Bionomics

Creating and developing innovative therapies

BNC105 Results Presentation

Dr Deborah Rathjen
CEO & Managing Director, Bionomics Limited

Dr José Iglesias
Chief Medical Officer, Bionomics Limited

Dr Tom Hutson
Director GU Oncology and Professor of Medicine Texas A&M HSC College of Medicine

Dr Gabriel Kremmidiotis
Vice President Research & Development, Bionomics Limited

Safe Harbor Statement

Factors Affecting Future Performance

This presentation contains "forward-looking" statements within the meaning of the United States' Private Securities Litigation Reform Act of 1995. Any statements contained in this presentation that relate to prospective events or developments, including, without limitation, statements made regarding Bionomics' development candidates BNC105, BNC210 (IW-2143), BNC101 and BNC375, its licensing agreements with Ironwood Pharmaceuticals and Merck & Co, its acquisition of Eclipse Therapeutics, drug discovery programs and pending patent applications 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 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. Results of studies performed on competitors products may vary from those reported when tested in different settings.

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 presentation.

Agenda

- Introduction (Deborah Rathjen)
- BNC105 mechanism of action and biological rationale supporting the clinical development strategy (Gabriel Kremmidiotis)
- The DISRUPTOR -1 trial evaluating BNC105 in combination with the mTOR inhibitor Afinitor in patients with metastatic renal cancer (José Iglesias)
- Significance of the DISRUPTOR-1 trial results (Tom Hutson)
- Phase I clinical trial evaluating BNC105 in combination with Gemcitabine and Carboplatin in Ovarian cancer patients – Phase I data and next steps (José Iglesias)
- Concluding remarks (Deborah Rathjen)

BNC105 displays three modes of anti-cancer action

Activation of acute tumour hypoxia by selective disruption of tumour vasculature without any effect on normal blood vessels - **tumour starvation**

Upregulation of pro-apoptotic proteins - **induction of cancer cell death**

Inhibition of cancer cell proliferation – **suppression of tumour growth**

The tri-modal activity of BNC105 can be utilized to boost the therapeutic effects of currently approved standard chemotherapies and targeted agents

BNC105 suppresses tumour growth and effects tumour cell kill through blood starvation and induction of apoptotic pathways

BNC105 hypoxia induces tumour dependency on mTOR and VEGF pathways for survival – oncogenic addiction

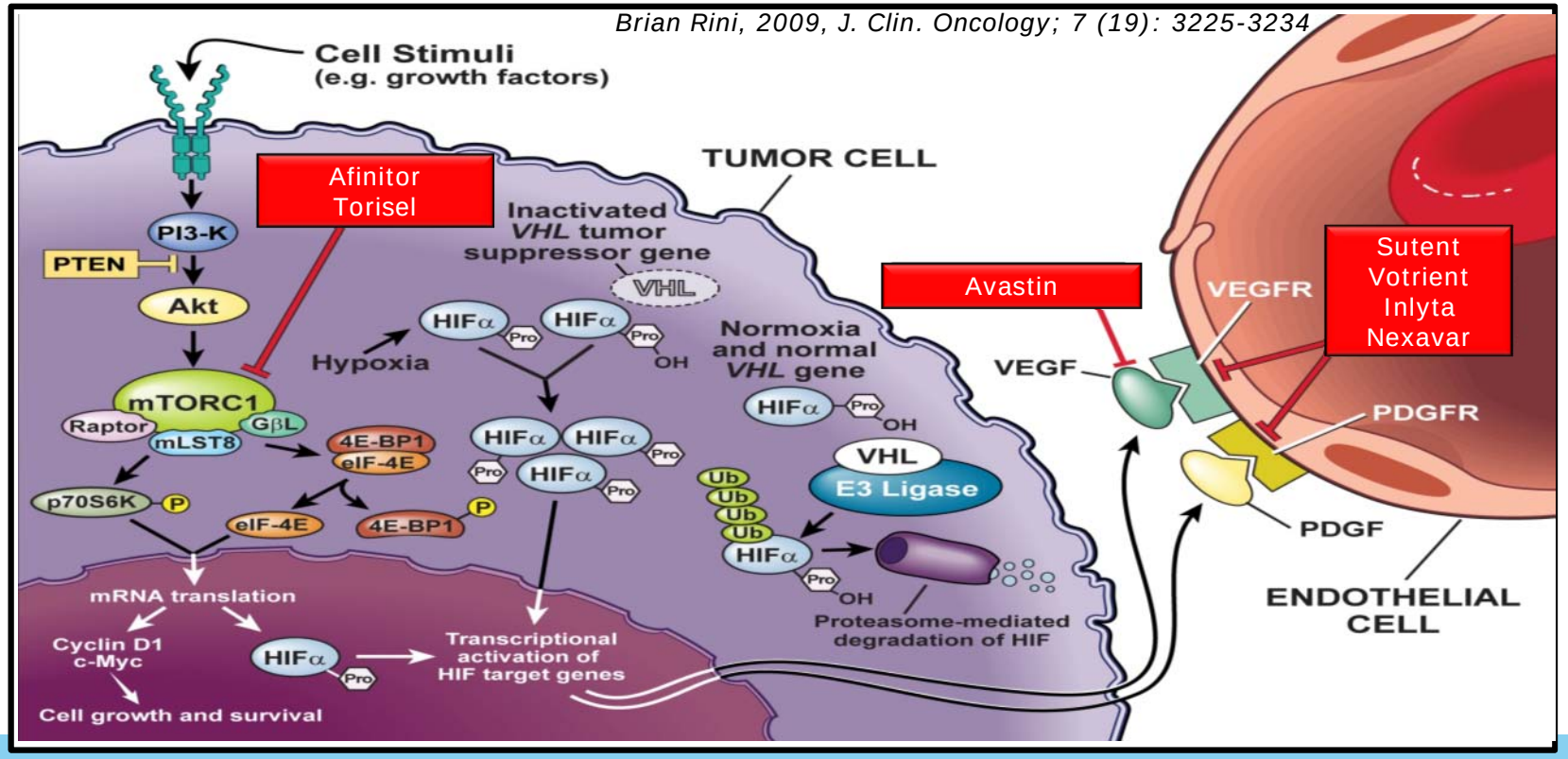
BNC105+Gemcitabine+Carboplatin
Ovarian Cancer

BNC105+Afinitor (mTOR)
Renal Cancer

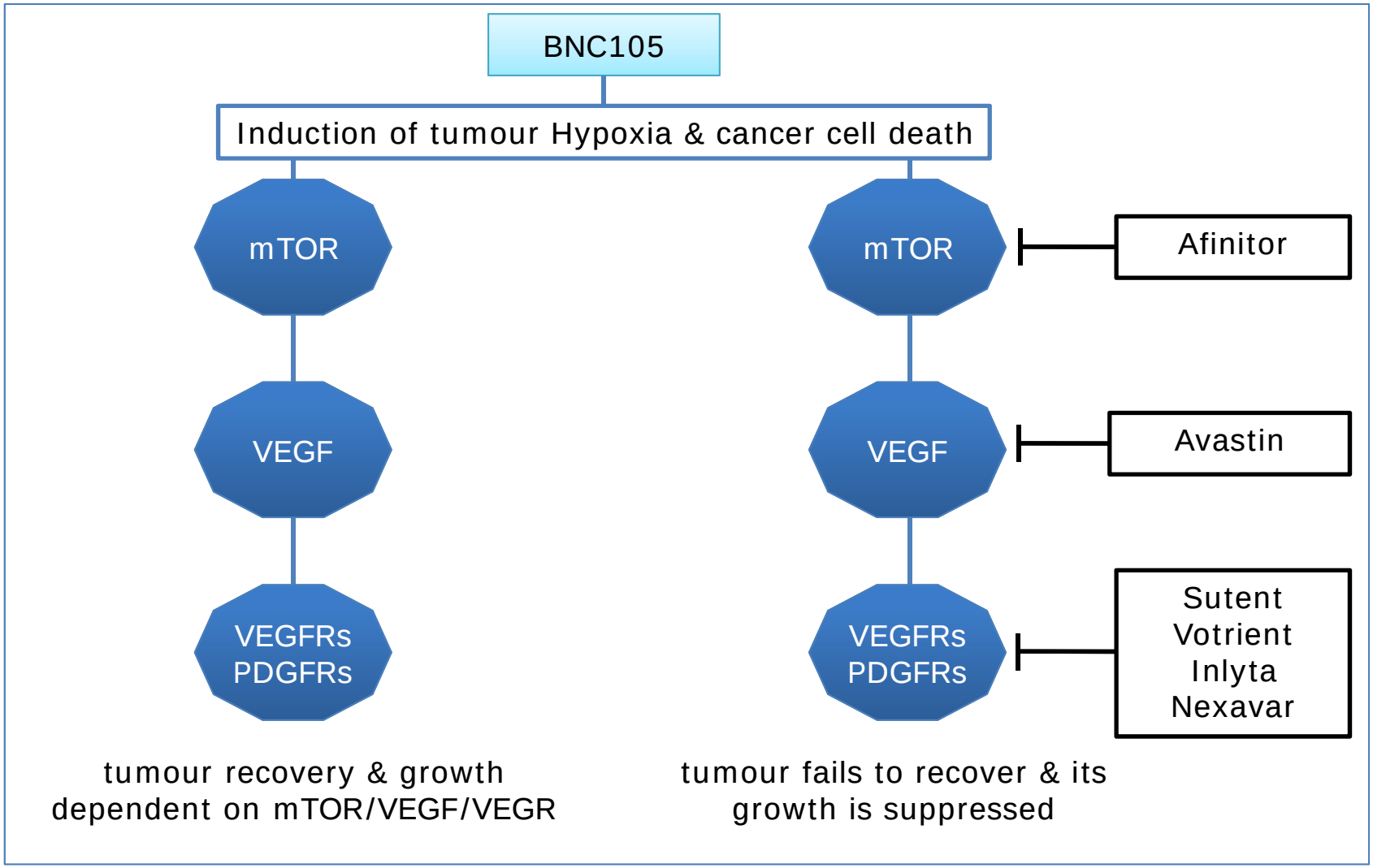
Rationale for combining BNC105 with inhibitors of the mTOR or VEGF signaling pathways

- Following BNC105 treatment renal tumours display significant increase in the expression of mTOR and VEGF signaling – oncogenic dependency for survival

- BNC105 combination treatment with an inhibitor of mTOR, VEGF or VEGFR has potential to improve therapeutic outcomes for mRCC patients



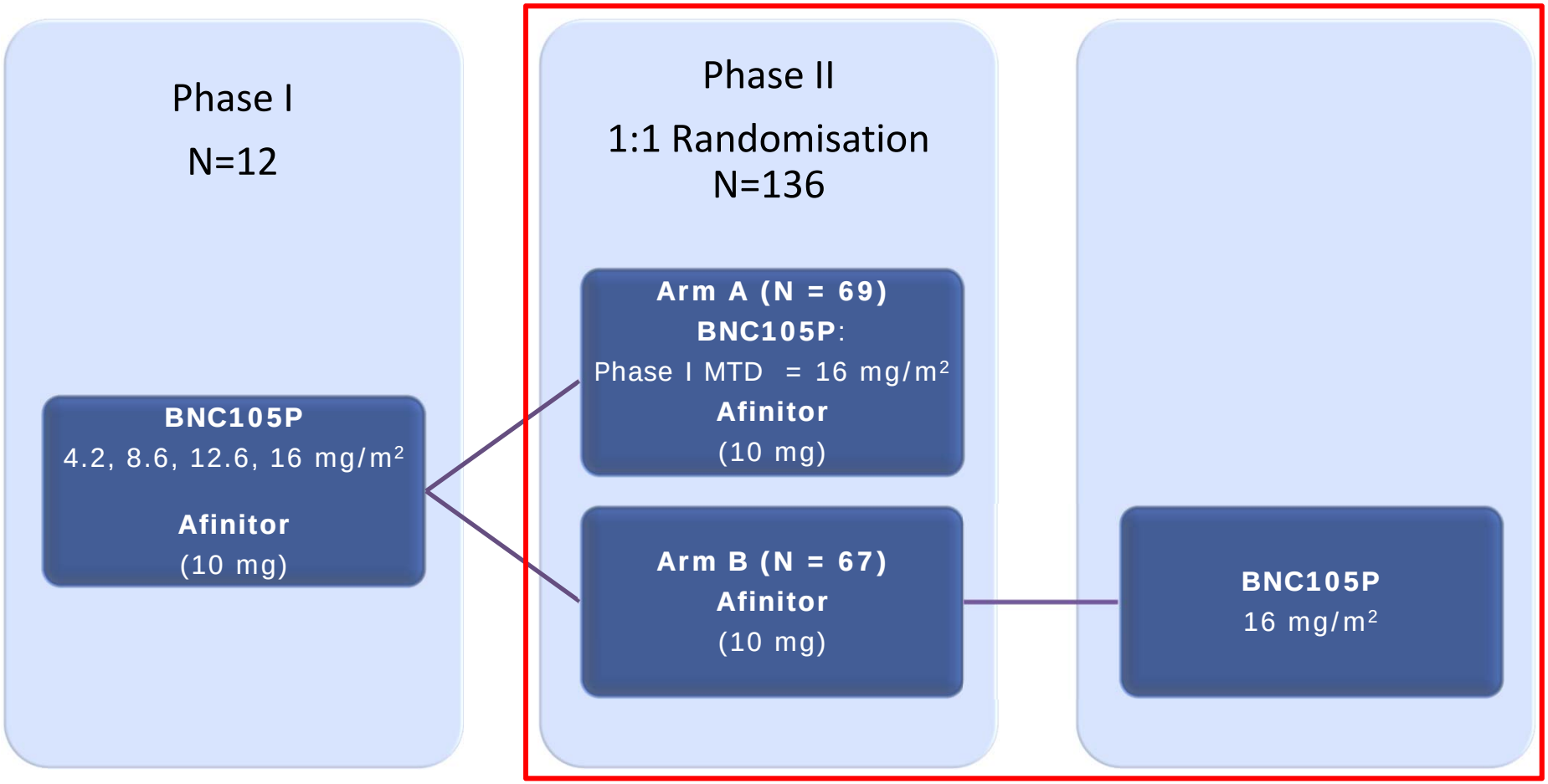
BNC105 combination regimens may enhance tumour response and patient outcomes in mRCC



Preclinical models demonstrate biological mechanism complementarity and additive anti-cancer activity of BNC105 combination with mTOR or VEGF pathway inhibitors

DISRUPTOR-1 Trial Design

- Metastatic Renal Cell Carcinoma (RCC)
- Patients progressed from prior Tyrosine Kinase Inhibitor (TKI) therapy



- Treatment schedule: BNC105P: IV, Days 1 and 8 of a 21-day cycle; Afinitor: PO, daily
- Treatment duration: Until disease progression, intolerable toxicity or consent withdrawal

DISRUPTOR-1: key patient selection criteria

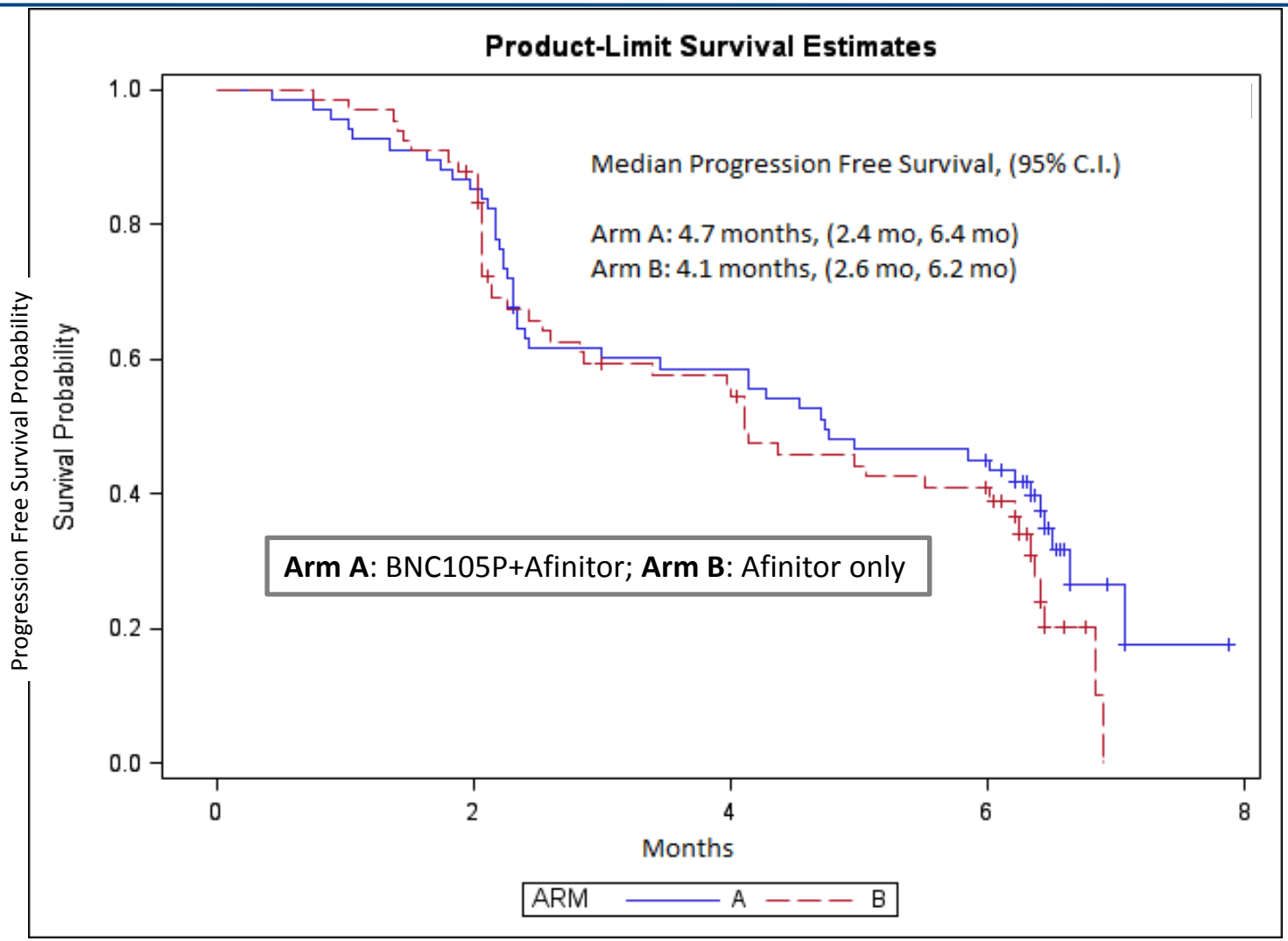
- Karnofsky Performance Score of ≥70
- Metastatic or locally advanced, inoperable RCC
- Progressive disease after 1-2 prior VEGF-directed TKIs
- Measurable disease
- No active brain metastases
- Good bone marrow, liver and kidney function

DISRUPTOR-1: study features

- Primary Objective:
  - Improvement in 6-month PFS (from 36% to 60%)

  (analysis power = 80%)
- Secondary Objectives:
  - PFS with BNC105P alone in patients progressing on Afinitor
  - Adverse events of the combination
- Exploratory Objective:
  - Evaluation of biomarkers of VDA action and correlation with clinical outcomes (PFS)
- Patient Stratification:
  - Prognostic (MSKCC) Risk Group – good, intermediate, poor
  - Number of prior TKIs – one, greater than one
- Subgroup Analysis:
  - Fuhrman grade, liver or bone metastasis, prior nephrectomy

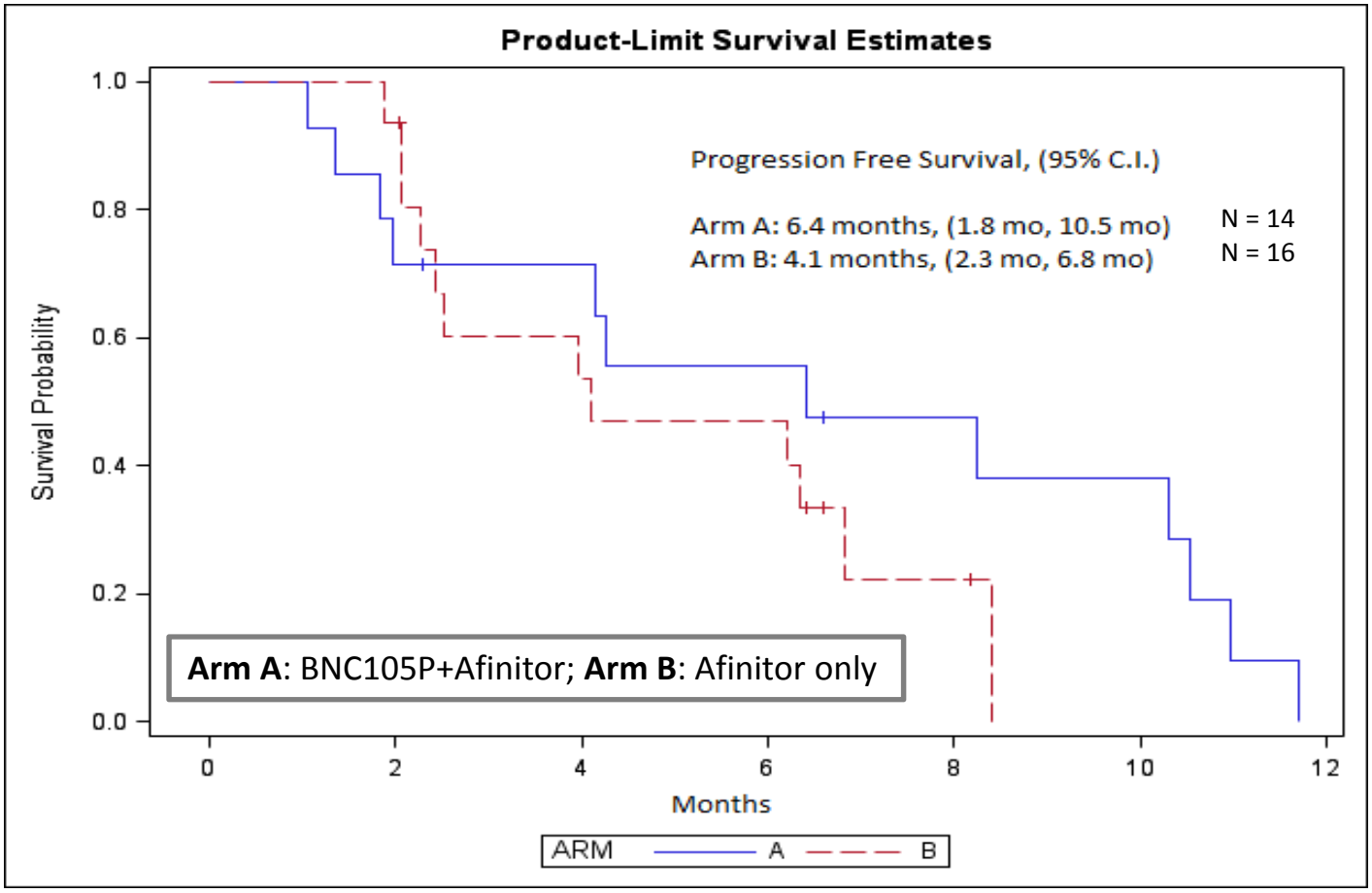
Progression Free Survival data – all patients



Primary endpoint - Similar proportion of patients free of progression at 6 months - 23 patients in the experimental arm, vs 20 patients in the control arm, approx. 1/3 of the patients in each arm, p=0.6625

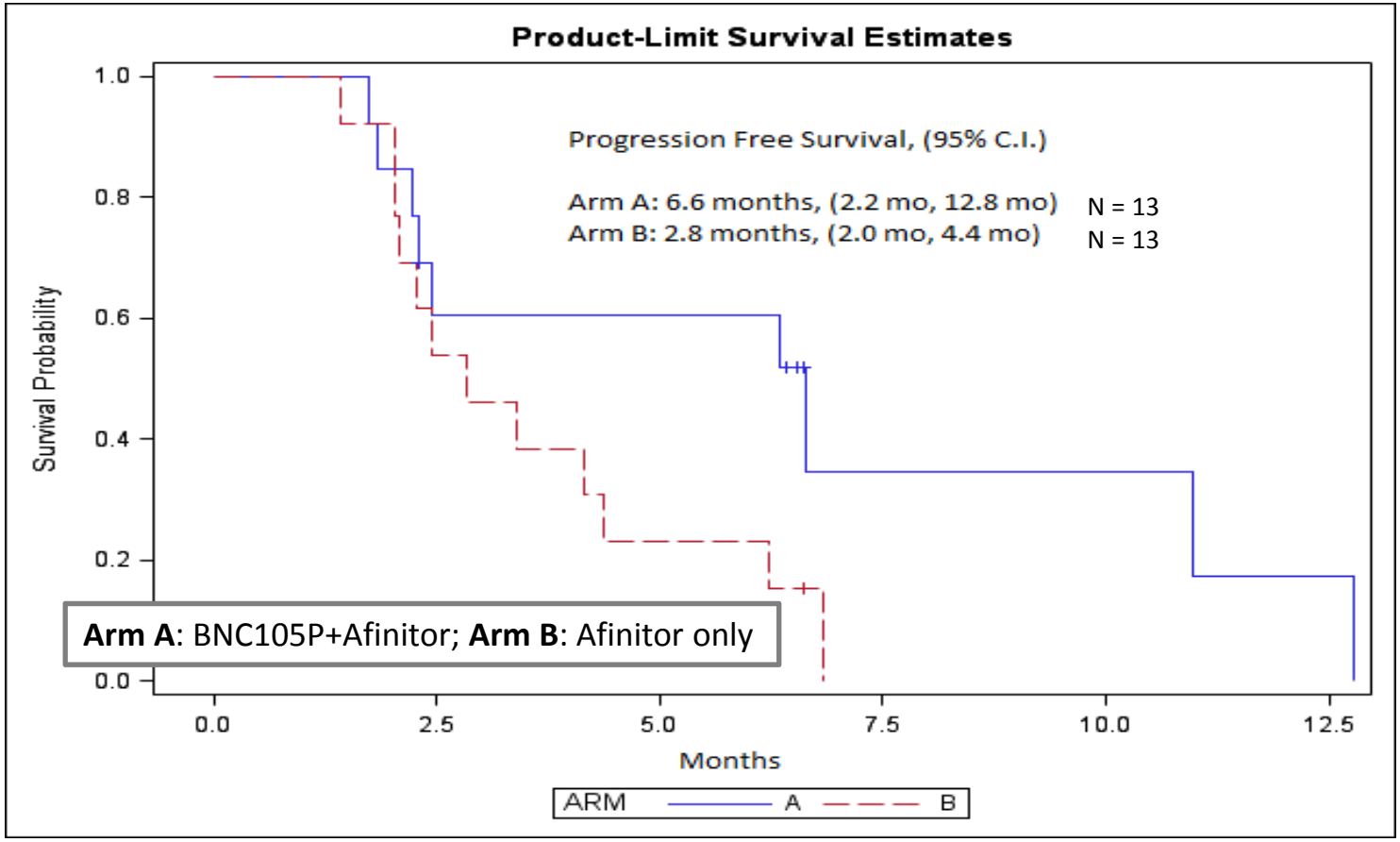
Progression Free Survival data
Fuhrman Grade II patients

Patients treated with BNC105P+Afinitor experience **2.3 month increase** in Progression Free Survival compared to patients treated with Afinitor alone



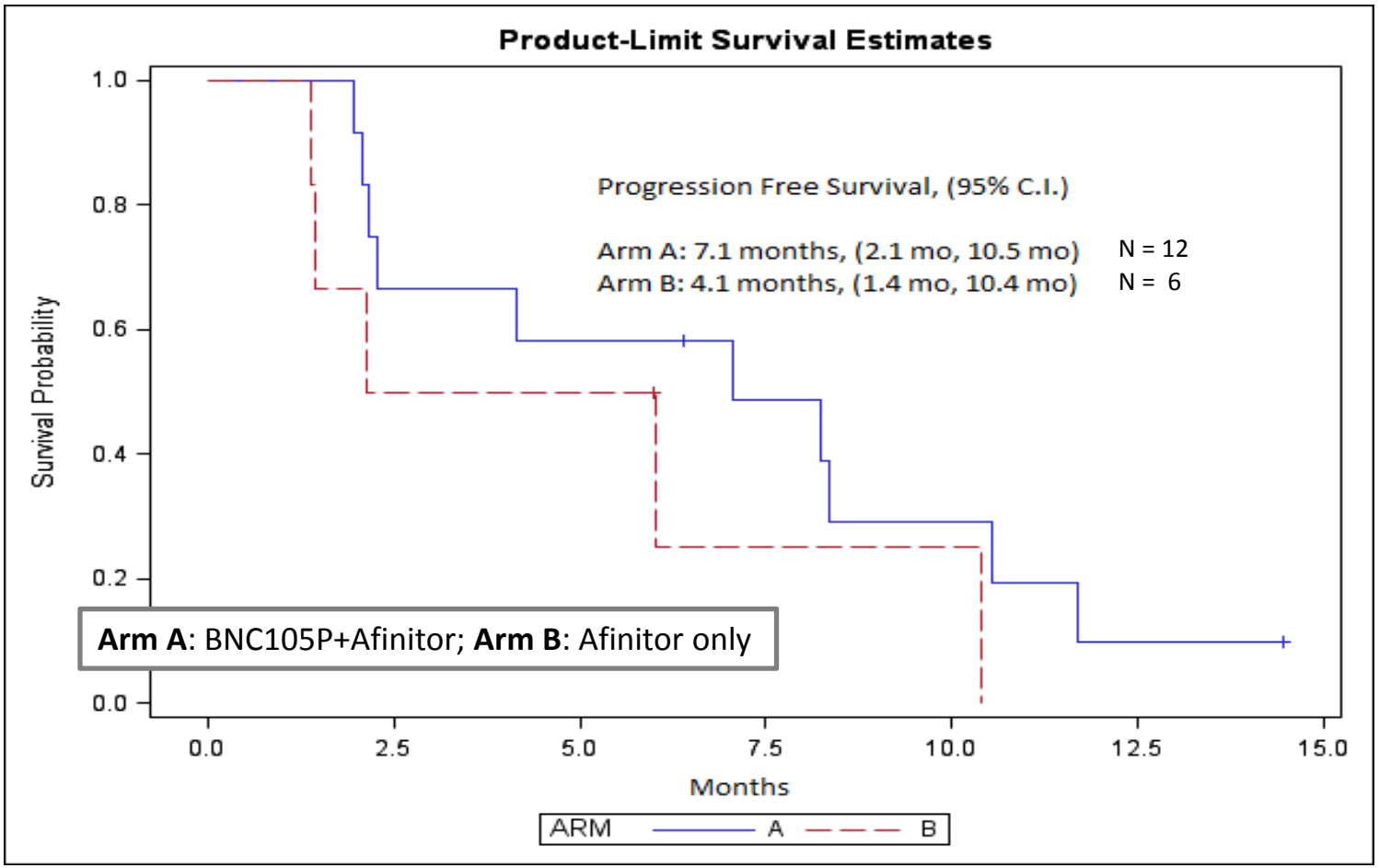
Progression Free Survival data
Patients with liver metastases

Patients treated with BNC105P+Afinitor experience **3.8 month increase** in Progression Free Survival compared to patients treated with Afinitor alone



Progression Free Survival data
Patients with prior nephrectomy

Patients treated with BNC105P+Afinitor experience **3 month increase** in Progression Free Survival compared to patients treated with Afinitor alone



Exploratory biomarkers associate with patient benefit

- Biomarker changes correlated with progression-free survival or lack thereof at 6 months, in a statistically significant manner (p-values of 0.0136 to 0.0348)
- This response was consistent with previous BNC105 clinical studies (Phase I study, Phase II study in mesothelioma and Phase I study in ovarian cancer)
- This is the first time biomarkers that correlate with PFS are reported for a VDA in renal cancer

Biomarkers correlating with clinical benefit from the BNC105+Afinitor treatment

- Macrophage Inflammatory Protein-1 beta
- Macrophage-Derived Chemokine
- Interleukin 1-beta
- Interleukin-12 Subunit p40
- Alpha-2-Macroglobulin
- Beta-2-Microglobulin
- Thyroxine-Binding Globulin

- ***The association of these biomarker variations with an important parameter of disease control such as progression-free-survival is demonstrated for the first time***

- ***The biomarkers have the potential to select for patients most likely to benefit from BNC105 treatment in future trials***

DISRUPTOR-1: Study summary and conclusions (1)

- Concerning the primary endpoint, similar proportion of patients free of progression at 6 months (23 patients in the experimental arm, vs 20 patients in the control arm, approx. 1/3 of the patients in each arm, p=0.6625)

- Median PFS was also similar between the study arms (4.7 months in the experimental arm vs 4.1 months in the control arm)

- Kaplan-Meier PFS curves show a separation in favor of BNC105 combination therapy after 4 months of treatment . Most of this benefit trend appears to be associated with patients having intermediate risk disease

DISRUPTOR-1: Study summary and conclusions (2)

- Positive PFS trends for the BNC105 + Afinitor combination compared to Afinitor alone, were observed on patient subgroups identified on the basis of metastases, prior nephrectomy and Fuhrman tumour differentiation Grade

- Biomarkers of BNC105 action displayed statistically significant correlation with clinical benefit status in patients treated with the BNC105+Afinitor combination therapy

- Clinical validation of these biomarkers in appropriate patient populations are warranted, with the aim of identifying those patients best fit to benefit from BNC105 treatment

The significance of the DISRUPTOR-1 trial data in the context of current treatment options for renal cancer

- *Several drugs are now available for RCC patients. The latest experience suggests that we need to be more targeted in matching up the right drug with the right patient subpopulation*

- *The latest clinical observations on Afinitor activity :*
  - *Profound benefit in a subset of patients that are difficult to identify pre-treatment (poor PS; undifferentiated histology; sites of metastasis).*
  - *The majority of the benefit is seen in stable disease NOT in tumour shrinkage (Stable disease drives Progression-Free and Overall Survival).*

- *Biomarker availability has been challenging in defining VDA activity and selecting responder populations.*
  - *DISRUPTOR-1 has produced a ground-breaking discovery of potential biomarkers that may allow pre-treatment selection of patients; further study is warranted.*

Next steps in the development of BNC105 for the treatment of renal cancer

- *Adaptive trial designs of the BNC105+Afinitor treatment:*
  - *confirm the utility of the BNC105+Afinitor combination in patients subgroups displaying increased clinical benefit in the DISRUPTOR-1 trial*
  - *utilize the biomarkers identified in DISRUPTOR-1 to select responder patient population*

- *Evaluate combinations of BNC105 with inhibitors of VEGF signaling:*
  - *Avastin - inhibitor of VEGFA*
  - *Votrient – inhibitor of VEGFR*

Prognosis remains poor for patients with advanced or metastatic Renal Cancer

Stage Distribution and 5-year Relative Survival by Stage at Diagnosis for 2003-2009, All Races, Both Sexes		
Stage at Diagnosis	Stage Distribution	5-year Relative Survival
Localized (confined to primary site)	63%	91.7%
Regional (spread to regional lymph nodes)	17%	64.2%
Distant (cancer has metastasized)	**17%**	**12.3%**

SEER Stat Fact Sheets: Kidney and Renal Pelvis
http://seer.cancer.gov/statfacts/html/kidrp.html

Based on NCI SEER Cancer Statistics Review 1975-2010
Updated June 14, 2013
http://seer.cancer.gov/csr/1975_2010/

Significant Market Opportunity for BNC105 in Renal Cancer

- Potential to extend sales of existing drugs through combination
- Many marketed drugs face patent expiries within the next 5 years

Drug	Company	2012 Sales (US$ MM)
Sutent	Pfizer	$1,300
Avastin	Roche	$2,400
Afinitor	Novartis	$800
Inlyta	Pfizer	$180
Nexavar	Onyx/Bayer	$1,000
Votrient	GSK	$340

BNC105 Phase I clinical trial in women with ovarian cancer

Name of Trial	Phase I/II BNC105 combination study in partially platinum sensitive ovarian cancer patients in first or second relapse
Primary Endpoints	Phase I: To determine the Recommended dose of BNC105 given with gemcitabine and carboplatin.
Correlative Endpoints	1. Effect of combining these drugs on the pharmacokinetics of BNC105 2. Associations between baseline biomarkers, ORR, PFS, OS and AE
Study Design	Single-arm Phase I (3-6 participants per dose level)
Treatment Method (route/frequency/dose levels)	Phase I: Carboplatin AUC 4 day 1, Gemcitabine escalations 800 and 1000mg/m^2 days 1 and 8, BNC105P at days 2 and 9, all q21 days for a maximum of 6 cycles, followed by single agent maintenance 16mg/m^2 BNC105 for a maximum of 6 additional cycles..
Number of Trial Subjects	Phase I: 15 participants.
Patient Population	The target population for Phase I was women with ovarian cancer with a progression-free interval > 4 months after first or second line platinum based chemotherapy.
Trial Locations	Australia, New Zealand, USA.
Trial Standard	ICH-GCP

BNC105 Phase I ovarian trial results (1)

- 15 patients enrolled
- 10 patients achieved a positive response according to RECIST 1.1 and/or GCIG CA125 criteria
- 12 patients completed six cycles of combination therapy and commenced with BNC105 monotherapy
- 1 patient has completed the protocol-prescribed 12 cycles of treatment comprised of 6 cycles of combination therapy and 6 cycles of BNC105 monotherapy, has continued on BNC105 monotherapy

BNC105 Phase I ovarian trial results (2)

- Current mean number of treatment cycles across the study is 8.8, 1 treatment cycle = 3 weeks
- Side-effects related to gemcitabine + carboplatin treatment backbone; haematological origin
- Recommended BNC105 Phase II dose:12mg/m^2 in combination with carboplatin and gemcitabine
- This dose level demonstrated a pharmacodynamic biomarker response consistent with the biological effects of BNC105 previously shown in other BNC105 clinical studies

BNC105 Phase I ovarian trial summary and conclusions

- Results are encouraging to continue BNC105 development in ovarian cancer
- Biomarker changes may assist with and refine patient selection in future studies – strongly supported by the latest biomarker correlation with patient benefit in the renal cancer trial
- The recently reported encouraging results of another VDA (Zybrestat) in ovarian cancer highlight the potential of these new compounds to improve on the treatment of this devastating disease.

Concluding remarks

- Latest BNC105 clinical data provide support for further clinical development in renal and ovarian cancer.
- In the ovarian cancer phase I trial BNC105 was well tolerated and produced clear indications of activity supporting Bionomics moving forward to the phase II component of the study design.
- In the renal cancer trial BNC105 displayed clear signs of increasing the therapeutic benefit of Afinitor in well defined patient subgroups and there was a strong, statistically significant correlation with biomarkers associated with clinical benefit.
  - These observations pave the way for the evaluation of the BNC105+Afinitor combination in a further clinical trial that will confirm the activity of the combination in the patient subgroups defined in DISRUPTOR-1.
  - The biomarkers identified in DISRUPTOR-1 are a “first” for the class of tumour Vascular Disruption drugs and provide an invaluable tool that can be incorporated in all future trials with BNC105 to increase probability of success through adaptive clinical trial designs.
- There are a number of clear value drivers to appeal to potential partners.

ASX:BNO

www.bionomics.com.au