will be whether GDC-0084 works sufficiently well as a single agent in GBM to justify filing for accelerated approval, or whether it will need to be used concurrently with radiotherapy or in combination with temozolomide (TMZ) or other chemotherapies in order to deliver sufficient efficacy in the target population. In our base case scenario, we assume that a confirmatory trial will be required to prove efficacy of GDC-0084, either as a single agent or as part of a combination therapy, delaying potential launch until 2025 versus 2021 under an accelerated approval scenario. While Novogen has funds to initiate the Phase II study of GDC-0084 in GBM, it would require additional funds of ~$19m over FY18 and FY19 to complete the planned trials, which could result in significant dilution of existing shareholders given the current market capitalization of ~$18m. The outcome of the ongoing Cantrixil Phase I will influence the prospects of Trilexium entering the clinic.

Cantrixil in the clinic, GDC-0084 headed to Phase II

Novogen is developing two groups of anti-cancer compounds, including GDC-0084, a Phase II-ready PI3K inhibitor licensed from Genentech (a subsidiary of Roche) that is intended for GBM. The company has transferred the GDC-0084 IND from Genentech and is finalizing the design for a Phase II study expected to start in H217. Its SBP drugs include Cantrixil and Trilexium, which are potent against cancer stem cells that are resistant to standard chemotherapy drugs, both *in vitro* and *in vivo*. A 60-patient Phase I trial of Cantrixil in ovarian cancer commenced in December 2016. Novogen has terminated development of its preclinical ATM drug Anisina, but has initiated a next-generation ATM drug discovery program supported by a $2m government grant. The company's product pipeline is summarized in Exhibit 1.

Exhibit 1: Novogen's product pipeline

Drug candidate	Indication	Stage	Next steps
GDC-0084	GBM	Phase II-ready	Initiate Phase II study in first-line GBM in H217.
Cantrixil	Malignant ascites	Phase I	Fully enroll Phase I study H2 CY17.
Trilexium	Melanoma	Preclinical	Complete animal efficacy studies. Initiate preclinical toxicology studies.
	Prostate cancer	Preclinical	
	Brain cancer	Preclinical	Demonstrate that TRXE-009 is effective against cancer cells growing in the brains of mice.

Source: Edison Investment Research

GDC-0084: Specifically developed to target GBM

Novogen in-licensed the Phase II-ready drug GDC-0084 from Genentech in October 2016. GDC-0084 is an orally administered small molecule phosphoinositide 3-kinase (PI3K) inhibitor that targets an important growth signaling pathway in cancer cells. The drug was specifically developed to cross the blood-brain barrier and target the aggressive brain cancer GBM, a disease with poor patient survival for which there are few effective therapies. The drug has completed a Phase I trial in patients with advanced disease, which confirmed that it readily crosses the blood-brain barrier and that it led to dose-dependent inhibition of tumor growth. Seven of the eight patients treated at the maximum tolerated dose of 45mg/day demonstrated levels of drug in the bloodstream that were associated with significant inhibition of tumor growth in preclinical models.

GBM: An aggressive brain cancer with few effective treatments

GBM is the most common and most aggressive primary malignant tumor of the brain and spinal cord. Approximately 11,500 patients are diagnosed with GBM each year in the US. GBM tumors are characterized by invasive and diffuse growth, which makes complete surgical removal difficult. Standard treatment for GBM entails surgical resection of the tumor followed by radiotherapy with concurrent chemotherapy with TMZ, followed by adjuvant chemotherapy with the same drug to treat the residual infiltrative component of the tumor. Despite this aggressive treatment the disease invariably returns, resulting in a five-year survival rate of only 5%.[1]

Preliminary design for GDC-0084 Phase II released

Novogen has outlined plans for a randomized Phase II study of GDC-0084 as first-line maintenance therapy in patients with recently diagnosed GBM, as shown in Exhibit 2. Patients will undergo surgery to remove the bulk of the tumor and receive a standard six-week course of radiotherapy in combination with TMZ before entering the study. Study participants will be randomized to receive

1 CBTRUS Statistical Report: Primary Brain and Central Nervous System Tumors Diagnosed in the United States in 2008-2012. Ostrom et al *Neuro-Oncology* 17:iv1–iv62, 2015.

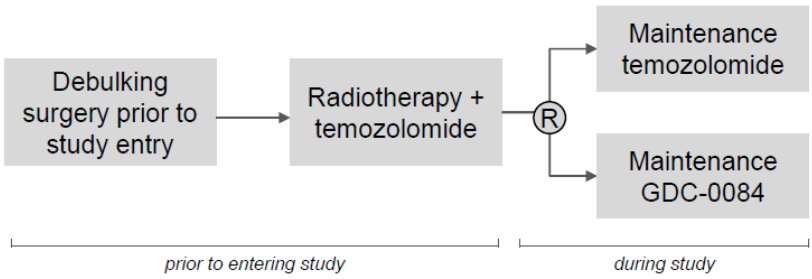
either 45mg of GDC-0084 for up to two years or to receive TMZ for up to six months (which is the approved duration of treatment with TMZ).

The trial will recruit patients where the promoter of the O6-methylguanine methyltransferase (MGMT) gene in the tumor cells is unmethylated. These patients receive only minimal benefit from treatment with TMZ and are in urgent need of more effective therapies. About 61%[2] of GBM patients have an unmethylated MGMT promoter, so GDC-0084 will be targeting use in the majority of recently diagnosed GBM patients.

The proposed Phase II trial design shown in Exhibit 2 is in line with the assumptions in our report dated October 2016, but the trial will be larger, recruiting 200 patients vs our prior assumption of 160 subjects. The trial is also expected to start slightly later (H2 CY17 vs Q2 CY17) and take longer to complete (2.5 years vs 21-24 months). Top-line PFS data are now expected in H1 CY20 vs our prior assumption of Q119.

Our previous budget estimate for the trial of $25m still seems adequate, despite the modest increase in trial size and duration.

Exhibit 2: Proposed design of GDC-0084 Phase II



Source: Novogen investor presentation, April 2017

Background: PI3K and history of GDC-0084

PI3K is a promising target for GBM drug development

The PI3K signaling pathway plays a crucial role in cellular proliferation, metabolism, survival and apoptosis (programed cell death). PI3K signaling is initiated by receptor tyrosine kinases or G-protein coupled receptors located at the cell surface, and by some oncogenic proteins such as Ras.

The PI3K pathway is frequently over-activated in cancer. The over-activation can occur through a variety of mechanisms including mutation and amplification of genes in the pathway, or by loss of function of the tumor suppressor PTEN, which is a negative regulator of PI3K signaling. Abnormal PI3K signaling is associated with over 80% of cases of the GBM.[3]

The first approved cancer drugs that target the PI3K pathway were the rapamycin analogues everolimus and temsirolimus, which inhibit mTORC1. The PI3K inhibitor idelalisib (Zydelig, Gilead Sciences) was first approved by the FDA in 2014 and is approved to treat several types of leukemia and lymphoma, providing validation for PI3K as a target for anticancer drug development. Idelalisib is a selective inhibitor of the delta isoform of PI3K (PI3Kδ).

In March 2016, Gilead halted six combination trials of idelalisib in newly diagnosed patients due to serious side effects including deaths from infections. Idelalisib inhibits the delta isoform of PI3K and

2 Average of Chinot et al *N Engl J Med* 2014; 17:708-717 (67%) and Hegi et al *N Engl JMed* 2005; 352:997-1003 (55%).

3 The Cancer Genome Atlas Research Network. Comprehensive genomic characterization defines human GBM genes and core pathways. Nature 2008, 455, 1061−1068.

inhibiting strongly PI3Kdelta affects the immune system. In contrast, GDC-0084 strongly inhibits PI3Kalpha and only weakly inhibits PI3Kdelta, and has not caused similar side effects in clinical trials.

Thorough GDC-0084 preclinical program

Novogen will benefit from the thorough preclinical development program that Genentech has conducted for GDC-0084.

GDC-0084 is a potent brain-penetrant small molecule inhibitor of PI3Kalpha (EC50 2nM) that was specifically designed for treatment of brain cancer. The drug is also deliberately designed to be a moderately potent inhibitor of mammalian target of rapamycin (mTOR) kinase (EC50 70nm) to avoid the toxicity seen with drugs that are potent inhibitors of both targets.

GDC-0084 was shown to freely cross the blood-brain barrier in the mouse, rat and dog. Studies showed that the drug inhibited PI3K activity in mouse brain, and strongly inhibited tumor growth in animal models using patient-derived tumors.

GDC-0084 combines with radiotherapy for increased efficacy

GDC-0084 showed increased efficacy when it was combined with radiotherapy under different treatment schedules in two separate studies performed in mice with GBM tumors implanted in the brain. However, it was not clear from the mouse studies whether GDC-0084 will give maximum benefit when administered as a monotherapy at the completion of a course of radiotherapy, or whether it would be more effective if it was administered at the same time as radiotherapy.

Phase I trial showed a trend to efficacy at higher doses

Genentech conducted a Phase I study of GDC-0084 in patients with progressive or recurrent high-grade gliomas (WHO Grade III–IV), including GBM and malignant astrocytoma. The study enrolled 47 patients in eight successive dose escalation cohorts (2-65mg). The maximum tolerated doses (MTD) was identified as 45mg.

Overall, the adverse event profile was consistent with PI3K/mTOR class effects; adverse events at the MTD were amenable to monitoring, manageable and reversible upon dose hold or discontinuation. The most common Grade 3 adverse events related to GDC-0084 were hyperglycemia (four patients) and mucositis (three patients).

Oral dosing of GDC-0084 demonstrated favorable pharmacokinetics in the Phase I trial, with sustained plasma levels following daily oral dosing. Analysis of tissue samples from a surgical brain specimen from one patient confirmed that the drug crosses the blood-brain barrier in humans, with concentrations seen in healthy brain and in tumor tissue higher than the levels in plasma (Exhibit 3).

Exhibit 3: GDC-0084 concentration in a surgical brain specimen*

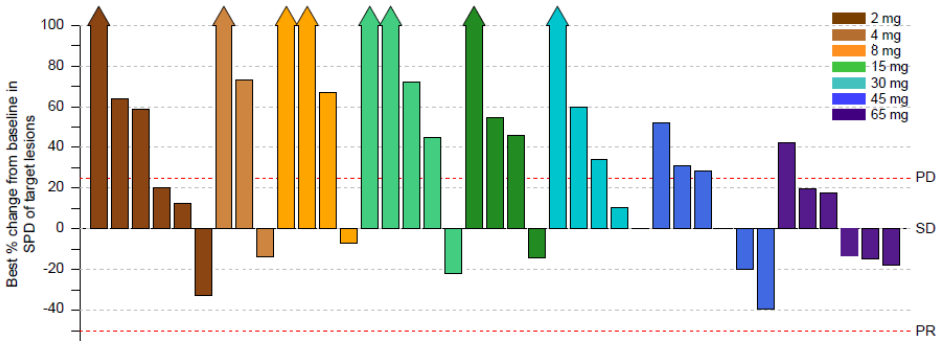
Sample	Total GDC-0084	Free GDC-0084
Plasma	0.56 uM	0.11 uM
Brain Tissue	0.86 uM	0.058 uM
Brain Tumor	0.80 uM	0.054 uM**

Source: Morrissey, Vora et al ASCPT 2016 poster. Notes: *Resection of brain tissue and tumor from a patient dosed at 45 mg QD; samples obtained 5.5 hours (plasma) and 7 hours (brain) post-dose. **Assumes same binding as brain.

Exhibit 4 summarizes the tumor responses for the patients in the Phase I study, grouped by dose cohort. Although none of the tumors reached the 50% reduction in tumor size that would qualify as a partial response, a dose response in tumor growth was apparent, with much less tumor growth in patients treated at 45mg (the MTD) or higher doses.

It is important to note that the Phase I study was performed in patients with late-stage disease and rapidly growing tumors. In the planned Phase II trial, Novogen will be testing whether this reduction in tumor growth is sufficient to improve PFS and/or overall survival in patients with early-stage disease who have undergone surgical resection and radiotherapy.

Exhibit 4: GBM patients in Phase I trial showed a trend to better disease control at higher doses of GDC-0084



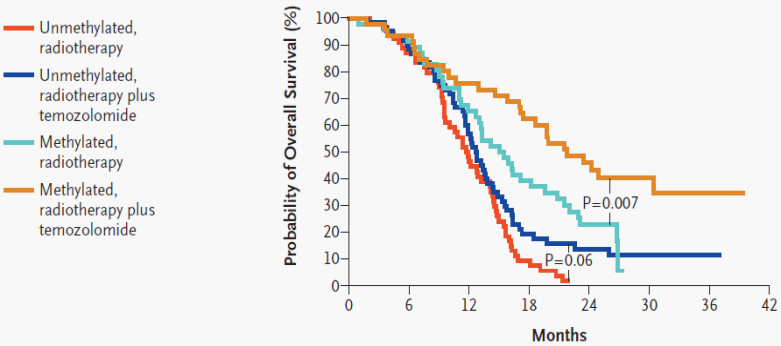
Source: Wen et al 2016 ASCO poster. Note: Maximum tolerated dose was identified as 45mg (blue bars).

Targeting the majority of GBM patients who get minimal benefit from current drug therapy

Novogen anticipates conducting a randomized Phase II trial of GDC-0084 as adjuvant therapy in newly diagnosed GBM patients with unmethylated MGMT promoter. In a seminal study reported in 2005, Hegi et al[4] found that GBM patients with an unmethylated MGMT promoter received only minimal additional benefit when standard of care drug TMZ was added to radiotherapy in first-line treatment of newly diagnosed disease.

Exhibit 5 shows that patients whose tumor contained a methylated MGMT promoter received a survival benefit when TMZ was added to standard radiotherapy; their median survival was 21.7 months, as compared with 15.3 months among those who received only radiotherapy (HR 0.51, P=0.007). In patients with an unmethylated MGMT promoter, there was a smaller and statistically insignificant difference in survival between patients who received TMZ and radiotherapy (orange line) compared to radiotherapy alone (blue line, 12.7 vs 11.8 months, HR 0.69, P=0.06).

Exhibit 5: Adding TMZ to radiotherapy in first line GBM provides little benefit to patients with unmethylated MGMT promoter



Source: Hegi et al *N Engl J Med* 2005;352(10):997-1003

Brain metastases offer potential upside

Although initial development of GDC-0084 will target GBM, it also has the potential to treat brain metastases for a range for different cancers. Brain metastases are quite common, but there are few

4 Hegi et al *N Engl J Med* 2005;352(10):997-1003.

drugs available to treat them. Lung, breast and melanoma represent the majority of brain metastases. Genentech has done preclinical studies showing that GDC-0084 improves survival in mouse models of brain metastases in HER2+ breast cancer. A large study[5] estimated that approximately 7% of HER2+ breast cancer patients eventually develop brain metastases.

The company has highlighted that the treatment of brain metastases from cancers that originate in other parts of the body is a potential opportunity for future partners. In order to provide a modest recognition of this opportunity, we have added a potential indication for the treatment of brain metastases of HER2+ breast cancer in our indicative valuation model.

Additionally, even though GDC-0084 has been specifically designed to cross the blood-brain barrier, it is also likely to be effective against tumors elsewhere in the body. However, at this stage we have not included potential applications of GDC-0084 for any indications other than GBM and breast cancer brain metastases in our valuation model.

Cantrixil Phase I underway – data expected H118

A Phase I study of Cantrixil in ovarian cancer enrolled its first patient on schedule in December 2016. Up to 60 patients are expected to be enrolled across six sites in the US and Australia. While the primary purpose of the trial is to demonstrate safety and tolerability, patients will also be assessed for tumor responses. The trial is expected to take around 18 months to complete, reporting data in H1 CY18. The US FDA has granted Cantrixil Orphan Drug status for ovarian cancer.

Cantrixil is being administered as an intraperitoneal (IP) therapy delivered directly into the abdominal cavity. IP administration delivers higher concentration of the drug to the site of the tumor for longer periods, and studies of advanced ovarian cancer patients have shown a survival benefit for IP delivery compared to intravenous administration of chemotherapy drugs.

Researchers at Yale University have shown that Cantrixil is active in a stringent, clinically relevant rodent model of human ovarian cancer. Cantrixil is the first drug to show uniformly high potency against the Yale library of ovarian cancer stem cells collected from tumors that had stopped responding to chemotherapy. Patients with ovarian cancer face a very poor prognosis, with a five-year survival rate of only 35%, so an urgent unmet clinical need remains for better treatment for ovarian cancer patients.

Trilexium

Trilexium is at an earlier stage of development than GDC-0084 and Cantrixil. The company is undertaking an ongoing program of drug formulation, preclinical efficacy and toxicology studies, but the drug is not expected to enter the clinic before 2018. If Cantrixil shows signs of efficacy in the ongoing Phase I trial, then we would expect to see increased focus on the development of Trilexium.

Trilexium has shown efficacy against cells from a wide range of cancers, including melanoma, colorectal, liver, lung, breast, prostate and brain cancers, in *in vitro* studies. Notably, the drug is highly cytotoxic against patient-derived explants of the childhood brain cancer known as diffuse intrinsic pontine glioma (DIPG) *in vitro*. Trilexium also inhibits tumor growth in flank models where GBM, melanoma and prostate cancer tumors are growing under the skin of rodents.

In addition, combination therapy with Trilexium and the BRAF inhibitor dabrafenib (Tafinlar, GlaxoSmithKline) inhibited melanoma tumor growth and improved survival in mice to a significantly greater extent than dabrafenib alone.

5 Pestalozzi et al *Ann Oncol*. 2006 Jun;17(6):935-44.

Additional orthotopic animal studies are planned where the human tumor cells are growing in the same organ as the original cancer. This allows the cancer cells to interact with the surrounding organ tissue, which affects the growth, differentiation and drug sensitivity of tumor cells. Mechanism of action and biomarker studies are underway, aimed at informing patient selection for future clinical trials.

Anisina terminated, new ATM discovery program funded

The company has terminated development of Anisina, following inconsistent efficacy and emerging toxicology findings in preclinical studies that raised concerns about whether a therapeutically active dose could be safely administered to patients. The scientific committee of the board of directors concluded that the available preclinical data did not support initiation of clinical trials for Anisina. Anisina had been scheduled to enter the clinic in H2 CY17.

Separately, a collaboration led by Novogen has been awarded a grant of up to $2m from the Australian government payable over three years to develop next-generation ATM therapies for cancer treatment. The research is distinct from the technology underlying the terminated Anisina program.

Novogen is the lead partner in the collaboration that also involves the University of New South Wales and the privately held CRO, ICP Firefly. Novogen will contribute $0.7m and the University of New South Wales will contribute $0.2m to funding the project.

While the project is at a very early stage, it could potentially provide a new ATM drug with a superior toxicity and activity profile to address the market opportunity that had previously been identified for Anisina.

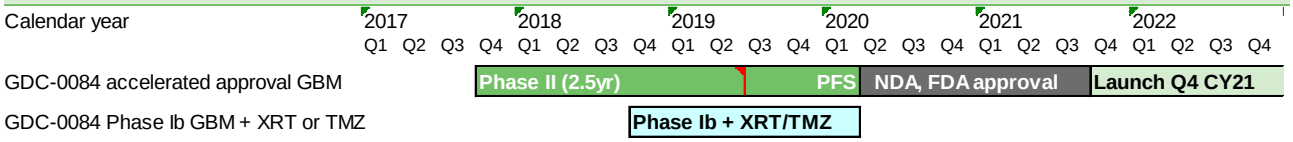
Development scenarios for GDC-0084 post-Phase II

We consider two potential development scenarios for GDC-0084 in GBM (accelerated approval post-Phase II or standard approval post-Phase III), as outlined below.

Potential for accelerated approval if Phase II is positive

If the upcoming Phase II trial of GDC-0084 in GBM demonstrates that treatment with GDC-0084 delivers a statistically significant and clinically meaningful improvement in PFS, then this would probably justify filing an application for accelerated approval. With PFS data anticipated in H1 CY20, this scenario could potentially see the drug launched in H2 CY21 as shown in Exhibit 6.

Exhibit 6: Assumed clinical trial and approval timeline for GDC-0084 accelerated approval

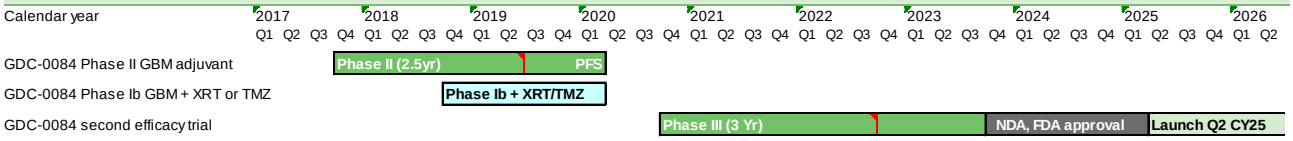


Source: Edison Investment Research

Potential timeline for Phase III approval scenario

Our second scenario assumes that the results of the first Phase II trial indicate that GDC-0084 is efficacious against GBM, but that additional evidence from a second clinical trial is required before filing for approval. We anticipate that this second trial would take three years to complete and note that it could potentially involve combining GDC-0084 with radiotherapy or TMZ. Exhibit 7 shows our forecast timeline for this two-trial scenario, which could potentially see a launch in H1 CY25.

Exhibit 7: Assumed clinical trial and approval timeline for GDC-0084 under two-trial scenario



Source: Edison Investment Research

An additional Phase Ib would give a partner more options

In our view, Novogen could give potential partners more options for future development of GDC-0084 by completing an additional Phase Ib trial while the Phase II trial is underway. One potential option for such a trial would be to identify the dose GDC-0084 can be safely administered while the patient is undergoing radiotherapy treatment (concurrent administration); a second option would be to identify a dose of GDC-0084 that can be safely used in combination with TMZ (ie adding GDC-0084 on top of TMZ therapy).

Both of these treatment strategies could potentially lead to higher overall efficacy. Adding GDC-0084 on top of standard TMZ therapy would have the added advantage of opening up the potential to treat GBM patients with a methylated MGMT promoter, as well as the unmethylated patient population to be targeted in the upcoming Phase II trial.

Novogen has not disclosed any plans to conduct an additional Phase Ib trial, but we have included one in Exhibits 6 and 7 to illustrate potential timing.

Valuation

We have substantially revised our valuation model for Novogen to reflect the termination of the Anisina development program, the addition of GDC-0084 following the completion of the in-licensing transaction, and longer development timelines for Cantrixil and Trilexium. We have valued GDC-0084 under two different development scenarios for GBM – in addition to our base case valuation, which assumes market launch in 2025 following completion of a Phase III trial, we have also valued GDC-0084 assuming accelerated approval with a launch in 2021.

As a result of these changes our base case valuation of Novogen has declined to $66m (previously $86m) or $3.39/ADR undiluted (vs $4.95/ADR) and $3.23/ADR after diluting for options and convertible notes. Novogen's primary listing is on the ASX under the code NRT; each NASDAQ-listed ADR represents 25 ordinary shares. Our undiluted base case valuation equals A$0.18 per ASX-listed ordinary share at current exchange rates. Note that the per-ADR value accounts for the shares issued as part of the acquisition of Glioblast ($1.1m in shares) but not the Glioblast milestone payments (potentially $1.0m of shares in FY18 on initiation of Phase II, and a further $1.0m potentially payable in FY20 on successful completion of Phase II).

In both valuation scenarios for GDC-0084, we assume that the program is out-licensed to a marketing partner in mid-2020 after reporting PFS data from the Phase II trial in a deal that includes $120m in clinical and regulatory milestone payments (but differing upfront payments; we risk-adjust milestone payments in our forecasts). We also assume that Novogen pays a royalty of 10% of net sales to Genentech and that global sales for GBM reach $1,050m in 2030.

Under both scenarios for GDC-0084 we also include a second indication for the treatment of brain metastases in patients HER2+ breast cancer, with a 2026 launch date.

The two scenarios assume different launch dates, upfront payment amounts and royalty rates payable to Novogen. For the post-Phase III approval scenario used in our base case valuation, we

assume a 2025 launch date, and that the license deal includes a $20m upfront payment and that Novogen receives a 15% royalty on net sales (the accelerated approval scenario valuation is discussed below Exhibit 8).

We have revised forecast development timelines for Cantrixil and Trilexium to include a Phase II trial duration of 2.5 years in line with the forecast for GDC-0084 (vs two years previously). Cantrixil is now assumed to be launched in 2025 (vs 2024). Trilexium is now assumed to commence clinical trials in 2018 (vs 2017) and launch in 2027 (vs 2026).

While our valuation reflects our understanding of the likely development path for Novogen's three lead drugs, it should be considered as indicative because of the early stage of development of Cantrixil and Trilexium. Our valuation is based on a risk-adjusted discounted cash flow model. Our cash flow forecasts extend out to 2035, but do not include any terminal valuation and apply a 12.5% discount rate. In calculating the diluted NPV/share, we assume that the $0.5m remaining balance of the Triaxial convertible note is converted to 24m shares on completion of Phase II trials. (the $1.1m convertible note was issued as part of the purchase of Triaxial and its SBP technology, $0.7m was converted in H1 FY17).

Exhibit 8 shows our base case market assumptions for GDC-0084, Cantrixil and Trilexium and the contribution of product royalties and milestone payments to the rNPV. We have offset the risk-adjusted trial cost against milestone revenue for each drug, rather than against royalty revenue. This understates the contribution of the milestone payments to the rNPV and overstates the contribution of royalties.

Exhibit 8: Novogen base case valuation (assumes confirmatory GDC-0084 pivotal trial required)

	Likelihood (%)	rNPV ($m)	rNPV/ ADR ($)	Assumptions
GDC-0084 – GBM	25%	13.0	0.67	Global peak sales* of $1,050m from GBM (11,500 US cases/year, 61% unmethylated MGMT promoter, 80% penetration); pricing of $50k. Global sales 2x US sales; launch 2025; assumes receives 15% royalty on sales, pays away 10% of royalty to Genentech.
GDC-0084 – brain metastases in HER2+ breast cancer	20%	5.4	0.28	Global peak sales of $570m (233,000 US breast cancer cases/year, 37% HER2+, 7% develop brain metastases, 50% penetration); pricing of $50k. Global sales 2x US sales; launch 2026; assumes receives 15% royalty on sales, pays away 10% of royalty to Genentech.
Ovarian and other abdominal cancers: Cantrixil	10%	20.2	1.04	Global peak sales of $680m from ovarian cancer (14,300 US deaths/year, 30% penetration) and bowel cancer (50,300 US deaths, 25% develop malignant ascites, 20% penetration); pricing of $50k. Global sales 2x US sales; launch 2025; assumes receives 15% royalty on sales, pays away 5% of revenue to Yale.
Melanoma: Trilexium	5%	3.2	0.17	Global peak sales of $$300m assuming 9,700 US deaths/year; 30% penetration; pricing of $50k. Global sales 2x US sales; launch 2027; assumes receives 15% royalty on sales.
Brain cancer: Trilexium	5%	2.9	0.15	Global peak sales of $300m assuming annual US incidence of GBM of 11,500 cases, 25% penetration; DIPG US incidence 275, 80% penetration; pricing of $50k. Global sales 2x US sales; DIPG launch 2027; 15% royalty on sales.
GDC-0084 milestones		2.2	0.11	Assumes potential licensing upfronts and milestones total $140m ($127m net of payments to Glioblast and Genentech; $38m after risk adjustment).
Cantrixil milestones		9.1	0.47	Assumes potential licensing upfronts and milestones total $140m ($23m after risk adjustment); assumes 5% of upfront and milestone payment paid away to Yale.
Trilexium milestones		3.6	0.18	Assumes potential licensing upfronts and milestones total $140m ($14m risk adjusted).
SG&A to 2020		-8.1	-0.42	
Portfolio total		51.4	2.66	
Cash (31 December 2016)		14.1	0.73	
Enterprise total		65.6	3.39	

Source: Edison Investment Research. Note: *Peak sales in actual dollars in forecast year. We had previously expressed peak sales in 2015 dollars based on current addressable market. We assume that the addressable markets grow at 4% per year. Launch dates listed are calendar years (in some cases the launch will be in the following financial year to the calendar year stated).

For our alternative accelerated approval valuation scenario, we assume a market launch in late 2021 and that Novogen receives a higher 20% royalty rate and a larger $40m upfront payment because the data are ready for filing, with other deal terms the same as for the Phase III approval scenario. Exhibit 9 shows that accelerated approval for GDC-0084 would increase our valuation for

Novogen to $111m or $5.74/ADR (undiluted) and $5.41/ADR after diluting for options and convertible notes.

Exhibit 9: Novogen valuation in GDC-0084 accelerated approval scenario

	Likelihood (%)	rNPV ($m)	rNPV/ ADR ($)	Assumptions
GDC-0084 – GBM	25%	45.6	2.36	As for Exhibit 8, except 2021 launch (vs 2025) and 20% gross royalty on sales (vs 15%).
GDC-0084 – brain metastases in HER2+ breast cancer	20%	10.7	0.55	As for Exhibit 8, except 20% gross royalty on sales (vs 15%).
GDC-0084 milestones		9.7	0.50	Assumes potential licensing upfronts and milestones total $160m ($147m net of payments to Glioblast and Genentech; $48m after risk adjustment). Milestones received earlier than base case (final milestone in 2021 vs 2025).
GDC-0084 total		66.0	3.41	
Remainder of portfolio		30.9	1.60	
Portfolio total		96.9	5.01	
Cash (31 December 2016)		14.1	0.73	
Enterprise total		111.0	5.74	

Source: Edison Investment Research. Launch dates listed are calendar years.

Sensitivities

The key sensitivity for Novogen will be the success of its three lead drugs in clinical trials. A crucial question regarding GDC-0084 will be whether it works sufficiently well as a single agent in adjuvant therapy to justify accelerated approval. If it needs to be used concurrently with radiotherapy or with TMZ to deliver sufficient efficacy in GBM then one or more additional efficacy trials may be required, as outlined in our base case scenario, delaying potential launch until 2025 vs 2021 under an accelerated approval scenario. There is also a significant risk that GDC-0084 may not provide sufficient survival benefit to justify approval either as a single agent or combination therapy.

We have assumed that a Phase Ib study of GDC-0084 in combination with either radiotherapy or TMZ is conducted in parallel with the planned Phase II trial, but that will be dependent on adequate funding.

While Novogen has funds to initiate the Phase II study of GDC-0084 in GBM, we estimate that it would require additional funds of ~$19m over 2018 and 2019 to complete all the planned trials, which could result in significant dilution of existing shareholders given the current market capitalization of ~$18m.

Our valuation includes revenues from the development of three drugs in five disease indications, as well as (risk-adjusted) upfront and milestone payments for three licensing deals. While each of these targeted indications is supported by the current preclinical efficacy studies and evidence of a dose response in the GDC-0084 Phase I trial, the company may not ultimately pursue development of the drugs for all of these indications. On the other hand, ongoing preclinical efficacy studies could identify additional disease indications that should be investigated in clinical trials. While we believe that the drug development timelines used in our forecasts are achievable, at this early stage it is hard to accurately predict how long it will take to get the drugs to market.

Financials: Additional funds likely required in FY18

Novogen's H1 FY17 results (six months ending 31 December 2016) showed a net loss of $3.2m, 6% larger than the previous corresponding period. R&D expenses were virtually unchanged at $3.7m compared to $3.8m in H1 FY16. Administration expenses rose to $3.0m (vs $2.3m in H116), including costs associated with the GDC-0084 transaction. Cash at 31 December was $14.1m.

Glioblast and the GDC-0084 license acquired in 2016 are valued in the accounts at $14.9m. The valuation comprises $5.4m cash consideration $5m to Genentech and $0.5m to Glioblast) and $1.1m shares issued to Glioblast vendors (17.2m shares at A$0.09), plus contingent consideration of $3.9m and deferred tax liability of $4.5m. The contingent consideration payable to Glioblast comprises four milestone payments, while the contingent consideration to Genentech comprises a single milestone payable on market launch of GDC-0084. Novogen has probability weighted the milestones and then discounted to present value in calculating the $3.9m valuation.

We have updated our financial forecasts to reflect termination of Anisina development and later timing of forecast spending on GDC-0084 and Trilexium clinical trials. We have reduced forecast R&D expenditure by 44% to $8.3m in FY17 and by 26% to $17.1m in FY18. We estimate that Novogen has sufficient funds to support operations to the end of FY17, but will require addition funds of ~$8m in FY18 and a further $12m in 2019 if Trilexium progresses to clinical trials and the GDC-0084 Phase II trial progresses as planned (part of the FY19 funding requirement could be met by upfront payments if Cantrixil is out-licensed at the completion of the Phase I trial). Note that we include unrisked clinical trial costs in our financial forecasts to show the potential funding requirement if the clinical trial program is conducted in line with our expectations (trial costs risk-adjusted for NPV calculation).

Exhibit 10: Financial summary

US$000s	2014	2015	2016	2017e	2018e
Year end 30 June	AASB	AASB	AASB	AASB	AASB
PROFIT & LOSS					
Sales, royalties, milestones	0	0	0	0	0
Other (includes R&D tax rebate)	260	1,244	2,786	3,344	7,241
Revenue	260	1,244	2,786	3,344	7,241
R&D expenses	(1,882)	(4,511)	(7,519)	(8,320)	(17,080)
SG&A expenses	(2,808)	(2,484)	(3,891)	(4,504)	(3,408)
Other	0	0	0	0	0
EBITDA	(4,430)	(5,751)	(8,625)	(9,480)	(13,246)
Operating Profit (before GW and except.)	(4,021)	(5,755)	(8,680)	(9,570)	(13,334)
Intangible Amortization	(433)	(433)	(433)	(50)	(1,213)
Exceptionals	0	848	(432)	0	0
Operating Profit	(4,454)	(5,340)	(9,546)	(9,620)	(14,547)
Net Interest	(477)	(213)	308	254	110
Profit Before Tax (norm)	(5,752)	(6,401)	(8,805)	(9,365)	(14,437)
Profit Before Tax (reported)	(5,752)	(5,553)	(9,237)	(9,365)	(14,437)
Tax benefit	0	0	0	0	0
Profit After Tax (norm)	(5,752)	(6,401)	(8,805)	(9,365)	(14,437)
Profit After Tax (reported)	(5,752)	(5,553)	(9,237)	(9,365)	(14,437)
Average Number of Shares Outstanding (m)	156.7	238.4	427.4	456.5	483.3
Average Number of ADRs Outstanding (m)	6.3	9.5	17.1	18.3	19.3
EPS - normalized (c)	(3.62)	(2.28)	(2.16)	(2.05)	(2.99)
EPS - diluted	(3.62)	(2.28)	(2.16)	(2.05)	(2.99)
Dividend per share (c)	0.0	0.0	0.0	0.0	0.0
Earnings per ADR - normalized (c)	(90.4)	(56.9)	(54.0)	(51.3)	(74.7)
Earnings per ADR - diluted (c)	(90.4)	(56.9)	(54.0)	(51.3)	(74.7)
Dividend per ADR (c)	0.0	0.0	0.0	0.0	0.0
BALANCE SHEET					
Fixed Assets	1,536	1,133	1,084	15,612	15,338
Intangible Assets	1,490	1,056	625	15,166	13,953
Tangible Assets	10	65	450	436	1,375
Investments	36	12	10	11	11
Current Assets	2,005	33,933	25,908	12,193	5,937
Stocks	0	0	0	0	0
Debtors	50	114	151	151	151
Cash	1,902	33,722	25,424	11,038	4,782
Other	53	96	333	1,003	1,003
Current Liabilities	(2,468)	(1,351)	(1,088)	(1,088)	(1,088)
Creditors	(197)	(1,230)	(988)	(988)	(988)
Short term borrowings	(2,057)	0	0	0	0
Other	(214)	(121)	(100)	(100)	(100)
Long Term Liabilities	0	0	(117)	(8,973)	(16,573)
Long term borrowings	0	0	0	0	(7,600)
Other long term liabilities	0	0	(117)	(8,973)	(8,973)
Net Assets	1,073	33,715	25,788	17,744	3,613
CASH FLOW					
Operating Cash Flow	(4,339)	(4,377)	(9,411)	(9,186)	(12,941)
Net Interest	0	0	308	254	110
Tax	0	0	0	0	0
Capex	(21)	(74)	(399)	(76)	(1,026)
Acquisitions/disposals	0	6	2	(5,394)	0
Equity Financing	2,123	36,035	594	15	0
Dividends	0	0	0	0	0
Other	0	0	0	0	0
Net Cash Flow	(2,237)	31,590	(8,906)	(14,386)	(13,856)
Opening net debt/(cash)	(1,005)	156	(33,722)	(25,424)	(11,038)
HP finance leases initiated	0	0	0	0	0
Other	1,076	2,288	608	0	0
Closing net debt/(cash)	156	(33,722)	(25,424)	(11,038)	2,818

Source: Novogen accounts, Edison Investment Research. Note: Solely for the convenience of the reader the financial summary table has been converted at a rate of US$0.76 to A$1. Novogen reports statutory accounts in Australian dollars. These translations should not be considered representations that any such amounts have been or could be converted into US dollars at the assumed conversion rate.

Contact details	Revenue by geography
Level 1 16-20 Edgeworth David Avenue Hornsby NSW 2077 Australia Tel: +61 2 9472 4100 www.novogen.com	N/A

Management team

CEO: Dr James Garner	Chairman: John O'Connor
Dr Garner is an experienced life sciences executive who has previously worked with companies ranging from small biotechs to multinational pharmaceutical companies such as Biogen and Takeda. His career has focused on regional and global development of new medicines from preclinical to commercialisation. Dr Garner is a physician by training and holds an MBA from the University of Queensland. He began his career in hospital medicine and worked for a number of years as a corporate strategy consultant with Bain & Company before entering the pharmaceutical industry. Prior to joining Novogen in 2016, he led R&D strategy for Sanofi in Asia-Pacific and was based in Singapore.	John has spent his working life in the financial industry. In this time he has worked both in fund management and as a stockbroker. He has worked in the UK, the US and in Australia. He has held management roles and been a partner in securities businesses. He served on the Board of Lonsec Securities, a Zurich Insurance owned business, for several years. He has been a consultant to several biotech businesses, including MEI Pharma, assisting with fundraising.

Principal shareholders	(%)
National Nominees	41.6
Hishenk Pty Ltd	2.1
Dr Andrew Heaton	1.2

Companies named in this report

Roche

Frankfurt +49 (0)69 78 8076 960
Schumannstrasse 34b
60325 Frankfurt
Germany

London +44 (0)20 3077 5700
280 High Holborn
London, WC1V 7EE
United Kingdom

New York +1 646 653 7026
245 Park Avenue, 39th Floor
10167, New York
US

Sydney +61 (0)2 9258 1161
Level 25, Aurora Place
88 Phillip St, Sydney
NSW 2000, Australia