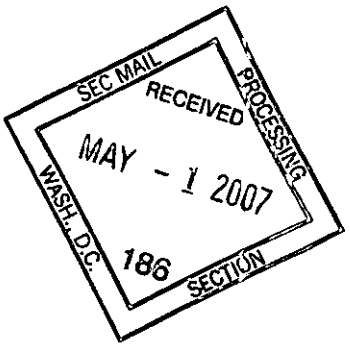
Bionomics Limited

17 April 2007



Securities and Exchange Commission
Judiciary Plaza,
450 Fifth Street,
Washington DC 20549

SUPPL

Re: Bionomics Limited - File number 82-34682

Please see attached provided pursuant to Section 12g3-2(b) file number 82-34682.

Yours sincerely

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FINANCIAL

Stephen Birrell
CFO & Company Secretary

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ASX ANNOUNCEMENT
17 April 2007

BIONOMICS PRESENTS CANCER DATA AT KEY INTERNATIONAL CANCER CONFERENCE

Tuesday 17 April 2007, Adelaide: Drug discovery company, Bionomics Limited (ASX:BNO), today presents the latest preclinical data for its cancer drug candidate, BNC105, at the 2007 Annual American Association for Cancer Research Conference.

Dr Gabriel Kremmidiotis, Bionomics' Vice President of Discovery Research presents the latest preclinical findings revealing that BNC105 has even greater capability to regress tumours than initially expected. The mouse studies showed that following two cycles of BNC105 treatment 14 per cent of mice carrying human breast cancer became tumour free.

"Although we have previously seen BNC105 stopping tumour growth or causing tumour regression, in our latest dose optimization experiments we saw for the first time that BNC105 caused some tumours to completely disappear", said Dr Kremmidiotis.

In studies involving 64 tumour bearing animals, four injections of BNC105 produced significant suppression of tumour growth or regression in 45% of the animals and an additional 14% of the animals were cleared of their tumour burden with the tumours not re-appearing. In this 70 day study BNC105 was administered on days 1, 8, 29 and 36.

"In addition, more recently we have obtained evidence that BNC105 is likely to be active against more than one tumour type," said Dr Kremmidiotis. Our studies showed that BNC105 exhibits very high potency in disrupting blood vessels in a model of human colon cancer. "This is a great result," he added.

Dr Deborah Rathjen, CEO of Bionomics said, "We are thrilled with the rapid progress BNC105 has made in this phase of its development and we look forward to commencing our phase I clinical trials later this year following our anticipated Investigational New Drug (IND) submission to the US Food and Drug Administration (FDA)".

BNC105 is a new type of drug called a Vascular Disruption Agent (VDA) that acts to rapidly shut down the blood supply within a tumour. It thereby "starves" the tumour of the oxygen and nutrients it needs to survive.

Vascular Disruption Agents have significant clinical potential in the treatment of cancer, as they may potentially be applied across a very wide variety of cancer types, including colon, lung and breast cancers. The market potential for VDAs has been estimated at approximately US$5 billion annually (ASInsights, 2003).

The 2007 Annual American Association for Cancer Research Conference poster presentation summarising the latest BNC105 preclinical data has been posted on Bionomics' website www.bionomics.com.au.

FOR FURTHER INFORMATION PLEASE CONTACT:

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About Bionomics Limited

Bionomics (ASX: BNO) discovers and develops innovative therapeutics for cancer and diseases of the central nervous system. Bionomics has small molecule product development programs in the areas of cancer, anxiety, epilepsy and multiple sclerosis. Bionomics' most advanced program, BNC105 for the treatment of cancer, is based upon the identification of a novel compound that potently and selectively restricts blood flow within tumours. Bionomics' discovery and development activities are driven by its three technology platforms: Angene®, the company's angiogenesis target and drug discovery platform, incorporates a variety of genomics tools to identify and validate novel angiogenesis targets. MultiCore® is Bionomics' proprietary, diversity orientated chemistry platform for the discovery of small molecule drugs. ionX® is a set of novel technologies for the identification of drugs targeting ion channels for diseases of the central nervous system. Bionomics was recently ranked in the top 10 in the Deloitte's Technology Fast 50 Australian technology companies.

For more information about Bionomics, visit **www.bionomics.com.au**

Factors Affecting Future Performance

This announcement contains "forward-looking" statements within the meaning of the United States' Private Securities Litigation Reform Act of 1995. Any statements contained in this press release that relate to prospective events or developments, including, without limitation, statements made regarding BNC105 and its' drug development programs are deemed to be forward-looking statements. Words such as "believes," "anticipates," "plans," "expects," "projects," "forecasts," "will" and similar expressions are intended to identify forward-looking statements. There are a number of important factors that could cause actual results or events to differ materially from those indicated by these forward looking statements, including risks related to our available funds or existing funding arrangements, a further downturn in our customers' markets, our failure to introduce new products or technologies in a timely manner, regulatory changes, risks related to our international operations, our inability to integrate acquired businesses and technologies into our existing business and to our competitive advantages, as well as other factors. Subject to the requirements of any applicable legislation or the listing rules of any stock exchange on which our securities are quoted, we disclaim any intention or obligation to update any forward-looking statements as a result of developments occurring after the date of this announcement.

Discovery and development of BNC105P, a novel tubulin polymerisation inhibitor with a superior therapeutic index

Gabriel Kremmidiotis, Tina Lavranos, Annabell Leske, Donna Beaumont, Jelena Gasic, Allison Hall, Michael O'callaghan, Gurmit Gill, Damien Grobelny, Bernard Flynn.

Bionomics Limited

Vascular Disruption Agents (VDA) target endothelial cells lining blood vessels in solid tumors, causing occlusion of tumor vasculature and tumor cell necrosis due to hypoxia. Tumor vascular disruption is a therapeutic strategy of great potential, however VDA compounds currently under development display a narrow therapeutic margin between efficacy and toxicity, with cardiovascular toxicity posing as the major dose limiting obstacle. Discovery of new VDA compounds that display a wide therapeutic margin will enable us to fully harness the therapeutic potential of blocking tumor vasculature. In order to identify such compounds we used a novel in vitro screening approach that exploits the different activation states displayed by endothelial cells stimulated by growth factors found in a solid tumor milieu versus endothelial cells that are present in normal tissues and are deprived of such growth factors. Our effort has yielded the compound BNC105. This compound displays 100-fold higher potency against endothelial cells that are actively proliferating or are engaged in angiogenic processes as compared to non-proliferating endothelial cells or endothelium found in stable capillaries. This selectivity profile was not seen with other tubulin polymerisation inhibitors currently in clinical development as VDAs. BNC105 disrupts the vasculature in human breast and colon solid tumors grown in nude mice but does not affect the vasculature in normal organs. One dose of 1mg/kg BNC105 administered iv disrupted 50% of tumor vasculature. Animals treated with 80mg/kg BNC105 did not exhibit any signs of toxicity, demonstrating a therapeutic margin of 80. A single 10mg/kg iv dose of BNC105 disrupted more than 95% of tumor vasculature in breast and colon cancer models. With repeated dosing this resulted in up to 75% tumor growth inhibition. With repeat dosing 40 mg/kg iv BNC105 caused 52% tumor regression and prolongation of survival time. Fourteen percent of tumor bearing animals were cleared of their tumor burden following 2 cycles of BNC105 treatment. BNC105 exhibits pharmacokinetic and pharmacodynamic profiles that justify commencement of clinical development.

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INTRODUCTION

The disruption of blood vessels that feed tumors represents one of the most promising therapeutic strategies for treating cancer. Until recently, the majority of research underlying this concept has focused on the discovery of agents that inhibit formation of new blood vessels in tumors, a process known as tumor angiogenesis. However, more recently, the importance of disrupting existing tumor vessels has been recognised and research efforts have expanded to the discovery of anti-vascular agents that cause shutdown of tumor vasculature, leading to extensive tumor death (Pilat et al *2004*; Cooney et al *2005*). Microtubules are filamentous intracellular structures that play a critical role in the function of cells. They act as a scaffold that determines cell shape and provides a network of "tracks" for intracellular vesicles and organelles to move on. Furthermore, microtubules are responsible for the formation of the mitotic spindle, a network of fibres that forms during cell division and guides the separation of chromosomes (Desai & Mitchison *1997*; Nogales *2000*). Compounds that target microtubule function by binding to of the protein tubulin have yielded very encouraging results in preclinical animal studies. These compounds, referred to as Vascular Disruption Agents (VDAs), elicit their anti-vascular effect through disruption of the cytoskeleton resulting in endothelial cell swelling (Siemann et al 2005; Tozer et al 2005). The swelling of endothelial cells can result in blood vessel occlusion and shutdown of the blood circulation. This effect is particularly pronounced in tumors. Certain aberrant features make tumor vasculature more susceptible to the cell swelling effects induced by VDAs. Despite encouraging results obtained in animal models the development of tubulin polymerisation inhibitors as vascular disruption agents in the clinic has been very slow, possibly due to toxicity issues associated with disruption of normal endothelial cells. Human endothelial cells may be more susceptible to the in vivo action of VDAs than endothelial cells in experimental animals. There is a clear need for the development of improved VDA compounds that are able to distinguish between tumor and normal endothelial cells. It is reasonable to hypothesise that compounds that exhibit selectivity for tumor vasculature may further enhance the specificity of VDA action. This is likely to alleviate some of the toxicity issues seen in the clinic to-date and result in significant increases in therapeutic index. The ability to influence the cell shape of actively proliferating versus non-proliferating endothelial cells in culture has been one of the most commonly used selection criteria for the identification of tubulin polymerisation inhibitors that have the ability to act as selective disruptors of tumor vasculature. Representative examples of this approach are the published work of Davis et al (*2002*) on ZD6126 and Dark et al (*1997*) on CA4P. We have utilised an in vitro system that allows comparative investigation of activated (tumor) versus quiescent (normal) endothelial cells as defined by endothelial cell proliferation under the influence of growth factors and the ability of endothelial cells to engage in the formation and maintenance of capillary tubes in vitro. We utilised these in vitro assays to evaluate a library of over 100 compounds exhibiting tubulin polymerisation inhibition (TPI) activity. The aim of this undertaking was to identify compounds that exhibit higher activity for activated endothelial cells than quiescent endothelial cells. It is reasonable to anticipate that such compounds will exhibit selectivity for the endothelium in tumors, sparing endothelium in normal tissues.

MATERIALS & METHODS

Proliferation assays were carried out in triplicate in 96-well plates using an MTT assay. Absorbance readings for each compound concentration were normalised to no-compound control cultures. For capillary formation assays cells were plated on Matrigel® at 25,000/well in 96-well plates and cultured for 22hrs. In vitro tubulin polymerisation assays utilised bovine neuronal tubulin that was allowed to polymerise in vitro in the presence of different concentrations of BNC105 or CA4. Fluorescence measurements were obtained over a period of 42 minutes at 1 minute intervals. Endothelial cell monolayer permeability was assessed using an in vitro Vascular Permeability Assay kit (ECM640, Chemicon) as previously described (Watts et al, 1997). All in vitro assays were carried out using endothelial cells derived from human umbilical vein (HUVEC) or human abdominal aorta (HAAEC). Primary in vivo evaluations of BNC105P efficacy were carried out using either an orthotopic human breast cancer model or a subcutaneous colon cancer model. The breast model involves the injection of MDA-MB-231 human breast cancer cells under the mammary fat pad of female Balb/c nu/nu mice; the colon model involves the injection of Colo205 cells subcutaneously on the right hind flank of female Balb/c nu/nu mice. The cells are allowed to grow for 2-3 weeks forming a solid tumor of approximately 50-100mm^3 in size. BNC105 has low solubility. For in vivo administration we synthesised BNC105 in a disodium phosphate "prodrug" chemical arrangement, BNC105P. BNC105P is completely soluble in saline and is rapidly converted into the BNC105 drug in vivo. BNC105P solutions were administered by single bolus intravenous injections through the tail vein.

RESULTS & DISCUSSION

Identification of BNC105, a compound that exhibits high activity against proliferating endothelial cells and comparatively low activity against quiescent endothelial cells. We have constructed a library of TPI compounds based on a benzofuran ring chemical core. We evaluated each of these compounds for its activity on human endothelial cells cultured in the presence or absence of growth factors that promote endothelial cell proliferation (VEGF, hFGF-B, IGF-1, hEGF, heparin). In the presence of these growth factors, cells were seeded at a density that allows further growth whereas, in the absence of growth factors cells were seeded at higher densities in order to promote survival and emulate close cell-cell contact interactions that are expected to be in operation between quiescent endothelial cells lining normal blood vessels. Our analyses identified a small number of compounds that exhibit selectivity for activated endothelial cells (Fig. 1). Compound BNC105 exhibited the highest degree of selectivity being 100 times more active against activated endothelial cells than quiescent endothelial cells (Figs. 1, 2). This selectivity was not seen with other TPI drugs currently in clinical trials, namely CA4 (Fig. 2) or ABT751 (Fig. 2). Furthermore, BNC105 exhibited significantly higher potency than CA4 and ABT751 against proliferating endothelial cells. In addition, to studying HUVEC we also investigated the activity of BNC105 against activated and quiescent HAAEC cells. As seen for HUVEC, BNC105 exhibited 100-fold selectivity for activated HAAEC cells (data not shown). These findings demonstrate that the selectivity displayed by BNC105 for activated endothelial cells is not restricted to HUVEC.

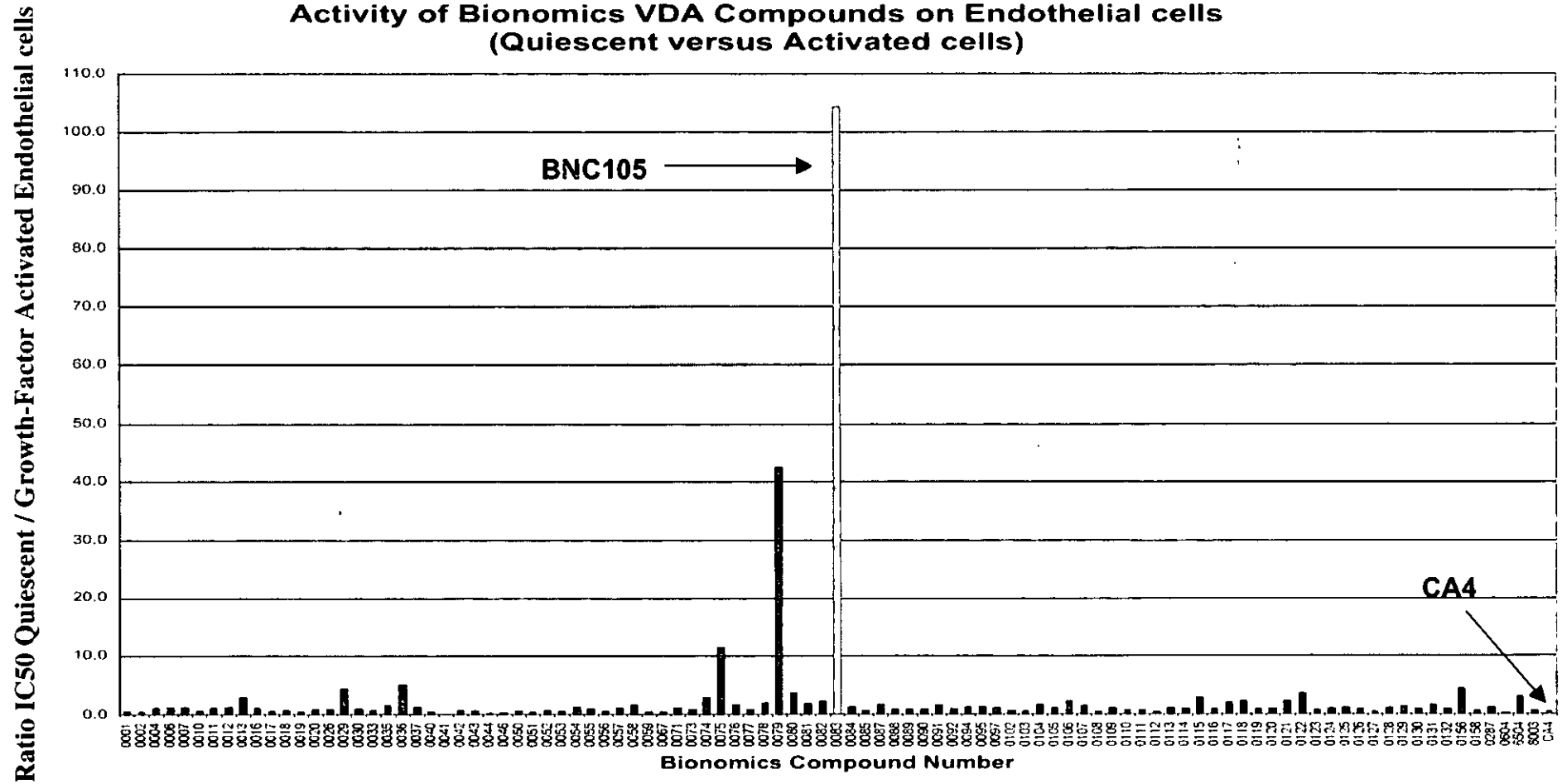


Figure 1. Activity exhibited by Bionomics' TPI compounds on HUVEC. HUVEC were cultured either in the presence (activated) or absence (quiescent) of growth factors. Activated and quiescent cell cultures were exposed to a range of concentrations for each of the compounds tested (0.1nM -1000nM). Following a 48hr incubation period cell proliferation was measured using an MTT assay (absorbance readings - 492nm). Absorbance readings were normalised to no-compound control cultures corresponding to activated and quiescent cells respectively. Normalised values were used to derive IC50 values for each compound for activated and quiescent cells. The graph in this figure displays the IC50-quiescent/IC50-activated ratio for each of the compounds tested. BNC105 (compound 0083 – shown in Blue) exhibited a ratio of over 100. The compound CA4 (shown in red) was used as a comparator.

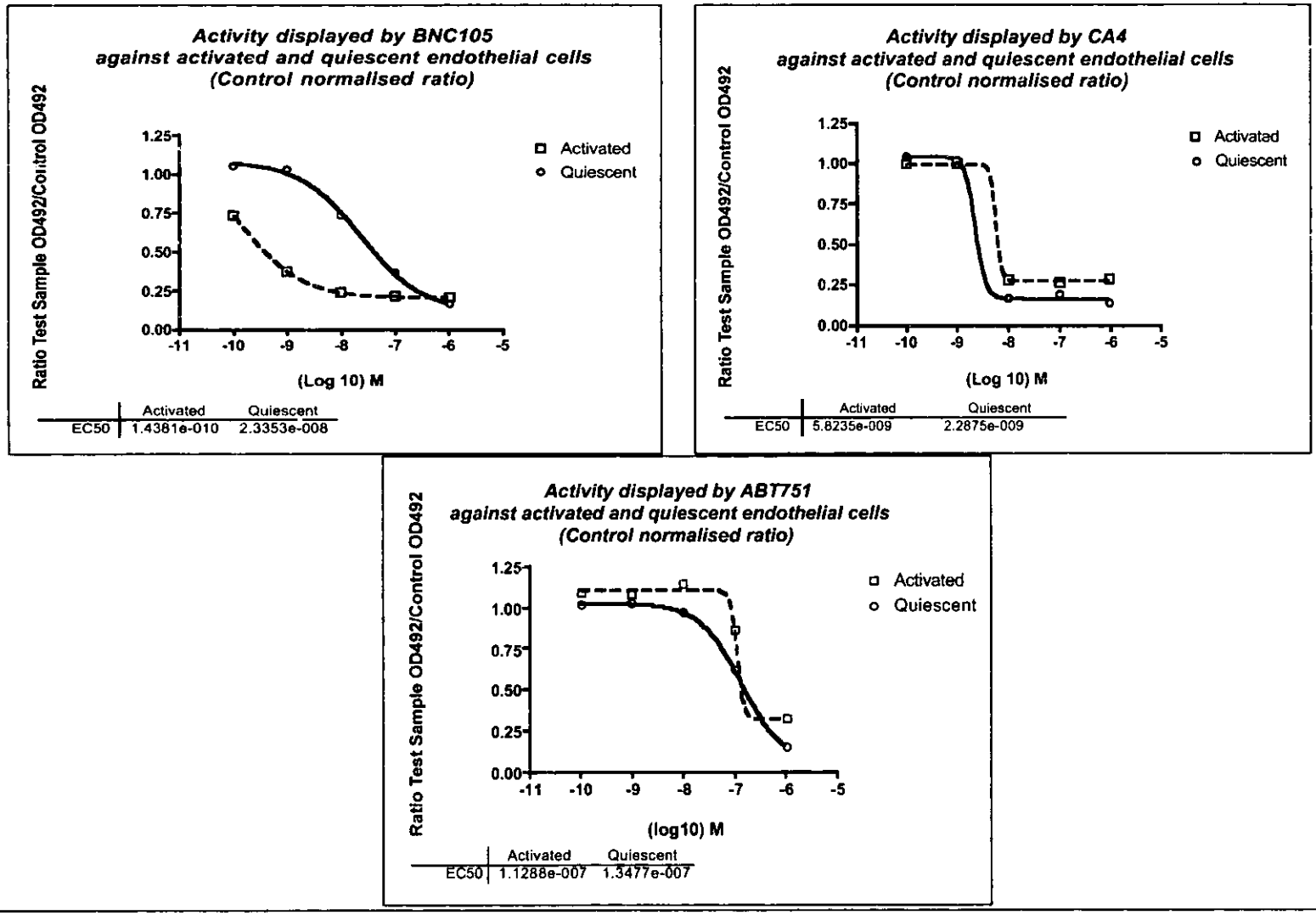


Figure 2. BNC105 exhibits 100-fold higher activity against activated HUVEC. HUVEC were cultured either in the presence (activated) or absence (quiescent) of growth factors. Activated and quiescent cell cultures were exposed to a range of concentrations of BNC105, CA4 and ABT751. Following a 48hr incubation period cell proliferation was measured using an MTT assay (absorbance readings - 492nm). Absorbance readings for each drug concentration were normalised to vehicle-treated control cultures corresponding to activated and quiescent cells respectively. The graphs in this figure display the activity of BNC105, CA4 and ABT751 against activated and quiescent HUVEC in the concentration range 0.1nM-1000nM.

BNC105 disrupts the formation of endothelial capillaries but does not disrupt preformed/quiescent capillaries. We investigated the activity of BNC105 on endothelial cells engaged in capillary tube formation in vitro. Endothelial cells were placed on a Matrigel® matrix and allowed to form capillary tubes in the presence or absence of the compound under evaluation. Each compound tested was used at concentrations found to display activity in the proliferation assay. BNC105 inhibited the formation of capillary tubes at 1nM (Fig.3). This activity was considerably higher than CA4 which inhibited capillary formation at 10nM and ABT751 that failed to inhibit capillary formation at ≤100nM (Fig. 3). These results clearly demonstrate that BNC105 exhibits very high potency against activated endothelial cells engaged in formation of capillaries. Subsequently, we investigated the activity of BNC105 on preformed capillaries. Endothelial cells were plated on Matrigel® and allowed to form capillary tubes for 22hrs. Subsequently, these capillary tubes were exposed to each of the compounds under study. Our results indicate that although BNC105 inhibited the formation of capillaries at 1nM (Fig. 3), it failed to disrupt preformed capillaries at that concentration (Fig. 4). This result is in agreement with the proliferation assay results providing further proof that this compound exhibits selectivity for activated endothelial cells. In contrast, CA4 disrupted preformed capillary tubes at the 10nM concentration (Fig. 4), at this concentration it also inhibited the formation of capillary tubes (Fig. 3).

BNC105 alters endothelial cell morphology and increases the permeability of endothelial cell monolayers. It has been previously shown that CA4 induces cytoskeletal alterations that manifest in a cell blebbing morphology in which actin accumulates around surface blebs (Kanthou & Tozer, 2002). We investigated whether BNC105 induces similar morphological changes. Exposure of HUVEC to 10nM of BNC105 for 15 minutes resulted in cell blebbing (Figure 5A). Drugs interfering with the morphology of endothelial cells compromise the integrity of endothelial cell layers lining blood vessels resulting in increased permeability. The consequences of the BNC105-induced cell morphology changes to endothelial cell permeability were evaluated. HUVEC monolayers were grown to confluency on microporous membranes. The ability of fluorescent dextran to cross the HUVEC monolayer in the presence of different concentrations of BNC105 was assessed. CA4 was used as comparator. This in vitro assay was carried out as previously described (Watts et al, 1997). Based on the effect of BNC105 on the cytoskeletal integrity of HUVEC it was not surprising to see that this drug led to an increase in the permeability of a HUVEC monolayer. Interestingly, CA4 was marginally more potent than BNC105 in this assay (Fig. 5B). This finding provides further support to the notion of BNC105 selectivity. Due to contact inhibition, endothelial cell monolayers in this assay comprise quiescent cells. BNC105 is less potent against these quiescent cells than CA4. In contrast, BNC105 was found to be 10-fold more potent than CA4 against endothelial cells that are either proliferating actively or are engaged in the formation of capillary tubes (Fig.2,3).

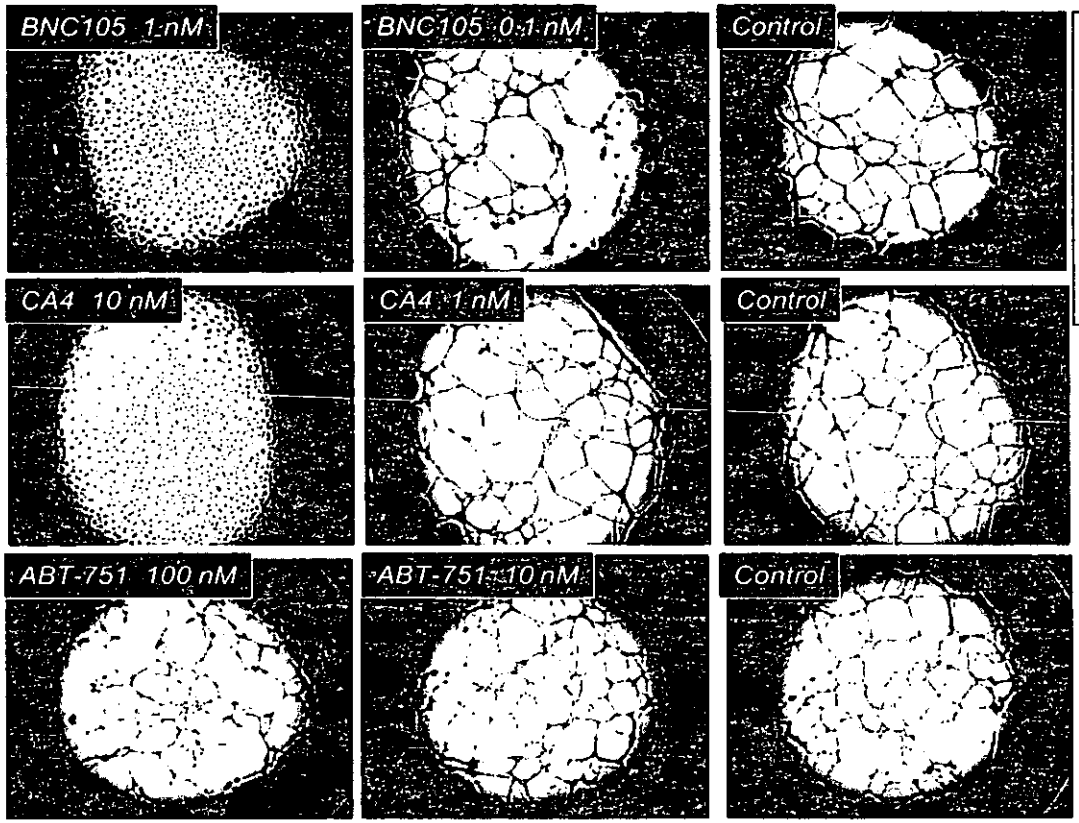


Figure 3. BNC105 inhibits HUVEC capillary formation in vitro. Cells were plated at 25,000/well in 96-well plates and cultured for 22hrs. The inhibitory activity exhibited by the compounds BNC105, CA4 and ABT751 on the formation of capillary tubes by HUVEC on Matrigel® was evaluated. DMSO vehicle negative control was included in the analysis.

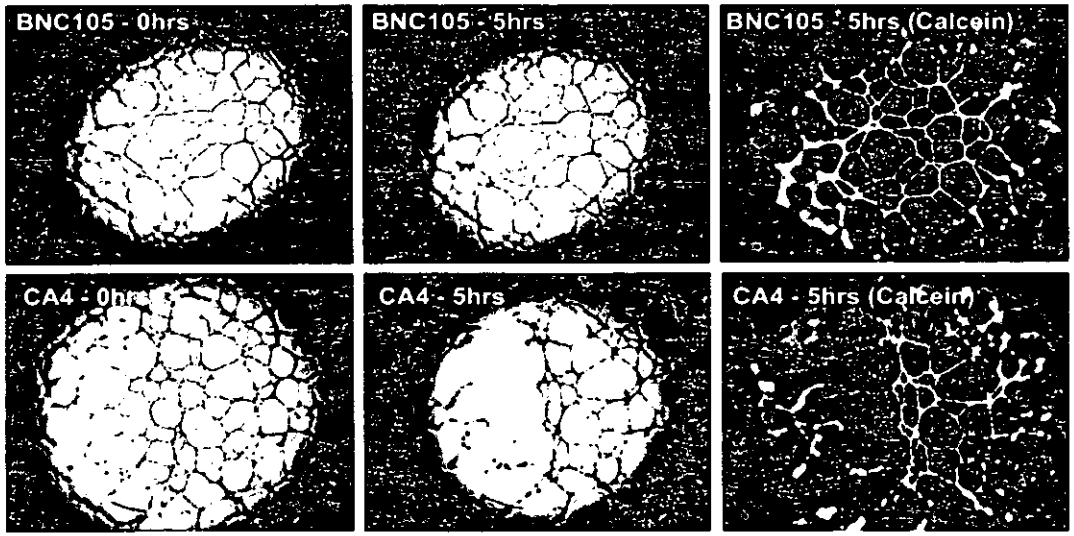
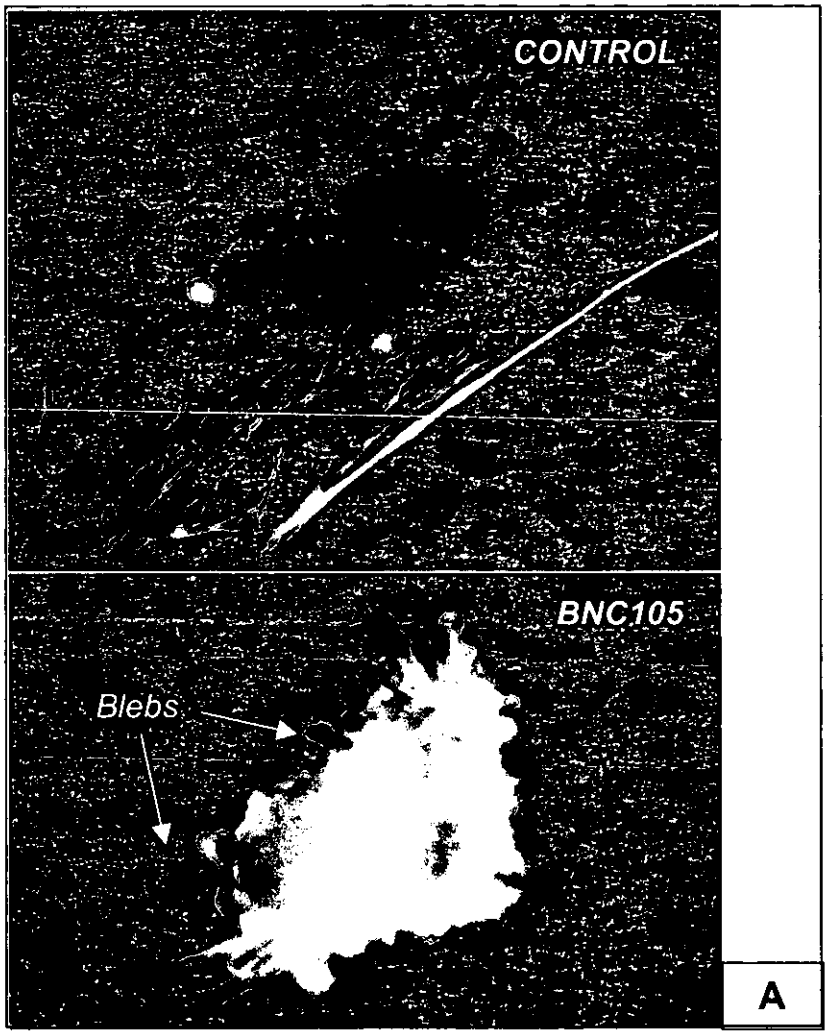


Figure 4. BNC105 does not disrupt preformed HUVEC capillaries in vitro. The inhibitory activity exhibited by the compounds BNC105 and CA4 on HUVEC capillary tubes formed on Matrigel® was evaluated. Pre-formed capillaries were exposed to BNC105 and CA4 concentrations that were found to inhibit capillary formation (Fig. 3). Capillary integrity was examined 5hrs after the addition of the compounds under study. This figure shows pictures of HUVEC capillaries immediately after addition of BNC105 and CA4 and 5hrs later. Capillaries were also stained with Calcein to confirm cell viability.



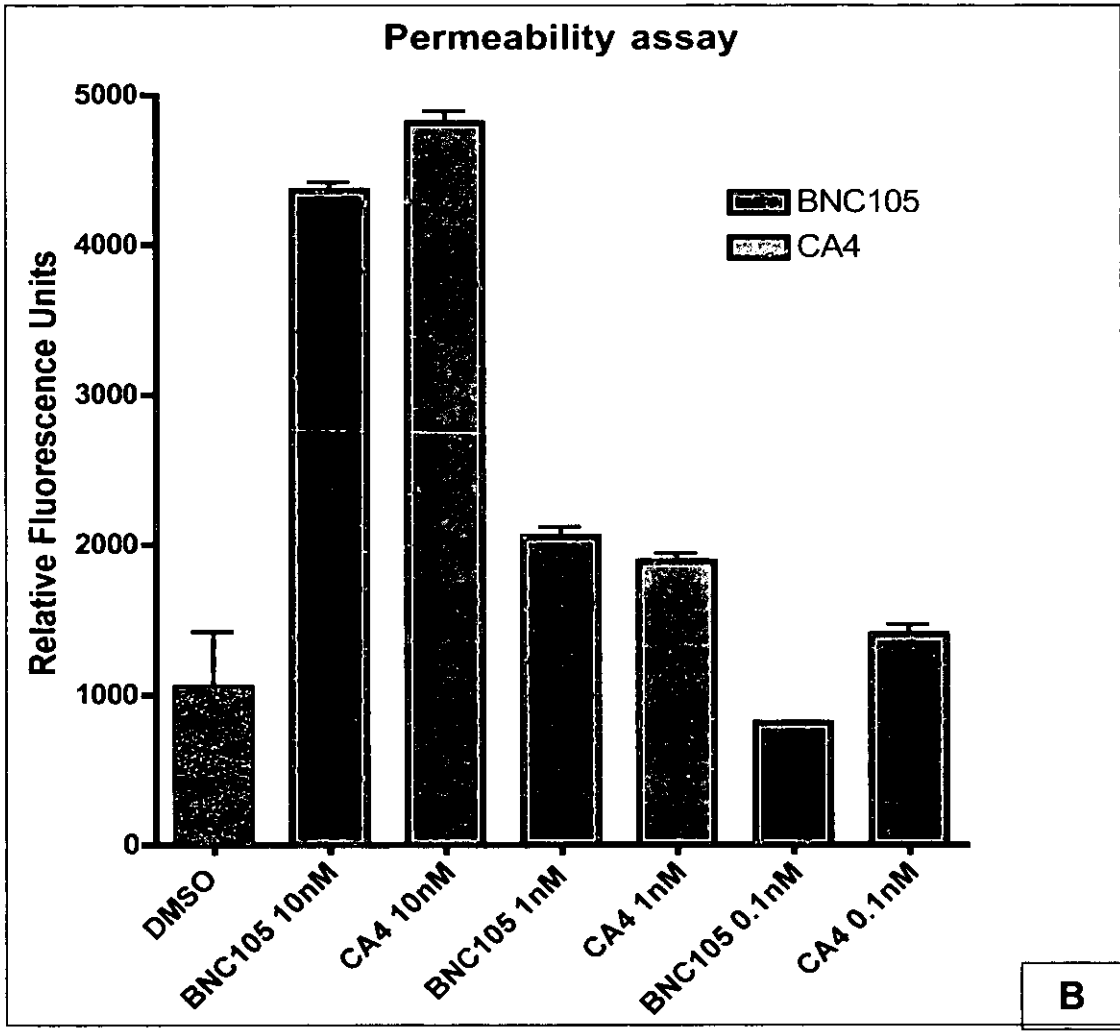
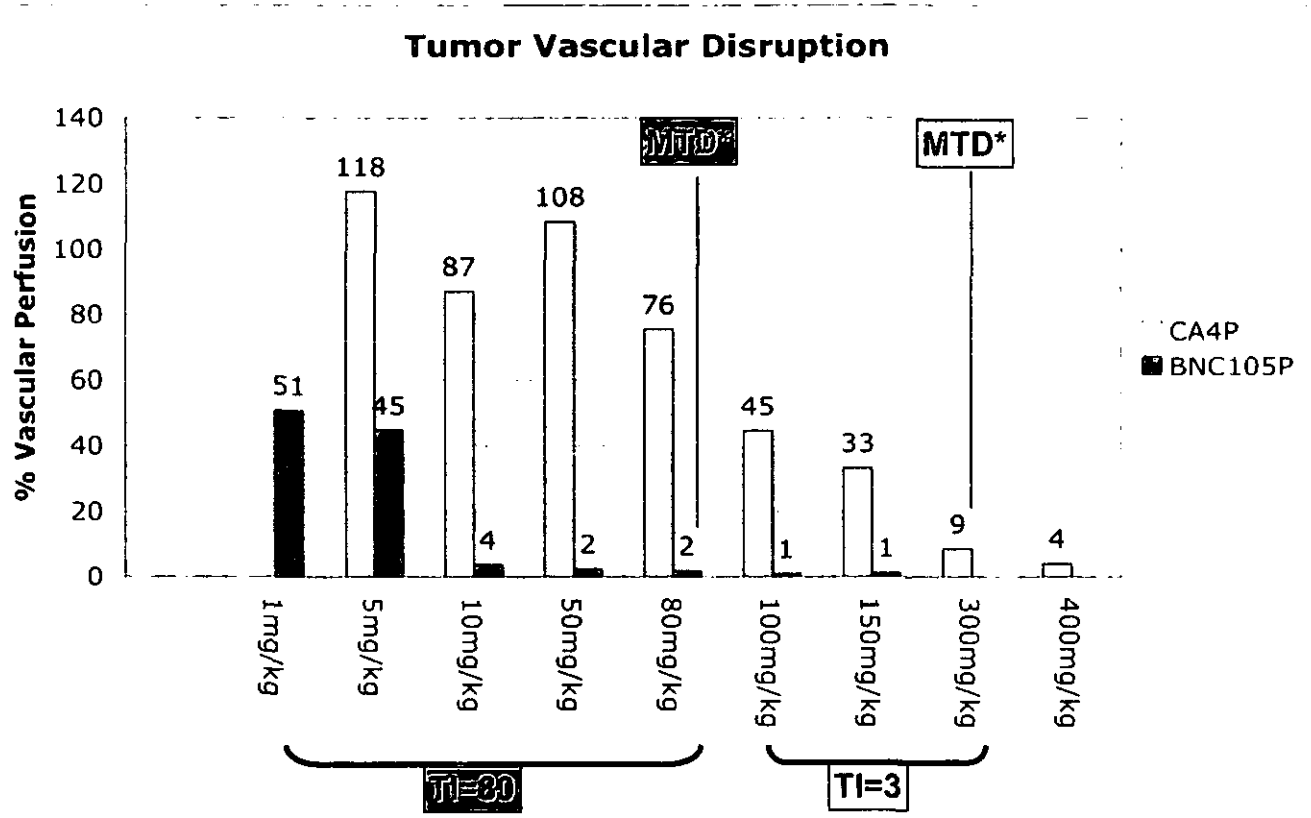


Figure 5. Effect of BNC105 on endothelial cell morphology (A) and permeability (B) in vitro. **(A)** HUVEC were cultured in the presence of 10nM BNC105 for 15min. Cells were stained for actin. BNC105 treated cells displayed clear evidence of "blebbing". **(B)** HUVEC monolayer permeability was assessed using an in vitro Vascular Permeability Assay kit (ECM640, Chemicon). HUVEC were seeded on a semi-permeable membrane and allowed to form a confluent monolayer. The HUVEC monolayer was treated with either BNC105, CA4 or vehicle control for 15min. The culture medium was replaced with an FITC-Dextran solution and incubated for 5 minutes. The extent of permeability was measured in terms of fluorescence allowed to pass through the cell monolayer.

Synthesis of a BNC105 prodrug - BNC105P. BNC105 does not have sufficient solubility to allow intravenous administration for future clinical use. In order to accommodate for this we synthesised BNC105P, a disodium phosphate ester form of BNC105. BNC105P is soluble in saline and is rapidly converted to the active drug BNC105 in vivo through the action of non-specific phosphatases.

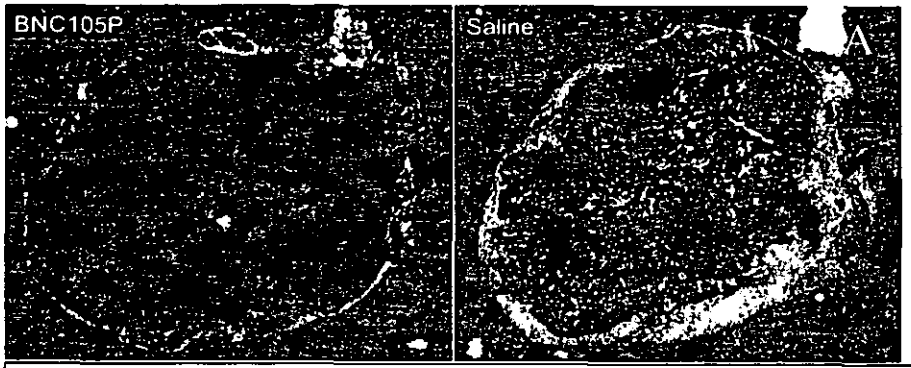
BNC105P disrupts vascular perfusion in human breast cancer xenografts. In order to further substantiate the anti-vascular action of BNC105P we investigated its ability to preferentially shut down the vasculature in solid tumors. Mice carrying solid breast tumors were treated with a single intravenous injection of either BNC105P (1mg/kg – 150mg/kg) or CA4P (5mg/kg - 400mg/kg). Twenty four hours after the injection of the compounds the animals were injected with the fluorescent dye H33342. H33342 acts as a marker of blood perfusion in tumors and normal tissues. Following the injection of the dye the animals were euthanized, the tumors were excised for histological examination. Quantitative analysis of H33342 staining in tumor sections revealed that BNC105P treatment caused ~50% vascular shutdown at 1 mg/kg and almost complete vascular shutdown at 10 mg/kg (Fig. 6). In comparison, CA4P caused ~50% vascular shut down at 100 mg/kg (Fig. 6). Interestingly, BNC105P was tolerated without any signs of toxicity at 80 mg/kg and CA4P at 300 mg/kg. These values translate into a TI of 80 for BNC105P and a TI of only 3 for CA4P. Qualitative examination of the data revealed that BNC105P caused dramatic vascular disruption within solid tumors at a dose of 10mg/kg (Fig. 7A). Staining of tumor sections with H&E showed that the vascular shutdown caused by BNC105P resulted in the initiation of necrosis in the core of the tumor (Fig. 7B). Investigation of vascular disruption achieved by a single iv dose of 10 mg/kg BNC105P at shorter time intervals revealed that BNC105P causes 98% vascular disruption as early as 3 hours post-administration and remained above 90% after 24hrs. Increased tumor necrosis became evident 24hrs after administration of BNC105P (data not shown). Quantitative analysis of vascular perfusion in normal organs of animals treated with BNC105P at the MTD (80mg/kg) revealed no changes compared to the organs of vehicle treated animals (Fig. 8).

BNC105P disrupts vascular perfusion in human colon cancer xenografts. Following the investigation of BNC105P efficacy in a solid breast cancer model we sought to investigate the efficacy of BNC105P treatment on tumor vasculature in a colon cancer model. For BNC105P treated groups, doses of 10mg/kg and above showed a statistically significant decrease in tumor perfusion (Fig.9A) and a corresponding increase in tumor necrosis (Fig. 9B) compared with the saline treated group. In the CA4P treated groups there was no significant difference in vascular perfusion between any of the CA4P doses tested and the saline treated group (Fig. 9A). There was a trend towards an increase in necrosis in a dose dependent manner in CA4P treated tumors but this was not statistically significant (Fig. 9B).



MTD - no observable signs of toxicity

Figure 6. Tumor vascular disruption caused by treatment with different doses of BNC105P and CA4P. Balb/c nu/nu mice bearing MDA-MB-231 solid tumors were treated with a single iv injection of BNC105P, CA4P or saline. BNC105P was injected at concentrations ranging at 1mg/kg-150mg/kg. CA4P was injected in the range of 5mg/kg-400mg/kg. 24hrs following this treatment the animals were injected with H33342 to label tumor vascular perfusion. Tumors were excised, sectioned and visualised for H33342 staining. H33342 staining was quantified using Image analysis software.



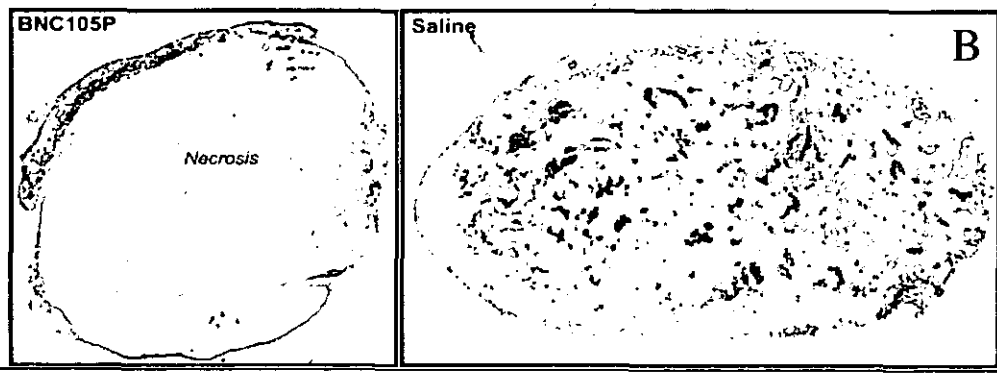


Figure 7. BNC105P disrupts the vasculature in solid tumors. Balb/c nu/nu mice bearing MDA-MB-231 solid tumors were treated with a single iv injection of 10mg/kg BNC105P or saline. 24hrs following this treatment the animals were injected with H33342 to label tumor vascular perfusion. Tumors were excised, sectioned and visualised for H33342 staining (A). Tumor sections were subsequently stained with H&E to detect necrotic cancer cells. H33342 staining (black) was superimposed to the H&E stain(B).

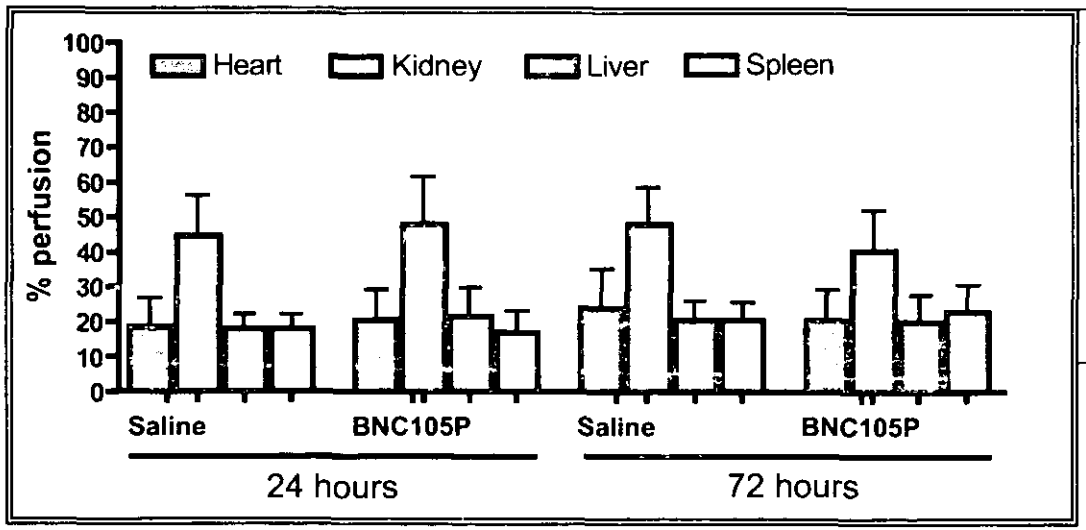


Figure 8. Effect of BNC105P treatment on the vascular perfusion in normal tissues. Balb/c nu/nu mice bearing MDA-MB-231 solid tumors were treated with a single iv injection of 80mg/kg BNC105P or saline. 24 and 72hrs following treatment the animals were injected with H33342 to label vascular perfusion within tumors and normal organs. A number of normal organs were excised, sectioned and visualised for H33342 staining.

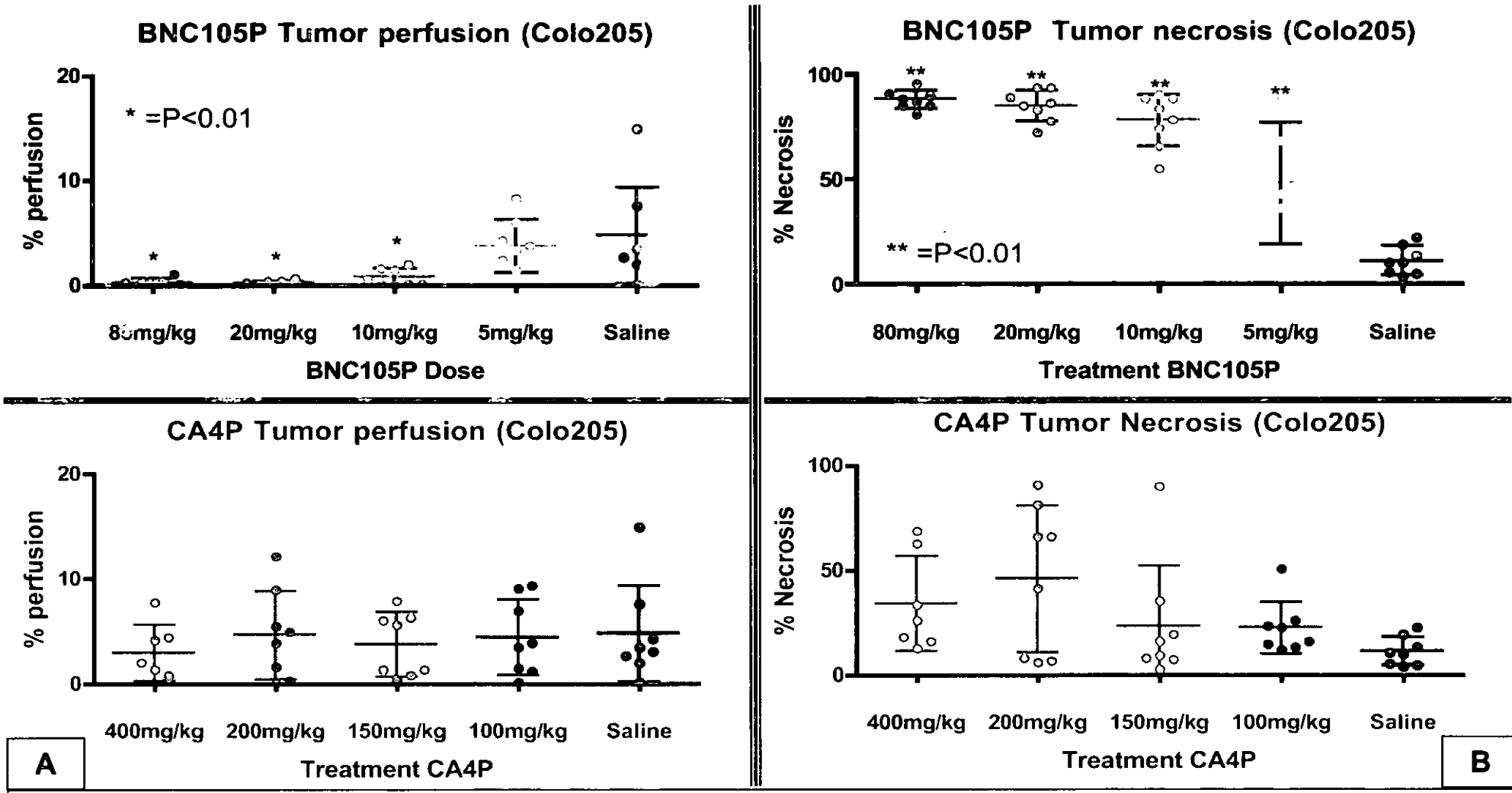


Figure 9. **(A)** Analysis of vascular perfusion in human colon tumor xenografts treated with BNC105P or CA4P. **(B)** Analysis of necrosis in human colon tumor xenografts treated with BNC105P or CA4P. Balb/c nu/nu mice bearing subcutaneous Colo205 tumors were treated with a single iv injection of saline, BNC105P, or CA4P at various concentrations. 24hrs following this treatment the animals were injected with H33342 to detect tumor vascular perfusion. Tumors were excised, sectioned and visualised for H33342 staining and were subsequently stained with H&E to visualise necrotic tumor areas. Percentage perfusion and necrosis is shown for each individual animal per group, staining was quantified using Image analysis software. Statistical analysis on perfusion and necrosis data utilized one-way ANOVA and Dunnett's multiple comparison post-test using Prism® Software.

Two cycles of BNC105P treatment suppresses tumor growth in a breast cancer model. Balb/c nu/nu mice bearing MDA-MB-231 orthotopic breast solid tumors were treated with two cycles of BNC105P at 40mg/kg. Tumor growth as well as animal health were monitored for up to 72 days post-day 1 of treatment. The results seen in this experiment (Fig. 11) clearly show tumor growth inhibition in animals treated with two cycles of BNC105P. Significant differences in tumor growth between BNC105P treated (n=64) and saline treated (n=20) animals were observed as early as day 4 ($p<0.001$; unpaired t-test; Prism® analysis) through to Day 70. In the BNC105P treated group, 34% of tumors showed delayed/slow growth, 4.7% exhibited no growth, 6.3% regressed and 14% of tumors were cleared. Fig. 10 depicts an example of one Balb/c nu/nu mouse from a total of 14% bearing a solid tumor in which tumor growth was arrested and the tumor disappeared over approximately 20 days following a second cycle of BNC105P treatment. There is a clear progressive drop in tumor volume following the second cycle of BNC105P treatment with the animal being cleared of its tumor burden by day 49. Cleared tumors did not reappear for the duration of this experiment.

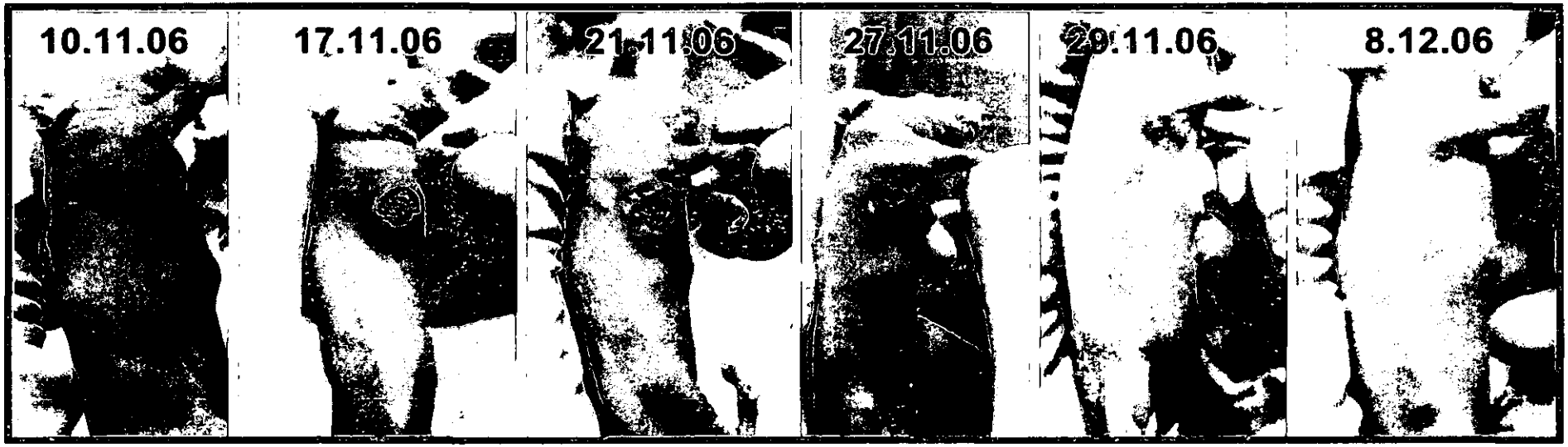


Figure 10. Example of one Balb/c nu/nu mouse from a total of 14% bearing a MDA-MB-231 solid tumor and treated with BNC105P at 40mg/kg iv 2 doses/1wk apart/3 wks rest, in which tumor growth was arrested and the tumor disappeared over 20 days following a second cycle of treatment.

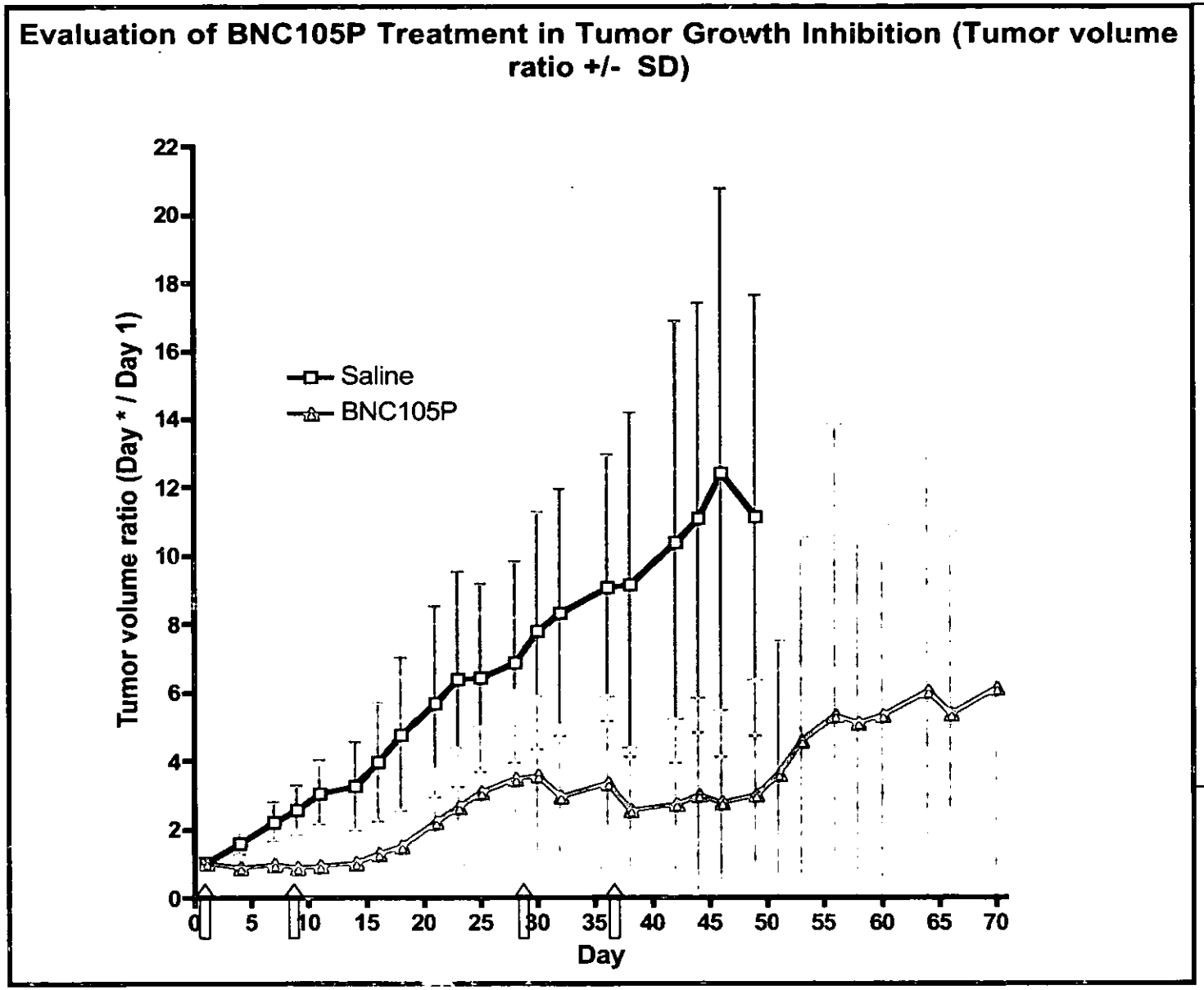


Figure 11. BNC105P tumor growth inhibition. Balb/c nu/nu mice bearing MDA-MB-231 solid tumors were treated with BNC105P. Animals were iv dosed with a total of two cycles of BNC105P treatment (dose timepoints shown with blue arrows). Tumor growth represented as a ratio to initial tumor volume is shown over a total of 72-days. Significant differences in tumor growth between BNC105P treated (n=64) and saline treated (n=20) animals were observed as early as day 4 ($p<0.001$; unpaired t-test; Prism® analysis) through to Day 49 at which timepoint the vehicle treated animals had to be euthanized due to the very large size of their tumors.

RESULTS & DISCUSSION

- BNC105P is a very potent Vascular Disruption Agent
- BNC105 exhibits selectivity for activated endothelium in two independent in vitro assays
- BNC105P is considerably more potent than CA4P in causing tumor vascular disruption, achieving a significantly improved Therapeutic Index
- BNC105P disrupts blood vessels in human breast and colon cancer in vivo tumor models
- BNC105P shows single agent efficacy in breast cancer with a 14% cure rate

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ABBREVIATIONS

HUVEC - Human umbilical vein endothelial cells

TPI - Tubulin Polymerisation Inhibitor

HAAEC - Human abdominal aorta endothelial cells

TI - Therapeutic Index

END