ProNAi

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Boston Entrepreneurs' Network (ENET)

Bay Colony Office Park, 1100 Winter Street, Waltham, MA

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ProNAi® Summary

- Established 2004 – “The DNAi® Company”
- Lead drug candidate PNT100 just months from clinic with multiple cancer treatment opportunities for blockbuster revenues
- Product business model with pipeline of six lead candidates; PNT200 entering preclinical studies
- DNAi-HiT™ provides ability to design additional leads for revenue generating partnership opportunities
- DNAi® solves the technical issues that have prevented the medical use of oligonucleotides
- “Can Do / Have Done It / Will Do It Again” Team
- $11M invested to date (Apjohn, Grand Angels, Amherst Fund, Sigvion, MEDC)

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DNAi® - Differentiated Approach to Nucleic Acid Drug Development

Targets: Genomic DNA disease loci	***Advantage:*** Multiple mechanisms to trigger apoptosis
Chemistry: Unmodified oligonucleotides	***Advantage:*** Improved safety profile
Delivery: Novosom Liposome encapsulation	***Advantage: Smarticles*** Enhanced delivery

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Emerging Pipeline of Cancer Drugs

Disease(s)	Product Candidate	Target	Discovery Lead	Development Preclinical	Development Clinical
Cancer (NHL, Prostate, Breast, etc.)	PNT100 (PNT225X)	*Bcl2*	1H2007		
Cancer (Breast, NHL, Colon, etc)	PNT200	***	2H2007		

Putative Leads to be proven out in DNAi-HiT™

Cancer (Prostate, Breast, Colon, etc.)	PNT300	***
Cancer (Breast, Colon, etc.)	PNT400	***
Cancer (Breast, Colon, etc.)	PNT500	***
Cancer (Prostate, Breast, Colon, etc.)	PNT600	***

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ProNAi® Intellectual Property

- One issued, 10 patent applications covering
  - DNAi® technology: US 5,874,416
  - Pipeline: US 2005/0287667, US 2006/0198828, US 2006/073596, US 2006/0135455 and WO 05/115524
  - Use in oncology and other diseases
  - Synergistic Combination therapy
  - Formulations
  - Platform: DNAi-HiT™
  - Registered Trademarks: DNAi® & ProNAi®

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Lead Drug Candidate - PNT100

- Targets Bcl2 oncogene chromosomal translocation breakpoint region to drive apoptosis and reduce gene expression
- Anti-tumor activity demonstrated in multiple cancers
- Initial indication: Non-Hodgkins Lymphoma
- Preclinical efficacy nearing completion
- IND-directed studies underway

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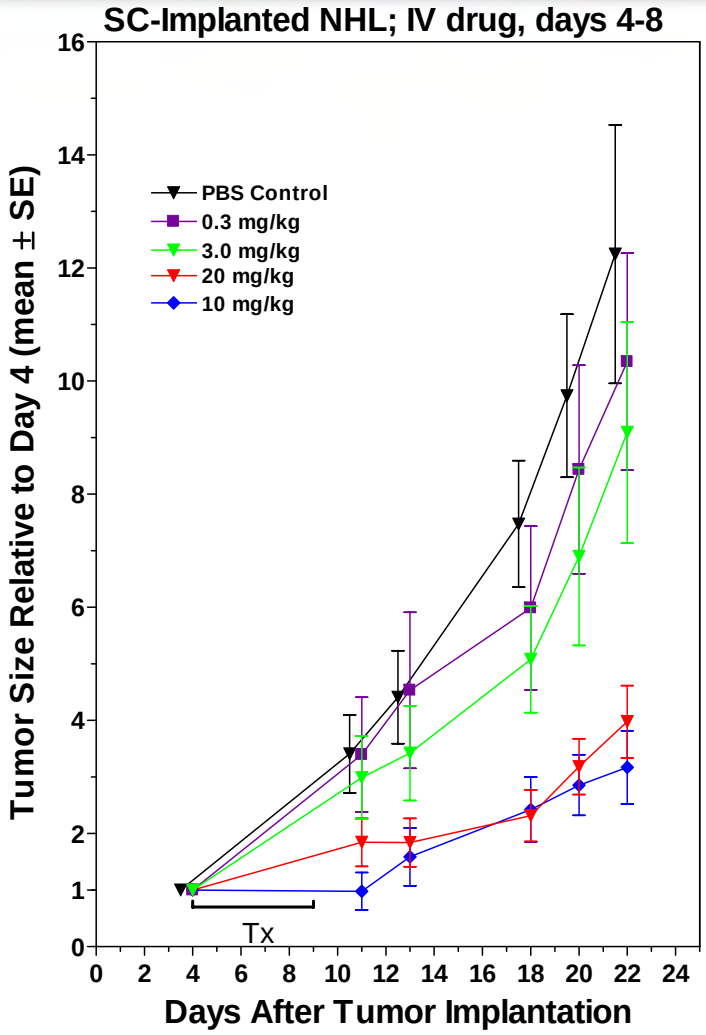
Drug Dose Response - PNT225X
Human Non-Hodgkin's Lymphoma Xenograft



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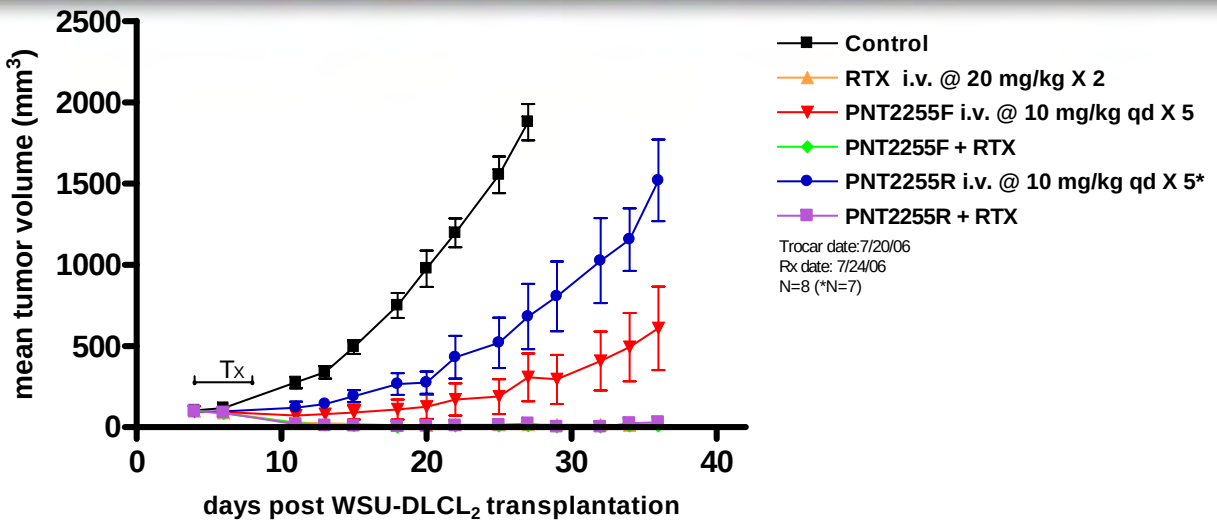
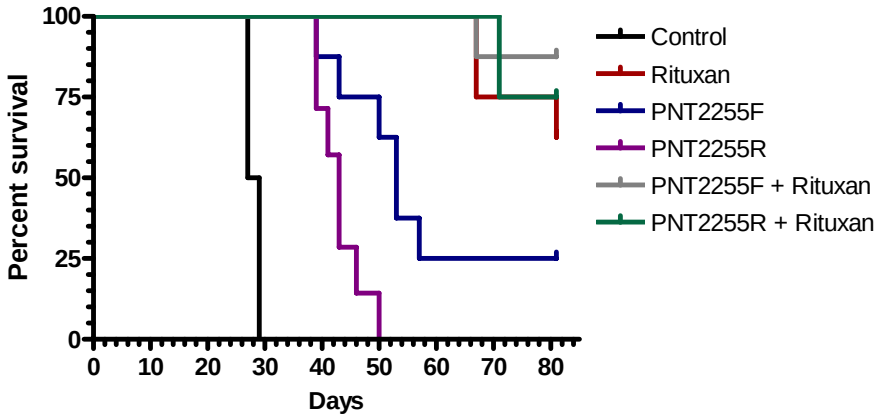
Single Agent Activity – PNT225X
WSU-DLCL2 Model: 2/8 tumor free survival



PNT2255 and Rituxan response:Survival proportions



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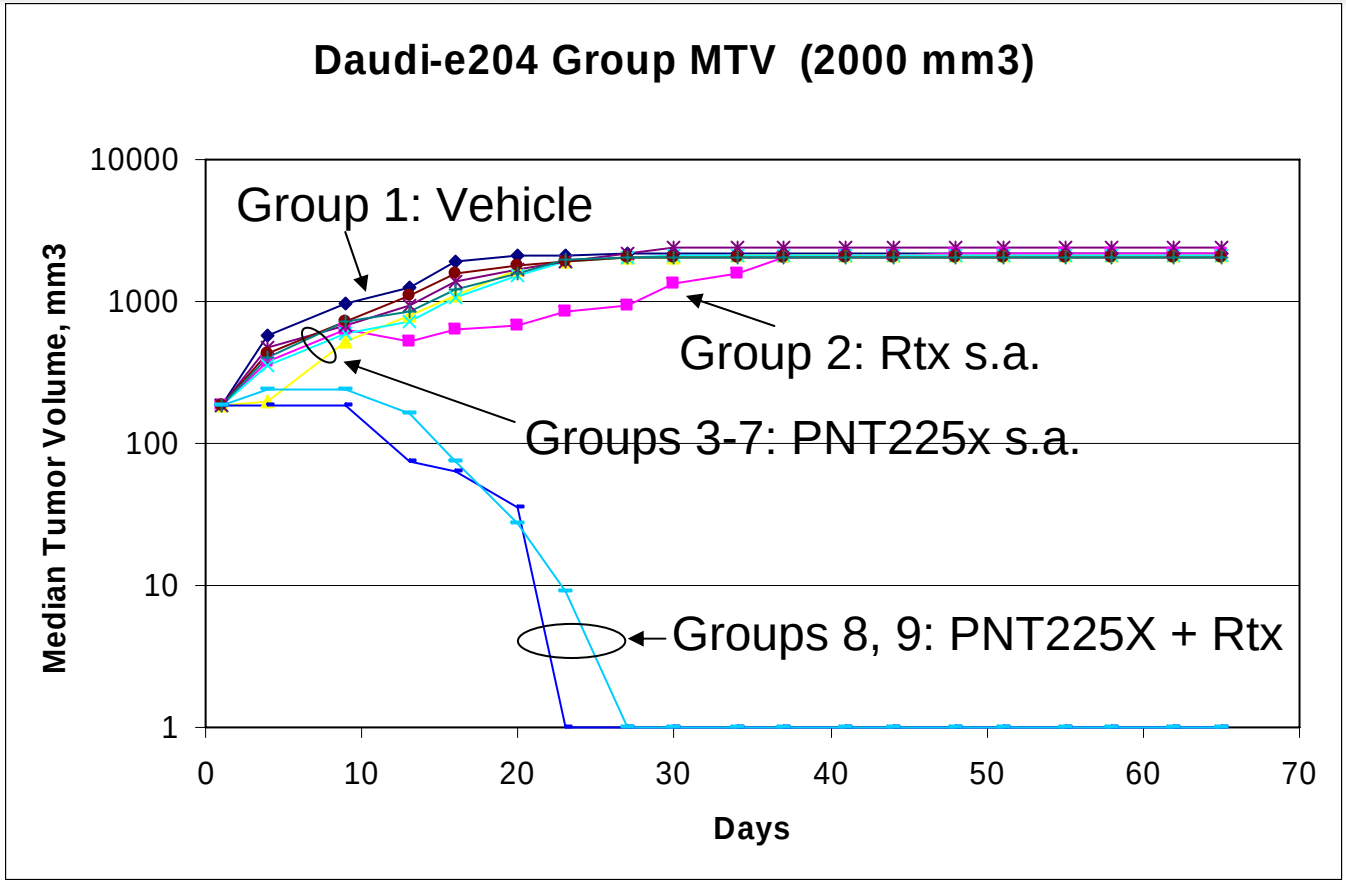
Combination Efficacy – PNT225X/Rituximab

Daudi Human Burkitt's Lymphoma Xenograft



Group 8: 7/10 CRs, 9/10 long-term survivors

Group 9: 7/10 CRs, 8/10 long-term survivors

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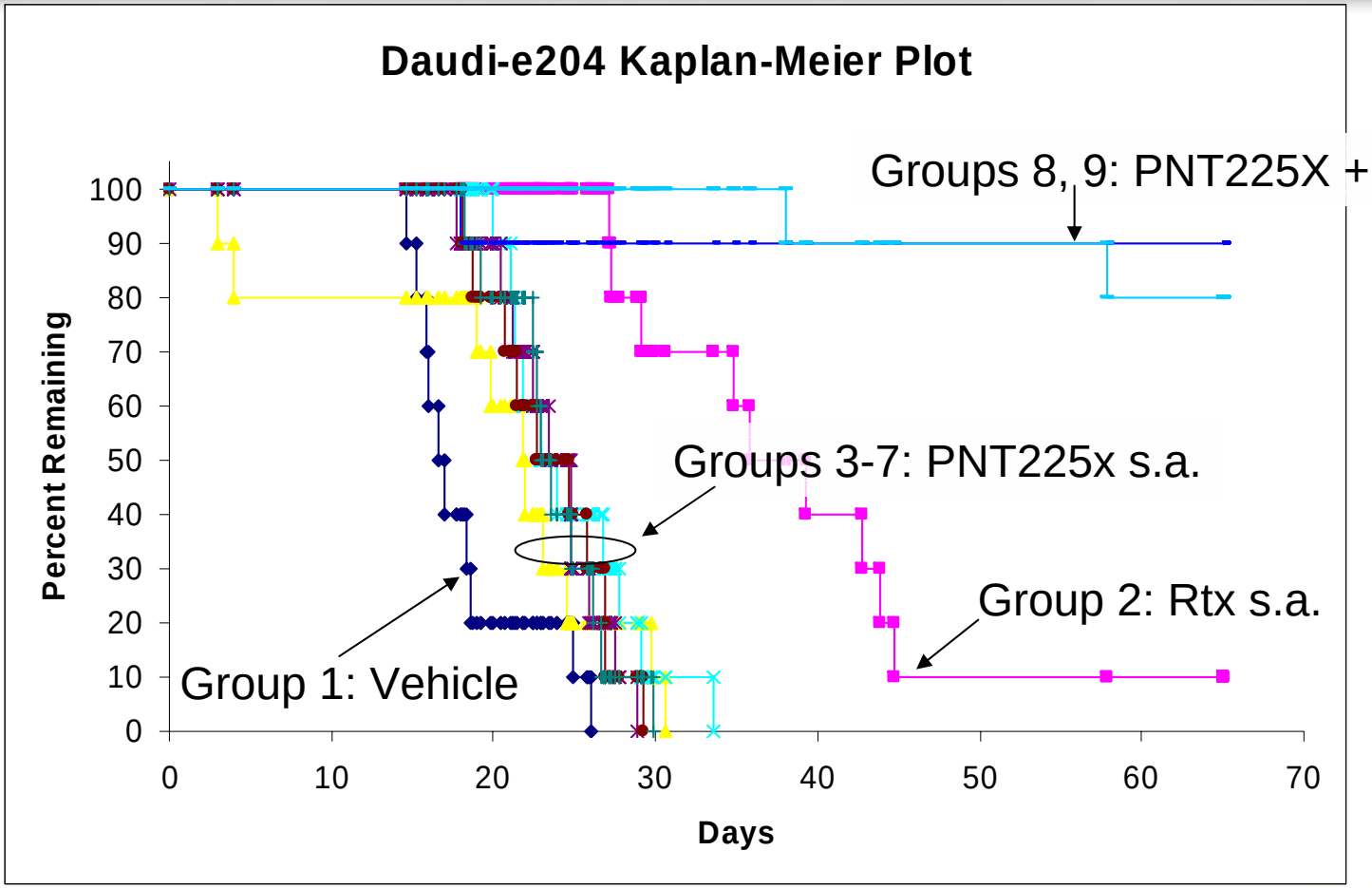
Combination Efficacy – PNT225X/Rituximab
Daudi Human Burkitt's Lymphoma Xenograft



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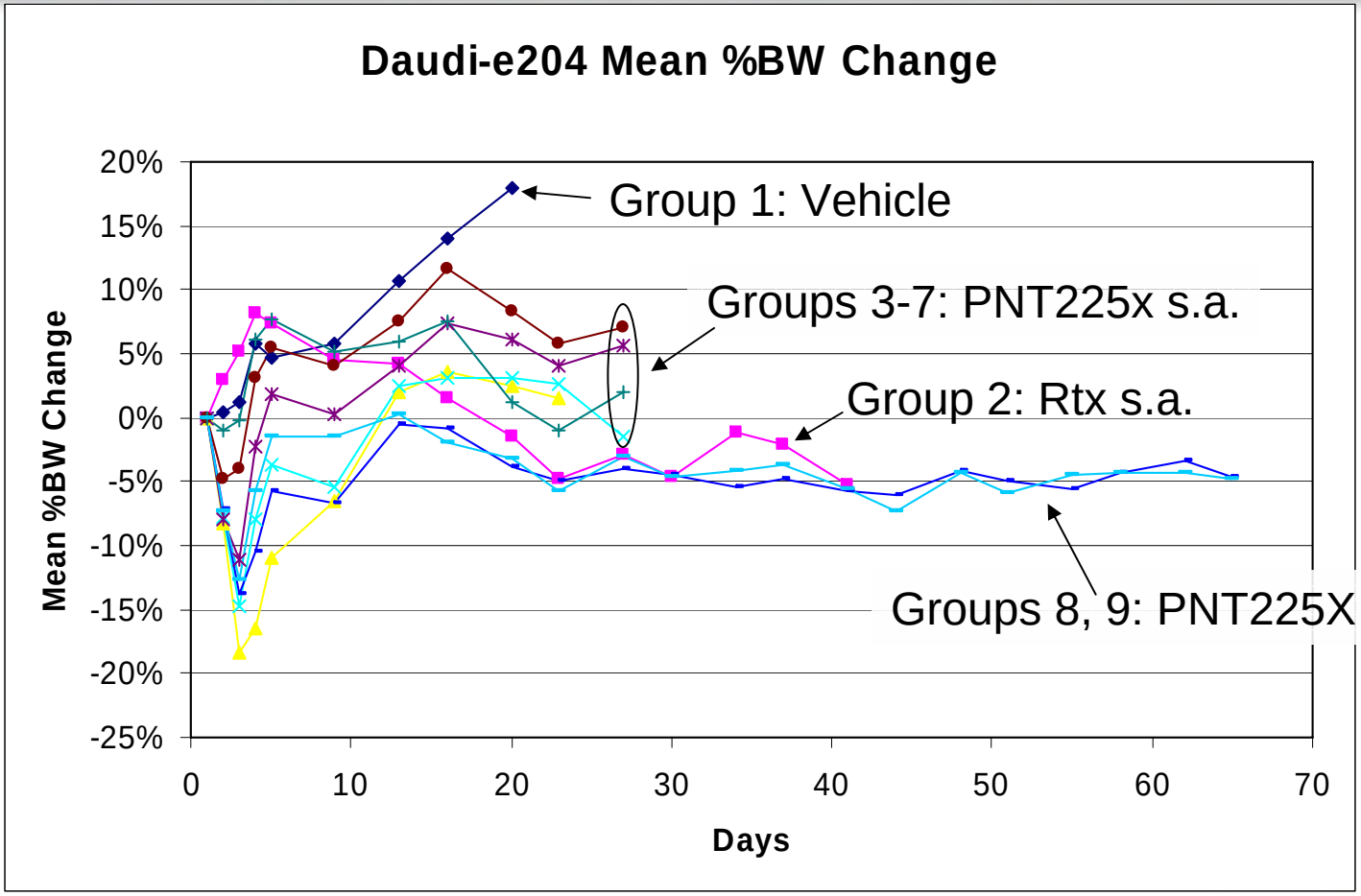
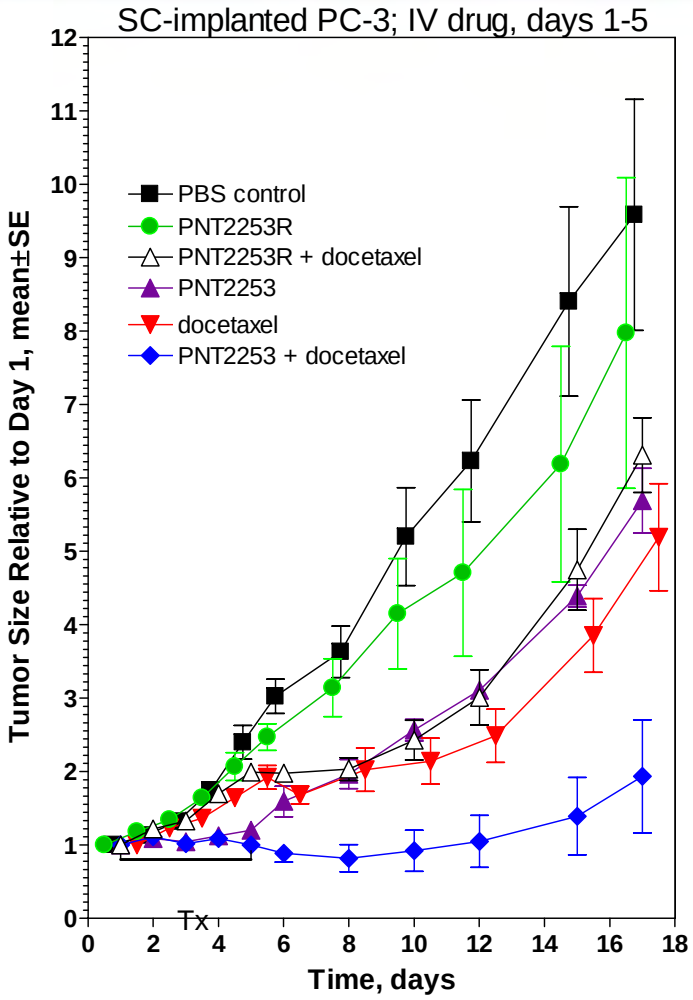
Combination Safety – PNT225X/Rituximab
Daudi Human Burkitt's Lymphoma Xenograft



Combination Efficacy – PNT225X/Docetaxel
Human Hormone Refractory Prostate Cancer



10 mg/kg PNT2253 q.d. X 5 (days 1-5)
10 mg/kg docetaxel q.d. X 1 (day 2)
5 mg/kg docetaxel q.d. X 1 (day 5)

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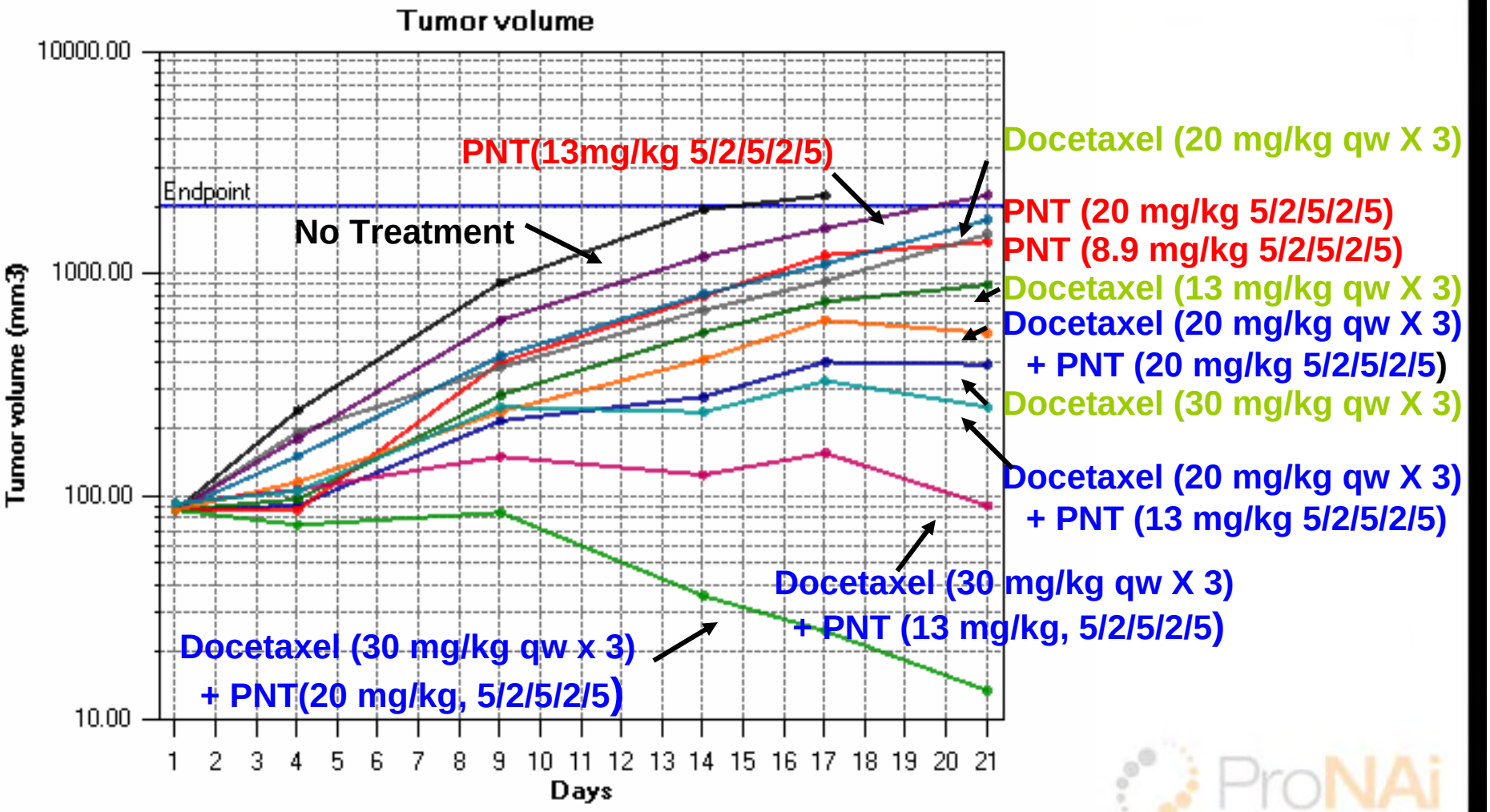
Combination Efficacy - PNT225X/Docetaxel

Melanoma



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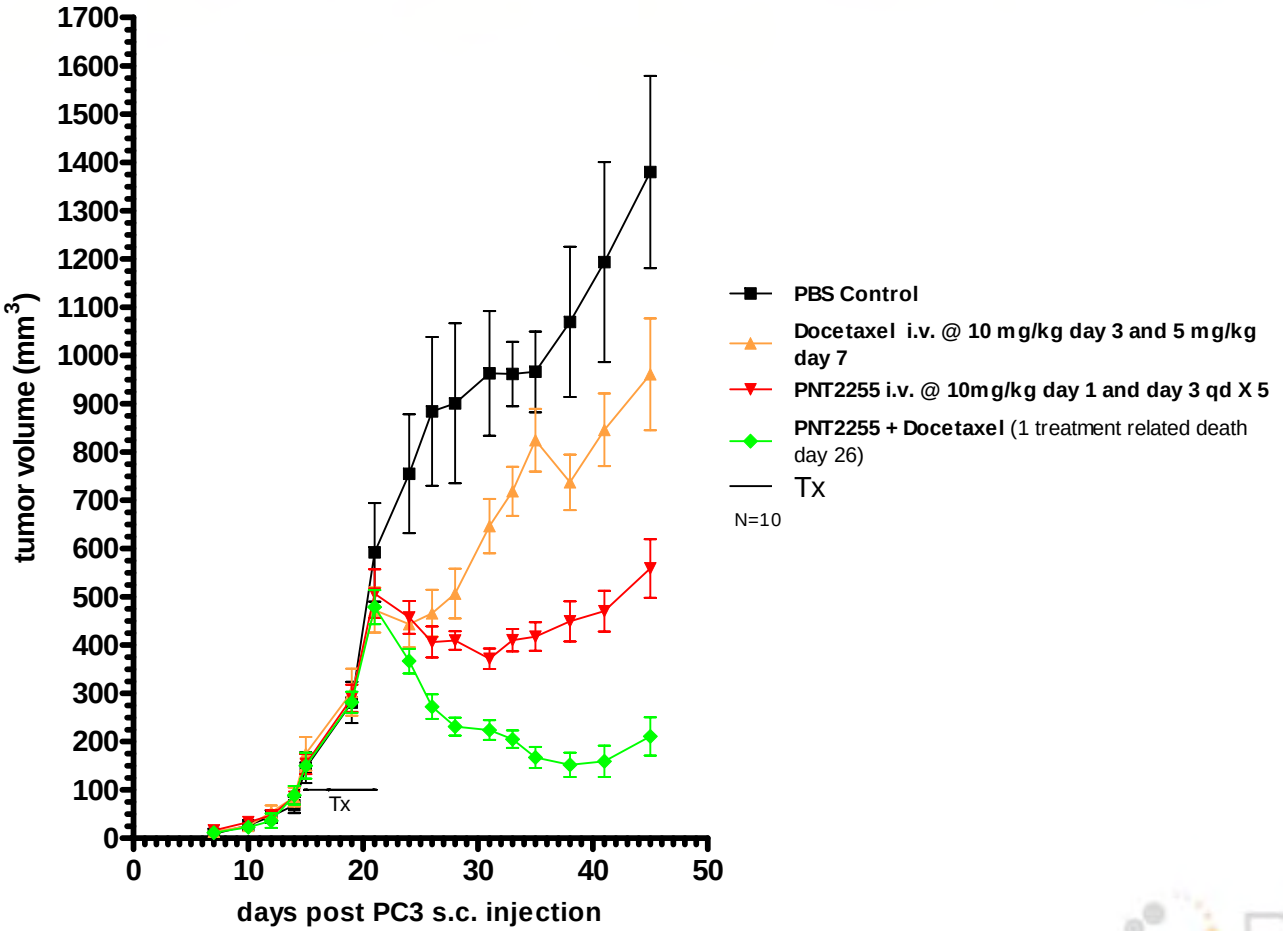
PC-3 PNT225X xenograft response

Mean tumor volume



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Specifications – PNT225X

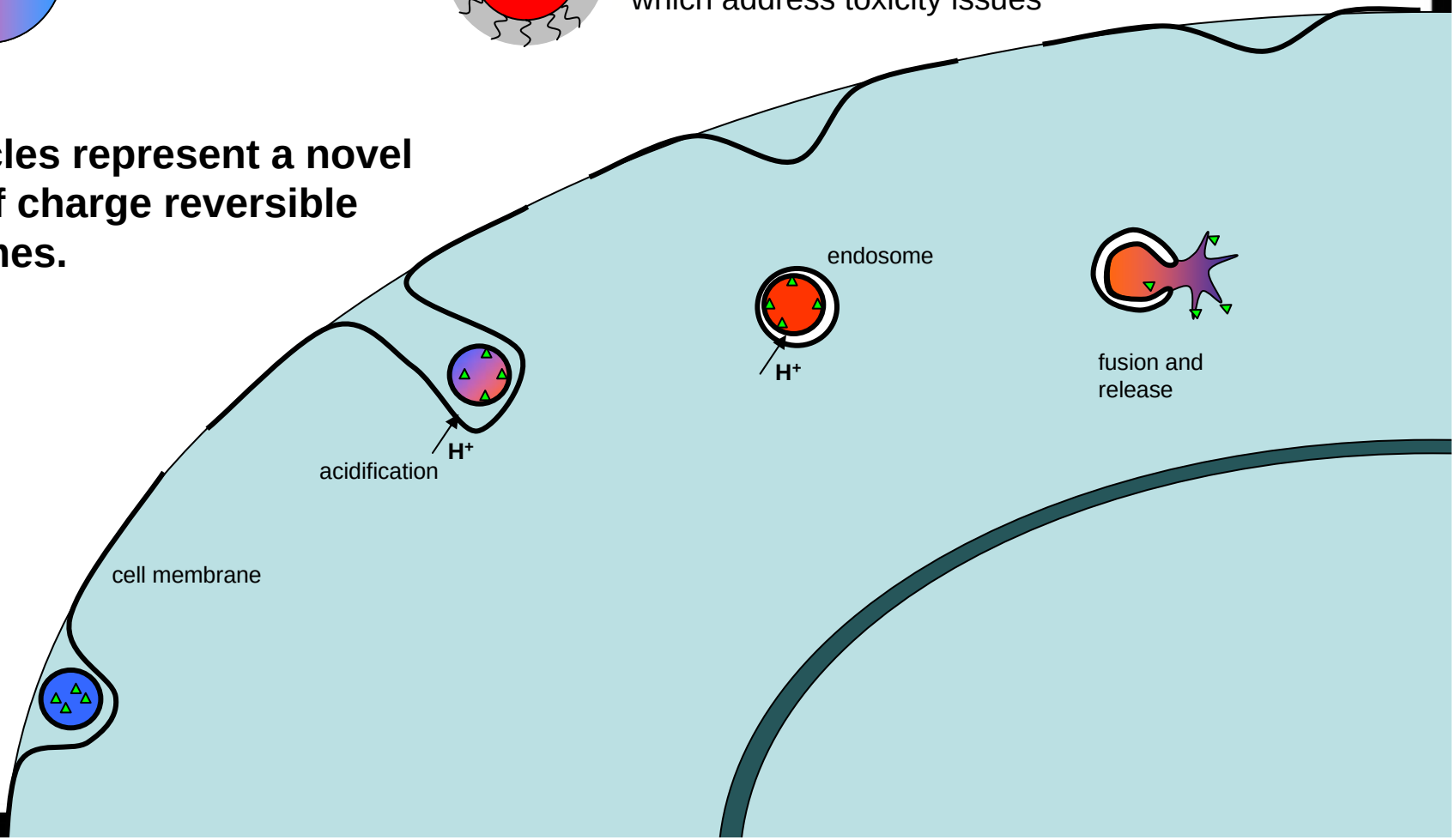
Characteristic	Test Method	Proposed Specifications
Appearance	Visual inspection	White-to-off white milky solution
Concentration (PNT100 content)	RP-HPLC	90 to 110% target
Free PNT100	HPLC	Report values
Related Impurities	RP-HPLC	≥ 85 Area %
	IEX-HPLC	≥ 85 Area %
Lysolipid content	HPLC	NMT 10% area
Free fatty acid content	HPLC	NMT 10% area
PNT100 lipid complex particle size	Dynamic light scattering	Report values
Ethanol content	USP/EP	Report values
Endotoxin	LAL	≤2 EU/mL
Osmolality	USP	280-350 mOsm
Sterility	USP	Sterile

Safe by Nature
- Efficient by Design (Novosom Smarticles)

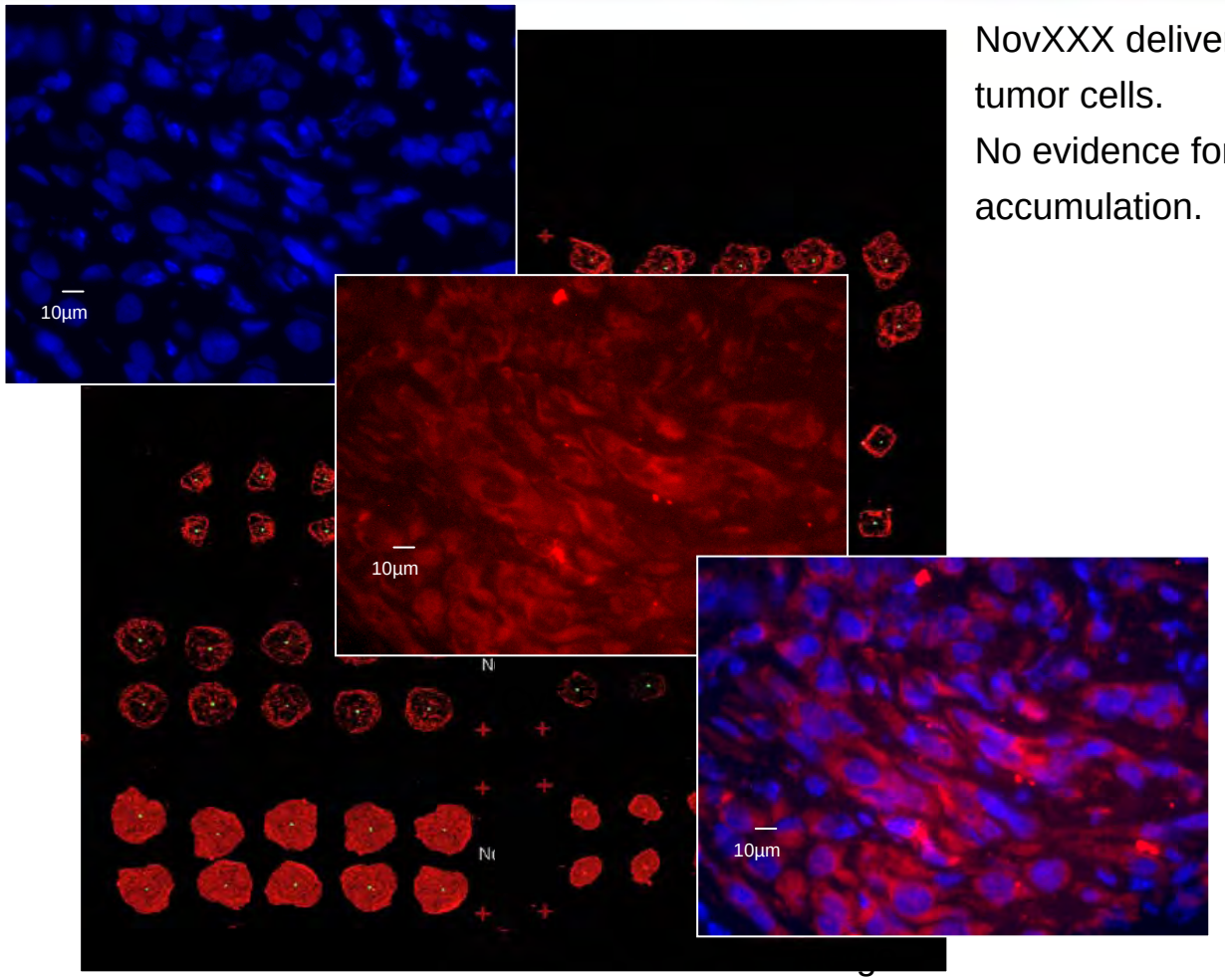
+/-

Competition is mainly cationic constructs with PEG “shields“ which address toxicity issues

Smarticles represent a novel class of charge reversible liposomes.



Cellular delivery
- ASO in tumors (Novosom Smarticles)



NovXXX delivers effectively into tumor cells.
No evidence for endosomal accumulation.

Cy5.5 labelled oligo was combined with NovXXX and injected into mice bearing a subQ tumor xenograft.
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Clinical Development - PNT225X
Rationale for Phase I/II Plan

- Consider a "Complete Phase I Design"
  - Establish the MTD/OBD of PNT225X monotherapy in solid tumor population (Phase Ia)
  - Establish safety and phase II dose for various drug combinations including PNT225X (Phase Ib)
  - Prioritize Phase II combination options among multiple indications of interest; expedite development plan towards best options
- Include exploratory studies to define biomarkers
  - Required for targeted drug development
  - Need to test molecular hypotheses re: MOA
  - Identify molecular markers predictive of drug response

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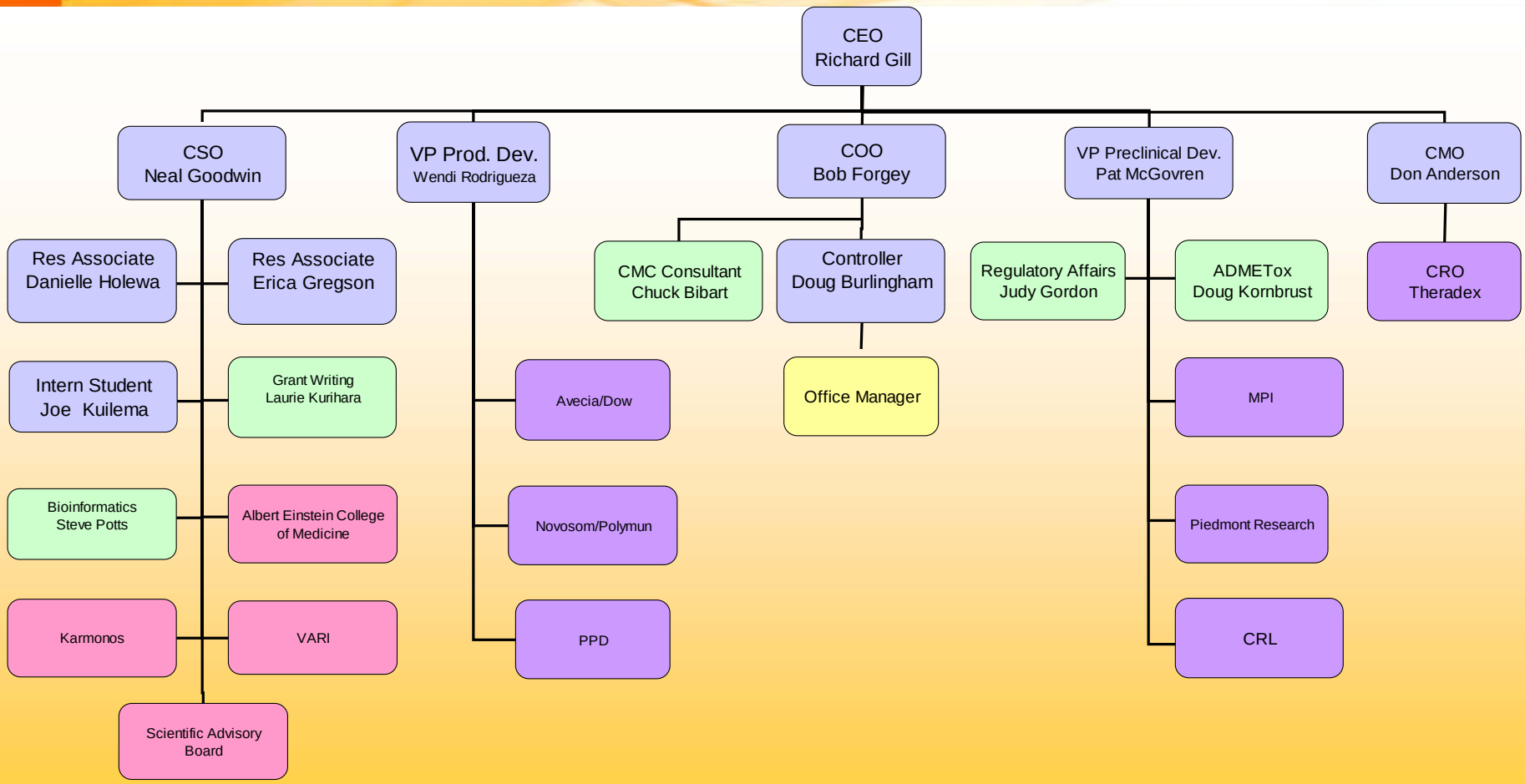
Organization Chart
- Team of 10 FTE's



ProNAi® Management Team

Richard D Gill, PhD ***President and CEO***	**Signet Laboratories, Genome Therapeutics, BTG, Unilever**
Robert Forgey ***COO***	**Pfizer, Pharmacia-Upjohn, Searle, Monsanto**
Donald Anderson, MD ***CMO***	**Advancis, Aventis, Pharmacia & Upjohn, Baylor**
Neal Goodwin, PhD	**Pharmacia, The Jackson Laboratory**
Patrick McGovren, PhD ***VP Preclinical Development***	**Pfizer, Pharmacia**
Wendi Rodriqueza, PhD ***VP Product Development***	***Novartis, Esperion***

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ProNAi® Board of Directors

Don Parfet ***Chairman***	**Apjohn Group/Apjohn Ventures**
Richard D Gill	**ProNAi**
Robert Forgey	**ProNAi**
Mike Pape	**Sigvion Ventures**
Mina Sooch	**Apjohn Ventures**

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ProNAi® Scientific Advisory Board

Nucleic Acid Chemistry

Tod Woolf, PhD (Chairman)
Founder Sequitur, Natick, sold to Invitrogen

Cy Stein, MD, PhD
Professor and Head Genitourological Cancer Albert Einstein COM, New York

Genomics

John Schimenti, PhD
Professor and Director Vertebrate Genomics, Cornell U., Ithaca

Terry Magnuson, PhD
Professor and Chair Genetics, U. North Carolina, Chapel Hill

Preclinical Efficacy

Ayad Al-Katib, MD
Head Oncology, St. Johns Medical Center, Detroit Professor of Medicine, Wayne State University Medical School, Detroit

Craig Webb, PhD
Director and Principle Investigator Tumor Metastasis and Angiogenesis Laboratory, Director Multiple Myeloma Laboratory Van Andel Research Institute, Grand Rapids

Clinical

Mace Rothenberg, MD
Ingram Professor of Cancer Research and Professor of Medicine, Vanderbilt Medical School, Nashville

Commercial

David Olson, PhD
Vice President Research PanCell, Co-founder Gentera

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ProNAi® Discovery Strategy

- Build on promising results of PNT100, PNT225X and PNT200 to expand portfolio
- Many cancers linked to chromosomal translocation
- Focus on cancer linked chromosomal translocation breakpoints
- Induce single stranded DNA formation at targeted translocation breakpoints
- DNAi® oligomers may interfere with chromosome structure to induce apoptosis

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Working Hypothesis for MOA
- PNT225X

Chromosome Translocation site 5' to BCL2 gene

Cancer causes genomic instability
- Relaxed chromosome structure
- Tumor genome susceptible to DNAi recognition

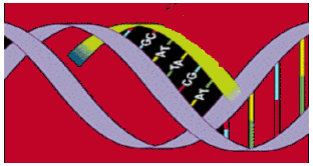
Lead candidates target oncogene translocation breakpoint regions
- *BCL2 & MYC*

Induction of ssDNA formation "*Primed Helix*"

DNAi® Data Evidence
- Strand specificity
- Sequence specificity
- +++ activity with DNA altering agents
- +++ activity with ↑ BCL2 expression

↑BCL2 → ↑Genomic Instability
(Predictive Biomarker)

PNT225X (single stranded DNAi® oligo +Lipid)



DNAi® Data Evidence
- Microarray Data (Predictive Biomarker)

Induction of p53/Sp1 response

Apoptosis in Cancer Cell Not Normal Cell

DNAi® Data Evidence
- *In vitro* tumor line efficacy
- *In vivo* xenograft response
- Exploratory monkey tox

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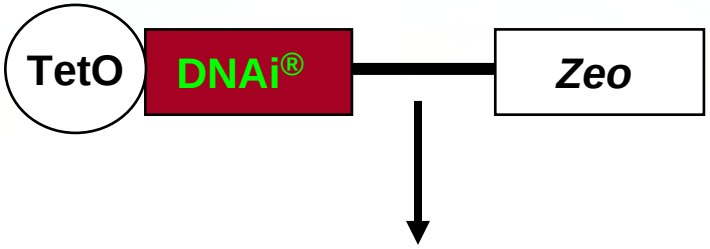
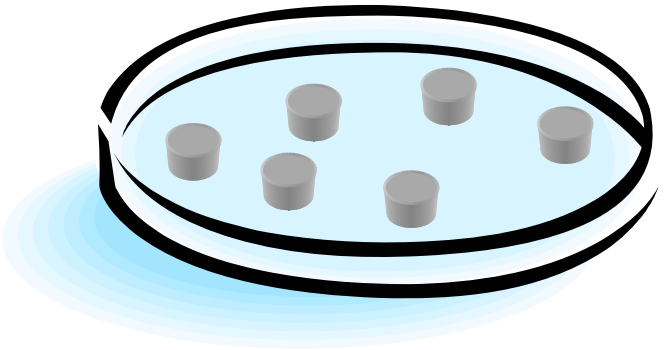
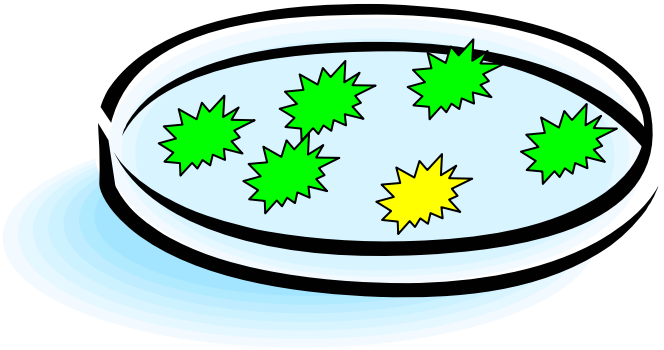
ProNAi® Platform – DNAi-HiT™





Doxycycline/Tet

Cell phenotyping protocol



Tumor cells (TetR)

Identify DNAi® responder cells

- Phenotype deviant detected
- DNAi® rescued by PCR/Sequencing

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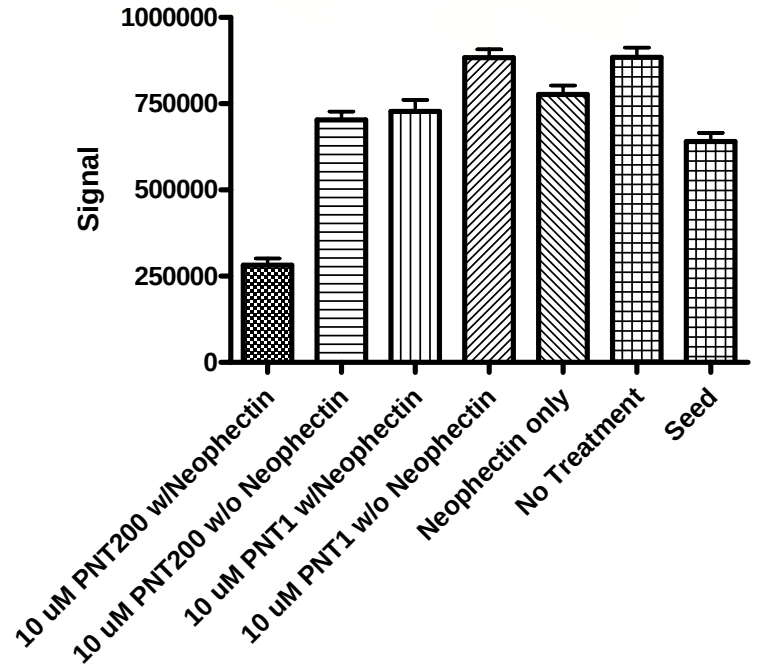
PNT200
- Inhibits Breast Cancer Cell Proliferation

PNT200 Inhibtion of MCF-7 Breast Cancer Cells (72 hr)



***DNAi-HiT™ and in vivo* efficacy next**

PNT200=*MYC* lead
PNT1=24mer randomer
PNT200 w/Neophectin vs. PNT1 w/Neophectin highly significant (P<0.0001; Mann-Whitney=0.00)
PNT200 w/o Neophectin vs. PNT1 w/o Neophectin highly significant (P<0.0001; Mann-Whitney=5.0)
note: Neophectin only demonstrates free liposome toxicity

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ProNAi® Financing Plan

- Funding to date ~$11M

- Series A Pre-Money Valuation $2.5 M
- Series A Financing $2.5 M
  - Angel Funds
  - Venture Capital
- Convertible Notes from MEDC $5.0M
- Bridge Financing $3.35M
  - Converts at Series B financing
  - Take PNT225X to IND submission
- Series B Financing $25M (~$17M new money)
  - Anticipated closing 1Q07 (Apjohn Ventures $1M)
  - Take PNT225X into the clinic
  - Complete Phase I thru Phase IIa

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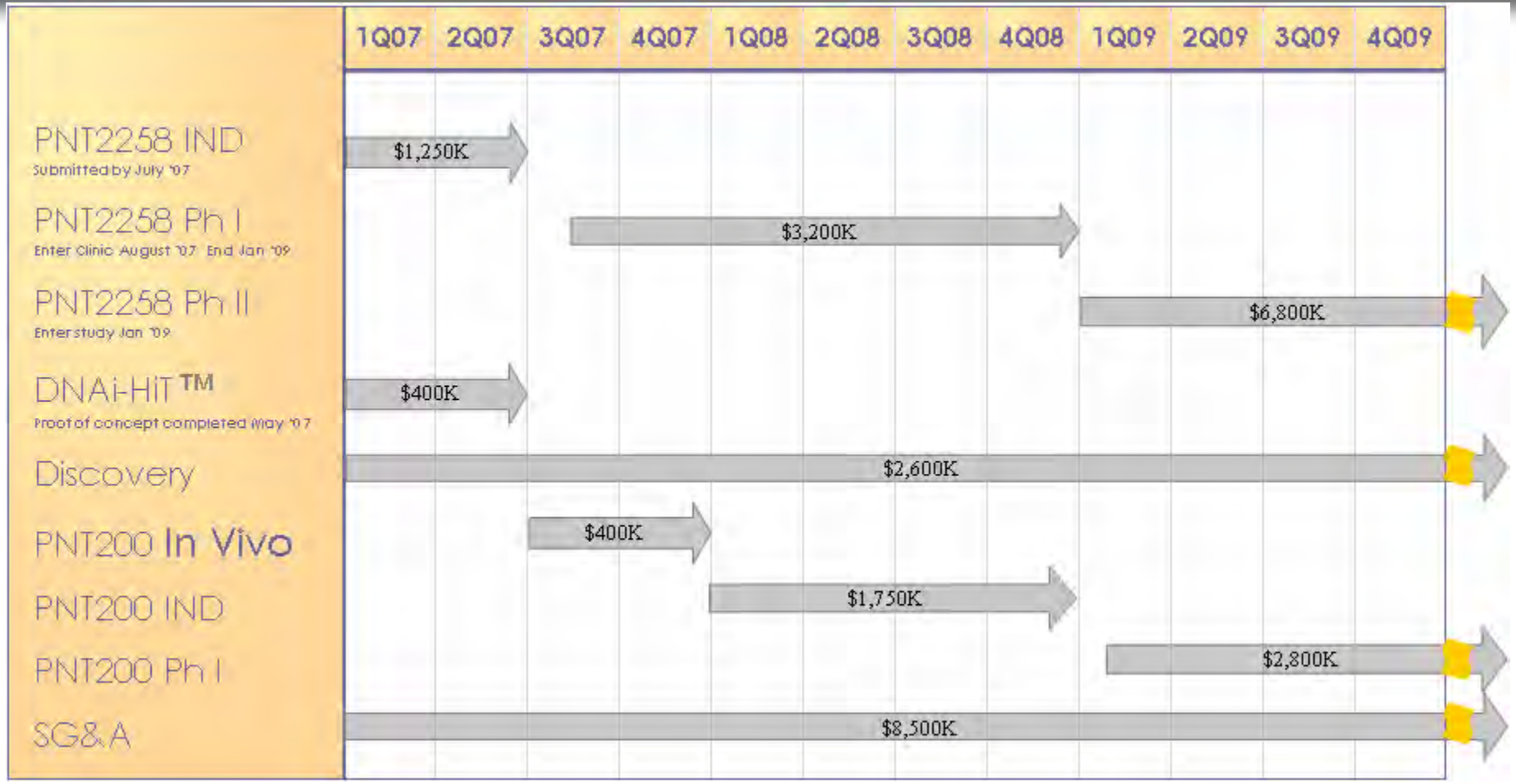
ProNAi® 2007 to 2009: $27.7M
- Portfolio Development/Use of Proceeds



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ProNAi® Key Milestones

- Publish/present PNT225X preclinical data
- Demonstrate Phase IIa proof-of-concept efficacy data for PNT225X
- Advance PNT200 into Phase I clinical trials
- Determine MOA in oncology
- Validate DNAi-HiT™ platform/identify new drug leads
- Position company for major alliance or acquisition

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ProNAi® Exit Opportunities

Liquidation Event	Timing	Potential Value
Out licensing IND and Ph I/II Package(s)	1-2 yrs	$20-50M Upfront $50-200M Milestones 8-12% Royalties
Pharma Development Partnership(s)	2-3 yrs	$250M
M&A	3-5 yrs	$100-500M

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Why are we all investing in ProNAi®?

- **Lead candidate PNT100 just months from clinic with multiple cancer treatment opportunities for blockbuster revenues**
- **Product business model with pipeline of six lead candidates; promising follow on PNT200**
- **DNAi-HiT™ provides ability to design additional leads for revenue generating partnership opportunities**
- **DNAi® solves the technical issues that have prevented the medical use of oligonucleotides**
- **“Can Do / Have Done It / Will Do It Again” Team**
  - **Upjohn, Pharmacia, Pfizer, Monsanto, GD Searle, sanofi-aventis, Unilever, BTG, Genome Therapeutics, Signet Laboratories, Esperion, Novartis**

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