# COMPANY PRESENTATION



AUGUST, 2010

# About MetronomX



- The company was founded in 2010 with the vision to be the leader in the development of metronomic therapies for cancer
  - Oral administration at low dose over prolonged periods
- The business strategy is to develop 'GenNext' cancer therapeutics used in metronomic therapy
  - Less regulatory, safety and efficacy risk
- Choose initial clinical path for fast approval; later expand
  - MNX-100 in Phase II relapsed and refractory neuroblastoma which has an historical PFS (progression free survival) of 42 days
- Series A closed
  - Seasoned investors in the generics industry
- The executive team members have demonstrated track records of building shareholder value and liquidity in the international biotech and pharmaceutical industry
  - Deep experience in development, partnerships, M&A, IPO's, reverse IPO's

# Clinical Product Candidates



**MNX-100 – PHASE II (INITIALLY NEUROBLASTOMA)**

**MNX-200 – Q1 2011, PHASE I**

# MNX – 100

4

## PHASE II NEUROBLASTOMA

# MNX-100 Overview



- Orally administered drug widely used for treatment of infectious disease
- MNX-100 has been prescribed to thousands of patients worldwide for over 45 years (currently distributed by WHO)
- Never formally approved in the US, EU or China
- Serendipitous human clinical data showed substantial clinical activity against neuroblastoma and medulloblastoma alone and combined with chemo
- Method of Use patents filed and licensed to MetronomX
- Proprietary formulation
- Substantial preclinical activity in other cancers

# Significant Value of Repurposed Cancer Drugs



- Bendamustine
  - tested in 1966 - sold to Cephalon in 2006 for $165M
- Thalidamide
  - the drug behind Celgene - $26B market cap
- Arsenic Trioxide
  - sold to CTIC for $100M; orphan drug designation
- Vidaza (5-azacitidine)
  - sold to Pharmion for $700K upfront by Pharmacia-Upjohn. Celgene acquired Pharmion for $2.9B; $200M annual sales in 2008; Celgen paid $425M to buy out royalties
- CAMPATH
  - patented in 1983; sold by Berlex Schering AG; $200M/yr revenues
- Aloxi (an old 5-HT3 antagonist)
  - MGI licensed from a Finish company (Helsinn) and got it approved in the US--sales of $300M before being acquired by Eisai in 2007 for $5.5B
- Debivon (an antihistamine)
  - Medivation, Inc. (non cancer) licensed it from Russia repurposed for Alzheimer's, sold for $225M to Pfizer in Phase III plus $500 M milestone

# Neuroblastoma – Current Treatment Outline



- Low Risk
  - Surgery and Observation
  - Survival > 90%
- Intermediate Risk
  - Chemotherapy (4 or 8 cycles)
    - Carboplatin, Etoposide, Cytoxan, Doxorubicin
  - Survival 80-90%
- High Risk- (overall 40% of the patients)
  - Chemotherapy, surgery, double autologous BMT, radiation, retinoic acid +/- antibody therapy
    - 60% relapse in < 1 year
  - First relapse treatment standard of care is cytoxan plus topotecan therapy
    - Progression free survival of this patient population is 42 days

# Neuroblastoma Development Strategy



- No other drugs ever approved for neuroblastoma
- It is an unmet medical need in this patient population
- The clinical read outs are fast (response, PFS and OS)
- Regulatory review by the FDA and EMEA will be 'fast track'
- It is an orphan disease with additional orphan disease designation protection
- Orphan diseases have special consideration for pricing and reimbursement
- Obama administration is pushing through legislation that will provide huge dividends for companies that are developing pediatric oncology drugs
- Develop in other indications later

# MNX-100 Phase I Clinical Study



- A dose escalation trial of daily oral MNX-100 in a therapeutic window, followed by continuation of MNX-100 with the addition of standard doses of cyclophosphamide and topotecan.
- Primary Objective
  - To test the safety of MNX-100 in children with relapsed or refractory neuroblastoma alone and in combination with cyclophosphamide and topotecan.
- Secondary Objectives
  - To evaluate the pharmacokinetic profile of MNX-100 alone and in combination with cyclophosphamide and topotecan.
  - To determine the response rate to treatment with MNX-100 combined with cyclophosphamide and topotecan

# MNX-100 Phase I Patient Population



- Multiply relapsed and refractory neuroblastoma patients (range = 1 to 6 relapses; average relapse number = 2.7)
- Most of the patients had been treated prior with either topotecan or with cytoxan plus topotecan, and had relapsed
- Median survival for this patient population (without further treatment) estimated to be <42 days

# Historical Data



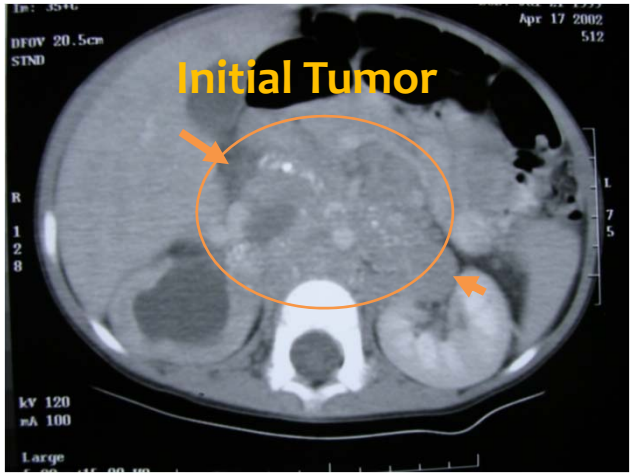
- There is currently no curative treatment for children with relapsed/refractory neuroblastoma, and for these children the 5 year survival rate is <10%. As such, new therapeutic approaches are needed to treat these children
- In a recent multicenter study by the COG (London et. al, in press), 119 patients with only one prior aggressive regime were evaluated for treatment response to topotecan (5 days at 2 mg/m2) or combination of topotecan and cyclophosphamide (0.75 mg/m2 and 250 mg/m2 respect.)

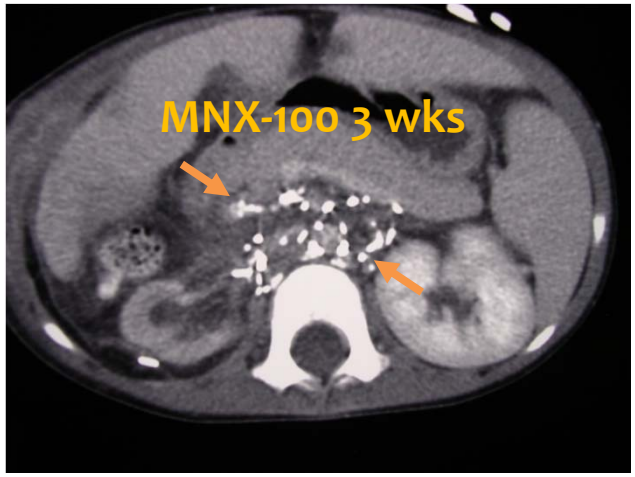
**Results of COG Phase II Study in First Relapsed Neuroblastoma**

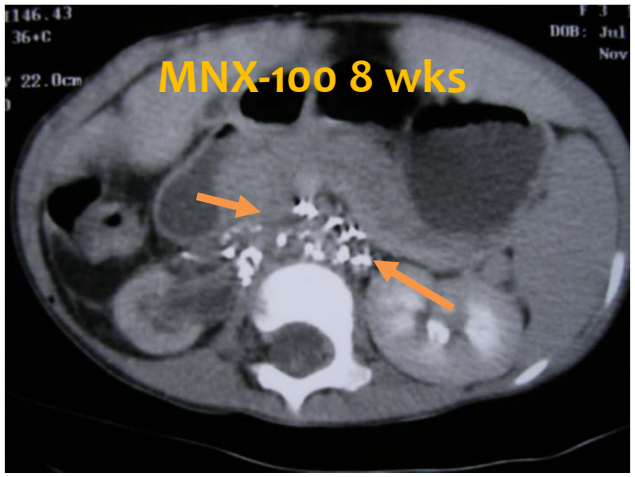
| Treatment | CR + PR | Percentage | PFS | OS at 3 years |
|---|---|---|---|---|
| TOPO | 11/59 | 19% | 3 months | 4% |
| TOPO + CYCLO | 18/57 | 32% | 6 months | 15% |

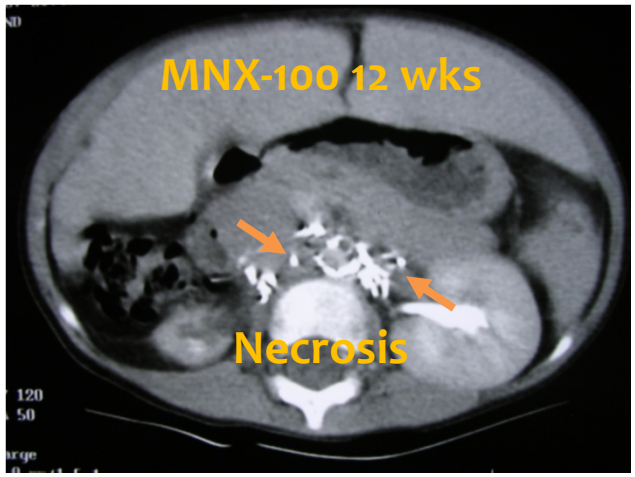
# MNX-100 – Initial Patient Treated





# Toxicities in MNX-100 Phase I Trial



Number of Patients Had Grade ≥2 Drug-Related Toxicities (CTC Version 3)

| MNX-100 Dose (mg/kg/day) | Stomach Pain | Anorexia or Nausea | Neuropathy (CNS/PNS) | Seizure | Pulmonary Hemorrhage |
|---|---|---|---|---|---|
| 20 (3 pts) | | | 1 | | |
| 30 (6 pts) | 2 | 4 | 3 | 1 | |
| 40 (5 pts) | | 2 | 2 (1-DLT) | 4 | 1 (DLT) |

CTC: Common Toxicity Criteria, DLT: Dose Limiting Toxicity

- All CNS/PNS neuropathy resolved after holding MNX-100.Three patients treated for seizures with Keppra displayed neurotoxicity that reversed after holding both medications. Seizures did not recur after decreasing MNX-100 dose without need for antiepileptics.
- No cardiotoxicity noted on 5 minute EKG's done throughout study

# Phase I Response Data



Evaluable criteria- at least 2 cycles (11 patients treated)

- 4 PR's = 34% response rate
  - PFS (3,5,10,10) mean = 7 months
- 5 SD = 44% response rate
  - PFS (1,3,8,11,12) mean = 7 months

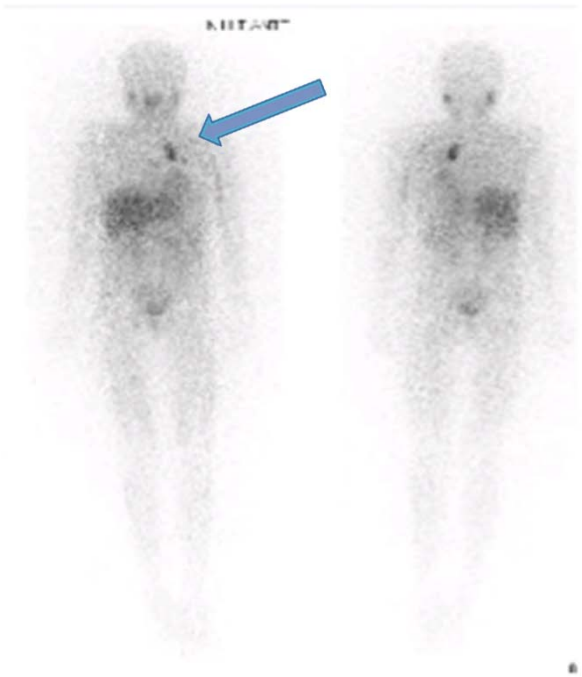
Evaluable criteria- at least 3 cycles (10 patients treated)

- 4 PR's = 40% response rate
  - PFS(3,5,10,10) mean = 7 months
- 4 SD = 40% response rate
  - PFS (3,8,11,12) mean = 6 months

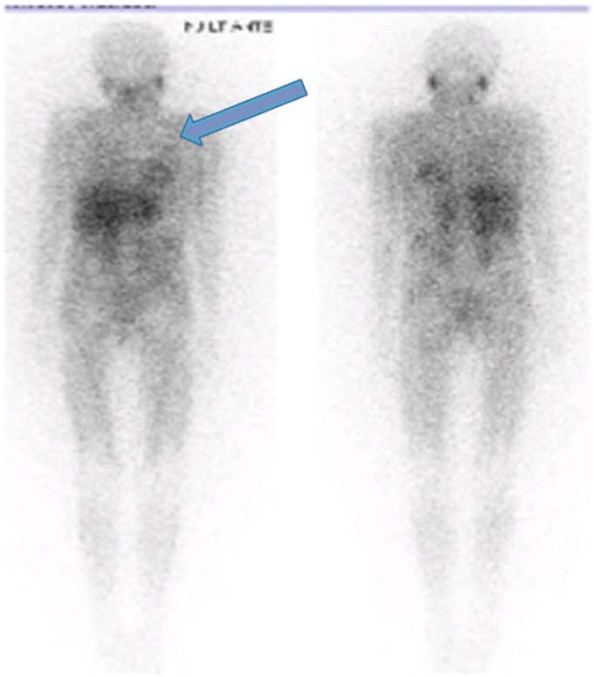
# An Example of Responses in Phase I



PRE-STUDY



END OF STUDY



The patient with neuroblastoma for 7 years multiply relapsed, treated with cyclo/topo for 2 cycles with stable disease prior to enrollment on Phase I study

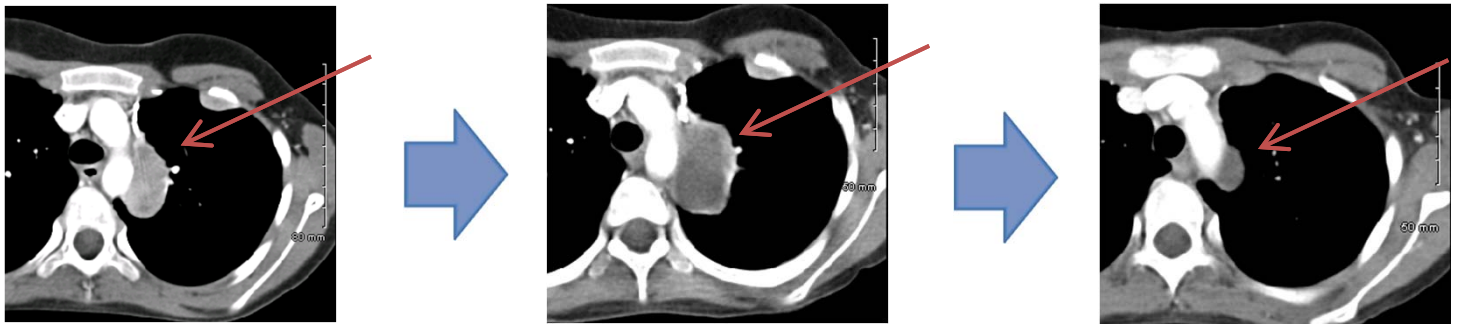
# An Example of Responses in Phase I



Pre Study

MNX-100 Alone
(Large Area of Necrosis Seen)

MNX-100 with Cyclo/Topo
(MIBG Negative)



The patient with neuroblastoma for 7 years multiply relapsed, treated with cyclo/topo for 2 cycles with stable disease prior to enrollment on Phase I study

# MNX-100 Phase I Results



- 6/14 alive 12 months following treatment
- Greatly improved quality of life including reduced narcotic use, improved mobility, return to school
- Exciting preliminary evidence of activity in drug resistant patient population

*Sydney is free of disease 24 months after relapse and start of MNX-100 trial*

# MNX-100 Phase IIa Clinical Study



- Primary Objective
  - Test the efficacy and safety of MNX-100 in children with relapsed or refractory neuroblastoma or medulloblastoma, both alone and in combination with cyclophosphamide/topotecan
- Secondary Objectives
  - Evaluate the correlation between the pharmacologic serum levels of MNX-100 (alone and combo with cyclo/topo) with tumor response
  - Quality of life and neurocognitive evaluation
  - Biology studies to include: genomic analysis of cells pre- and post-treatment, correlation of in vitro response to in vivo response, flow cytometry of tumor burden in bone marrow and biomarker development.

# MNX-100 – Phase IIa Treatment Plan



**Initial Evaluation**

- MNX-100 at 30 mg/kg/day, daily X 42 days, divided TID (Cycle 1-2)

**Re-evaluation**

- Continue MNX-100 at 30 mg/kg/day, daily divided TID, plus
- Cyclophosphamide and Topotecan daily for 5 days every 21 days with zoledronic acid 4 mg/m$^2$ on Day 1 (Cycles 3-12)

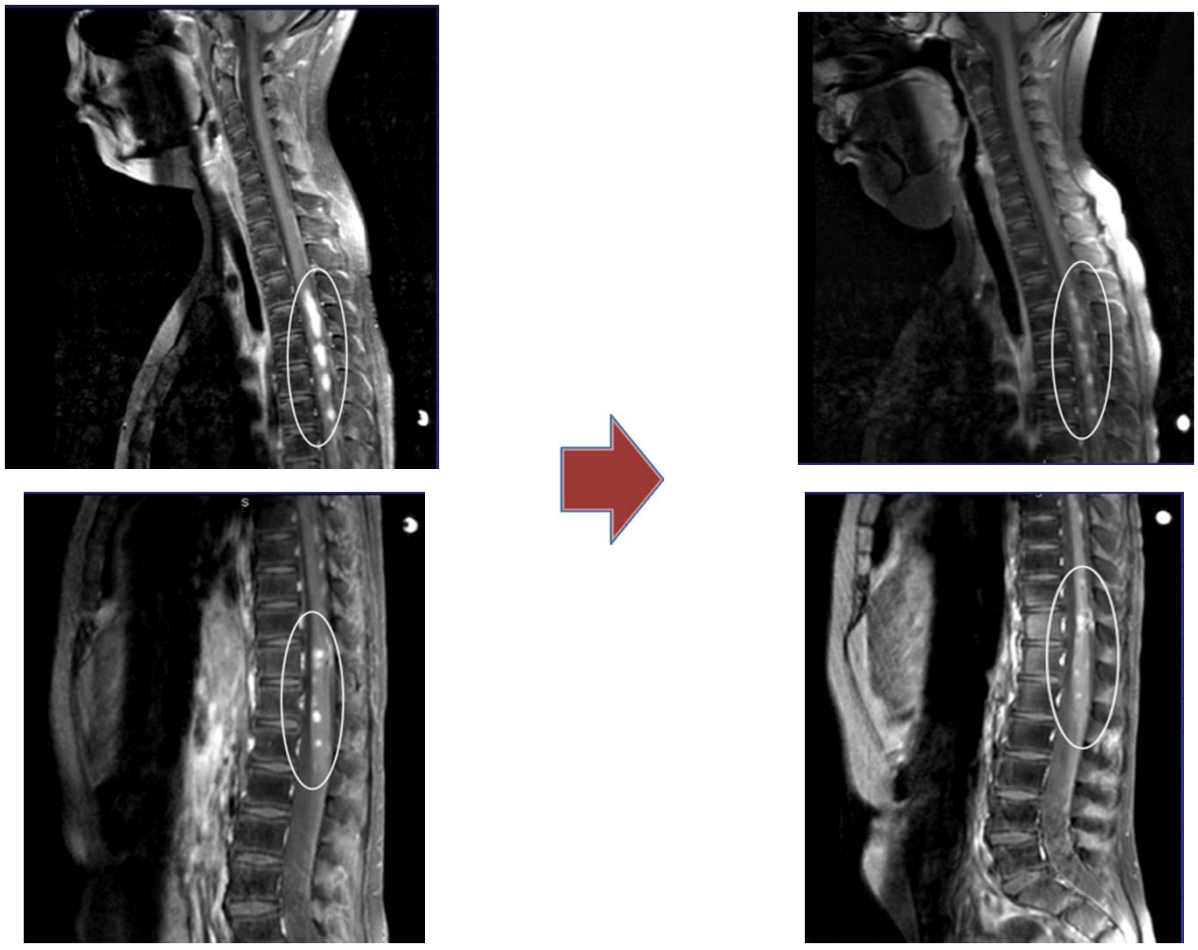
**Final Evaluation**

# An Example of Responses in Phase IIa



Pre Study

6 weeks on MNX-100 Alone

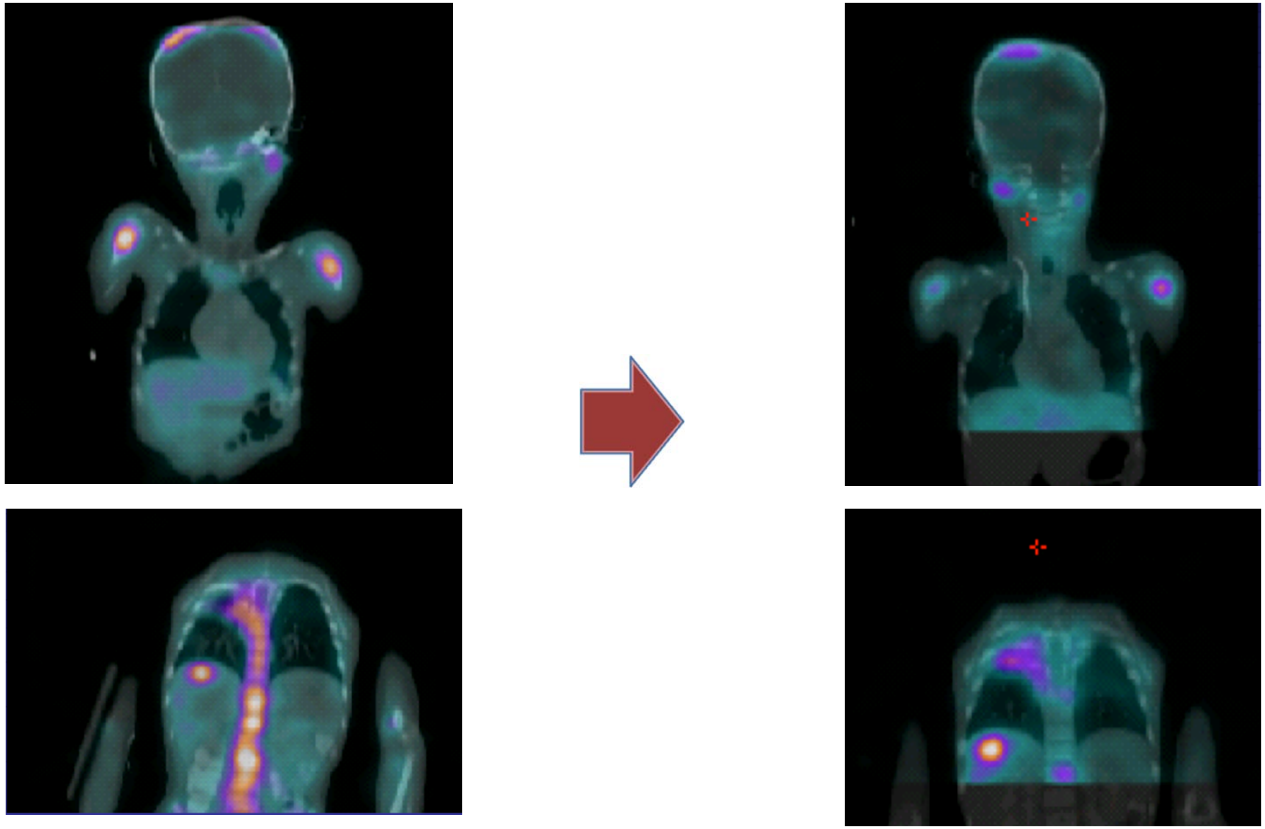


# An Example of Responses in Phase IIa



Pre Study

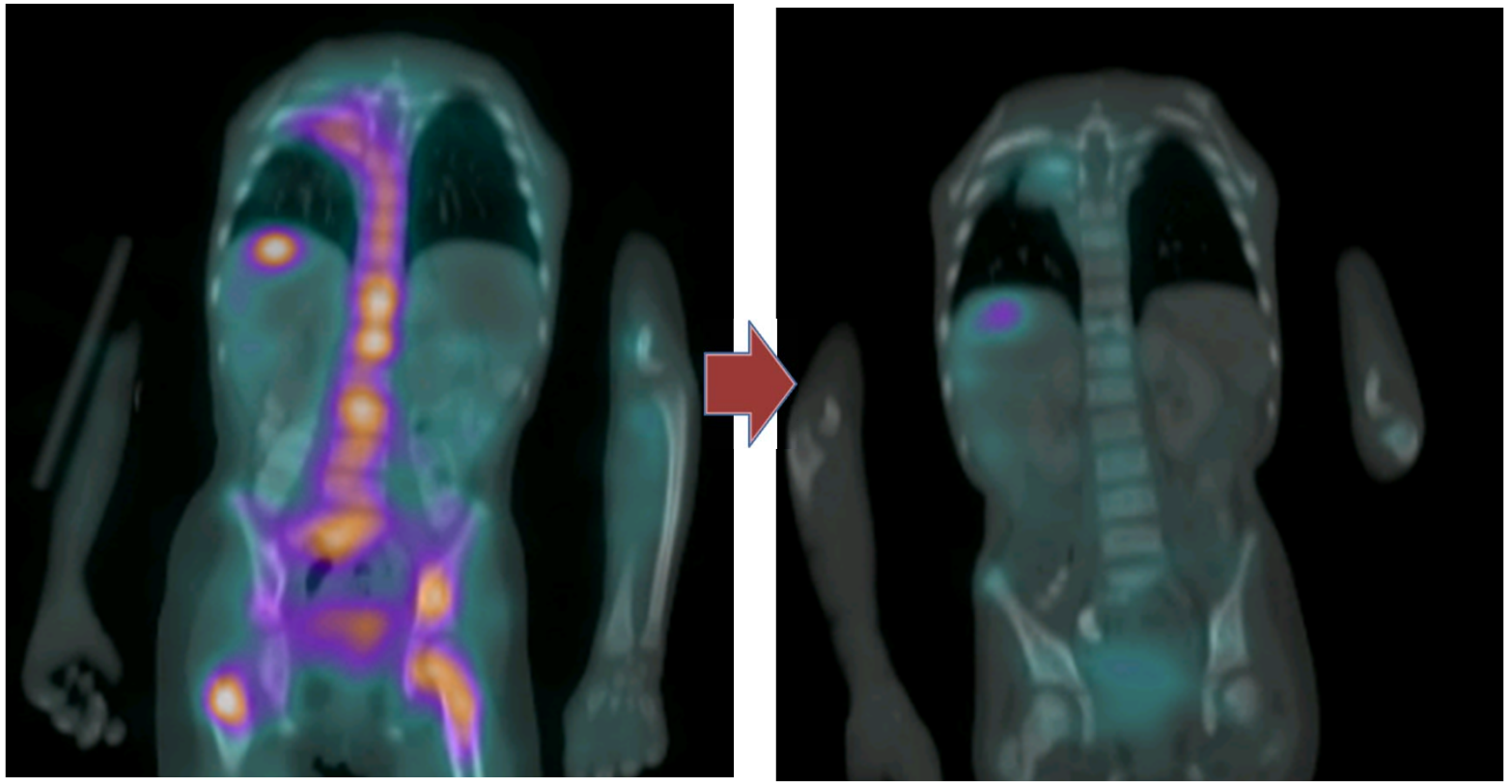
3 weeks on MNX-100 Alone



# An Example of Responses in Phase IIa



Patient before and after 6 weeks of MNX-100 therapy alone



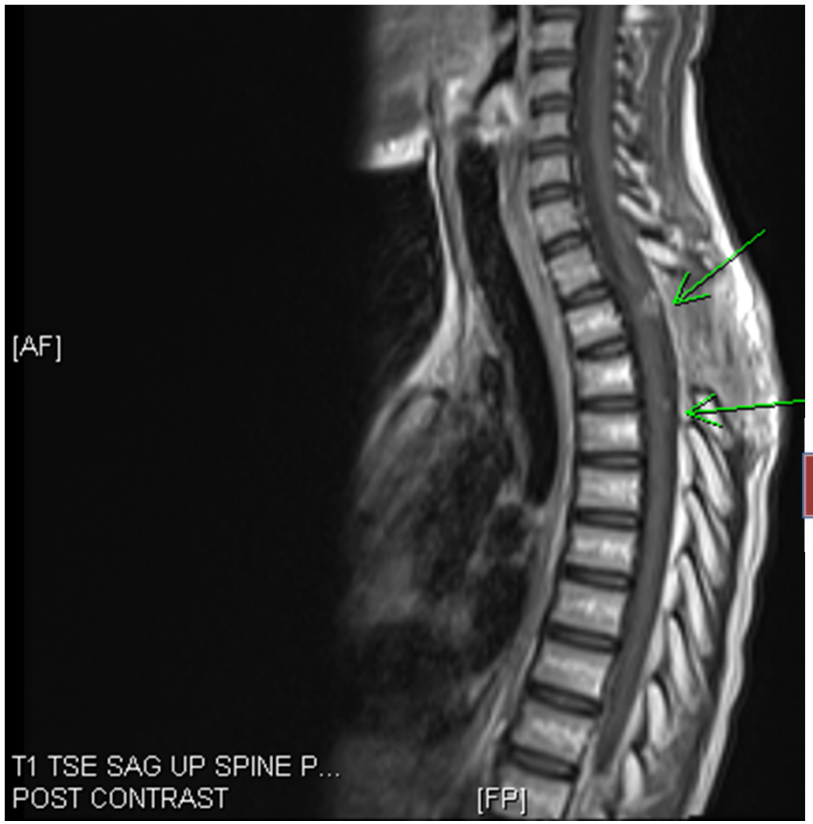
VMA: 441

VMA: 329

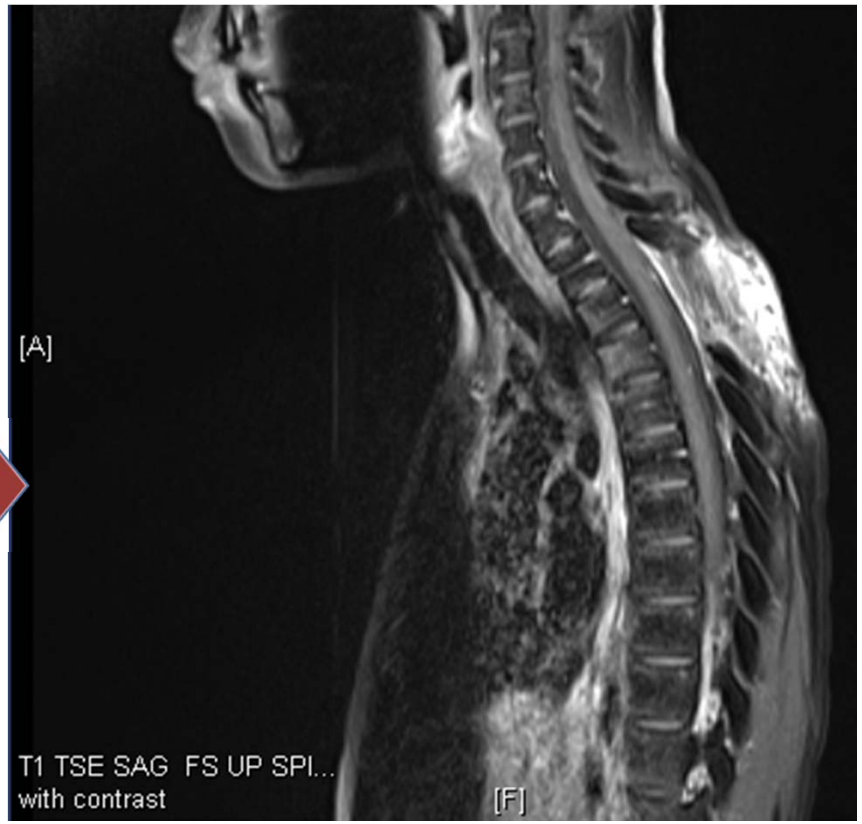
# An Example of Medulloblastoma Responses



3/18/10



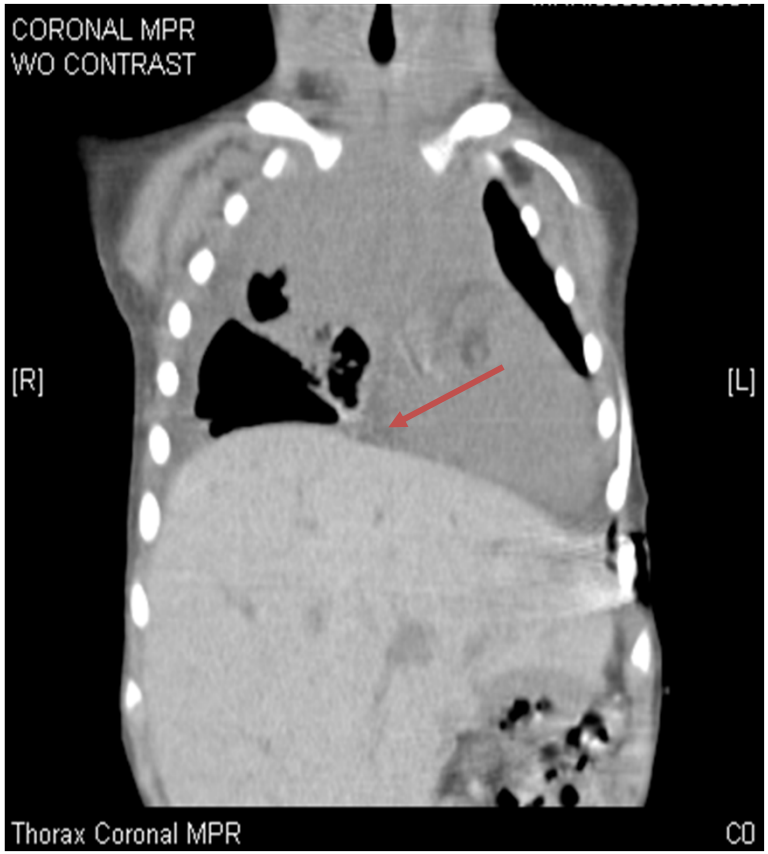

4/28/10



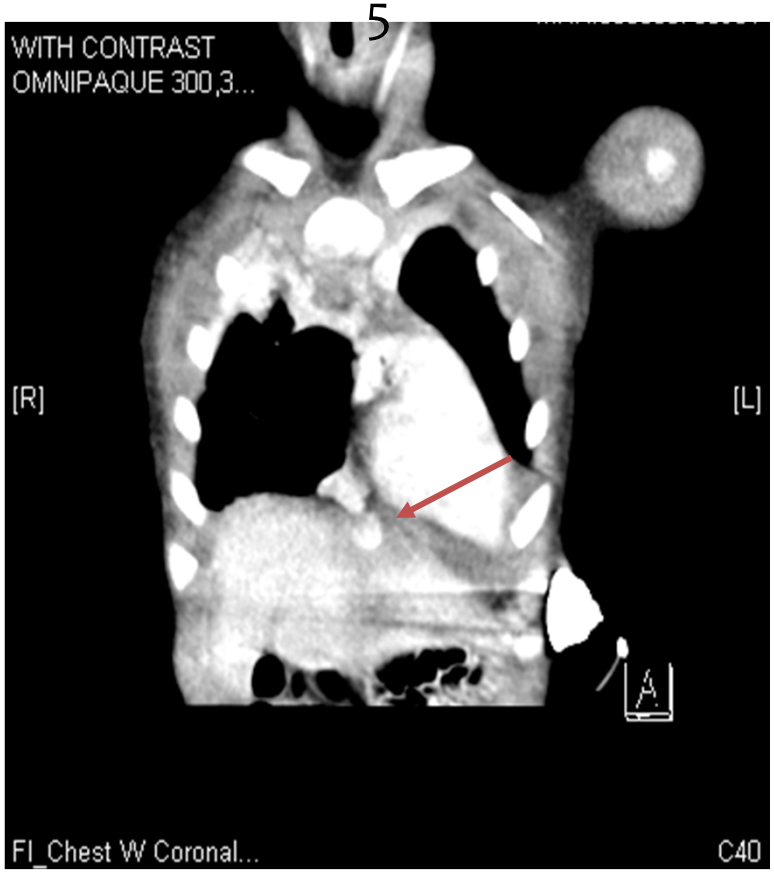
# An Example of Responses in Phase IIa



MNX-100, D10



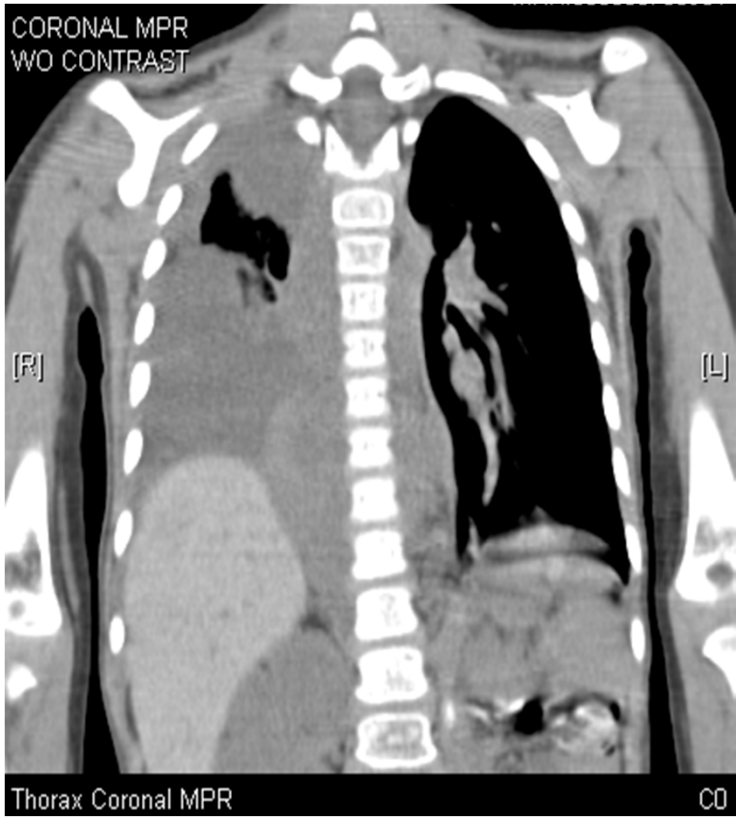

MNX-100 with Topo/Cyclo, end of cycle 5



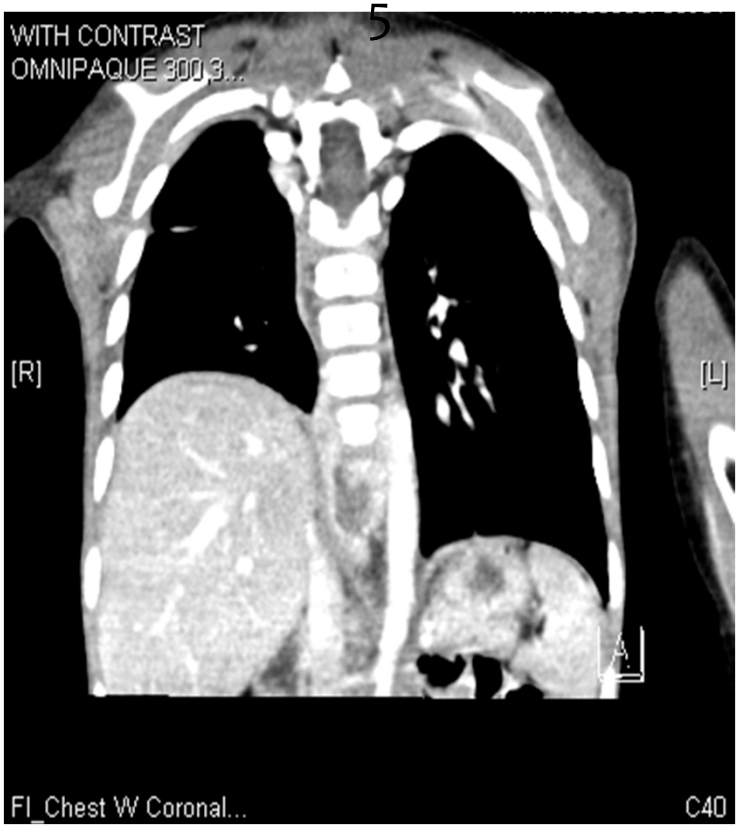
# An Example of Responses in Phase IIa



MNX-100, D10




MNX-100 with Topo/Cyclo, end of cycle 5



# Site update



## Number at each site:

- UVM – 20 subjects
- St. Louis – 3 subjects
- Orlando – 4 subjects
- North Carolina – 4 subjects
- San Diego – 1 Subject

## Sites are open:

- UVM – Open
- St. Louis – Open
- San Diego – Open
- Orlando – Open
- MD Anderson, TX – Not Open – IRB approved
- South Carolina –Open
- North Carolina – Open
- Michigan – Open
- Connecticut – Not Open –at IRB
- Kansas- Open
- Oregon- Open

# Patient Accrual



Number of patients enrolled in each strata:

- Stratum I (first relapse) – 0
- Stratum II (multiple relapse/refractory) – 28
  - New protocol – 8 at other sites + 1 at our site = 9
  - Old Protocol – 19
- Stratum III (medulloblastoma) – 4
  - New Protocol – 1
  - Old Protocol – 3

# MNX-100 Phase II Response to Date



| Response | Results |
|---|---|
| PR | 43% |
| SD | 43% |
| PD | 14% |

# MNX-100 – Phase IIb Treatment Plan



**Initial Evaluation**

- Continue MNX-100 at 30 mg/kg/day, daily divided TID, plus
- Cyclophosphamide and Topotecan daily for 5 days every 21 days with zoledronic acid 4 mg/m$^2$ on Day 1 (Cycles 1 - 2)

**Re-evaluation prior to each two cycles**

# MNX-100 Phase IIb Analysis



- A sample size of n = 39 subjects will be required to test the 30% vs. 50% response rate hypotheses for subject group using a two-stage minimax design
- There will be an interim look at the data after accrual of 18 patients. Need 4/18 PR to continue to a total of 39 patients to power the study

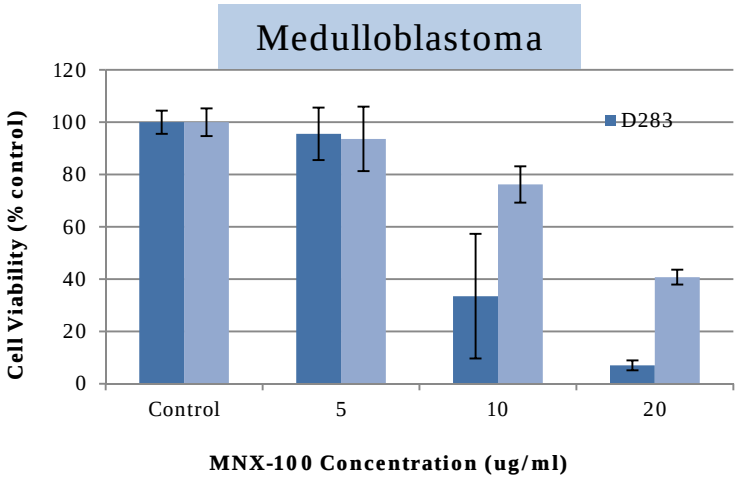
# MNX-100 Approval Path

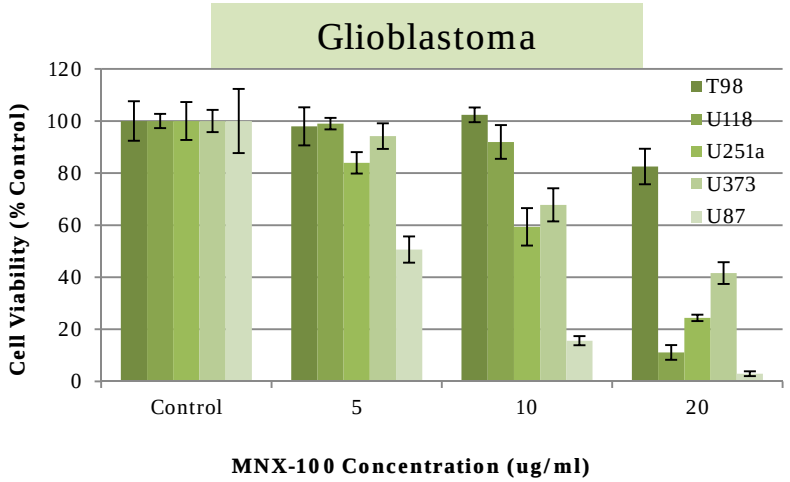


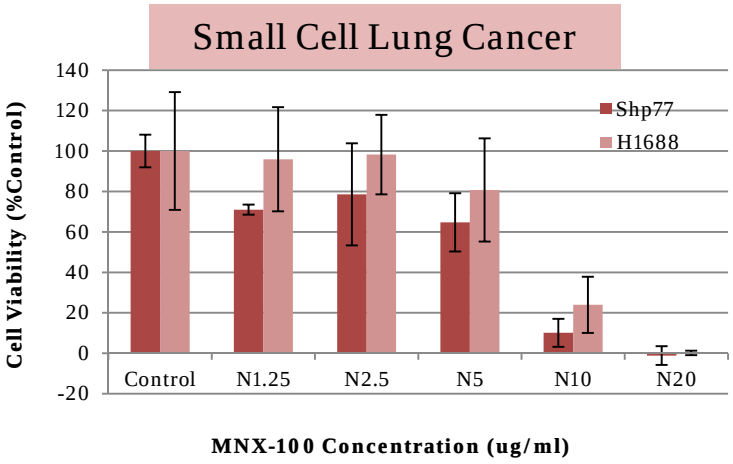
- Special protocol amendment with FDA Q1 2011
- Initiate a pivotal Phase III sometime soon thereafter
  - Additional US centers have requested participation including the NCI
  - Open clinical sites in India, UK and Germany (requested) which would pave the way for EMEA regulatory filing
  - Partner in China for neuroblastoma and lung cancer
- Randomized study against cytoxan/topotecan with cross over design if progression on control arm
- Estimated 40 patients per arm (80 total)
- Primary endpoints would be response rate and progression free survival; secondary endpoints quality of life
- Fast track approval and orphan disease designation
- File with EMEA (Europe) at the same time

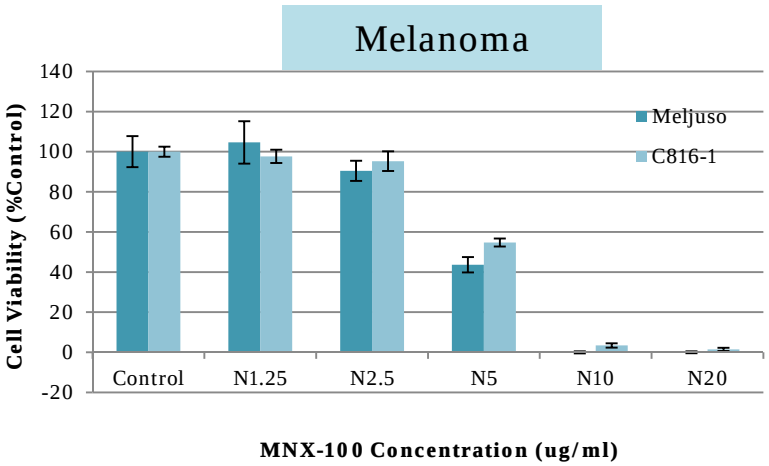
# MNX-100 has Activities Against Other Cancer Types





# Small Cell Lung Cancer Study



- Significant unmet medical need- long term survival <15%; multiply relapsed patients particularly
- Excellent potential for significant activity and well positioned for China trial
- Open label dose escalation of MNX-100 plus rapamycin or combined with chemotherapy
- Other cancer indications which use topotecan, cytoxan or rapamycin (renal, NSCLC, ovarian, breast, other) should have significant activity and would be well suited for China trial

# MNX-100 – Summary



- Discovered through surprising and unexpected clinical outcomes
- Increases the level of reactive oxygen species (ROS) in cancer cells where the level of ROS is already abnormally elevated, causing oxidative stress
- Activates caspase pathway and induces apoptosis
- Encouraging results from phase 1 and phase 2 trials for treating neuroblastoma and medulloblastoma
- Anti tumor activities observed in other solid tumors from cell based assays
- World-wide exclusive license
- Potential significant value as seen in other repurposed cancer therapeutics

# MNX-200

35

## PHASE I EXPECTED Q1 2011

# MNX-200 Overview



- Proprietary oral metronomic formulation of a cancer cytotoxic
- This cytotoxic drug is currently approved in the US, Europe and Japan as an i.v. formulation for first line colon and rectum carcinoma
- Current US sales of i.v. formulation are $550 million (2007 sales)

# MNX-200 i.v. formulation also has single-agent activity in clinical trials against other malignancies



- SCLC
  - 16-33% PT; 50% NPT
- NSCLS
  - 15-32%
- Gastric ca.
  - 20-30%
- Esophageal ca.
  - 20%
- Hematologic
- Breast ca.
  - 8-25%
- Cervical ca.
  - 21%
- Ovarian ca.
  - 24%
- Pancreatic ca.
  - 9-11%
- Glioma
  - 5-15%

# Metronomic Dosing

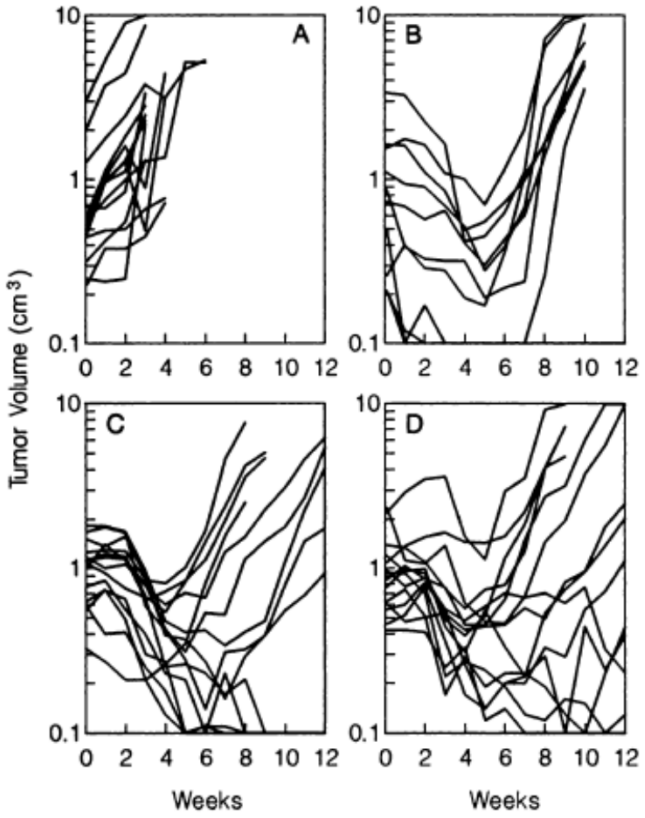


- Metronomic dosing means oral administration using low doses over extended periods of time
- Anti-tumor activity is substantially greater than traditional formulations using preclinical models
- MetronomX is developing a proprietary formulation that allows for optimal metronomic dosing with minimal toxicity
- Metronomic reformulation has potential with multiple cancer drugs

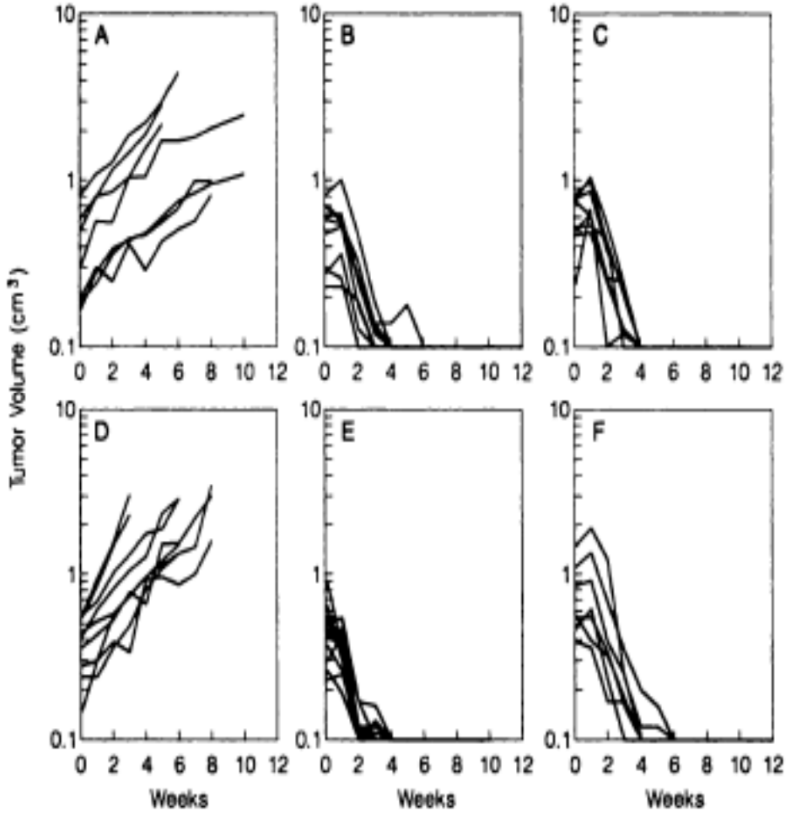
# Effects of Metronomic Dosing vs. MTD



Traditional MTD Dosing
of colon carcinoma model (B,C,D)




Metronomic Dosing of same
colon carcinoma model (B,C,E,F)



# Rationales for MNX-200 Phase I



- Eight Phase I studies have been conducted with oral, ***non-metronomic*** formulation of MNX-200
- Similar single agent efficacy was observed compared with the i.v. formulation
- Activity was seen in multiple tumor types
- Acceptable toxicity profile
- Metronomic formulation should provide dramatic additional activity
- MNX-200 Phase I dose escalation to begin later 2010 or early 2011

# Rationales for MNX-200 Development




Approved
Generic

$500 M sales in
the US

Eight Phase 1
Studies

Clinical activities in
multiple tumors

Metronomic
Proprietary

Low clinical risks
with significant
market potential

# Thank You



**DANONG CHEN**
**CEO**
**DCHEN@METRONOMXGROUP.COM**
**GLENN RICE**
**PRESIDENT**
**GRICE@METRONOMXGROUP.COM**